Associations Between the Presence or Absence of a Lifetime History of Prostate Cancer Diagnosis and Current Mental Health Issues in a Sample of Canadian Men: A Secondary Analysis of the Canadian Longitudinal Study on Aging (CLSA)

by

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Dedication

This is dedicated to the members of the Catholic congregation at the Veterans' Memorial Hospital for their prayers and patience as I completed my thesis.

I also want to express my gratitude to Saint Jude and Saint Anthony for their intercessions.

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Abstract

The present study examined the prevalence of lifetime history of prostate cancer (PCa) in a cross-sectional sample of Canadian men (N = 25, 183) and investigated the contribution of presence or absence of history of a PCa diagnosis to current mental health outcomes. This study used baseline data from the Canadian Longitudinal Study on Aging (2010-2015). Logistic regression analyses, controlled for the complexity of the design, demographics, and lifestyle factors, evaluated the association between history of a lifetime PCa diagnosis and current mental health outcomes. The prevalence of lifetime history of PCa diagnosis in this sample was 4% (95% CI: 3.7, 4.4). Our results indicate statistically significantly greater odds of psychological distress (aOR= 1.52, 95% CI: 1.09, 2.11) and depressive symptoms (aOR = 1.24, 95% CI: 1.02, 1.51) among Canadian men who self-reported a lifetime history of PCa diagnosis, compared to men with no history of a PCa diagnosis, even when multimorbidity and substance use were statistically controlled.

List of Abbreviations Used

PCa – Prostate Cancer

CLSA – Canadian Longitudinal Study on Aging

SRMH – Self-Rated Mental Health

QoL – Quality of Life

ADT – Androgen Deprivation Therapy

ED – Erectile Dysfunction

CCHS – Canadian Community Health Survey

WHO – World Health Organization

MI – Multiple Imputation

PCaPRO – Prostate Cancer Patient-Reported Outcomes

DSM – Diagnostic and Statistical Manual

MCMC – Markov Chain Monte Carlo

FSC – Fully Conditional Specification

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"Never doubt that you are valuable, powerful and deserving of every chance and opportunity in the world to pursue and achieve your own dreams." - HRC

CHAPTER 1 INTRODUCTION

Prostate cancer (PCa) is the most common form of non-skin cancer among Canadian males. In 2017, 21% of all new diagnosed cancer cases were PCa and, on average, 58 Canadian men were diagnosed with PCa every day (1,2). Among all cancers currently affecting Canadian men, PCa has the highest incidence (2). Research indicates that 1 in 7 Canadian men will develop PCa during their lifetime (1,3). The incidence of PCa increases faster with age than any other major cancer; and, therefore, PCa is a disease associated with aging (3). About 97% of all PCa is diagnosed in men 50 years of age and older; 60% occur in men over 65 (4,5). The majority of PCa patients will become long-term survivors (>5 years), with over 70% of patients expected to live 10 years or more from the time of diagnosis (6).

The prevalence of PCa is projected to increase due to a burgeoning older population – the number of adults over the age of 65 is expected to represent between 23%-25% of the total population by 2036 (7). This increasing prevalence, combined with the cumulative number of years men live post-diagnosis, is bound to pose significant challenges to our healthcare system. In 2008, Courneya et al. analyzed data from the 2005 Canadian Community Health Survey (CCHS) to provide population-based estimates of cancer prevalence for the Canadian population. They found the prevalence of history of PCa cancer to be 1.3% among adults aged 18 to 65 (N = 114, 355) (8). In a forthcoming report, the prevalence estimate of history of PCa diagnosis in Atlantic Canada (2009-2015) was found to be 4% (males aged 49-69) (9). This suggests an increase in lifetime prevalence of history of PCa diagnosis in the last 10 years, however

comparisons between these estimates cannot be made due to differences between the two studies in both the age range and the surveillance time period assessed.

Recently, there has been increasing interest in mental health outcomes of the PCa survivor population. Fervaha et al. (2019) provided a focused review on depression and PCa aimed at educating clinicians on the prevalence of depression within this population. According to Fervaha, 1 in 6 men with a PCa diagnosis will experience clinically significant depression (10). Several studies have suggested that PCa patients are at increased risk for mental health issues such as depression, anxiety and suicide (6,11). Watts et al. (2014) reviewed 27 studies and their findings suggest that the prevalence of depression and anxiety in men with PCa is elevated in comparison to the general population (6). Their reported prevalence rates identified for pre-treatment, on-treatment and post-treatment were 17.3%, 14.7% and 18.4%, respectively; and anxiety prevalence rates were 27%, 15% and 18%, respectively (6). In comparison, the prevalence of clinical depression and anxiety in general population men aged over 65 years is estimated to be less than 9% and 6%, respectively (6). Watts et al. included studies from several different countries, including Germany, Sweden, USA and Holland. Two Canadian papers were included in their analysis: Savard (2005) and Hervouet (2005), and they had the two largest sample sizes (327 and 861, respectively) out of the 27 journal articles that met inclusion criteria for entry (6). Hervouet (2005) found that the prevalence rates of clinical levels of depression and anxiety were 17% and 23.7%, respectively, within their sample of patients with diverse stages and treatments (12). In comparison to the general Canadian population, approximately 8% and 5% of Canadian adults are expected to experience depression and anxiety, respectively, at some time in their lives (13).

Overall, it is well-accepted in the literature that there is above-average occurrence of depression among PCa patients and survivors, as supported by recent reviews and meta-analyses (6,10). However, several researchers, as well as the American Society of Clinical Oncology, have called for additional population-based studies to better understand mental health outcomes among the PCa population (6,14).

Multimorbidity, usually defined as the co-occurrence of two or more chronic conditions within a person, is becoming the norm rather than the exception (15,16). The link between multimorbidity and mental health has already been well documented in the literature, and has been shown to be positively related with age (17,18). Rice et al (2018) examined male-specific depression symptoms in men with a diagnosis of PCa for those with and without multimorbidity. They found a consistent pattern of higher scores for major depression symptoms for those men with PCa reporting multimorbidities, such as cardiovascular disease and arthritis (19). When multimorbidity is high at PCa diagnosis, physicians are more cautious about active treatment due to concerns that compounding effects of treatment and multimorbidities could increase patients' risk of mortality (20,21). Matthes (2018) found that age is a stronger predictor of PCa treatment choice than additional morbidities, but morbidities have a larger influence on mortality (22). Given the known association between multimorbidity and mental health within cancer populations (17,18,23), and multimorbidity's growing importance in PCa treatment choice (22), we consider it critical to examine this factor in relation to mental health issues in Canadian men with a lifetime history of a PCa diagnosis.

Furthermore, the stress caused by a PCa diagnosis and the side effects caused by active forms of treatment can exacerbate unhealthy behaviours, such as alcohol

consumption and smoking (24). Smoking has been shown to be associated with mental health conditions such as depression, as well as with alcohol use (25). Han (2017) found that stress and depressive symptoms were associated with smoking, alcohol consumption, number of chronic conditions and unmet needs for healthcare in cancer survivors (26). Continued substance use can complicate treatment, increase risk for further malignancy and contribute to secondary health problems such as cardiovascular disease and diabetes for cancer patients and survivors (24). Therefore, it is particularly important to examine the contributions of these factors in relation to mental health outcomes in this population.

Our study used a national, cross-sectional sample of adult men ages 49-86 from the Canadian Longitudinal Study on Aging (CLSA). This project will contribute substantially to our understanding of the adverse health conditions associated with mental health outcomes in survivors of PCa, in addition to fulfilling the CSLA's strategic objective of attempting to understand why some people age in a healthy fashion while others do not. Furthermore, it will contribute to the evidence needed to inform the implementation of prevention strategies to help improve quality of life (QoL) of PCa survivors, such as routine screening for mental health issues as well as the adoption of multi-disciplinary teams for PCa care. Evidence gained from this research could lend support to the development and adoption of innovative, holistic intervention programs that have the potential to address the depression risk in this population (9).

This thesis examines the prevalence of lifetime history of PCa diagnosis and the association between lifetime history of PCa diagnosis and mental health outcomes – depressive symptomology, psychological distress and self-rated mental health. Secondarily, we assess whether holding constant the contribution of multimorbidity and

substance use changes the association between lifetime history of PCa diagnosis and mental health outcomes. The thesis is divided into a background review (Chapter 2), objective (Chapter 3), one manuscript (Chapter 4) and a general conclusion (Chapter 5). The background review examines the previous findings on PCa, multimorbidity and substance use in relation to mental health outcomes in men. The manuscript examines the associations between lifetime history of PCa diagnosis, multimorbidity, substance use and mental health outcomes among Canadian men. The concluding chapter summarizes the findings, considers strengths and limitations, and discusses the implications for both future research and policy.

CHAPTER 2 BACKGROUND

2.1 OVERVIEW

While aging is not synonymous with the development of chronic disease, many older people live with conditions that impact their QoL. Improvements in early detection techniques and treatments have shifted the view of PCa from that of a terminal illness to a chronic condition. Although PCa is a serious disease, most men diagnosed with PCa do not die from it. It is widely accepted that rates of mood and anxiety disorders are higher among older adults with multiple chronic conditions. However, little is known about how multimorbidity and substance use impact mental health outcomes among Canadian men with a lifetime history of a PCa diagnosis. Thus, assessing the contribution of multimorbidity and substance use to the relationship between a history of a PCa diagnosis and mental health issues in this population of older Canadian adults, fills an important gap in the literature. To the best of our knowledge, this is the first study to assess these associations in a large national population dataset and also report on the prevalence of lifetime history of PCa diagnosis among older Canadian adults since 2005 (8)

2.2 MENTAL HEALTH AMONG MEN WITH PROSTATE CANCER

Despite the increased focus on disease-specific health-related QoL among men with PCa, mental health is an aspect of PCa care that is largely overlooked (10,27,28). Primarily, this is the case because the biomedical model focuses on treating the disease rather than the whole person. The recognition and diagnosis of mental illness in older individuals, and specifically in patients with cancer, is challenging (29). Yet, depression and anxiety occur at an increased rate in cancer populations, including among PCa survivors (10,11,30–32). For example, Steginga et al. (2004) found that 60% of men with PCa

experience some form of psychological distress, a well-known precursor to development of mental health issues (30). The Watts et al. (2014) meta-analysis included 27 studies with a pooled sample size of over 4000 PCa patients with either localized or advanced disease, and estimated a prevalence rate of clinically significant depression between 15% and 18% (6). However, other research has found the prevalence of depressive symptomology in patients diagnosed with PCa ranging from 16%-30% (33,34). Younger patients (<65) with PCa, when compared to those over 65, have been noted to have higher rates of depression, anxiety and psychological distress (35,36). These findings have been supported by the preliminary results from the Prostate Cancer Patient Reported Outcomes (PCaPRO) Maritime Survey, which found that 13.7% and 17.1%, of Nova Scotian PCa survivors (N=108) in the 47-65 age category, reported depression distress and anxiety distress, respectively (37).

Depression and anxiety among cancer patients, including PCa patients, have been shown to contribute to treatment noncompliance and poorer long-term treatment outcomes (6,32,38). Men with PCa and a depression diagnosis are more likely to experience worse overall QoL, oncological outcomes and survival (39). Depressed men were found to be less likely to undergo definitive therapy (surgery or radiation), and they experienced worse overall mortality (39). Furthermore, higher risks of depression (6,10,40), anxiety (6,40), and suicide (41,42) are often reported among men with a history of PCa, and the development of mental illness among survivors has been shown to increase rates of emergency department usage, hospitalization, and mortality (43). The heightened risk of depression for this population is hypothesized to be related to unmet psychosocial needs, PCa-related symptoms and side-effects from different treatment

modalities (44). Treatment side-effects often include urinary incontinence, sexual dysfunction, and intimacy and relationship issues (19,37,44,45). Many men with PCa suffer from additional health problems such as heart disease that may contribute to depressive symptoms (19). More and better information regarding the interaction of complex health issues within the PCa population will help clinicians and researchers better understand these issues and develop interventions that reduce their occurrence and impact.

2.3 Multimorbidity and mental health

Multimorbidity is commonly defined as the presence of two or more chronic conditions in an individual (46). Multimorbidity burden is common among older adults, including cancer patients, and is a significant predictor of poorer psychological well-being and mental health (17,18,23,47,48). Various age-related health conditions and chronic illnesses can have adverse consequences on daily functioning, independent living and, ultimately, QoL (49,50). The majority of PCa cases are diagnosed in men 65 or older. PCa is therefore likely to be concurrent with other conditions that affect older individuals. Recent literature has suggested it is important to control for multimorbidity when assessing mental health outcomes, especially in older adults (18).

Prostate cancer cells need hormones called androgens to grow. The main male androgen is testosterone. The PCa treatment modality, uses hormone therapy to either stops the body from producing testosterone or block the action of testosterone, which can slow tumor growth or shrink the tumor for a period of time. The selection of hormone therapy, also known as androgen deprivation therapy (ADT), for men with PCa is common. In their international survey of ADT use for localized PCa in 19 countries,

Liede et al. (2016) found that 38% of PCa patients (N = 76 386) received ADT (51). Hormone therapy has multiple known side-effects, including some health risks. One known risk of ADT is the thinning or weakening of bones (osteoporosis) (52). Diabetes and cardiovascular disease are already common in older men – ADT increases the risk for these diseases. Other risks include fatigue, erectile dysfunction, weight gain, liver inflammation and hot flashes (52). Therefore, the selection of hormone therapy can actually cause further morbidity among the PCa population.

The presence of chronic conditions and illnesses has been shown to result in unhappiness and distress, leading to lower QoL (53). Both the presence of elevated depressive symptoms and diagnosed clinical depression are higher among persons with some chronic conditions, such as diabetes, stroke, cardiac disease, respiratory conditions and cancer, compared with the general population (47,54). Studies of older adults have indicated that those with depressive symptoms have poorer functioning (55). In addition to poor functioning, depression can lead to the development of chronic diseases and thereby increase the utilization of medical services and healthcare costs (55). Studies of patients with early-stage PCa have suggested that those with more morbidities have lower QoL during the diagnosis and treatment period (56), but little is known about the effect of morbidities on the survivorship period.

There are few studies that specifically investigate the impact of multimorbidity on the mental health outcomes of PCa patients. Relevant studies have focused mainly on morbidities that affect sexual and urinary health, and their impact on the QoL of PCa survivors (57,58). Research has found erectile dysfunction (ED) is strongly associated with depression and significant distress in PCa survivors (58,59). ED is often the result of

side-effects from PCa treatment and/or specific chronic conditions that occur in older men such as obesity, diabetes, osteoporosis and metabolic syndromes (58). Men who simultaneously experience PCa and multimorbidity burden may perceive their sense of masculinity to be threatened, which can evoke unregulated anger and aggression in response to their compromised health (19).

A higher number of multimorbidities can negatively influence patients' mental health, including producing symptoms of anxiety and depression through poor physical functioning and increased problems in daily life (47). Monitoring the psychological status of patients with multiple morbidities is thus of utmost importance, in particular because the variability in clinical presentation and types of morbidities present may hinder the detection of psychological distress. The current study explored how multimorbidity contributes to the mental health outcomes of Canadian men with a history of a PCa diagnosis.

2.4 Substance use and mental health

Mental health issues and substance use problems are common concurrent disorders. The links between mental health and substance use are complex. These problems can develop independently as a result of common risk factors, or one can lead to the other as a result of self-medication or prolonged distress (60).

Substance use among elderly patients with PCa can pose unique challenges to the delivery of effective and efficient care. A study by Kuerbis et al (2014) concluded that screening for alcohol use as well as other substances among middle-aged and older adults is essential, so problematic use does not go unrecognized (61). The Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 depression definition has been criticized

for being insufficient to comprehensively evaluate depression in men (19,62). This has led to a research focus on highlighting male-specific depressive symptoms in this population (19). Systematic reviews and population studies have echoed these critiques and have suggested the creation of a subtype of depression in men characterized by alcohol/substance use and externalizing symptoms including anger and irritability (63). This expansion of the assessment for depression may be of particular importance for PCa research.

Substance use is considered a common type of coping behaviour to reduce stress (64). It is well known that men with PCa experience high levels of stress related to diagnosis, treatment, side-effects and relapse. Prostate cancer-related side-effects such as sexual dysfunction and urinary incontinence have been shown to increase levels of psychological distress (37,65). These side-effects may contribute to adherence to harmful coping mechanisms in this population.

The literature suggests that the intersection of aging and advanced-stage disease can exacerbate substance use, leading to adverse outcomes such as psychological distress. However, there is little research on the effect of substance use on mental health outcomes in men with PCa (66). In the reviewed literature, the term “substance use” refers to the use of drugs or alcohol, and includes many substances including cigarettes, cannabis, illegal drugs, and prescription drugs. However, for the purpose of our study the term “substance use” specifically refers to alcohol and cigarettes. Alcohol is by far the most commonly-used drug by Canadians. According to the Canadian Tobacco, Alcohol and Drugs Survey (CTADS), in 2015 66.2% of older adults (65+) reported drinking in the past year, including 70.4% of males (67).

Alcohol consumption and cigarette smoking have long been explored as possible causes of PCa, but the research has produced controversial and contradictory results over the years due to methodological limitations (68–70). There is little research that explores the role of alcohol consumption and cigarette smoking on the mental health of men with a history of PCa.

A systematic review conducted by De Nunzio (2015) synthesized evidence of the role of cigarette smoking on PCa development and progression. Although the underlying pathophysiology remains unclear, they found that smokers had higher PCa mortality and worse outcomes after treatment (68). In a more recent review, Foerster (2018) examined data from previous studies with a total of 22 549 men with a history of PCa who had been treated with either surgery or radiation. During follow-up, compared to men who never smoked, current smokers were 40% more likely to have tumors return after treatment and more than twice as likely to have cancer spread beyond the prostate (71). The authors also found that former smoking was associated with higher risk of relapse, but not with spread or cancer-specific death, which underlines the importance of smoking cessation in improving disease outcomes (71). The evidence from both these reviews suggests that smoking-cessation counseling should be available for PCa patients, to help with physical outcomes.

Farris et al. (2018) explored post-PCa diagnosis alcohol intake and survival. They found a statistically significant increased risk of mortality with increased alcohol consumption, particularly PCa-mortality (72). Although the biological mechanisms that explain how alcohol consumption is associated with PCa-specific mortality remain

largely unknown, it is known that men who are heavy drinkers have worse survival rates than those of moderate or non-drinkers (72).

Our study looked at how substance use, specifically alcohol consumption and tobacco use, contributes to the association between poor mental health among Canadian men with or without a history of a PCa diagnosis. Our findings may support the development of depressive measurements that are more male-specific, with the potential for inclusion of substance use subtypes. Additionally, exploring substance use in this population could lead to new interventions and educational resources that address these maladaptive coping mechanisms.

2.5 Aging and mental health

According to the World Health Organization (WHO), the world's population is aging rapidly. Between 2015 and 2050, the proportion of the world's older adults is estimated to double from 12% to 22% (73). This is an expected increase from 900 million to 2 billion people over the age of 60 (73). Older individuals face special physical and mental challenges that need to be recognized. With aging comes many changes and many new sources of stress, such as: declines in physical functioning which can lead to less independence; increases in chronic conditions and illnesses; losing loved ones and a decrease in socialization; and, major life transitions, including retiring, which can lead to a drop in socioeconomic status. All of these stressors can result in isolation, loneliness or psychological distress in older people (73).

Aging is an important risk factor associated with the development of multimorbidity, including PCa (74). Physical health has an impact on mental health and vice versa . For example, untreated depression in an older person with heart disease can

negatively affect their outcomes for both illnesses (73). However, aging is not the only important risk factor for the development of chronic physical conditions. Others include habits such as tobacco smoking and alcohol consumption (74). Additionally, the Geriatric Mental Health Foundation includes alcohol/substance use and long-term illness, such as cancer or heart disease, in their list of potential triggers for mental illness in older adults (75).

Mental health and physical health are fundamentally connected. Co-existing mental and physical conditions can diminish QoL, lead to longer illness duration, worse health outcomes and add to the overall burden of disability (76). This interaction generates economic costs to society in the form of lost work productivity and increased health services use (77,78). A better understanding of the links between mental and physical health in older adults is the first step in developing clinical strategies to reduce the burden of co-existing conditions, and to support the mental health of those individuals living with chronic physical conditions such as PCa with the hope of improving their QoL.

The CLSA was launched in 2010 as a unique research platform with the goal of investigating the complexities of the aging process. This landmark study of over 50, 000 Canadian residents provides researchers with data that has the potential to advance our understanding of the transitions and trajectories of aging. As our nation faces the burden of several decades of rapid population aging, the CLSA provides the data needed for interdisciplinary, population-based research that may lead to evidence-based decisions that could provide both economic and societal relief. The depth and breadth of data collected by the CLSA provides an ideal opportunity to evaluate associations between

mental health, multimorbidity and substance use patterns among older Canadian men with a history of PCa diagnosis.

CHAPTER 3 OBJECTIVES

Due to the gaps identified in the literature and in light of the extended survivorship period for PCa survivors, there is a great need to conduct research on the link between PCa diagnosis and mental health issues. We *hypothesize* that men with a history of a PCa diagnosis have more current mental health issues than their healthy counterparts. Our proposed study will add to the existing state of knowledge on the mental health of older men with and without a PCa diagnosis.

Our **first objective** is to examine the prevalence of lifetime history of PCa diagnosis and the contribution of the presence or absence of history of a PCa diagnosis to current mental health outcomes, as measured by two validated scales (CES-D10 and K10) and self-rated mental health, in a national cross-sectional sample of Canadian men. This objective will be addressed by two research questions: 1) What is the prevalence of a lifetime PCa diagnosis in this national sample of Canadian older adults, and what demographic characteristics describe them? 2) Do Canadian men with a history of a PCa diagnosis have higher odds of current mental health issues compared to Canadian men without a history of a PCa diagnosis?

A **secondary objective** is to assess the role of substance use and multimorbidity in the association between current mental health outcomes and a history of a PCa diagnosis to see if together these adverse health conditions lead to a change in the odds of poor mental health among these men. The research question we will be attempting to answer is: Is the presence of a history of a PCa diagnosis associated with increased probability of poorer mental health outcomes holding constant the contribution of the presence of multimorbidity and substance use?

CHAPTER 4

Associations Between the Presence or Absence of a Lifetime History of Prostate Cancer Diagnosis and Current Mental Health Issues in a Sample of Canadian Men: A Secondary Analysis of the Canadian Longitudinal Study on Aging (CLSA)

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4.1 Introduction

Prostate cancer (PCa) is the most commonly diagnosed cancer among Canadian men, making up an estimated 21% of all new male cancer cases (2). Currently, 1 in 7 Canadian men will be diagnosed with prostate cancer in their lifetime (2). The incidence rate of PCa increases faster with age than any other cancer. Fortunately, PCa mortality rates have been declining in most Western countries including Canada (79,80). The majority of PCa patients will become long-term survivors (>5 years), with over 70% of patients expected to live 10 years or more from the time of diagnosis (6). By 2030, Canadians aged 65 or older will make up 23% of our population (81). The rise in incidence with aging combined with the low mortality rate of PCa has important implications for the Canadian healthcare system. PCa diagnosis is often only the beginning of an array of inter-related health issues for affected men. Therefore, finding ways to improve the QoL among men with PCa is a Canadian health priority (81,82).

According to Fervaha et al. (2019), 1 in 6 men with a PCa diagnosis will experience clinically significant depression (10). A meta-analysis by Watts and colleagues found rates of depression and anxiety to be higher (across several PCa treatment phases) than those found in the general population (6). Depression and anxiety among PCa survivors have been shown to contribute to poorer long-term treatment oncological outcomes (6,32,38). Men with PCa and a depression diagnosis are more likely to experience worse overall QoL and survival (39). Depressed men were found to be less likely to undergo definitive therapy (surgery or radiation), and they experienced worse overall mortality (38,39).

Due to the increasing longevity of PCa patients, recent statistics tell us that 90% of Canadians aged 65 and over live with at least one chronic disease or condition, such as cancer, cardiovascular disease, diabetes, and arthritis (81). Multimorbidity is strongly associated with a range of adverse outcomes, including poor mental health outcomes (83,84). Individuals with multimorbidity have worse physical, social and psychological QoL (85). Read et al. (2017) found that depression is two to three times more likely in people with multimorbidity than in those who have no chronic physical conditions (84). There is a lack of existing evidence that explores the association between multimorbidity and mental health outcomes among PCa patients and survivors. Therefore, given that multimorbidity is well known in the literature to be associated with poorer mental health outcomes, combined with the fact that the mean number of morbidities per person increases with age, we feel it is essential to examine this factor in our exploration of mental health among men with PCa.

Additionally, the stress caused by a PCa diagnosis and the side-effects caused by active forms of treatment may lead to unhealthy coping mechanisms, such as alcohol consumption and smoking (24,64,86). These health behaviours have known associations with mental health outcomes (87,88). Smoking has been shown to be associated with mental health conditions such as depression, as well as with alcohol use in cancer survivors (25). Additionally, continued substance use can complicate treatment, increase risk for further malignancy and contribute to secondary health problems such as cardiovascular disease and diabetes for cancer patients and survivors (24). There is little research exploring the associations between alcohol use and smoking in relation to

mental health outcomes among men with PCa and, therefore, it is particularly important to examine the contributions of these factors in this population.

This study examines a large sample of older Canadian men who participated in the baseline data collection for the Canadian Longitudinal Study on Aging (CLSA) between 2010-2015 with the goal of answering the following research questions:

1) What is the prevalence of a lifetime PCa diagnosis in this national sample of Canadian older adults and what demographic characteristics describe them?
2) Do Canadian men with a history of a PCa diagnosis have higher odds of current mental health issues compared to Canadian men without a history of a PCa diagnosis?
3) Is the presence of a history of a PCa diagnosis associated with increased probability of poorer mental health outcomes holding constant the contribution of the presence of multimorbidity and substance use?

This investigation provides the first Canadian population-based data on the relationship between history of PCa, multimorbidity, substance use, and mental health in a large sample of older Canadian adults.

4.2 Methods

4.2.1 Study sample

The data we used for this investigation are from the Canadian Longitudinal Study on Aging. The CLSA is a national cohort study of adults aged 45 to 85 years of age at recruitment. Slightly more than 50,000 men and women across Canada's ten provinces were recruited and assessed at baseline between 2010 and 2015. A total of 21,241 individuals participated in a telephone interview (Tracking cohort) and 30,111

individuals participated in an in-home interview (Comprehensive cohort). The current sample is based on baseline data from 25,183 men who participated in either the Tracking or Comprehensive cohorts of the CLSA. Details about CLSA design, recruitment, study procedure and measures have been described elsewhere (89).

4.2.2 Mental health

The CLSA used two validated tools to assess the construct of mental health. The Andresen short form of the Center for Epidemiological Studies Depression Scale (CES-D10) and Kessler's Psychological Distress Scale (K10) were used to measure constructs of emotional distress. The CLSA also included the single-item measure of self-rated mental health (SRMH). These three indicators measure different dimensions of the mental health construct: K10 is a global measure of distress based on anxiety and depressive symptoms, CES-D10 is a screening tool for depression and SRMH is a measure of one's perception of their overall mental health.

Psychological distress was measured in the CLSA Comprehensive cohort only using the K10. The K10 has been used to assess psychological distress across multiple settings and populations. Many national population surveys have successfully adopted the K10, including in the USA, Canada, and Australia (90) This tool has been translated into more languages than any other mental health tool, and has been found to be highly reliable and valid when compared to other tools for screening for mental health (90). The K10 assessment involves 10 items about a person's emotional state, asking individuals how often they felt a certain way in the last 30 days. The cut-off score for psychological distress recommended by Kessler is a score greater than or equal to 20 (91). Therefore

screening positive for distress (score ≥ 20) was coded 1, and screening negative for distress (score < 20) was coded 0.

Depressive symptoms assessments were collected in both the CLSA Tracking and Comprehensive samples using the Andresen short form of the Center for Epidemiologic Studies – Depression (CES-D10) Scale. CES-D10 is a brief, self-reported, screening test for depression. It is one of the best-known instruments for identifying current (past week) symptoms of depression among community-residing older adults (89), however it is not used as a diagnostic tool for clinical depression. The CES-D10 includes ten items comprising six scales reflecting major facets of depression: depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite and sleep disturbance. The cut-off score for depressive symptoms recommended by Andresen et al (1994) is a score greater than or equal to 10 (92). Screening positive for depressive symptoms (score ≥ 10) was coded 1, and screening negative for depressive symptoms (score < 10) was coded 0.

Self-rated mental health (SRMH) was assessed in both the CLSA Tracking and Comprehensive cohorts, as part of the general health module. The standard item used to measure SRMH asked "*In general, would you say your mental health is excellent, very good, good, fair or poor?"* Research suggests that SRMH measures are a good proxy for clinical criteria. Paralleling the literature on clinical mental health diagnoses, the literature highlights a positive association between "poor" self-perceived mental health status, depressive symptoms, and healthcare expenditure (93). We dichotomized SRMH to presence of poor mental health (e.g. fair and poor) coded 1, and absence of poor

mental health (e.g. excellent, very good and good) coded 0. This dichotomization is common through most SRH literature for both general health and mental health (94).

4.2.3 Exposure variables

Lifetime History of a PCa Diagnosis

History of prostate cancer (ICD10) diagnosis is our main, binary independent variable of interest. CLSA participants were asked about their history of cancer via questionnaire. The question stem read: "Has a doctor ever told you that you had cancer?" If the participant responded "yes" to this question, then they were asked the follow-up question(s) which were part of a skip pattern: "What type(s) of cancer were you diagnosed with?" In the Comprehensive cohort, 813 participants answered yes to having received a PCa diagnosis. In the Tracking cohort, 545 participants answered yes to a PCa diagnosis. In total, 1358 Canadian men who participated in the baseline of CLSA had received a PCa diagnosis at some point during their lifetime.

Multimorbidity

To determine the occurrence of chronic health conditions, respondents were asked whether a doctor had ever told them that they have any one of 34 chronic conditions. From the list of chronic conditions, we included the following 26 physical health conditions: heart attack or myocardial infarction; angina (or chest pain due to heart disease); stroke or CVA (cerebrovascular accident); high blood pressure or hypertension; heart disease (including congestive heart failure); peripheral vascular disease or poor circulation in limbs and mini-stroke or TIA (Transient Ischemic Attack); diabetes, borderline diabetes or high blood sugar; over-active thyroid (hyperthyroidism); and under-active thyroid (hypothyroidism); emphysema, chronic bronchitis, chronic

obstructive pulmonary disease (COPD), or chronic changes in lungs due to smoking; asthma; macular degeneration; osteoarthritis in one or both hands, osteoarthritis in one or both hips, osteoarthritis in the knee; osteoporosis; other type of arthritis; rheumatoid arthritis; kidney disease or kidney failure; intestinal or stomach ulcers; bowel disorder; epilepsy, multiple sclerosis and Parkinsonism/Parkinson's disease; dementia or Alzheimer's disease; and cancer.

The types of chronic conditions included in multimorbidity studies vary widely, as does the number of conditions, which have ranged from 11 to 130 (95,96). We included the 26 chronic physical conditions listed above as they either fit the definition of a chronic condition or have been included in previous multimorbidity studies (95,96). Consistent with previous research, presence of multimorbidity was coded 1, and was defined as the presence of two or more chronic physical health conditions (46,84). For PCa survivors, this meant one or more conditions in addition to their lifetime history of PCa.

Substance Use – Alcohol Use and Smoking

CLSA participants in both cohorts were asked about the frequency of their alcohol consumption in the past 12 months. This item was assessed using four categories: daily drinker (4-5 times a week or almost every day) (coded 3), weekly drinker (once a week or 2-3 times a week) (coded 2), occasional drinker (less than once a month or about once a month or 2-3 times a month) (coded 1), and non-drinkers (coded 0). CLSA participants in both cohorts were asked about the frequency of their smoking in the last 30 days. This item was assessed using three categories: daily (at least one cigarette every day for the past 30 days) (coded 2), occasionally (at least one cigarette in the past 30 days, but not

every day) (coded 1), and not at all (you did not smoke at all in the past 30 days) (coded 0).

4.2.4 Covariates

Covariates, potential confounders to be adjusted for, were selected based on previous literature indicating these variables are associated with mental health and/or PCa (73,97–100). The following six covariates were employed: age (<65, 65-74, 75+); province (Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec and Saskatchewan); education (less than post-secondary degree/diploma, post-secondary degree/diploma); household income (<$50 000 a year; ≥ $50 000, less than $100 000 a year; ≥ $100 000, less than $150 000 a year; ≥$150 000 a year); marital status (married or common-law; not married/not common-law) and ethnicity [other (non-whites), white only, to account for the limited counts in some cells that would have otherwise limited our analyses].

4.2.5 Statistical Analysis

Complex survey data typically violates the assumption of independence of observations. Therefore estimation methods that accommodate such data sampling must be used, otherwise variances will be understated (101). To adjust the complex survey data, variances were estimated using Taylor Series Linearization available in the Complex Sample module in SPSS 25.0 (101). For the Pooled CLSA data, our analyses were based on a design employing normalized inclusion weights of 25,183 adult men drawn from 34 equally allocated strata. For the Comprehensive CLSA data, our analyses were based on a design employing normalized inclusion weights of 14,777 adult men drawn from 14 equally allocated strata. Covariate-adjusted logistic regressions assessed the association

between lifetime history of a PCa diagnosis and three mental health outcomes – psychological distress, depressive symptoms, and self-rated mental health. Covariate-adjusted multivariate logistic regressions considered lifetime history of PCa, multimorbidity and substance use (alcohol use and smoking) simultaneously to predict each of the mental health outcomes. Listwise deletion reduced the estimation sample for depressive symptoms to 25,060 from 25,183 and for self-rated mental health to 25,159 from 25,183. For psychological distress, listwise deletion reduced the estimation sample to 13,960 from 14,777. Based on 5.5% of our data missing for psychological distress, multiple imputation (MI) was performed using IBM SPSS 25.0 (102).

The imputation method selected was the Automatic method (the software scans the data and decides on which method of imputation (monotone or fully conditional) should be specified based on the pattern of missing data. Fully conditional specification (FCS) was selected, which is an iterative Markov Chain Monte Carlo (MCMC) method. The MCMC method can be used when the pattern of missing data is arbitrary (103). We specified 20 iterations, as recommended by the literature (102,104). For each iteration, and for each variable in the order specified in the variable list, the FCS method fits a univariate model using all other available variables in the model as predictors, then imputes missing values for the variable being fit. This method continues until the maximum number of iterations is reached. For each of our analyses using MI, sensitivity analyses were performed to determine how the missing data affected the results. Analyses for psychological distress are reported for both original and multiple imputation (MI) pooled data.

To make the estimates generalizable to the Canadian population and address the complexity of the CLSA survey design, we used trimmed (inflation) weights in the descriptive analyses and analytic weights in the regression analyses, as recommended by CLSA (105). Weights were calculated by CLSA and were provided in the dataset that was released to researchers (105).

4.3 Results

In this population-based sample, the estimated prevalence of lifetime history of PCa diagnosis was 4% (95% CI: 3.7, 4.4) in Canadians males aged 47-65. Table 4.3.1 displays the estimates of lifetime history of PCa diagnosis by demographic characteristics. Of the Canadian men who reported a lifetime history of a PCa diagnosis, 72.8% were over the age of 65. The majority of men who reported a lifetime history of PCa diagnosis were married or common-law, 83.7%. Additionally, over 70% of the men who reported a history of PCa had a household income of less than $100, 000 per year; and of those, 29% reported a household income of less than $50, 000 per year.

Table 4.3.2 shows the logistic regression model for lifetime history of PCa diagnosis by screening positive for psychological distress. Men with a lifetime history of PCa diagnosis showed statistically significantly higher adjusted odds of screening positive for psychological distress, as measured by the K10 (aOR= 1.52, 95% CI: 1.09, 2.11; aOR^{MI} 1.57, 95% CI: 1.18, 2.08), compared to men who never received a PCa diagnosis.

History of PCa diagnosis was statistically significantly associated with depressive symptoms and, compared to men without a lifetime history of PCa diagnosis, those with a lifetime history of PCa diagnosis showed higher adjusted odds of screening positive for

depressive symptoms, as measured by CES-D10 (aOR = 1.24, 95% CI: 1.02, 1.51) (see Table 4.3.3).

History of PCa diagnosis and poor self-rated mental health were not statistically significantly associated (Table 4.3.4).

Table 4.3.5 shows the logistic regression analyses for screening positive for psychological distress by multimorbidity, alcohol use and smoking. All three predictors were statistically significantly associated with psychological distress. Individuals who self-identified as having multimorbidity showed statistically significantly higher odds of screening positive for psychological distress (aOR = 1.73, 95% CI: 1.50, 2.01); aOR^{MI} = 1.78, 95% CI: 1.56, 2.03), compared to those who did not. Compared to non-drinkers, daily or weekly drinkers showed statistically significantly higher odds of screening positive for psychological distress (aOR = 1.66, 95% CI: 1.31, 2.11; aOR^{MI} = 1.69, 95% CI: 1.38, 2.07 and aOR = 1.46, 95% CI: 1.16, 1.84; aOR^{MI} = 1.55, 95% CI: 1.27, 2.07, respectively). Lastly, compared to non-smokers, those who were daily smokers showed statistically significantly higher odds of screening positive for psychological distress (aOR = 1.81, 95% CI: 1.43, 2.27; aOR^{MI} = 1.83, 95% CI: 1.58, 2.13). The results for the original data set and the MI pooled data were comparable.

Multimorbidity, alcohol use and smoking were statistically significantly associated with depressive symptoms (see Table 4.3.6). Compared to those with no multimorbidity, those with multimorbidity (two or more chronic conditions, other than PCa diagnosis) showed statistically significantly higher odds of screening positive for depressive symptoms (aOR = 1.69, 95% CI: 1.53, 1.85). Compared to non-drinkers, those who were daily, weekly or occasional drinkers showed statistically significantly higher odds of

screening positive for depressive symptoms (aOR= 1.48 (95% CI:1.28, 1.71), 1.64 (95% CI: 1.42, 1.89), and 1.23 (95% CI: 1.06, 1.41), respectively). Compared to non-smokers, those who were daily smokers showed statistically significantly higher odds of screening positive for depressive symptoms (aOR = 1.58, 95% CI: 1.37, 1.83).

Multimorbidity, alcohol use and smoking were statistically significantly associated with self-rated mental health (see Table 4.3.7). Compared to those with no multimorbidity, those with multimorbidity showed statistically significantly higher odds of self-reporting poor mental health (aOR = 2.27, 95% CI: 1.96, 2.62). Compared to non-drinkers, those who were daily, weekly or occasional drinkers showed statistically significantly higher odds of self-reporting poor mental health (aOR = 1.76 (95% CI: 1.43, 2.18), 2.07 (95% CI: 1.68, 2.56), and 1.51 (95% CI: 1.23, 1.85), respectively). Compared to non-smokers, those who were daily smokers showed statistically significantly higher odds of self-reporting poor mental health (aOR = 1.58, 95% CI: 1.29, 1.93).

Table 4.3.8, provides synopsis of Model 1, which displays the association between lifetime history of PCa diagnosis and psychological distress, and Model 2, which displays a covariate-adjusted multivariate logistic regression assessing the contributions of lifetime history of a PCa diagnosis, multimorbidity, and substance use (alcohol use and smoking) to screening positive for psychological distress. Lifetime history of PCa diagnosis no longer predicts psychological distress when multimorbidity and substance use are included in the Model, using the original data. However, in the pooled MI data model (see Table 4.3.9 – Model 2) lifetime history of a PCa diagnosis remains statistically significantly associated with psychological distress when multimorbidity and substance use (alcohol use and smoking) are included in the model. The results for the

multivariate logistic regression (Model 2) were not consistent between the complete case (original data) analysis and pooled multiple imputation analysis.

Table 4.3.10, provides a synopsis of the results of Model 1, which assessed lifetime history of PCa diagnosis with screening positive for depressive symptoms and displays covariate-adjusted multivariate logistic regression (Model 2) examining the association between depressive symptoms and lifetime history of a PCa diagnosis, multimorbidity, and substance use (alcohol use and smoking). Lifetime history of PCa diagnosis remains significantly associated with depressive symptoms when multimorbidity and substance use (alcohol use and smoking) were included in the model.

Lastly, Table 4.3.11 displays a covariate-adjusted multivariate logistic regression evaluating the association between poor self-rated mental health and lifetime history of a PCa diagnosis, multimorbidity, and substance use (alcohol use and smoking). Lifetime history of PCa diagnosis remained not statistically significantly associated with poor self-rated mental health when multimorbidity and substance use (alcohol use and smoking) were included in the model.

4.4 Discussion

The estimated prevalence of lifetime history of PCa diagnosis was 4% (95% CI: 3.7, 4.4), males aged 47-65, in this secondary analysis of the baseline (2010-2015) CLSA data. This estimate is comparable to the 4% prevalence estimate of history of lifetime PCa in Atlantic Canada (2009-2015) reported most recently (males aged 49-69 years old) and 2.7% higher than the previous estimate reported by Courneya et al (2008) based on 2005 data (males aged 18 to 65) (8,9) . Our results suggest that the prevalence of PCa survivors has increased in the last 10 years, which is consistent with the increasing number of

adults over the age of 65, as well as better detection and treatment practices. However, comparisons between our prevalence and Courneya et al. are precluded due to the differences in the age range and the surveillance time period assessed between the two studies. The results we report here indicate statistically significant greater psychological distress and depressive symptoms among Canadian men who self-reported a lifetime history of PCa diagnosis, compared to men who had no history of a PCa diagnosis. In analyses controlled for multimorbidity and substance use, lifetime history of PCa is still associated with increased probability of poorer mental health outcomes. This suggests that preventative efforts to reduce mental health burden during PCa survivorship is a health priority.

The results reported here complement studies that indicate the PCa population deals with higher levels of poor mental health than the non-PCa population (6,10). To our knowledge this is the first investigation looking at mental health outcomes among Canadian men with a history of PCa diagnosis, compared to men in the general population, that also models simultaneously the contribution of multimorbidity and substance use, both factors that have been shown to contribute to mental health burden in the general population. Our results show that PCa is an additional adverse health correlate for mental health, irrespective of multimorbidity and substance use. The implication of this novel research is the potential for increased focus on acknowledging and addressing the psychological needs of PCa patients and survivors. Results here point to the need to identify the struggles of PCa survivors in order to ensure their proper care and good QoL long-term. This could therefore be informative to clinicians and health policy makers, who want to improve the QoL for Canadian PCa patients and survivors.

This might be accomplished via innovative and integrative care plans such as holistic interventions that aim to ease the psychosocial and physical needs of this population. Such programs are already in development, including the TrueNTH programs developed by Prostate Cancer Canada and the Prostate Cancer – Patient Empowerment Program (PC-PEP) based out of the Soillse Scientist in Prostate Cancer Quality of Life Research Laboratory in Halifax, Nova Scotia. These programs share the common goal of fostering networks of healthcare professionals, researchers and patient representatives to improve the QoL of men with PCa (106,107).

Our results are consistent with the literature, where those with multimorbidity have a greater probability of poor mental health outcomes compared to those without multimorbidity (84). Additionally, our results corroborate findings that those who are more frequent drinkers and smokers have higher probability of worse mental health outcomes (87,108).

Our results indicate absence of an association between history of PCa diagnosis and self-rated mental health (SRMH) for this sample of men. This finding is inconsistent with the results produced from the two validated questionnaires, CES-D10 and K10. This suggests the importance of using validated questionnaires for assessing mental health. The use of validated measures reduces the influence of social desirability bias that is associated with self-reported data, especially when it comes to states of being that are stigmatized in our society.

The results reported here, however, are subject to various limitations. Firstly, the nature of the data used for our analyses is retrospective and self-reported, and thus is subject to recall bias that may have affected the results. Second, as with many

population-based studies, the first wave of the CLSA had a lower than expected response rate. The overall response proportion was approximately 10%, which, although adjusted for by the use of population-based weights, may have introduced non-response bias (109). CLSA respondents were slightly more educated than the non-responders (90). Therefore, we can speculate that non-response bias in the CLSA may have led to an underestimate of the prevalence of history of PCa diagnosis due to adults with higher educational attainment living healthier and longer lives (97). Survival bias is another potential concern. This bias occurs since men who survived their PCa diagnosis are more likely to enter our study than other cases. On average, these men are likely to be healthier, have less multimorbidity and less substance use, than men who did not survive. Since multimorbidity and substance use increase the risk of mortality, the proportion of cases with high multimorbidity and heavy substance use will be lower in our data and could consequently lead to an underestimate of the odds ratios for the associations between multimorbidity/substance use and mental health outcomes (110–112). Survival bias describes our tendency to focus on the individuals that have passed some kind of selection process, such as surviving their PCa diagnosis. This type of selection bias is of particular relevance in cross-sectional studies which measure prevalent rather than incident cases, and the data will always reflect determinants of survival. Therefore, using long-term data from the CLSA may help reduce this type of bias in future studies as researchers will be able to assess survivorship time of individuals as well as incident cases. Both survivorship time and incidence would give researchers a better picture of the population of interest and allow for comparisons between survivors and non-survivors at each interval, which could reduce survival bias. An additional limitation for the current

study is the comparison group (men without a history of lifetime PCa diagnosis) rather than comparing PCa with other forms of cancer. Results here preclude us from concluding whether a lifetime history of PCa or a lifetime history of cancer is associated with poor mental health when the covariates assessed are held constant. Future studies should consider including this additional control group and examine if the results we observed here are restricted to PCa or include other forms of cancer (10).

Nonetheless, the results reported here provide important contributions, by providing evidence of poor mental health outcomes among Canadian men with a history of PCa diagnosis via examining data from a large-scale, national, population-based survey that used a standard protocol. Another strength of our study is the use of two validated mental health measures, CES-D 10 and K10, which allowed us to capture different dimensions of the mental health construct. Another important consideration is that we were able to capture 26 chronic conditions for inclusion into our multimorbidity variable. In contrast, many previous studies examining multimorbidity in the Canadian population were based on only a limited number of chronic conditions (113).

Future CLSA longitudinal data should be used to assess longitudinal changes in the prevalence of mental health outcomes among men with a history of a PCa diagnosis. Future cycles of CLSA data could be used to identify incident cases of PCa, which will also allow for a comparison between the mental health outcomes of newly diagnosed men (incident cases) and those of men with a lifetime history of a PCa diagnosis at baseline.

In conclusion, data from a nationally representative sample of men indicate that those with a lifetime history of PCa diagnosis have worse mental health outcomes than those with no history of PCa diagnosis, when all literature-derived main relevant factors

to poor mental health outcomes in the population are held constant. This research may have implications related to care of prostate cancer survivors, by informing new interventions and care plans that acknowledge and address the psychological issues of these men.

Table 4.3.1 Weighted and unweighted estimates with 95% CI of lifetime history of PCa diagnosis by demographic characteristics for Canadian men from the baseline cycle of the CLSA, 2010-2015 (N = 25 183).

	Lifetime history of PCa diagnosis	
	No (n = 23825)	Yes (n = 1358)
Age		
> 75 (n)	(4133)	(641)
Weighted **%**[a] (95% CI)	10.2 (9.7, 10.7)	36.2 (32.3, 40.3)
Unweighted % (95% CI)	17.3 (16.8, 17.8)	47.2 (44.5, 49.9)
65-74 (n)	(5516)	(452)
Weighted **%**[a] (95% CI)	18.3 (17.5, 19.1)	36.6 (32.2, 41.2)
Unweighted % (95% CI)	23.2 (22.7, 23.7)	33.3 (30.8, 35.8)
< 65 (n) (Reference)	(14176)	(265)
Weighted **%**[a] (95% CI)	71.5 (70.6, 72.4)	27.2 (23.3, 31.6)
Unweighted % (95% CI)	59.5 (58.9, 60.1)	19.5 (17.4, 21.6)
Provincial Residence		
Saskatchewan (n)	(641)	(38)
Weighted **%**[a] (95% CI)	2.9 (2.8, 3.0)	3.1 (2.2, 4.3)
Unweighted % (95% CI)	2.7 (2.5, 2.9)	2.8 (1.9, 3.7)
Quebec (n)	(4465)	(223)
Weighted **%**[a] (95% CI)	24.6 (24.2, 25.0)	22.9 (19.6, 26.7)
Unweighted % (95% CI)	18.7 (18.2, 19.2)	16.4 (14.4, 18.4)
Prince Edward Island (n)	(517)	(48)
Weighted **%**[a] (95% CI)	0.4 (0.4, 0,5)	0.7 (0.5, 1.0)
Unweighted % (95% CI)	2.2 (2.0, 2.4)	3.5 (2.5, 4.5)
Ontario (n)	(5210)	(298)
Weighted **%**[a] (95% CI)	38.1 (37.7, 38.6)	39.3 (34.7, 44.1)
Unweighted % (95% CI)	21.9 (21.4, 22.4)	21.9 (19.7, 24.0)
Nova Scotia (n)	(2177)	(129)
Weighted **%**[a] (95% CI)	3.0 (2.9, 3.1)	2.7 (2.0, 3.6)
Unweighted % (95% CI)	9.1 (8.7, 9.5)	9.5 (7.9, 11.1)
Newfoundland and Labrador (n)	(1622)	(85)
Weighted **%**[a] (95% CI)	1.7 (1.7, 1.8)	1.6 (1.2, 2.3)
Unweighted % (95% CI)	6.7 (6.5, 7.1)	6.4 (5.0, 7.6)
New Brunswick (n)	(634)	(34)
Weighted **%**[a] (95% CI)	2.4 (2.4, 2.5)	2.3 (1.6, 3.2)
Unweighted % (95% CI)	2.7 (2.5, 2.9)	2.5 (1.7, 3.3)
Manitoba (n)	(2137)	(107)
Weighted **%**[a] (95% CI)	3.4 (3.3, 3.4)	3.1 (2.5, 3.9)
Unweighted % (95% CI)	9.0 (8.6, 9.4)	7.9 (6.5, 9.3)
British Columbia (n)	(4089)	(264)
Weighted **%**[a] (95% CI)	13.9 (13.6, 14.1)	15.3 (12.9, 17.9)
Unweighted % (95% CI)	17.2 (16.7, 17.7)	19.4 (17.3, 21.5)
Alberta (n) (Reference)	(2333)	(132)
Weighted **%**[a] (95% CI)	9.6 (9.4, 9.8)	9.0 (7.2, 11.1)
Unweighted % (95% CI)	9.8 (9.4, 10.2)	9.7 (8.1, 11.3)

	Lifetime history of PCa diagnosis	
	No (n = 23825)	Yes (n = 1358)
Education [(1)]		
Less than post-secondary degree/ diploma (n)	(5721)	(400)
Weighted **%**[a] (95% CI)	25.2 (24.3, 26.1)	31.2 (27.2, 35.5)
Unweighted % (95% CI)	24.1 (23.6, 24.6)	29.5 (27.1, 31.9)
Post-secondary degree/ diploma (n) (Reference)	(18032)	(955)
Weighted **%**[a] (95% CI)	74.8 (73.9, 75.7)	68.8 (64.5, 72.8)
Unweighted % (95% CI)	75.9 (75.4, 76.4)	70.5 (68.1, 72.9)
Total Household Income [(2)]		
< $50 000/year (n)	(5744)	(373)
Weighted **%**[a] (95% CI)	23.1 (22.3, 24.0)	29.2 (25.2, 33.4)
Unweighted % (95% CI)	25.3 (24.7, 25.8)	28.9 (26.5, 31.3)
≥ $50 000, less than $100 000/ year (n)	(8356)	(561)
Weighted **%**[a] (95% CI)	37.0 (35.9, 38.0)	41.4 (37.0, 46.0)
Unweighted % (95% CI)	36.8 (36.2, 37.4)	43.5 (40.9, 46.1)
≥ $100 000, less than $150 000/year (n)	(4644)	(221)
Weighted **%**[a] (95% CI)	21.0 (20.2, 21.9)	18.5 (15.0, 22.5)
Unweighted % (95% CI)	20.4 (19.9, 20.9)	17.1 (15.1, 19.1)
≥ $150 000 year (n) (Reference)	(3987)	(136)
Weighted **%**[a] (95% CI)	18.9 (18.0, 19.8)	10.9 (8.3, 14.3)
Unweighted % (95% CI)	17.5 (17.0, 18.0)	10.5 (8.9, 12.1)
Marital Status [(3)]		
Non-married/non-common-law (n)	(5365)	(274)
Weighted **%**[a] (95% CI)	18.7 (18.0, 19.5)	16.3 (13.5, 19.4)
Unweighted % (95% CI)	22.5 (22.0, 23.0)	20.2 (18.1, 22.3)
Married/common-law (n) (Reference)	(18454)	(1084)
Weighted **%**[a] (95% CI)	81.3 (80.5, 82.0)	83.7 (80.6, 86.5)
Unweighted % (95% CI)	77.5 (77.0, 78.0)	79.8 (77.7, 81.9)
Ethnicity [(4)]		
Other (n)	(992)	(53)
Weighted **%**[a] (95% CI)	4.8 (4.3, 5.3)	3.8 (2.3, 6.2)
Unweighted % (95% CI)	4.4 (4.1, 4.7)	4.0 (3.0, 5.0)
White only (n) (Reference)	(21800)	(1273)
Weighted **%**[a] (95% CI)	95.2 (94.7, 95.7)	96.2 (93.8, 97.7)
Unweighted % (95% CI)	95.6 (95.3, 95.9)	96.0 (95.0, 97.0)

Notes:
[(1)] Listwise deletion resulted in the following: n = 25 108
[(2)] Listwise deletion resulted in the following: n = 24 022
[(3)] Listwise deletion resulted in the following: n = 25 177
[(4)] Listwise deletion resulted in the following: n = 24 118
In complex samples, df = (#PSUs) – (# strata);
*** significant at $p < 0.001$;
** significant at $p < 0.01$;
* significant at $p < 0.05$
[a] complex sample analysis design adjusted – inflation weights used.

Table 4.3.2 Estimates of psychological distress, as measured by K10, by lifetime history of PCa for Canadian men from the Comprehensive cohort during the baseline cycle of the CLSA, 2010-2015 (N = 14 777).

	Listwise Deletion (n = 13 960)			**Multiple Imputation (pooled n = 14 777)**		
	Screened positive for psychological distress			Screened positive for psychological distress		
	No (n= 12623)	**Yes** (n = 1337)			**No** (pooled n = 13349)	**Yes** (pooled n = 1428)
Model [(1)]	*F (7, 12689) = 39.29****		**Model** [MI]	*F (7, 14757) = 49.48****		
Lifetime history of PCa diagnosis	*F (1, 12695) = 6.24**		**Lifetime history of PCa diagnosis** [MI]	*F (1, 14763) = 9.70***		
Yes (n)	(681)	(79)	**Yes** (n)	(728)	(85)	
Weighted %[a] (95% CI)	3.7 (3.4, 4.0)	4.7 (3.5, 6.3)		3.8 (3.5, 4.1)	4.7 (3.6, 6.2)	
aOR[b] (95% CI)	**1.00 (Reference)**	**1.52 (1.09, 2.11)****	**aOR[MI] (95% CI)**	**1.00 (Reference)**	**1.57 (1.18, 2.08)****	
No (n) (Reference)	(11942)	(1258)	**No** (n)	(12621)	(1343)	
Age	*F (1, 12695) = 83.88****		**Age** [MI]	*F (1, 14763) = 102.44****		
♦**Province**	*F (1, 12695) = 4.79**		♦**Province** [MI]	*F (1, 14763) = 5.74**		
Education	*F (1, 12695) = 7.22***		**Education** [MI]	*F (1, 14763) = 5.83**		
Household Income	*F (1, 12695) = 95.43****		**Household Income** [MI]	*F (1, 14763) = 117.23****		
Marital Status	*F (1, 12695) = 20.77****		**Marital Status** [MI]	*F (1, 14763) = 30.72****		
Ethnicity	*F (1, 12695) = 9.99***		**Ethnicity** [MI]	*F (1, 14763) = 17.39****		

Notes:
[(1)] Listwise deletion resulted in the following: n = 12 709
♦ Participants recruited to the Comprehensive cohort were required to live within 25-50 km of one of 11 Data Collection Sites (DCS) across 7 Canadian provinces.
In complex samples, df = (# PSUs)—(# strata);
*** significant at P < 0.001;
** significant at P < 0.01;
* significant at P < 0.05 (two-tailed)
a. complex sample analysis design adjusted – inflation weights used;
b. complex sample analysis design adjusted – analytical weights used;
F – design and covariate adjusted Wald *F* tests;
adjusted ORs (aORs) were calculated using logistic regression – aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity;
PCa, prostate cancer.

Table 4.3.3 Estimates of depressive symptoms, as measured by CES-D 10, by lifetime history of PCa diagnosis for Canadian men from the baseline cycle of the CLSA, 2010-2015 (N = 25 183).

	Screened positive for depressive symptoms (n = 25 060)	
	No (n= 21 750)	**Yes** (n = 3310)
Model [(1)]	*F (7, 22777)= 94.98****	
Lifetime history of PCa diagnosis	*F (1, 22783) = 4.51**	
Yes (n)	(20582)	(3125)
Weighted %[a] (95% CI)	4.0 (3.6, 4.4)	4.1 (3.2, 5.3)
Unweighted % (95% CI)	5.4 (5.1, 5.7)	5.6 (4.8, 6.4)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.24 (1.02, 1.51)***
No (n) **(Reference)**	(1168)	(185)
Age	*F (1, 22783) = 107.72****	
Province	*F (1, 22783) = 9.01***	
Education	*F (1, 22783) = 16.18****	
Total Household Income	*F (1, 22783) = 217.49****	
Marital Status	*F (1, 22783) = 147.13****	
Ethnicity	*F (1, 22783) = 1.81*	

Notes:
[(1)] Listwise deletion resulted in the following: n = 22 817
In complex samples, df = (#PSUs) – (# strata);
*** significant at $p < 0.001$;
** significant at $p < 0.01$;
* significant at $p < 0.05$ (two-tailed)
[a] complex sample analysis design adjusted – inflation weights used
[b] complex sample analysis design adjusted – analytical weights used
F – design and covariate adjusted Wald *F* tests
adjusted ORs (aORs) were calculated using logistic regression – aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity;
PCa, prostate cancer.

Table 4.3.4 Estimates of self-rated mental health (SRMH) by lifetime history of PCa diagnosis for Canadian men from the baseline cycle of the CLSA, 2010-2015 (N = 25 183).

	Poor self-rated mental health (SRMH) n = 25 159	
	No n = 22 564	Yes n = 1238
Model [(1)]	*F (7, 22860) = 53.87****	
Lifetime history of PCa diagnosis	*F (1, 22866) = 0.11*	
Yes (n)	(1302)	(55)
Weighted %[a] (95% CI)	4.0 (3.7, 4.4)	4.3 (2.8, 6.6)
Unweighted % (95% CI)	5.5 (5.2, 5.8)	4.3 (2.9, 5.7)
aOR[b] (95% CI)	**1.00 (Reference)**	**0.95 (0.68, 1.32)**
No (n) **(Reference)**	(22564)	(1238)
Age	*F (1, 22866) = 96.31****	
Province	*F (1, 22866) = 19.82****	
Education	*F (1, 22866) = 0.75*	
Total Household Income	*F (1, 22866) = 114.57****	
Marital Status	*F (1, 22866) = 71.41****	
Ethnicity	*F (1, 22866) = 4.43**	

Notes:
[(1)] Listwise deletion resulted in the following: n = 22 866
In complex samples, df = (#PSUs) – (# strata);
*** significant at $p < 0.001$;
** significant at $p < 0.01$;
* significant at $p < 0.05$ (two-tailed)
[a] complex sample analysis design adjusted – inflation weights used;
[b] complex sample analysis design adjusted – analytical weights used;
F – design and covariate adjusted *Wald F* tests.
adjusted ORs (aORs) were calculated using logistic regression – aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity.
PCa, prostate cancer.

Table 4.3.5 Multiple logistic regression analyses predicting presence of current (past 30 days) psychological distress, as measured by K10, by fitting multimorbidity, alcohol use and smoking, respectively, while controlling for age, province, education, household income, marital status and ethnicity.

	Listwise Deletion (n = 13 960)		**Multiple Imputation** (pooled n =14 777)	
	Screening positive for psychological distress		Screening positive of psychological distress	
	No (n = 12623)	**Yes** (n = 1337)	**No** (n=13345)	**Yes** (n = 1432)
Model [(1)]	*F (7, 12689) = 47.68****		*F (7, 14757) = 60.08****	
Multimorbidity	*F (1, 12695) = 52.99****		*F (1, 14763) = 72.16****	
Yes (n)	(6146)	(825)	(6549)	(888)
Weighted %[a] (95% CI)	40.4 (39.3, 41.5)	54.2 (50.8, 57.6)	40.7 (39.7, 41.8)	54.3 (51.5, 57.6)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.73 (1.50, 2.01)*****	**1.00 (Reference)**	**1.78[MI] (1.56, 2.03)*****
No (n) (Reference)	(6477)	(512)	(6796)	(544)
	59.6 (58.5, 60.7)	45.8 (42.4, 49.2)	59.3 (58.2, 60.3)	45.7 (42.4, 48.9)
Age	*F (1, 12695) = 112.60****		*F (1, 14763) = 140.76****	
Province	*F (1, 12695) = 4.68**		*F (1, 14763) = 6.17**	
Education	*F (1, 12695) = 5.40**		*F (1, 14763) = 3.39*	
Household Income	*F (1, 12695) = 82.02****		*F (1, 14763) = 101.97****	
Marital Status	*F (1, 12695) = 21.19****		*F (1, 14763) = 31.11****	
Ethnicity	*F (1, 12695) = 11.23***		*F (1, 14763) = 18.05****	
Model[(2)]	*F (9, 12469) = 32.91****		*F (9, 14755) = 42.57****	
Alcohol Use	*F (3, 12475) 7.78****		*F (3, 14761) = 12.18****	
Daily drinker (n)	(4091)	(329)	(4341)	(353)
Weighted %[a] (95% CI)	32.0 (31.0, 33.1)	24.1 (21.3, 27.1)	32.0 (30.9, 33.0)	24.0 (21.3, 26.9)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.66 (1.31, 2.11)*****	**1.00 (Reference)**	**1.69 [MI] (1.38, 2.07)*****
Weekly drinker (n)	(4268)	(384)	(4564)	(415)
Weighted %[a] (95% CI)	37.3 (36.2, 38.5)	31.3 (28.1, 34.6)	37.3 (36.2, 38.4)	31.1 (28.0, 34.4)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.46 (1.16, 1.84)****	**1.00 (Reference)**	**1.55 [MI] (1.27, 2.07)*****
Occasional drinker (n)	(2857)	(390)	(3090)	(431)
Weighted %[a] (95% CI)	21.6 (20.7, 22.5)	30.3 (27.2, 33.6)	21.7 (20.8, 22.6)	30.4 (27.4, 33.6)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.15 (0.92, 1.45)**	**1.00 (Reference)**	**1.15 [MI] (0.95, 1.40)**
Non-drinker (n) (Reference)	(1194)	(204)	(1350)	(233)
Age	*F (1, 12477) = 76.43****		*F (1, 14763) =92.05****	
Province	*F (1, 12477) = 6.77***		*F (1, 14763) = 7.59***	
Education	*F (1, 12477) = 6.39**		*F (1, 14763) = 4.44**	
Household Income	*F (1, 12477) = 76.10****		*F (1, 14763) = 96.19****	
Marital Status	*F (1, 12477) = 19.60****		*F (1, 14763) = 29.69****	
Ethnicity	*F (1, 12477) = 4.25**		*F (1, 14763) = 8.92***	
Model[(3)]	*F (8, 9070) = 27.42****		*F (8, 14756) = 50.67****	
Smoking	*F (2, 9076) = 13.00****		*F (2, 14762) = 32.26****	

	Listwise Deletion (n = 13 960)		**Multiple Imputation** (pooled n =14 777)	
	Screening positive for psychological distress		Screening positive of psychological distress	
	No (n = 12623)	**Yes** (n = 1337)	**No** (n=13345)	**Yes** (n = 1432)
Daily smoker (n)	(738)	(191)	(1116)	(273)
Weighted %[a] (95% CI)	8.9 (8.1, 9.7)	20.0 (17.1, 23.3)	8.6 (8.0, 9.2)	19.4 (17.1, 21.9)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.81 (1.43, 2.27)*****	**1.00 (Reference)**	**1.83 [MI] (1.58, 2.13)*****
Occasional smoker (n)	(196)	(29)	(304)	(41)
Weighted %[a] (95% CI)	2.7 (2.3, 3.3)	3.4 (2.2, 5.2)	2.8 (2.5, 3.2)	3.3 (2.4, 4.7)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.42 (0.87, 2.32)**	**1.00 (Reference)**	**1.26 [MI] (0.91, 1.75)**
Non-smoker (n) (Reference)	(8050)	(807)	(11925)	(1118)
Age	*F (1, 9077) = 47.16****		*F (1, 14763) = 74.51****	
Province	*F (1, 9077) = 1.45*		*F (1, 14763) = 5.17**	
Education	*F (1, 9077) = 1.02*		*F (1, 14763) = 2.87*	
Household Income	*F (1, 9077) = 62.45****		*F (1, 14763) = 103.50****	
Marital Status	*F (1, 9077) = 12.51****		*F (1, 14763) = 19.53****	
Ethnicity	*F (1, 9077) = 3.76*		*F (1, 14763) = 15.51****	

Notes:

(1) Listwise deletion resulted in the following: n = 12709
(2) Listwise deletion resulted in the following: n = 12491
(3) Listwise deletion resulted in the following: n = 9091

In complex samples, df = (# PSUs)—(# strata);
*** significant at P < 0.001;
** significant at P < 0.01;
* significant at P < 0.05 (two-tailed);
[a] complex sample analysis design adjusted – inflation weights used;
[b] complex sample analysis design adjusted – analytical weights used;
F – design and covariate adjusted Wald *F* tests;
aORs were calculated using logistic regression and evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity.

Table 4.3.6 Multiple logistic regression analyses predicting presence of current depressive symptoms, as measured by CES-D 10, by fitting multimorbidity, alcohol use and smoking, respectively, while controlling for age, province, education, household income, marital status and ethnicity.

	Screening positive for depressive symptoms (n = 25060)	
	No	**Yes**
Model	*F (7, 22777) = 109.66***	
Multimorbidity	*F (1, 22783) = 114.68***	
Yes (n)	(10637)	(2045)
Weighted %[a] (95% CI)	43.2 (42.1, 44.3)	56.2 (53.4, 58.9)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.69 (1.53, 1.85)*** **
No (n) (Reference)	(11113)	(1265)
Weighted %[a] (95% CI)	56.8 (55.7, 57.9)	43.8 (41.1, 46.6)
Age	*F (1, 22783) = 160.30***	
Province	*F (1, 22783) = 9.18***	
Education	*F (1, 22783) = 12.77***	
Household Income	*F (1, 22783) = 188.35***	
Marital Status	*F (1, 22783) = 148.92***	
Ethnicity	*F (1, 22783) = 2.65*	
Model	*F (9, 22310) = 78.78***	
Alcohol Use [(1)]	*F (1, 22316) = 18.22***	
Daily drinker (n)	(6525)	(835)
Weighted %[a] (95% CI)	29.2 (28.2, 30.2)	25.8 (23.5, 28.3)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.48 (1.28, 1.71)*** **
Weekly drinker (n)	(7288)	(898)
Weighted %[a] (95% CI)	36.3 (35.2, 37.3)	29.0 (26.5, 31.6)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.64 (1.42, 1.89)*** **
Occasional drinker (n)	(5205)	(956)
Weighted %[a] (95% CI)	24.5 (23.6, 25.5)	30.0 (27.5, 32.7)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.23 (1.06, 1.41)****
Non-drinker (n)	(2273)	(556)
Age	*F (1, 22318) = 101.74***	
Province	*F (1, 22318) = 7.00***	
Education	*F (1, 22318) = 12.88***	
Household Income	*F (1, 22318) = 178.46***	
Marital Status	*F (1, 22318) = 139.93***	
Ethnicity	*F (1, 22318) = 0.45*	
Model	*F (8, 16647) = 63.21***	
Smoking [(2)]	*F (2, 16653) = 19.83***	

	Screening positive for depressive symptoms (n = 25060)	
	No	**Yes**
Daily smoker (n)	(1452)	(462)
Weighted %[a] (95% CI)	10.6 (9.8, 11.4)	18.8 (16.4, 21.4)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.58 (1.37, 1.83)*** **
Occasional smoker (n)	(340)	(78)
Weighted %[a] (95% CI)	2.7 (2.3, 3.2)	3.3 (2.3, 4.7)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.23 (0.93, 1.64)**
Non-smoker (n) (Reference)	(13998)	(2057)
Age	*F (1, 16654) = 53.27****	
Province	*F (1, 16654) = 7.65***	
Education	*F (1, 16654) = 6.39**	
Household Income	*F (1, 16654) = 129.28****	
Marital Status	*F (1, 16654) = 94.45****	
Ethnicity	*F (1, 16654) = 6.81***	

Notes:

(1) Listwise deletion resulted in the following: n = 24 536

(2) Listwise deletion resulted in the following: n = 18387

In complex samples, df = (# PSUs)—(# strata);

*** significant at P < 0.001;

** significant at P < 0.01;

* significant at P < 0.05 (two-tailed)

[a] complex sample design adjusted – inflation weights used;

[b] complex sample design adjusted – analytical weights used;

F – design and covariate adjusted Wald *F* tests;

aORs were calculated using logistic regression – aORs were evaluated while holding fixed values of the complexity of design, age, province, education, household income, marital status and ethnicity.

Table 4.3.7 Multiple logistic regression analyses predicting presence of poor self-rated mental health (SRMH), by fitting multimorbidity, alcohol use and smoking, respectively, while controlling for age, province, education, household income, marital status and ethnicity.

	Poor self-rated mental health (SRMH)	
	No	Yes
Model	*F (7, 22860) = 68.71***	
Multimorbidity (1)	*F (1, 22866) = 121.33***	
Yes (n)	(11844)	(883)
Weighted %[a] (95% CI)	43.8 (42.8, 44.9)	65.7 (61.3, 70.0)
aOR[b] (95% CI)	**1.00 (Reference)**	**2.27 (1.96, 2.62)*** **
No (n) (Reference)	(12022)	(410)
Weighted %[a] (95% CI)	56.2 (55.1,57.2)	34.3 (30.0, 38.7)
Age	*F (1, 22866) = 147.70***	
Province	*F (1, 22866) = 20.36***	
Education	*F (1, 22866) = 0.13*	
Household Income	*F (1, 22866) = 93.86***	
Marital Status	*F (1, 22866) = 74.89***	
Ethnicity	*F (1, 22866) = 3.36*	
Model	*F (9, 22393) = 48.82***	
Alcohol Use (2)	*F (3, 223399) = 16.31***	
Daily drinker (n)	(7083)	(301)
Weighted %[a] (95% CI)	29.1 (28.2, 30.0)	22.2 (18.7, 26.0)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.76 (1.43, 2.18)*** **
Weekly drinker (n)	(7882)	(326)
Weighted %[a] (95% CI)	35.9 (34.9, 36.9)	23.6 (20.0, 27.6)
aOR[b] (95% CI)	**1.00 (Reference)**	**2.07 (1.68, 2.56)*** **
Occasional drinker (n)	(5809)	(382)
Weighted %[a] (95% CI)	24.9 (24.0, 25.8)	33.0 (28.7 37.7)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.51 (1.23, 1.85)*** **
Non-drinker (n) (Reference)	(2592)	(259)
Weighted %[a] (95% CI)	10.1 (9.5, 10.7)	21.2 (17.7 25.0)
Age	*F (1, 22401) = 100.32***	
Province	*F (1, 22401) = 15.49***	
Education	*F (1, 22401) = 0.08*	
Household Income	*F (1, 22401) = 92.20***	
Marital Status	*F (1, 22401) = 68.81***	
Ethnicity	*F (1, 22401) = 5.23**	
Model	*F (8, 16711) = 42.44***	
Smoking (3)	*F (2, 16717) = 10.65***	
Daily smoker (n)	(1714)	(206)
Weighted %[a] (95% CI)	11.1 (10.4, 11.9)	23.6 (19.4, 28.4)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.58 (1.29, 1.93)*** **
Occasional smoker (n)	(384)	(35)
Weighted %[a] (95% CI)	2.8 (2.3, 3.2)	4.4 (2.6, 7.3)
aOR[b] (95% CI)	**1.00 (Reference)**	**1.47 (0.98, 2.22)**
Non-smoker (n) (Reference)	(15369)	(756)
Weighted %[a] (95% CI)	86.1 (85.3, 87.0)	72.0 (67.0, 76.5)
Age	*F (1, 16718) = 59.99***	
Province	*F (1, 16718) = 19.77***	
Education	*F (1, 16718) = 0.004*	
Household Income	*F (1, 16718) = 84.68***	
Marital Status	*F (1, 16718) = 48.63***	
Ethnicity	*F (1, 16718) = 2.33*	

Notes:

(1) Listwise deletion resulted in the following: n = 25159
(2) Listwise deletion resulted in the following: n = 24634
(3) Listwise deletion resulted in the following: n = 18464

In complex samples, df = (# PSUs)—(# strata);
*** significant at P < 0.001;
** significant at P < 0.01;
* significant at P < 0.05 (two-tailed)
[a] complex sample design adjusted – inflation weights used;
[b] complex sample design adjusted – analytical weights used;
F – design and covariate adjusted Wald *F* tests;
aORs were calculated using logistic regression – aORs were evaluated while holding fixed values of the complexity of design, age, province, education, household income, marital status and ethnicity.

Table 4.3.8 Multivariate logistic regression, using listwise deletion, predicting current psychological distress, measured by K10, by fitting multimorbidity, alcohol use and smoking to the model, while controlling for age, province, education, household income, marital status and ethnicity.

	Screening positive for psychological distress vs. screening negative **aOR[a] (95% CI)**	
	Model 1 [(1)] *F (7, 12689) = 39.29****	Model 2 [(2)] *F (13, 8997) = 20.63****
Lifetime history of PCa diagnosis	*F (1, 12695) = 6.24**	*F (1, 9009) = 1.63*
Yes	**1.52 (1.09, 2.11)***	**1.28 (0.88, 1.86)**
No	**1.00 (Reference)**	**1.00 (Reference)**
Multimorbidity	–	*F (1, 9009) = 25.07****
Yes	–	**1.56 (1.31, 1.85)*****
No	–	**1.00 (Reference)**
Alcohol Use	–	*F (3, 9007) = 4.75***
Daily drinker	–	**1.52 (1.16, 2.00)****
Weekly drinker	–	**1.38 (1.05, 1.81)***
Occasional drinker	–	**1.08 (0.82, 1.42)**
Non-drinker	–	**1.00 (Reference)**
Smoking	–	*F (2, 9008) = 12.75****
Daily smoker	–	**1.82 (1.43, 2.30) *****
Occasional smoker	–	**1.46 (0.90, 2.40)**
Non-smoker	–	**1.00 (Reference)**
Age	*F (1, 12695) = 83.88****	*F (1, 9009) = 60.96****
Province	*F(1, 12695) = 4.79**	*F (1, 9009) = 2.11*
Education	*F (1, 12695) = 7.22***	*F (1, 9009) = 0.26*
Household Income	*F (12695) = 95.43****	*F (1, 9009) = 41.74****
Marital Status	*F (1, 12695) = 20.77****	*F (1, 9009) = 15.10****
Ethnicity	*F (1, 12695) = 9.99***	*F (1, 9009) = 1.56*

Notes:

(1) Listwise deletion resulted in the following n = 12709

(2) Listwise deletion resulted in the following n = 9023

In complex samples, df = (# PSUs)—(# strata);

*** significant at P < 0.001;

** significant at P < 0.01;

* significant at P < 0.05 (two-tailed);

a – complex sample design adjusted – analytical weights used; *F* – design and covariate adjusted Wald *F* tests;

aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity;

PCa, prostate cancer

Table 4.3.9 Multivariate logistic regression, using multiple imputation, predicting current psychological distress, measured by K10, by fitting multimorbidity, alcohol use and smoking to the model, while controlling for age, province, education, household income, marital status and ethnicity.

	Screening positive for psychological distress vs. screening negative **aOR[a] (95% CI)**	
	Model 1 **MI** *F (7, 14757) = 49.65****	Model 2 **MI** *F (13, 14751) = 39.87****
Lifetime history of PCa diagnosis	*F (1, 14763) = 10.08***	*F (1, 14763) = 10.96***
Yes	**1.57 (1.18, 2.08)****	**1.62 (1.22, 2.16)****
No	**1.00 (Reference)**	**1.00 (Reference)**
Multimorbidity	–	*F (1, 14763) = 66.54****
Yes	–	**1.74 (1.52, 1.98)*****
No	–	**1.00 (Reference)**
Alcohol Use	–	*F (3, 14761) = 9.98****
Daily drinker	–	**1.62 (1.32, 1.98)*****
Weekly drinker	–	**1.44 (1.18, 1.75)*****
Occasional drinker	–	**1.12 (0.93, 1.36)**
Non-drinker	–	**1.00 (Reference)**
Smoking	–	*F (2, 14762) = 31.64****
Daily smoker	–	**1.85 (1.59, 2.15)*****
Occasional smoker	–	**1.28 (0.92, 1.79)**
Non-smoker	–	**1.00 (Reference)**
Age	*F (1, 14763) = 104.37****	*F (1, 14763) = 107.24****
Province	*F(1, 14763) = 6.02**	*F (1, 14763) = 6.61**
Education	*F (1, 14763) = 5.36**	*F (1, 14763) = 0.97*
Household Income	*F (1, 14763) = 120.05****	*F (1, 14763) = 69.05****
Marital Status	*F (1, 14763) = 30.40****	*F (1, 14763) = 21.68****
Ethnicity	*F (1, 14763) = 15.98****	*F (1, 14763) = 10.96***

Notes:
MI - Multiple Imputation under taken with 20 iterations for all variables included in Model 4
a – complex sample design adjusted – analytical weights used;
F – design and covariate adjusted Wald *F* tests;
aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity;
PCa, prostate cancer

Table 4.3.10 Multivariate logistic regression predicting depressive symptoms, measured by CESD-10, by fitting multimorbidity, alcohol use and smoking to the model, while controlling for age, province, education, household income, marital status and ethnicity.

	Screening positive for depressive symptoms vs. screening negative **aOR[a] (95% CI)**	
	Model 1 [(1)] *F (7, 22777) = 94.98****	Model 2 [(2)] *F (13, 16488) = 48.18****
Lifetime history of PCa diagnosis	*F (1, 22783) = 4.51**	*F (1, 16500) = 5.81**
Yes	**1.24 (1.02, 1.51)***	**1.31 (1.05, 1.63)***
No	**1.00 (Reference)**	**1.00 (Reference)**
Multimorbidity	–	*F (1, 16500) = 71.80****
Yes	–	**1.59 (1.43, 1.78)*****
No	–	**1.00 (Reference)**
Alcohol Use	–	*F (3, 16498) = 14.85****
Daily drinker	–	**1.49 (1.27, 1.75)*****
Weekly drinker	–	**1.69 (1.44, 1.99)*****
Occasional drinker	–	**1.26 (1.08, 1.49)****
Non-drinker	–	**1.00 (Reference)**
Tobacco	–	*F (2, 16499) = 18.75****
Daily smoker	–	**1.57 (1.36, 1.82)*****
Occasional smoker	–	**1.23 (0.92, 1.64)**
Non-smoker	–	**1.00 (Reference)**
Age	*F (1, 22783) =107.72****	*F (1, 16500) = 88.52****
Province	*F(1, 22783) = 9.01***	*F (1, 16500) = 6.18**
Education	*F (1, 22783) = 16.18****	*F (1, 16500) = 3.41*
Household Income	*F (1, 22783) = 217.49****	*F (1, 16500) = 86.57****
Marital Status	*F (1, 22783) = 147.13****	*F (1, 16500) = 99.90****
Ethnicity	*F (1, 22783) = 1.81*	*F (1, 16500) = 4.17**

Notes:

(1) Listwise deletion resulted in the following n: 22 817

(2) Listwise deletion resulted in the following n: 16 534

In complex samples, df = (# PSUs)—(# strata);

*** significant at $p < 0.001$;

** significant at $p < 0.01$;

* significant at $p < 0.05$ (two-tailed);

[a] complex sample design adjusted – analytical weights used;

F – design adjusted Wald F tests; ORs and adjusted ORs (aORS) were calculated using logistic regression. aORs were evaluated while holding fixed values of the complexity of the design, age group, provincial residence, education level, total household income, marital status and ethnicity;

PCa, prostate cancer

Table 4.3.11 Multivariate logistic regression predicting poor self-rated mental health (SRMH), by fitting multimorbidity, alcohol use and smoking to the model, while controlling for age, province, education , household income, marital status and ethnicity.

	Poor self-rated mental health vs. good self-rated mental health **aOR [a] (95% CI)**	
	Model 1 [(1)] *F (7, 22860) = 53.87****	Model 2 [(2)] *F (13, 16553) = 31.78****
Lifetime history of PCa diagnosis	*F (1, 22866) = 0.11*	*F (1, 16565) = 0.002*
Yes	**0.95 (0.68, 1.32)**	**1.01 (0.70, 1.45)**
No	**1.00 (Reference)**	**1.00 (Reference)**
Multimorbidity	–	*F (1, 16565) = 62.99****
Yes	–	**1.97 (1.67, 2.33)*** **
No	–	**1.00 (Reference)**
Alcohol Use	–	*F (3, 16563) = 10.12****
Daily drinker	–	**1.65 (1.30, 2.09)*** **
Weekly drinker	–	**1.95 (1.53, 2.48)*** **
Occasional drinker	–	**1.52 (1.20, 1.91)*** **
Non-drinker		**1.00 (Reference)**
Tobacco	–	*F (2, 16564) = 9.61****
Daily smoker	–	**1.54 (1.25, 1.89)*** **
Occasional smoker	–	**1.53 (1.00, 2.32)***
Non-smoker	–	**1.00 (Reference)**
Age	*F (1, 22866) = 96.31****	*F (1, 16565) = 84.15****
Province	*F(1, 22866) = 19.82****	*F (1, 16565) = 18.08****
Education	*F (1, 22866) = 0.75*	*F (1, 16565) = 0.17*
Household Income	*F (1, 22866) = 114.57****	*F (1, 16565) = 59.19****
Marital Status	*F (1, 22866) = 71.41****	*F (1, 16565) = 50.35****
Ethnicity	*F (1, 22866) = 4.43**	*F (1, 16565) = 2.06*

Notes:

(1) Listwise deletion resulted in the following: n = 22 900

(2) Listwise deletion resulted in the following: n = 16 599

In complex samples, df = (# PSUs)—(# strata);

*** significant at P < 0.001;

** significant at P < 0.01;

* significant at P < 0.05 (two-tailed)

a – complex sample design adjusted – analytical weights used; and covariate adjusted;

aORs were evaluated while holding fixed values of the complexity of the design, age, province, education, household income, marital status and ethnicity; PCa, prostate cancer

CHAPTER 5 CONCLUSION

The increasing prevalence of PCa, combined with the cumulative number of years men live post-diagnosis, has led to an increased interest in the mental health of this population. This thesis examined the relationship between lifetime history of PCa diagnosis and mental health outcomes among a sample of Canadian men. The main objectives were to: (1) identify the prevalence of a lifetime PCa diagnosis in a national sample of older Canadian men (Chapter 4); (2) examine the association between lifetime history of PCa diagnosis and current mental health symptoms (Chapter 4); and (3) examine the contribution of multimorbidity and substance use in the association between lifetime history of PCa and mental health (Chapter 4).

We found the national prevalence estimate of lifetime history of PCa diagnosis to be 4% (95% CI: 3.7, 4.4), in males aged 47-65 years old. This result is a much-needed update on the national prevalence which was last reported in 2008 (8). Courneya et al (2008) found the prevalence of history of a PCa diagnosis to be 1.3% in their sample of Canadians males aged 18 to 65. Our results suggest that the prevalence of PCa survivors in our population has increased since 2005, which is consistent with the increasing number of adults over the age of 65 in our population. However, the difference in age range as well as surveillance period prevents us from making accurate comparisons between these two studies. Additionally, our national prevalence estimate is more comparable to that found by Ilie et al (2019) among the Atlantic Canadian population, which was also 4% (males aged 49-69 years old, between 2009-2015) (9).

We demonstrated that there is significantly greater psychological distress and depressive symptoms among Canadian men who self-reported a lifetime history of PCa

diagnosis, compared to men who had no history of a PCa diagnosis. Additionally, we demonstrated that when analyses are controlled for multimorbidity and substance use, lifetime history of PCa is still associated with increased probability of poorer mental health outcomes.

Our results indicate absence of an association between history of PCa diagnosis and self-rated mental health (SRMH) for this sample of men. One explanation of these results may be that the single-item perceived mental health measure (SRMH) is not robust enough to capture the complexity of the mental health issues these men are facing. Another explanation could be the influence of social desirability and/or masculine ideals, such as stoicism, on SRMH. This suggests the importance of using validated, multi-faceted questionnaires for assessing mental health outcomes among older men.

Some possible mechanisms for explaining the association between history of PCa and mental health, as suggested in the literature, include survivorship needs which may include any or a combination of the following: physical symptoms (e.g., urinary, bowel and sexual function impairments), spiritual issues, practical/social problems (e.g., financial concerns) and/or emotional problems (114). Physical symptoms may be related to disease progression or treatment modality, and include pain, fatigue, sexuality/reproduction issues, and other treatment-specific issues such as menopausal symptoms and memory problems associated with hormonal therapy (20). Spiritual issues may be related to religious concerns, and fear of death (114). Practical/social problems may include transitioning back to work, and financial problems. Emotional issues may be related to fear of progression or relapse, or intimacy and social support issues. Therefore, these aspects should be the targets of future psycho-oncological interventions.

Relevant factors that future research may want to examine also include treatment modality, disease stage and survivorship time. Examination of these factors would lead to a better understanding of the issues that men with PCa face. The direction of the association between these factors and mental health outcomes would remain substantially the same as we have found, however the strength of the association might differ based on deeper analysis of treatment modality (related side-effects), disease stage, survivorship time. The CLSA data would not allow us to explore these factors as they were not available in the survey. One possibility may be that men who selected hormonal therapy or underwent radical prostatectomy would be more likely to report adverse mental health outcomes than those who underwent other forms of treatment, based on the known intensity of the hormonal treatments side-effects which include menopausal symptoms (e.g. hot flashes and hormonal mood swings), erectile dysfunction, weight gain, etc.

The literature suggests a few possible mechanisms to explain the relationship between our predictor variables, history of PCa diagnosis, substance use and multimorbidity, relative to our outcome variable, mental health. Both multimorbidity and substance use could be risk factors for mental health issues before the development of PCa. Multimorbidity burden is common among older adults, and could be an issue prior to a PCa diagnosis. Research supports the negative effect of multimorbidity on QoL and mental health (85,115). Substance use may lead to mental health symptoms such as depression and anxiety (116). In contrast, both multimorbidity and substance use may be consequences of a PCa diagnosis. The addition of PCa increases multimorbidity burden in men who have other conditions, such as heart disease or diabetes. Furthermore, addition of physical side-effects from PCa treatment can also increase multimorbidity.

Increased substance use may also be a consequence of PCa, as a stress-coping mechanism (24). Therefore, it is difficult to speculate on the temporal order between the predictor variables in relation to the outcome measures.

5.1 Limitations

This thesis had several limitations. First, as this study is cross-sectional, and therefore is a snap-shot in time, it can only show associations, and causation cannot be inferred. However, according to the Bradford Hill criteria of causation, temporality is only one of nine components needed to provide epidemiological evidence of a causal relationship (117). The other components include strength of association, consistency, specificity, dose-response relationship, biological plausibility, experimental evidence, coherence and analogy. Our results provided *statistically significant associations* between lifetime history of PCa and mental health outcomes – depressive symptoms and psychological distress. These results are *consistent* with a large majority of studies that have also examined the association between PCa and poor mental health (6). 7/31/2019 12:26:00 PMAs of yet, no strong *evidence* has demonstrated a strong effect of psychosocial interventions on distress and depression in men with PCa (118). There are *biological* variables that may place men with PCa at an increased risk for depression, such as greater burden of physical symptoms, advanced age and type of treatment modality such as hormone therapy (10).

Second, one of the most important limitations with our data is that the nature of the information collected is retrospective and self-reported. Therefore, our results may be subject to recall bias.

Third, the analysis conducted in this study is limited by information available in the CLSA survey. For example, the CLSA did not collect additional information regarding time of PCa diagnosis and PCa treatment modality, both of which could have strengthened our analysis and, therefore, our conclusions.

Finally, there is a possibility of selection bias in the CLSA study. As with many population-based studies, the first wave of the CLSA had a lower than expected response rate. The overall response proportion was approximately 10%, which, although adjusted for by the use of population-based weights, may have introduced non-response bias. Non-response or refusal to participate can increase the risk of selection bias and reduces the likelihood of having a representative sample, which occurs when those who participate differ in some systematic way from those who do not. This issue was examined, in part, in the 2009 CLSA pilot. Very few differences were found between responders to the CLSA pilot questionnaire and non-responders. However, responders were slightly more educated than the non-responders (90). Research on population-based surveys has shown that older individuals and individuals with higher education are more prone to complete questionnaires (119). Our sample of men is highly selective, that is, the majority are white, educated, married and have moderate to high income. These factors may reduce the generalizability of our results to the entire Canadian PCa population. Only by obtaining relevant information on non-respondents can investigators accurately estimate response bias and its effects on the odds ratio. However, we can speculate that non-response bias in the CLSA may have led to an underestimate of the prevalence of history of PCa diagnosis due to adults with higher educational attainment living healthier and longer lives (97).

Survival bias is another potential concern for our study. This bias occurs since men who survived their PCa diagnosis are more likely to enter our study. On average, these men are likely to be healthier, and have less multimorbidity and less substance use, than men who did not survive. Since multimorbidity and substance use increase the risk of death from PCa, the proportion of cases with high multimorbidity and heavy substance use will be lower in our data. Therefore, we are excluding patients who have died (severe cases) and focusing on those who survived their diagnosis. This may have consequently led to an underestimate of the prevalence estimate of history of PCa, as we are only capturing those men in the population who survived their diagnosis. Using follow-up data from the CLSA may help reduce this type of bias in future research.

5.2 Strengths

The main strength of this research is the use of a large-scale, national, population-based survey that used a standard protocol to examine detailed characteristics of aging. This is the most recent study documenting the national prevalence of lifetime history of PCa diagnosis among older Canadian adults. The breadth of data collected allows for comparison across a number of patient-important outcomes that are not usually available in other routinely collected data sources. Additionally, the information collected allows for several covariates to be assessed and controlled for in analysis. Another strength is the availability, use and comparison of two validated measures, CES-D 10 and K10, and a self-rated mental health (SRMH) item for our outcome variable, mental health. The use of these measures is a strength of our study because it has the potential to minimize measurement bias by capturing different dimensions of the mental health construct. Another important consideration is that we were able to capture 26 chronic conditions for

inclusion into our multimorbidity variable. In contrast, many previous studies examining multimorbidity in the Canadian population were based on only a limited number of chronic conditions (113).

5.3 Implications for future research and clinicians

The first clinical implication of our results is the increased need for multi-disciplinary healthcare teams to assess mental health outcomes among men with PCa, so that issues do not go undiagnosed as they can lead to dire consequences such as worse treatment outcomes, higher risk of suicide, and overall poorer QoL (38,39,41,42). Another clinical implication of our results is the support they provide for the development and adoption of holistic intervention programs that target this population and help provide men with tools to alleviate the burden of mental health issues, such as support groups, meditation and physical activity (9).

Future research needs to consider the use of multiple validated mental health measures to accurately capture the complexity of the mental health construct. Our results indicated the presence of an association between history of PCa diagnosis and both depressive symptoms, measured by CES-D10, and psychological distress, measured by K10, for this sample of men. However, our results did not demonstrate the presence of an association between history of PCa diagnosis and self-reported mental health (SRMH) among these men. This suggests the importance of using multi-faceted measures for assessing mental health, rather than a single-item perceived health measure. Although SRMH is a validated measure, its simplicity does not seem to capture the complex psychological issues within the PCa population. The SRMH item may be subject to social desirability bias that is often associated with self-reported data, especially when it comes

to states of being that are stigmatized in our society. Therefore, future studies examining mental health among PCa patients should employ several tools to assess and screen for the different psychological issues these men face during their cancer journeys.

Additionally, the findings from our research should inform clinicians who may want to screen their patients for mental health issues. That is, they should employ a validated, short-form questionnaire, such as the CES-D10 or K10, rather than relying on self-reports from patients about their perceived mental health status.

There is a need for further research. The future CLSA follow-up data should be used to assess longitudinal changes in prevalence of mental health outcomes among men with a history of a PCa diagnosis. Future cycles of CLSA data could be used to identify incident cases of PCa. Then, the mental health outcomes between newly diagnosed men (incident cases) and those with a history of a PCa diagnosis at baseline could be compared and evaluated. Future cycles of the CLSA, and other population-based surveys, may benefit from inclusion of the date of diagnosis in their questionnaires which would allow for the assessment of survivorship time.

Additionally, future research should explore the social construct of masculinity in relation to mental health outcomes of men with PCa. There are several aspects of masculine socialization that may have positive or negative implications for men with urogenital cancers (120). For example, strength and resiliency may play a positive role in dealing with the psychological effects of PCa (121). Conversely, ideals such as stoicism and reluctance to disclose vulnerability may negatively influence emotional coping in men with PCa (121). The inter-play of these aspects are vital to bettering our understanding of mental health among this population. The knowledge gained from this

type of future research may enable the development of interventions that harness masculine ways of coping, thereby maximizing the emotional supports needed by men at all stages of their cancer journeys.

Avenues for future work using future cycles of CLSA could include an exploration of the association between history of PCa and mental health outcome over time, and an exploration of the role of survivorship time in this association. The examination of the interaction between age and lifetime history of PCa constitutes yet another avenue to extend the results of the current study. Knowledge gained from this research will give a better picture of who is suffering the most in this population, and therefore lead to age-specific interventional programs. Lastly, assessing the role played by treatment modality and social support in the relationship between history of PCa diagnosis and mental health it would allow researchers to identify the populations most at need. Both treatment modality and social support (e.g. marital status) could be explored as potential mediators in the causal pathway. Knowledge from this exploration could lead to the creation of improved care plans and better targeted interventional practices, such as spousal/partner educational programs or individualized group support programs based on treatment type.

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