AN EXAMINATION OF THE ASSOCIATION BETWEEN PROSTATE CANCER, LIFESTYLE FACTORS AND MENTAL HEALTH OUTCOMES IN A MATCHED SAMPLE OF MEN FROM ATLANTIC CANADA

by

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Dedication

This thesis is dedicated to my late Maman, Gisèle Pilon-Blackman, who passed away in 2002 at the age of 46 from breast cancer. I am forever grateful for her showing me constant inspiration and for teaching me to persevere in the face of challenges. I have felt her presence with me throughout this journey, encouraging me forward.

In addition, I would also like to dedicate this thesis to the individuals who have lost their life to COVID-19 and to the healthcare workers and researchers who have worked tirelessly to end the pandemic.

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Abstract

This cross-sectional study aims to examine the association between the presence or absence of a lifetime history of prostate cancer (PCa) diagnosis and current mental health outcomes (anxiety and depression) among men in Atlantic Canada. It will also examine the individual contribution of modifiable lifestyle factors (diet, physical activity, sleep, alcohol and smoking) on this association. Using the Atlantic PATH database, logistic regression analyses and pooled sensitivity analyses evaluated these associations. Our target population had 2.39 (95% CI: 1.03, 5.57) higher odds of screening positive for current depressive symptoms. This association was no longer significant when physical activity or smoking were included. Diet, physical activity, sleep or smoking, but not PCa status, resulted in significant associations with screening positive for current anxiety symptoms. This study can inform and support the development of multidisciplinary patient education and empowerment programs to help improve the quality of life of men living with PCa.

List of Abbreviations Used

PCa	Prostate Cancer
PATH	Partnership for Tomorrow's Health
PEI	Prince Edward Island
RP	Radical Prostatectomy
ADT	Androgen Deprivation Therapy
PSA	Prostate Specific Androgen
EBRT	External Beam Radiation Therapy
PA	Physical Activity
PHQ-9	Patient Health Questionnaire (Nine-Item)
CanPath	Canadian Partnership for Tomorrow's Health
IPAQ	International Physical Activity Questionnaire
GAD-7	Generalized Anxiety Disorder (Seven-Item)
WHO	World Health Organization
MET	Metabolic Equivalent Minutes
MI	Multiple Imputation
PC-PEP	Prostate Cancer Patient Empowerment Program

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Chapter 1 Introduction

Prostate cancer (PCa) is the most commonly diagnosed non-skin cancer among Canadian men with one in nine men expected to be diagnosed in their lifetime (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2019). The prevalence of PCa in Canada is projected to increase due to the burgeoning elderly population and high survival rates. The incidence of PCa sharply increases with age, and 60% of cases are diagnosed in men 65 years or older (American Cancer Society, 2019). By 2036, the number of individuals 65 years and older in Canada is expected to double and will account for 25% of the total population (Government of Canada, 2015).

Survival rates for men with localized PCa are high, with approximately 99% surviving the first five years after diagnosis and 98% surviving ten years after diagnosis (American Cancer Society, 2018). Furthermore, survival rates remain high when men with all types and stages of PCa are included in the analyses, with 70% of men surviving ten years after diagnosis (Watts et al., 2014).

One implication of increased prevalence as men age with PCa is the substantial impact of decreased quality of life for men with a lifetime history of a PCa diagnosis as well as for their family members (Ilie, 2018). Studies also show that poor mental health outcomes can negatively affect PCa oncological outcomes (Fervaha et al., 2019). The increased prevalence of PCa is also associated with an increase economic burden due to indirect and direct costs on the healthcare system (Canadian Mental Health Association, 2019; Trautmann et al., 2016).

Recent literature provides evidence that men with a lifetime history of a PCa diagnosis are at a higher risk for depression and anxiety compared to the general population

(Fervaha et al., 2019; Ilie et al., 2020b; Watts et al., 2014). In a recent study, Fervaha et al. (2019) found that approximately one in six men with PCa will be diagnosed with clinically significant depression during their PCa journey (Fervaha et al., 2019). A meta-analysis with a pooled sample size of 4,494 men with a lifetime history of a PCa diagnosis estimated that the prevalence of anxiety and depression are highest in men who have yet to receive treatment (27.4% and 17.3%, respectively) and lowest in men who are currently receiving treatment (15.9% and 14.7%, respectively) (Watts et al., 2014). In comparison, the lifetime prevalence of anxiety and depression is significantly lower among the general Canadian adult population and is estimated as 6% and 8%, respectively (Watts et al., 2015). The PCa population is also at a higher risk of suicidal ideation and death by suicide compared to the general population (Fervaha et al., 2019; Llorente et al., 2005; Matthew & Elterman, 2014). For instance, Llorente et al. (2005) found that the risk of suicide in the PCa population is 4.24 times higher than the general population (Llorente et al., 2005). These early findings show that screening for psychological distress experienced among men with a lifetime history of a PCa diagnosis can be overlooked and underprioritized.

Increased survivorship time due to improved active treatment options may result in a variety of life altering side effects, which include sexual, urinary and bowel dysfunction, as well as psychological distress (American Cancer Society, 2018). The side effects may differ depending on the selected treatment modality; therefore, treatment modalities may have a differential influence on mental health and should be further investigated (Hanly et al., 2014; Hervouet et al., 2005; Ravi et al., 2014).

There is currently limited research on the association between modifiable lifestyle factors and mental health outcomes among men with a lifetime history of a PCa diagnosis.

Modifiable lifestyle factors are behaviours and exposures that can positively or negatively influence an individual's risk of developing chronic illnesses, including PCa and poor mental health (Blanchard et al., 2004; Poirier et al., 2019). Therefore, modifiable lifestyle factors may contribute to the complex relationship between a lifetime history of a PCa diagnosis and current mental health (Poirier et al., 2019). Among individuals with cancer, research has typically focused on the association between modifiable lifestyle factors and risk of cancer and has yet to examine the association between these lifestyle factors and mental health outcomes, particularly in men with a history of a PCa diagnosis (Poirier et al., 2019). In addition, other studies have focused on examining the association between men with a lifetime history of a PCa diagnosis and the association with mental health by identifying non-modifiable variables, such as sociodemographic factors (e.g., socioeconomic status, age, marital status), disease stage, and disease-related decisions (e.g., selection of treatment modality, confidence in selection of treatment modality) (Aarts et al., 2010; Linden et al., 2012; Steginga et al., 2004; Vodermaier et al., 2011).

The aim of this study is to expand the current literature by not only examining the association between a lifetime history of a PCa diagnosis and mental health outcomes in Atlantic Canada, but also by including various modifiable lifestyle factors in the evaluation of this association. In addition, we will also examine the association between PCa treatment modality and current mental health outcomes among participants who report a lifetime history of a PCa diagnosis. These relationships will be examined using cross-sectional data from the first cycle of the Atlantic Partnership for Tomorrow's Health (PATH) study, which includes 179 men with a lifetime history of a PCa diagnosis matched (1:3) by

propensity scores using age, marital status, income, province, education level, and ethnicity to men without a lifetime history of a PCa diagnosis.

Chapter 2 Background & Literature Review

This literature review will first introduce the current prevalence of PCa in Atlantic Canada and justify the rationale of the focus of this research. Secondly, an overview of the current studies examining mental health and PCa in Atlantic Canada will be discussed. The literature review will then present evidence on the association of PCa treatment modalities and mental health. Finally, an in-depth review of the association between modifiable lifestyle factors and mental health in men with a lifetime history of a PCa diagnosis will be examined.

2.1 PCa in Atlantic Canada

The prevalence of a lifetime history of a PCa diagnosis is 3.9% among men aged 49 to 69 years old in Atlantic PATH data set (Ilie et al., 2020b). This finding is similar to a recently reported prevalence (4%) of PCa across Canada among the Canadian Longitudinal Study on Aging data set (Moodie et al., 2019). As previously discussed, the prevalence of PCa in Canada is expected to increase due to the burgeoning older population and the increased number of years men live post-diagnosis. This burden will disproportionally affect Atlantic Canada, as these provinces have the highest proportion of Canadian men and women aged 65 or older and have the overall highest incidence of cancer in Canada (Government of Canada, 2015). The incidence rates of PCa in Atlantic Canada range from a low of 146.3 per 100,000 (New Brunswick) to a high of 169.8 per 100,000 [Prince Edward Island (PEI)] (Government of Canada, 2019). Therefore, the investigation of mental health among men with a lifetime history of a PCa diagnosis should be a health priority in Atlantic Canada.

2.2 Mental Health & PCa

It has been well established in the literature that men with a lifetime history of a PCa diagnosis are predisposed to developing depression and anxiety compared to the general population (Fervaha et al., 2019; Ilie, 2018; Ilie et al., 2020b; Sharp et al., 2016; Watts et al., 2014). The main findings of the recent meta-analysis by Watts et al. (2014) reported an 18% prevalence for both depression and anxiety in post-treatment PCa patients (Watts et al., 2014). These findings were corroborated by Sharp et al. (2016) who reported a 17% and a 16% prevalence for depression and anxiety respectively, in PCa survivors (Sharp et al., 2016). These findings have only recently been examined in the Maritimes and Atlantic Canada.

The preliminary results of the "Prostate Cancer Patient Reported Outcomes Maritimes Survey Preliminary Results" mirror the levels of depression and anxiety reported by Watts et al. (2014) in a Canadian population (Ilie, 2018). For instance, 13.7% and 17.1%, of Nova Scotian PCa survivors (n=108) in the 47-65 age category reported depression and anxiety distress, respectively; 12.5% of New Brunswick PCa survivors (n=32) reported depression and anxiety distress. In this study, there was no available data for PEI, and it did not include Newfoundland and Labrador (Ilie, 2018). In a recent report, Ilie et al. (2020a) found that 19.5% of men with a lifetime history of a PCa diagnosis in the Maritimes scored positive for poor mental health (Ilie et al., 2020a). These preliminary findings provide evidence of distress among PCa survivors in the Maritimes and highlights the need for further research that includes all of Atlantic Canada.

In a similar study utilizing the Atlantic PATH dataset, Ilie et al. (2020b) compared participants with a lifetime history of a PCa diagnosis to participants with no lifetime

history of a cancer diagnosis; and to participants with a lifetime history of other cancer diagnosis but no lifetime history of a PCa diagnosis (Ilie et al., 2020b). They found that men with a lifetime history of a PCa diagnosis in Atlantic Canada had a 2.54 and 2.05 statistically significantly higher odds of screening positive for current anxiety and depressive symptoms (Ilie et al., 2020b).

Finally, the distress among the PCa population has been shown to be long-term. Evidence presented at the European Association of Urology in March 2019 showed that men with a lifetime history of a PCa diagnosis who were treated with a radical prostatectomy (RP) and androgen deprivation therapy (ADT) were at an increased risk for depression up to 18 years after surgery (European Association of Urology, 2019). Here we propose to evaluate the association between the presence or absence of a lifetime history of a PCa diagnosis and current mental health outcomes in an Atlantic Canadian matched sample of men.

2.3 PCa Treatment Modalities

There are multiple therapeutic treatment modalities available for men with a PCa diagnosis. Treatment modalities are guided by disease stage, prostate specific androgen (PSA) tests, biopsies, and patient values (Heidenreich et al., 2014). The treatment modalities available for men with a PCa diagnosis include radiation therapy (brachytherapy or external beam radiation therapy [EBRT]), surgery (RP), hormonal therapy (ADT), active surveillance, chemotherapy or any combination of the treatment modalities mentioned above (Keyes et al., 2013).

2.4 Mental Health & Treatment Modality

The side-effects as a result of treatment for PCa can also result in increased anxiety and depressive symptoms. It should be noted that each treatment modality can cause different side effects and therefore the type of treatment modality may result in different mental health outcomes, and the literature is inconsistent in its findings. Hervouet et al. (2005) compared anxiety and depression across three treatment modalities: radiation therapy (EBRT and brachytherapy), and RP (Hervouet et al., 2005). This study found that men with a PCa diagnosis who received EBRT had a higher score of depression symptoms compared to men who received brachytherapy and RP, and had a higher score of anxiety symptoms compared to men who received brachytherapy (Hervouet et al., 2005). Similar to this study, Ilie et al. (2020a) compared psychological distress across three treatment modalities (radiation therapy, RP and hormonal therapy), and found that men with a PCa diagnosis who were treated with radiation therapy had 7.15 higher odds of screening positive for psychological distress compared to those treated without radiation therapy (e.g., RP and hormonal therapy) (Ilie et al., 2020a). Ravi et al. (2014) compared anxiety and depression across three treatment modalities, including RP, radiation therapy and active surveillance, and found that men with a PCa diagnosis who were treated with RP or radiation therapy had a lower risk of developing anxiety and depression compared to those undergoing active surveillance (Ravi et al., 2014). In contrast, Donovan et al. (2016) found no difference in anxiety and depressive symptoms across the same treatment modalities (Donovan et al., 2016). Furthermore, Fervaha et al. (2019) stated that there is no difference between the choice of a definitive treatment modality (RP or radiation therapy) compared to active surveillance on depressive symptoms (Fervaha et al., 2019). However, this study

reports that individuals who select ADT may have worse depressive symptoms compared to other available treatment modalities (Fervaha et al., 2019).

2.5 Mental Health & Modifiable Lifestyle Factors

Modifiable lifestyle factors such as diet, physical activity (PA), sleep, alcohol consumption, and smoking can contribute to an individual's poor mental health. Studies show that men with a PCa diagnosis changed various lifestyle factors to accommodate different adverse post-treatment side effects that are negatively affecting their quality of life (Blanchard et al., 2004; Hanly et al., 2014). For example, some men reduced alcohol intake to improve urinary incontinence and psychological health, while others used alcohol as a negative coping mechanism despite its negative effect on urinary incontinence and emotional struggles (Hanly et al., 2014). It is important to identify modifiable lifestyle factors that can improve mental health and further research is required to better understand what factors contribute to the complex relationship between a lifetime history of a PCa diagnosis and current mental health. This study will examine five modifiable lifestyle factors (diet, PA, sleep, alcohol, and smoking) and their contribution on the association between men with or without a lifetime history of a PCa diagnosis and current mental health.

2.5.1 Diet

In recent years, the association between fruit and vegetable intake and mental health has received growing attention. Existing literature suggests that there is a positive relationship between high intake of fruit and vegetables and improved mental health (Liu et al., 2016; Lopresti et al., 2013; McMartin et al., 2013). For instance, a recent meta-

analysis with a large population size found that high intake of fruit and vegetables was significantly associated with a decreased risk of depression in the general population (Liu et al., 2016). However, this study is limited and does not include anxiety as an indicator for mental health. Nevertheless, a study using the Canadian Community Health Survey found that in the general population (aged 12 years and older), an increased frequency of fruit and vegetable consumption was associated with lower odds of self-reported depression and anxiety symptoms (McMartin et al., 2013).

Few studies have examined the association between fruit and vegetable intake and mental health in individuals with a cancer diagnosis and those that have are inconsistent with findings in the general population. For instance, in contrast to these findings in the general population, Blanchard et al. (2004) found that there was no association between health-related quality of life (including mental health) and fruit and vegetable intake in individuals with a breast, colorectal, or PCa diagnosis (Blanchard et al., 2004). Nonetheless, they found that survivors who met more than one lifestyle behavior recommendation (diet, PA and smoking) had significantly higher health-rated quality of life than those who only met one recommendation. Despite these benefits, studies show that only 26.2% of cancer survivors meet the daily recommended servings for fruits and vegetables (Blanchard et al., 2004).

To the best of our knowledge, no studies have looked at the association between fruit and vegetable intake and mental health in a PCa specific population. Therefore, given this potential association between a lifetime history of a PCa diagnosis and mental health, the current study will investigate the contribution of diet to mental health outcomes in our population of interest.

2.5.2 Physical Activity

During early survivorship, PA is an effective intervention for improving quality of life. In men with a lifetime history of a PCa diagnosis, studies have found that vigorous exercise, such as running, swimming, bicycling, and playing squash or tennis is significantly associated with improved PCa specific-survival (Kenfield et al., 2011). PA can also reduce many common side effects associated with PCa, such as nausea, fatigue, weight gain and erectile, urinary, and bowel dysfunction (Dahn et al., 2005; Ilie et al., 2019; Menichetti et al., 2016; Vashistha et al., 2016).

In the general population, it has been hypothesized that PA is associated with improved mental well-being; however, current research has reported conflicting results. Few studies have examined the association between PA with both depression and anxiety, but Harvey et al. (2017) found that regular PA was only protective against depression and not anxiety (Harvey et al., 2017). However, research on the association between PA and depression has been more thoroughly examined and two meta-analyses found that PA is an effective intervention to improve mild and moderate depression (Cooney et al., 2013; Kvam et al., 2016). In addition, a more recent cross-sectional study (n=1.2 million participants) found that individuals who regularly participated in PA had 1.5 fewer days of poor self-reported mental health per month compared to individuals who did not engage in PA (Chekroud et al., 2018).

These findings are also reflected in studies examining individuals with a cancer diagnosis and more specifically, studies that focus on men with a lifetime history of a PCa diagnosis. Research among individuals with a cancer diagnosis has shown that moderate to intense PA was associated with decreased anxiety and depressive symptoms, and 150

minutes per week or more of PA was significantly associated with higher health-related quality of life and mental well-being (Blanchard et al., 2004; Bock et al., 2017; Campbell et al., 2019; Ilie et al., 2019). In contrast, a meta-analysis by Vashistha et al. (2016) found that pooled data from 13 randomized control trials did not reveal a significant improvement in depression or anxiety among men with a lifetime history of a PCa diagnosis who participated in PA interventions (Vashistha et al., 2016).

It is difficult to determine how many individuals with a lifetime history of a cancer diagnosis meet the recommended PA guidelines due to an overestimation of self-reported activity levels; however, it is estimated that between 29.6%-70.0% individuals with a lifetime history of a cancer diagnosis meet the PA recommendations (Blanchard et al., 2004; Blanchard et al., 2008). In a more recent review, Schmitz et al. (2019) state that studies indicate that 30.0%-47.0% of individuals with a lifetime history of a cancer diagnosis engage in the recommended PA guidelines (Schmitz et al., 2019). Therefore, as PA has an important role throughout the entire cancer journey (e.g., improvement in survival and physical function) and can potentially improve aspects of mental health, it is an important variable to consider when examining lifestyle factors among men with a lifetime history of a PCa diagnosis.

2.5.3 Sleep

Sleep problems are characterized by having either a poor quality or decreased quantity of sleep (American Psychiatric Association, 2013). Disruptions in sleep can cause a magnitude of health issues that include both physical and mental health. For example, existing literature has established that there is a significant association between decreased sleep duration and increased mortality in the general population (Cappuccio et al., 2010).

This association has only recently been observed in individuals with a lifetime history of a cancer diagnosis, with an association between decreased sleep duration and decreased survivorship (Collins et al., 2017). In addition, this study also found that more than half the of the individuals with a cancer diagnosis who reported clinically significant levels of depression had shorter sleep duration ($p=0.02$). Sleep problems are known to have detrimental effects on mental health by increased risk of developing psychiatric disorders, decreased cognitive thinking, experiencing a lack of daily accomplishments, and a lack of enjoyment of relationships (Hanisch et al., 2011). Sleep duration is also used as an indication of depression in diagnostic screening tools, such as the Patient Health Questionnaire (PHQ-9) and the Kessler Psychological Distress Scale (Andrews & Slade, 2001; Kroenke et al., 2001).

Disruptions in sleep can have negative effects on mental health and studies have found that sleep problems are very common in men with a lifetime history of a PCa diagnosis (Dirksen et al., 2009; Maguire et al., 2019). It has been shown that ongoing adverse treatment side effects, such as nocturia, hot flashes, night sweats, and urinary dysfunction are significantly associated with the development of sleep problems, and that these sleep problems are associated with a significant increase in depressive symptoms (Dirksen et al., 2009; Maguire et al., 2019). Maguire et al. (2019) also found that sleep problems due to adverse PCa treatment side effects are associated with increased symptoms of anxiety. Sleep is important to mental health and can be disrupted by the ramifications of a PCa diagnosis. It is unclear whether long term sleep disturbances may continue to affect mental health outcomes in this population. Therefore, to expand our understanding of the

current literature on this association, its contribution to the association between a lifetime history of a PCa diagnosis and current mental health will be examined.

2.5.4 Substance Use

The literature typically defines substance use as the use of drugs or alcohol, and includes substances such as cigarettes, illegal drugs, prescription drugs, inhalants and solvents (American Psychiatric Association, 2013). For the purpose of this thesis, substance use will be defined as alcohol consumption and cigarette smoking. The relationship between poor mental health symptoms and substance use is complex, and it can be difficult to determine the causal relationship between the two. For instance, both poor mental health symptoms and substance use can independently develop due to common risk factors, such as difficulties with family or friends, problems in the community, and genetic predisposition (Canadian Centre on Substance Abuse, 2013; Swendsen & Merikangas, 2000). Subsequently, when given a PCa diagnosis, men may engage in increased alcohol consumption in order to cope with their diagnosis (Hanly et al., 2014).

In the general population, a considerable amount of evidence has found that both smoking and alcohol consumption are associated with many comorbidities, such as depression and anxiety. For instance, Stranges et al. (2014) found that individuals who heavily smoked (>20 cigarettes/day) had a 1.98 statistically significantly higher odds of screening for low mental health compared to individuals who never smoked (Stranges et al., 2014). A recent meta-analysis, found that smoking cessation is associated with reduced symptoms of depression and anxiety and improved positive mood and quality of life compared to individuals who continue to smoke (Taylor et al., 2014). Additionally, studies found that individuals who regularly consumed a moderate amount of alcohol are

associated with better mental health outcomes compared to non-drinkers and heavy drinkers (Awaworyi Churchill & Farrell, 2017; Stranges et al., 2014).

Few studies have examined this association in individuals with a history of a cancer diagnosis, particularly among men with a lifetime history of a PCa diagnosis. Bock et al. (2017) found that men who had low alcohol consumption and/or were non-smokers pre-surgery were less likely to be associated with a depressed mood compared to individuals who had a high alcohol intake and/or were smokers (Bock et al., 2017). Additionally, high alcohol consumption was associated with poor mental health after surgery (Bock et al., 2017). As substance use is a widely recognized risk factor for poor mental health, smoking and alcohol consumption will be included as a modifiable lifestyle factor in the examination of the association between a lifetime history of a PCa diagnosis and current mental health.

2.5.5 Conclusion

In summary, the literature review supports that diet, PA, sleep, alcohol, and smoking are important modifiable lifestyle factors to be considered as they are associated with mental health. The literature review further supports that these modifiable lifestyle factors require more investigation among men with a lifetime history of a PCa diagnosis.

Chapter 3 Objectives

The goal of this research is to examine the association between a lifetime history of a PCa diagnosis on current mental health outcomes in a matched sample of men who participated in the Atlantic PATH study. To meet this goal, this research will focus on the following three research objectives:

1. The primary objective of this study is to examine the association between the presence or absence of a lifetime history of a PCa diagnosis and current mental health (anxiety and depression) in a propensity score matched sample of individuals who participated in the Atlantic PATH survey.
2. The second objective is to investigate the individual contribution of diet, PA, sleep, and substance use (alcohol and smoking) on the association between a lifetime history of a PCa diagnosis and mental health outcomes (anxiety and depression).
3. The third objective is to examine the association between PCa treatment modality and current mental health outcomes among participants who reported a lifetime history of a PCa diagnosis.

Chapter 4 Methodology

4.1 Sample

Data for this study was derived from the first cycle (2009-2015) of the Atlantic PATH study, a multicenter prospective cohort study of 31,173 residents aged 35-69 living in one of four Atlantic provinces (Sweeney et al., 2017). For the purpose of this study, men with a lifetime history of a PCa diagnosis (n=179) were matched by propensity scores (1:3) to men without a lifetime history of a PCa diagnosis to be included in the analyses. Propensity scores estimate the probability that an individual with certain characteristics will be exposed to a treatment or condition by adjusting for the impact of observed covariates (Rosenbaum & Rubin, 1984). The main objective of using propensity scores is to reduce selection bias when matching case to controls from the larger sample size and to ensure that the distribution of observed baseline covariates is similar between the case and control groups. For the purpose of this study propensity scores were matched on age, marital status, income, province, education level, and ethnicity.

4.2 Design

Atlantic PATH is part of the Canadian Partnership for Tomorrow's Health (CanPath, formerly the Canadian Partnership for Tomorrow Project), which has recruited more than 300,000 participants across five cohorts in eight provinces including Atlantic PATH, Alberta's Tomorrow Project, the Ontario Health Study, British Columbia Generations Project, and Quebec's CARTaGENE (Dummer et al., 2018; Sweeney et al., 2017). The Atlantic PATH survey data is very well suited for the examination of the proposed objectives as its main objective is to examine the complex interplay of genetic, behavioural and environmental factors that lead to the development of cancer and other

chronic diseases.

Participants were recruited through a range of outreach activities, such as invitations from the Provincial Health Insurance provider (Nova Scotia only), advertisement, media coverage, community and workplace events, and incentive programs (Airmiles) (Sweeney et al., 2017). Participants provided data in person at assessment centres, via online questionnaires or by mail. Participants also provided physical measurements (height, weight, waist and hip circumference, body composition and blood pressure) and biological samples (blood, urine, saliva and toenails) (Sweeney et al., 2017).

Two questionnaires were administered, one was administered to the entire Canadian sample (core) and the other was administered only to the Atlantic PATH participants (supplementary). The core questionnaire asked participants about their health and well-being, including demographic information, personal health history, family history of disease, provincial residence, household income, health behaviours, and PA [short form of the International Physical Activity Questionnaire (IPAQ)]. The supplementary questionnaire assessed diet, depression, anxiety, additional questions on PA (long form of the IPAQ), and occupational and environmental exposures specific to Atlantic Canada. Detailed descriptions of survey questions, physical measures, and biological measures are discussed in Sweeney et al. (2017). Data for the proposed study was derived from both the core and supplementary questionnaires.

All Atlantic PATH participants in the 2009-2015 cycle completed the core questionnaire, and 68% of the Atlantic PATH participants completed the supplementary questionnaire specific to Atlantic Canada. Importantly, all participants have given permission for their data and samples to be used for research purposes (with approval from

a Research Ethics Board and the Atlantic PATH Data Access Committee).

4.3 Ethics Approval and Data Access

The Dalhousie University Health Sciences Research Ethics Board granted the ethics approval for this study in August 2018 (File # 4462). The Atlantic PATH data access agreement was granted in October 2018.

4.4 Exposure Variables

The exposure variable for addressing the first two research objectives was the presence or absence of a lifetime history of a PCa diagnosis. To address the third objective only participants with a lifetime history of a PCa diagnosis were selected and the association between treatment modality and mental health outcomes were assessed.

Lifetime history of a PCa diagnosis: Participants were asked, "[h]as a doctor ever told you that you had cancer or a malignancy of any kind?" and then asked to select a cancer type from a list of common cancers and indicate the age of diagnosis. A lifetime history of a PCa diagnosis was coded (0) (reference category) for the absence of a PCa diagnosis and (1) for the presence of a PCa diagnosis.

Treatment Modality: Participants were asked to further indicate the type of active treatment they received. Responses were coded (0) for surgery (reference), (1) for radiation therapy, and (2) for two or more forms of active treatment.

4.5 Outcome Variables

Anxiety: Anxiety was assessed using the Generalized Anxiety Disorder (GAD-7) self-report questionnaire that allows for the rapid detection and severity of generalized anxiety disorder (Spitzer et al., 2006). Surveyed participants were asked if they were bothered by

anxiety related problems over the past two weeks prior to responding to the survey by answering seven questions on a 4-point scale (not at all, several days, more than half the days, nearly every day). The total scores ranged from 0 to 21. The GAD-7 has a sensitivity of 90% and a specificity of 79% for detecting generalized anxiety disorder compared with a structured psychiatric interview (Spitzer et al., 2006). The GAD-7 has been used extensively in general population health studies, and is considered to have excellent internal consistency (Cronbach=0.92) and good test-retest reliability (r=0.83) (Spitzer et al., 2006).

The Atlantic PATH survey questions on anxiety have five possible response options: not at all, several days, more than half the days, nearly every day, or skip this question. Scores of 0-4, 5-9, 10-14, and 15-21 represent positive screening for minimal, mild, moderate, and severe anxiety, respectively (Löwe et al., 2008). Screening positive for mild, moderate, or severe anxiety (scores ≥ 5) was coded as (1) for the presence of current anxiety symptoms; minimal anxiety (scores <5) was coded as (0) for the absence of current anxiety symptoms. The dichotomization of mental health variables are common in the literature (Ialomiteanu et al., 2018; Kroenke et al., 2007).

Depression: Depression was assessed using the PHQ-9 which is a 9-item depression module from the full PHQ for mental health disorders (Kroenke et al., 2001). Surveyed participants were asked if they were bothered by depression related problems over the past two weeks prior to responding to the survey by answering nine items on a 4-point scale. The total scores ranged from 0 to 27. The PHQ-9 has a sensitivity of 95% and a specificity of 84% for detecting depression compared with a structured psychiatric interview (Kroenke et al., 2001). The PHQ-9 has also been cited as having excellent construct validity and

reliability as a measure of depression (Kroenke et al., 2016). Studies have found that there is a strong association between increasing PHQ-9 depression score and worsening function status (mental, social, role, general, pain, and physical) (Kroenke et al., 2001). Additionally, internal consistency of the PHQ-9 is excellent (Cronbach=0.85) and test-retest reliability is also excellent (r=0.89) (Bian et al., 2011; Kroenke et al., 2016).

The Atlantic PATH survey questions on depression have five possible response options: not at all, several days, more than half the days, nearly every day, or skip this question. Scores of 0-4, 5-9, 10-14, 15-19, and 20-27 represent positive screening for minimal, mild, moderate, moderately severe, and severe depression, respectively. Screening positive for mild, moderate, moderately severe or severe depression (scores ≥5) was coded as (1) for the presence of current depressive symptoms; minimal depression (scores <5) was coded as (0) for the absence of current depressive symptoms.

4.6 Modifiable Lifestyle Factors

To address research objective two, there are five modifiable lifestyle factors of interest, which include diet, PA, sleep, and substance use (alcohol and smoking).

Diet: All participants were asked about their food intake in a typical day and asked, "[h]ow many total servings of vegetables and fruit do you eat a day?" Atlantic PATH defines one serving as ½ a cup or 125mL. For the fruit and vegetable categorization, sufficient intake (≥5 servings/day) and insufficient intake (<5 servings/day), as recommend by the World Health Organization (WHO), were coded 0 and 1, respectively. The WHO recommends having a minimum of 400g or 2 cups of fruits and vegetable per day for the prevention of chronic diseases in adults (Ashfield-Watt et al., 2004).

Physical Activity: PA indices were derived from both the short and long form of the IPAQ, which asks participants how often (days and time) they participated in light, moderate, and vigorous activity during the week (Craig et al., 2003; Keats et al., 2017b). IPAQ is a valid and widely used measure of PA among individuals with a cancer diagnosis and the limitations of self-reported health behaviours are well established (Ruiz-Casado et al., 2016). Test- retest-reliability is excellent with scores ranging from (0.65 to 0.88) (Craig et al., 2003). The construct validity, a limitation of IPAQ, is moderate at best (Cronbach=0.70**)**, as studies have found that compared to the use of an accelerometer, the IPAQ overestimates PA levels (across all intensities) and underestimates physical inactivity level (Mannocci, A. et al., 2010; Mirzaei et al., 2016).

PA was assessed using both the long and short form of the IPAQ. In accordance with the IPAQ scoring protocol, total PA was calculated using the metabolic equivalent minutes (MET) per week for each participant. The MET scores were ranked intro tertiles and levels of PA were classified and coded as low (2), medium (1), and high (0) based on MET scores for this specific sample.

Sleep: Participants were asked, "[o]n average how many hours per day do you usually sleep, including naps?" and asked to write the hours and minutes. Based on the time they spent sleeping the participants were categorized based on the National Sleep Foundation's updated "*Sleep Duration Recommendations: Final Report"* (Hirshkowitz et al., 2015). The recommended duration of sleep varies by age. Men aged 24-64 years old are recommended to sleep between seven and nine hours per day, and men aged 65 or older are recommended to sleep between seven and eight hours per day (Hirshkowitz et al., 2015). Participants

were coded as meeting the recommended guidelines (0), or not meeting the recommended sleep guidelines (1) based on their age group (Hirshkowitz et al., 2015).

Alcohol Use: To examine drinking behaviour participants were asked, "[o]n average, over the last year, how often did you drink alcohol?" Participants were asked to select from a 9-item list and were classified as (0) abstainers (reference), (1) occasional drinker (>0 to <2–3 times/month), (2) regular drinker (≥1 time/week to ≤2–3times/week), and (3) habitual drinker (≥4–5times/ week) (Yu et al., 2018).

Smoking Use: For cigarette use, participants who reported never having smoked 100 cigarettes in their life were defined as never smoked (0), participants who reported having smoked at least 100 cigarettes in their lifetime, but did not smoke any within the previous 30 days were defined as former smokers (1), and participants who reported smoking at least 100 cigarettes in their lifetime and smoked during the past 30 days were defined as current smokers (2) (Keats et al., 2017b).

4.7 Covariates

The literature review identified nine covariates as potential confounders to be included in the analysis (American Psychiatric Association, 2019; Sareen et al., 2011; Spiker, 2014; World Health Organization, 2017; Zajacova & Lawrence, 2018). These covariates were selected as they were associated with mental health and/or PCa diagnosis. For objectives one and two the following eight covariates were employed: age, ethnicity (white and non-white, as all categories other than white were less than 5% which is representative of the Atlantic Provinces); education (high school or less, college or trade level, and university degree or higher); income in the past calendar year before taxes (≤$49,999, $50,000 – 99,999, and ≥$100,000); marital status (married or living with a

partner, and not-married); region (New Brunswick, Newfoundland and Labrador, Nova Scotia, and PEI); working status (full-time employment >30 hours/week, part-time employment ≤30 hours/week, unemployed, sick-leave and retired), and multimorbidity. For objective three all of the above covariates were included with the addition of survivorship time. The coding of multimorbidity and survivorship time are described below.

Multimorbidity: Multimorbidity has been shown to be associated with poor mental health; therefore, the number of chronic illnesses reported by a participant was included in the model as a covariate (Fortin et al., 2004; Gould et al., 2016). A recent study reported a high prevalence of multimorbidity in Atlantic Canada with 34.3% of male participants reporting at least two chronic conditions (Keats et al., 2017a). Participants were asked to select one or more chronic diseases from a list of 18 possible conditions (asthma, chronic obstructive pulmonary disease, liver cirrhosis, chronic hepatitis, myocardial infarction, stroke, hypertension, type I and II diabetes, inflammatory bowel disease, psoriasis, eczema, multiple sclerosis, arthritis, systemic lupus erythematosus, osteoporosis, major depression, Crohn's disease, and ulcerative colitis), and were given the opportunity to describe any other long-term conditions they might have. Multimorbidity was defined as having two or more chronic diseases and was coded based on the participant's history of a PCa diagnosis. A participant with a presence of a lifetime history of a PCa diagnosis and no additional chronic diseases was coded as (0) for no multimorbidity and was coded as (1) if they have any other comorbidities in addition to a lifetime history of a PCa diagnosis. A participant with an absence of a lifetime history of a PCa diagnosis and ≤1 comorbidity was coded as (0) for no multimorbidity and was coded as (1) if they have two or more comorbidities.

Survivorship Time: After a cancer diagnosis, survivorship time has been shown to have a long-term effect on poor mental health. A meta-analysis of 43 studies showed that survivorship time after a cancer diagnosis is also associated with anxiety and depression (Mitchell et al., 2013). Survivorship time was defined as the time from cancer diagnosis to the time that the participant completed the Atlantic PATH questionnaire.

4.8 Statistical Analyses

All analyses, including the propensity scores matching previously described, were performed using SPSS version 25.0 software package. Logistic regression was used to examine the association between the presence or absence of a lifetime history of a PCa diagnosis and the separate evaluation of two mental health outcomes (depression and anxiety). To address objective two, several logistic regressions were used to investigate the additional contribution of diet, PA, sleep, and substance use (alcohol and smoking) on current mental health outcomes by the presence or absence of a lifetime history of a PCa diagnosis. These analyses were repeated while controlling for age, ethnicity, education, income, marital status, region, working status, and multimorbidity. Finally, to address objective three, unadjusted and adjusted (age, ethnicity, education, income, marital status, region, working status, multimorbidity, and survivorship time) logistic regressions evaluated the association between treatment modality and depression or anxiety among men with a lifetime history of a PCa diagnosis.

For objectives one and two, listwise deletion reduced the analytic sample for evaluating anxiety symptoms from 716 to 337 and depressive symptoms from 716 to 338. For objective three, listwise deletion reduced the sample for both anxiety and depressive

symptoms from 158 (total sample of PCa sample) to 56. Given that several variables far exceeded the 5.0% tolerable threshold of missing data, multiple imputation (MI) was performed as a sensitivity analysis to assess the comparability of the results as recommended by the literature (White et al., 2011). These variables included anxiety (45.1%), depression (44.8%), PA (22.6%), and income (8.1%). Using SPSS' automatic option, the statistical software determined what MI method should be used (monotone or fully conditional) based on the pattern of missing data. Fully conditional specification was selected, which is an iterative of the Markov Chain Monte Carlo method. We specified 20 iterations, as recommended by the literature (White et al., 2011). Results from the original dataset, using listwise deletion (n=337 and 338, for anxiety and depression), were compared to iterations from the pooled MI dataset (n=654) for objective one and two. Original dataset for objective three (n=56 for anxiety and depression) was compared to the MI pooled iteration dataset (n=126). For each analysis, pooled sensitivity analyses were used to determine how missing data affected the results by comparing the pooled MI results to the original propensity based matched data set (Carpenter et al., 2007).

Given the design of this study and the use of propensity scores, we recognize that this is clustered data. We conducted one analysis (objective one, depression) that included cluster variance estimators, and found that the results were comparable to those obtained from the original analyses (Appendix A, Table 8). Therefore, we elected to proceed with the original analyses rather than with the cluster variance estimator sample design analyses, as there is a large amount of missing data in the outcome variables of interest (anxiety and depression). Additionally, sensitivity analyses using the MI method ensured that the results from the original dataset were comparable to the pooled dataset.

Chapter 5 Results

A detailed description of the demographics of this sample are shown in Table 1. The average age of men who reported a lifetime history of a PCa diagnosis was 61.61 (±4.79). Among the men with a lifetime history of a PCa diagnosis, the majority were white (94.7%), married or living with a partner (87.7%), were working full time (42.9%) or were retired (42.4%).

The results of the logistic regression model predicting anxiety shows that a lifetime history of a PCa diagnosis was not statistically significantly associated with screening positive for current anxiety symptoms after adjusting for age, ethnicity, income, marital status, region, working status, and multimorbidity (Table 2). In comparison, men with a lifetime history of a PCa diagnosis had a 2.39 (95% CI: 1.03, 5.57) statistically significantly higher odds of screening positive for current depression symptoms compared to men without a lifetime history of a PCa diagnosis after adjusting for age, ethnicity, education, income, marital status, province, working status, and multimorbidity (Table 3). In the pooled MI models, a lifetime history of a PCa diagnosis was not significantly associated with screening positive for current anxiety or depressive symptoms (Tables 2 and 3, respectively).

Tables 4 and 5 show the results of the unadjusted and covariate-adjusted logistic regression models for a lifetime history of a PCa diagnosis and the individual contribution of modifiable lifestyle factors by anxiety and depression, respectively. A lifetime history of a PCa diagnosis became significantly associated with screening positive for current anxiety symptoms when diet (aOR = 2.95 CI: 1.00, 8.75), PA (aOR = 3.61 CI: 1.03, 12.69), sleep (aOR = 3.00 CI: 1.00, 8.94), or smoking (aOR = 3.04 CI: 1.04, 8.89) were included

in the models (Table 4). Therefore, diet, PA, sleep, and smoking significantly contributed to the association between a lifetime history of a PCa diagnosis and current anxiety symptoms. In the pooled MI dataset, a lifetime history of a PCa diagnosis was not significant for screening positive for current anxiety symptoms when any modifiable lifestyle factor (diet, PA, sleep, alcohol, and smoking) were included in the models (Table 4).

The association between a lifetime history of a PCa diagnosis and screening positive for depressive symptoms, was no longer significant when PA (aOR = 2.58 CI: 0.95, 6.99) or smoking (aOR = 2.25 CI: 0.95, 5.32) were included in the models (Table 5). As such, only PA and smoking significantly contributed to the association between a lifetime history of a PCa diagnosis and current depressive symptoms. When examining this association with the pooled MI dataset, a lifetime history of a PCa diagnosis was not significant when any of the modifiable lifestyle factors (diet, PA, sleep, alcohol, and smoking) were included in the models (Table 5).

Treatment modality was not significantly associated with screening positive for current anxiety or depressive symptoms among individuals with a lifetime history of a PCa diagnosis. This association is comparable with the results using the pooled MI dataset (Table 6 & 7).

Table 1 Frequency of demographic characteristics among men with and without a lifetime history of a PCa diagnosis residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015).

Variables	Lifetime History of PCa Diagnosis		No Lifetime History of PCa Diagnosis	
	n = 179		*n* = 537	
	n	%	*n*	%
Age, mean (SD)	61.61 (4.79)		56.16 (9.57)	
Ethnicity				
Non-white	9	5.3	36	7.0
White	162	94.7	475	93.0
Education				
High School or less	38	21.5	108	20.2
College or trade level	68	38.4	204	38.1
University level or higher	71	40.1	223	41.7
Income				
CAD ≤$49,999	40	23.8	99	20.2
CAD $50,000 – 99,999	71	42.3	207	42.2
CAD ≥$100,000	57	33.9	184	37.6
Marital Status				
Non-married	22	12.3	70	13.2
Married or living with a partner	157	87.7	461	86.8

	n	%	*n*	%
Region				
Nova Scotia	36	20.1	212*	39.5
New Brunswick	88	49.2	178	33.1
Newfoundland and Labrador	45	25.1	120	22.3
Prince Edward Island	10	5.6	27	5.0
Working Status				
Full time	76	42.9	302	57.2
Part time	16	9.0	28	5.3
Unemployed/Sick	10	5.6	30	5.7
Retired	75	42.4	168	31.8

Notes:
SD Standard Deviation
* Two participants who did not indicate province of residence were combined with Nova Scotia participants, as the majority of participants who completed the survey reside in Nova Scotia.

Table 2 Logistic Regression analysis predicting anxiety symptoms by a lifetime history of a PCa diagnosis among men residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, and multimorbidity.

		No anxiety vs. anxiety symptoms	
		n=337[a] OR (95% CI)	n=654[b] OR (95% CI)
Model		**$X^2(15)=36.14$****	-
Lifetime History of PCa Diagnosis		*$X^2(1)=3.45$**	-
Yes		2.22 (1.08, 4.53)*	1.48 (0.80, 2.73)
	aOR	2.75 (0.95, 8.02)	1.47 (0.63, 3.37)
No		1.0 Reference	1.0 Reference
Age		*$X^2(1)=3.30$*	-
		0.95 (0.90, 1.00)	0.97 (0.93, 1.01)
Ethnicity		*$X^2(1)=0.25$*	-
Non-White		0.57 (0.06, 5.24)	0.61 (0.09, 3.92)
White		1.0 Reference	1.0 Reference
Education		*$X^2(2)=0.36$*	-
High school or less		0.80 (0.27, 2.37)	0.89 (0.37, 2.13)
College or trade level		0.76 (0.30, 1.93)	0.90 (0.42, 1.94)
University level or higher		1.0 Reference	1.0 Reference
Income		*$X^2(2)=9.16$***	-
CAD ≤$49,999		3.92 (1.30, 11.79)**	2.80 (0.96, 8.13)
CAD $50,000 – 99,999		0.82 (0.31, 2.22)	0.80 (0.29, 2.19)
CAD ≥$100,000		1.0 Reference	1.0 Reference
Marital Status		*$X^2(1)=0.04$*	-
Non-Married		0.89 (0.28, 2.79)	0.97 (0.38, 2.50)
Married or living with a partner		1.0 Reference	1.0 Reference
Region		*$X^2(3)=1.49$*	-
New Brunswick		1.26 (0.49, 3.20)	1.58 (0.69, 3.60)
Newfoundland and Labrador		1.82 (0.64, 5.15)	1.48 (0.58, 3.78)
Prince Edward Island		2.10 (0.21, 20.83)	1.26 (0.20, 8.08)
Nova Scotia		1.0 Reference	1.0 Reference
Working Status		*$X^2(3)=10.42$**	-
Part time		2.12 (0.51, 8.92)	1.69 (0.50, 5.75)
Unemployed/Sick		4.25 (1.09, 16.56)*	2.56 (0.74, 8.83)
Retired		0.29 (0.07, 1.23)	0.74 (0.28, 1.92)
Full time		1.0 Reference	1.0 Reference

		OR (95% CI)	OR (95% CI)
Multimorbidity		*$X^2(1)=0.01$*	-
	Yes	0.97 (0.39, 2.38)	1.05 (0.49, 2.23)
	No	1.0 Reference	1.0 Reference

Notes:
[a]Original data
[b]Multiple Imputation
X^2 Wald Chi-square value
* significant at $p<0.05$
** significant at $p<0.01$

Table 3 Logistic Regression analysis predicting depression symptoms by a lifetime history of a PCa diagnosis among men residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, and multimorbidity.

		No depression vs. depressive symptoms	
		n=338[a]	n=654[b]
		OR (95% CI)	OR (95% CI)
Model		**$X^2(15)=40.20$*** **	**-**
Lifetime History of PCa Diagnosis		*$X^2(1)=4.07$**	-
Yes		2.05 (1.14, 3.69)**	1.37 (0.86, 2.18)
	aOR	2.39 (1.03, 5.57)*	1.31 (0.74, 2.31)
No		1.0 Reference	1.0 Reference
Age		*$X^2(1)=2.19$*	-
		0.97 (0.93, 1.01)	0.98 (0.95, 1.01)
Ethnicity		*$X^2(1)=0.16$*	-
Non-White		0.72 (0.15, 3.57)	0.65 (0.21, 2.01)
White		1.0 Reference	1.0 Reference
Education		*$X^2(2)=1.13$*	-
High school or less		0.84 (0.35, 2.04)	0.83 (0.40, 1.73)
College or trade level		1.29 (0.64, 2.61)	1.28 (0.67, 2.47)
University level or higher		1.0 Reference	1.0 Reference
Income		*$X^2(2)=5.77$**	-
CAD ≤$49,999		2.93 (1.17, 7.33)	2.34 (0.94, 5.79)
CAD $50,000 – 99,999		1.25 (0.60, 2.58)*	1.08 (0.54, 2.14)
CAD ≥$100,000		1.0 Reference	1.0 Reference
Marital Status		*$X^2(1)=2.22$*	-
Non-Married		1.89 (0.82, 4.38)	1.49 (0.74, 2.97)
Married or living with a partner		1.0 Reference	1.0 Reference
Region		*$X^2(3)=2.86$*	-
New Brunswick		0.65 (0.32, 1.35)	0.95 (0.55, 1.64)
Newfoundland and Labrador		0.49 (0.20, 1.24)	0.69 (0.30, 1.54)
Prince Edward Island		1.10 (0.19, 6.34)	0.68 (0.13, 3.67)
Nova Scotia		1.0 Reference	1.0 Reference
Working Status		*$X^2(3)=6.90$*	-
Part time		1.58 (0.48, 5.16)	1.30 (0.47, 3.61)
Unemployed/Sick		1.37 (0.38, 4.96)	1.44 (0.51, 4.10)
Retired		0.34 (0.13, 0.92)	0.64 (0.31, 1.34)
Full time		1.0 Reference	1.0 Reference

		OR (95% CI)	OR (95% CI)
Multimorbidity		*$X^2(1)=2.22$*	-
	Yes	1.69 (0.85, 3.39)	1.47 (0.86, 2.52)
	No	1.0 Reference	1.0 Reference

Notes:
[a]Original Data
[b]Multiple Imputation
X^2 Wald Chi-square value
* significant at p<0.05
** significant at p<0.01
*** significant at p<0.001

Table 4 Logistic Regression analysis predicting current anxiety symptoms by fitting a lifetime history of a PCa diagnosis and the individual association of modifiable lifestyle factors (diet, PA, sleep, alcohol, and smoking) among men residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, and multimorbidity.

	No anxiety vs. anxiety symptoms			
	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Model	**$X^2(2)=7.03$***	**$X^2(16)=38.12$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=4.97$**	*$X^2(1)=3.84$**	-	-
Yes	2.27 (1.10, 4.67)*	2.96 (1.00, 8.75)*	1.50 (0.80, 2.80)	1.45 (0.62, 3.39)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Diet	*$X^2(1)=2.40$*	*$X^2(1)=2.61$*	-	-
Insufficient intake	1.85 (0.85, 4.04)	2.16 (0.85, 5.47)	1.30 (0.69, 2.44)	1.36 (0.70, 2.65)
Sufficient intake	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=4.40$**	-	-
	-	0.94 (0.89, 1.00)*	-	0.97 (0.92, 1.01)
Ethnicity	-	*$X^2(1)=0.45$*	-	-
Non-White	-	0.46 (0.05, 4.42)	-	0.56 (0.09, 3.43)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.64$*	-	-
High school or less	-	0.77 (0.26, 2.29)	-	0.86 (0.36, 2.05)
College or trade level	-	0.68 (0.26, 1.77)	-	0.86 (0.40, 1.86)
University level or higher	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Income	-	*$X^2(2)=8.77$***	-	-
CAD ≤$49,999	-	3.92 (1.28, 11.96)**	-	2.77 (0.97, 7.95)*
CAD $50,000 – 99,999	-	0.85 (0.31, 2.32)	-	0.79 (0.29, 2.18)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=0.00$*	-	-
Non-Married	-	0.99 (0.31, 3.16)	-	0.99 (0.38, 2.56)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=1.89$*	-	-
New Brunswick	-	1.33 (0.52, 3.46)	-	1.58 (0.69, 3.61)
Newfoundland & Labrador	-	1.81 (0.64, 5.15)	-	1.44 (0.56, 3.75)
Prince Edward Island	-	3.20 (0.31, 32.98)	-	1.30 (0.20, 8.35)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=10.68$***	-	-
Part time	-	2.39 (0.56, 10.15)	-	1.73 (0.51, 5.88)
Unemployed/Sick	-	4.82 (1.20, 19.31)*	-	2.63 (0.78, 8.91)
Retired	-	0.32 (0.08, 1.38)	-	0.76 (0.29, 2.00)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=0.011$*	-	-
Yes	-	0.95 (0.38, 2.37)	-	1.05 (0.49, 2.23)
No	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Model	**$X^2(3)=8.60$***	**$X^2(17)=35.19$****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=8.35$***	*$X^2(1)=4.00$**	-	-
Yes	3.36 (1.48, 7.64)**	3.61 (1.03, 12.69)*	1.49 (0.81, 2.74)	1.45 (0.62, 3.37)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Physical Activity	*$X^2(2)=0.61$*	*$X^2(2)=0.32$*	-	-
Low	0.88 (0.32, 2.46)	0.73 (0.20, 2.71)	1.13 (0.39, 3.29)	1.02 (0.29, 3.55)
Medium	0.69 (0.26, 1.80)	1.00 (0.31, 3.21)	0.83 (0.29, 2.42)	1.12 (0.31, 4.01)
High	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=4.23$**	-	-
	-	0.93 (0.87, 1.00)*	-	0.97 (0.93, 1.01)
Ethnicity	-	*$X^2(1)=0.02$*	-	-
Non-White	-	0.86 (0.09, 8.32)	-	0.60 (0.10, 3.76)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=1.54$*	-	-
High school or less	-	0.40 (0.09, 1.74)	-	0.89 (0.37, 2.15)
College or trade level	-	0.67 (0.22, 2.10)	-	0.90 (0.41, 2.00)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=8.17$**	-	-
CAD ≤$49,999	-	5.50 (1.34, 22.53)**	-	2.88 (0.98, 8.50)*
CAD $50,000 – 99,999	-	0.85 (0.24, 3.00)	-	0.79 (0.29, 2.20)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Marital Status	-	*$X^2(1)=0.08$*	-	-
Non-Married	-	0.82 (0.21, 3.22)	-	0.98 (0.37, 2.55)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=5.57$*	-	-
New Brunswick	-	2.43 (0.69, 8.62)	-	1.59 (0.70, 3.60)
Newfoundland & Labrador	-	4.15 (1.07, 16.04)*	-	1.48 (0.58, 3.78)
Prince Edward Island	-	9.22 (0.72, 117.82)**	-	1.26 (0.20, 8.13)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=5.32$*	-	-
Part time	-	3.44 (0.60, 19.65)	-	1.69 (0.48, 5.91)
Unemployed/Sick	-	3.38 (0.50, 22.80)	-	2.56 (0.75, 8.76)
Retired	-	0.49 (0.08, 2.82)	-	0.73 (0.27, 1.96)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=0.17$*	-	-
Yes	-	1.27 (0.41, 3.92)	-	1.05 (0.50, 2.22)
No	-	1.0 Reference	-	1.0 Reference
Model	**$X^2(2)=9.33$****	**$X^2(16)=39.45$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=5.12$**	*$X^2(1)=3.86$**	-	-
Yes	2.31 (1.12, 4.78)*	3.00 (1.00, 8.94)*	1.49 (0.80, 2.77)	1.46 (0.62, 3.44)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Sleep	*$X^2(1)=4.69$**	*$X^2(1)=1.01$*	-	-
Not recommended sleep	2.10 (1.07, 4.11)*	1.54 (0.66, 3.56)	1.45 (0.82, 2.57)	1.20 (0.62, 2.35)
Recommended sleep	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=4.23$**	-	-
	-	0.95 (0.90, 1.00)*	-	0.96 (0.92, 1.01)
Ethnicity	-	*$X^2(1)=0.38$*	-	-
Non-White	-	0.49 (0.05, 4.83)	-	0.58 (0.09, 3.66)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.11$*	-	-
High school or less	-	0.86 (0.28, 2.64)	-	0.91 (0.38, 2.21)
College or trade level	-	0.86 (0.33, 2.24)	-	0.96 (0.44, 2.09)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=9.06$***	-	-
CAD ≤$49,999	-	3.65 (1.18, 11.26)*	-	2.69 (0.93, 7.76)
CAD $50,000 – 99,999	-	0.69 (0.24, 1.93)	-	0.73 (0.26, 2.06)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=0.12$*	-	-
Non-Married	-	0.81 (0.25, 2.66)	-	0.95 (0.36, 2.51)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Region	-	*$X^2(3)=1.75$*	-	-
New Brunswick	-	1.28 (0.49, 3.36)	-	1.65 (0.71, 3.84)
Newfoundland & Labrador	-	1.99 (0.68, 5.80)	-	1.56 (0.59, 4.09)
Prince Edward Island	-	2.00 (0.19, 21.02)	-	1.34 (0.21, 8.65)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=10.23$***	-	-
Part time	-	2.14 (0.48, 9.55)	-	1.81 (0.52, 6.30)
Unemployed/Sick	-	4.82 (1.20, 19.44)	-	2.72 (0.78, 9.44)
Retired	-	0.34 (0.07,1.49)	-	0.81 (0.30, 2.17)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=0.00$*	-	-
Yes	-	1.00 (0.40, 2.49)	-	1.07 (0.50, 2,29)
No	-	1.0 Reference	-	1.0 Reference
Model	**$X^2(4)=8.64$**	**$X^2(18)=44.07$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=4.62$**	*$X^2(1)=3.33$*	-	-
Yes	2.23 (1.07, 4.65)*	2.73 (0.93, 8.03)	1.51 (0.82, 2.79)	1.50 (0.63, 3.32)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Alcohol Use	*$X^2(3)=3.65$*	*$X^2(3)=5.75$*	-	-
Habitual drinker	0.42 (0.13, 1.37)	1.04 (0.21, 5.08)	0.54 (0.20, 1.49)	0.94 (0.27, 3.26)
Regular drinker	1.04 (0.38, 2.85)	3.65 (0.89, 15.04)	1.02 (0.42, 2.50)	1.81 (0.60, 5.48)
Occasional drinker	0.80 (0.27, 2.36)	2.12 (0.54, 8.43)	0.86 (0.33, 2.23)	1.20 (0.36, 3.94)
Abstainers	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Age	-	*$X^2(1)=3.50$*	-	-
	-	0.95 (0.90, 1.01)	-	0.97 (0.92, 1.01)
Ethnicity	-	*$X^2(1)=0.30$*	-	-
Non-White	-	0.57 (0.06, 5.74)	-	0.61 (0.09, 4.22)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.97$*	-	-
High school or less	-	0.74 (0.24, 2.34)	-	0.95 (0.38, 2.37)
College or trade level	-	0.63 (0.23, 1.70)	-	1.16 (0.48, 2.85)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=11.29$***	-	-
CAD ≤$49,999	-	6.17 (1.67, 22.75)**	-	0.26 (0.09, 0.77)**
CAD $50,000 – 99,999	-	0.81 (0.27, 2.43)	-	0.33 (0.11, 1.01)*
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=0.03$*	-	-
Non-Married	-	0.94 (0.29, 3.10)	-	1.01 (0.37, 2.72)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=2.32$*	-	-
New Brunswick	-	1.45 (0.55, 3.85)	-	0.77 (0.11, 5.16)
Newfoundland & Labrador	-	2.15 (0.72, 6.45)	-	1.26 (0.19, 8.33)
Prince Edward Island	-	2.80 (0.27, 29.38)	-	1.18 (0.17, 8.30)
Nova Scotia	-	1.0 Reference	-	1.0 Reference

		OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Working Status		-	*$X^2(3)=9.96$***	-	-
	Part time	-	1.90 (0.42, 8.53)	-	0.39 (0.11, 1.42)
	Unemployed/Sick	-	4.17 (1.00, 17.35)*	-	0.30 (0.08, 1.19)
	Retired	-	0.25 (0.05, 1.18)	-	0.66 (0.12, 3.50)
	Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity		-	*$X^2(1)=0.56$*	-	-
	Yes	-	1.06 (0.41, 2.69)	-	1.06 (0.82, 1.39)
	No	-	1.0 Reference	-	1.0 Reference
Model		**$X^2(3)=8.23$***	**$X^2(17)=39.01$****	**-**	**-**
Lifetime History of PCa diagnosis		*$X^2(1)=5.33$**	*$X^2(1)=4.11$**	-	-
	Yes	2.34 (1.14, 4.83)*	3.04 (1.04, 8.89)*	1.49 (0.81, 2.74)	1.49 (0.65, 3.42)
	No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Smoking Use		*$X^2(2)=3.70$*	*$X^2(2)=2.29$*	-	-
	Current smoker	2.5 (0.98, 6.55)*	2.28 (0.67, 7.73)	1.94 (0.86, 4.34)	1.58 (0.57, 4.34)
	Former smoker	1.29 (0.62, 2.69)	1.75 (0.72, 4.30)	1.12 (0.56, 2.24)	1.34 (0.59, 3.03)
	Never smoked	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age		-	*$X^2(1)=3.92$**	-	-
		-	0.95 (0.90, 1.00)*	-	0.97 (0.92, 1.01)
Ethnicity		-	*$X^2(1)=0.28$*	-	-
	Non-White	-	0.55 (0.06, 5.04)	-	0.58 (0.09, 3.78)
	White	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Education	-	*$X^2(2)=0.70$*	-	-
High school or less	-	0.70 (0.23, 2.09)	-	0.81 (0.34, 1.96)
College or trade level	-	0.69 (0.26, 1.78)	-	0.85 (0.39, 1.86)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=8.37$***	-	-
CAD ≤$49,999	-	3.70 (1.23, 11.15)*	-	2.73 (0.93, 8.00)
CAD $50,000 – 99,999	-	0.82 (0.30, 2.23)	-	0.79 (0.28, 2.22)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=0.09$*	-	-
Non-Married	-	0.84 (0.26, 2.71)	-	0.96 (0.37, 2.52)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=1.09$*	-	-
New Brunswick	-	1.39 (0.54, 3.57)	-	1.58 (0.69, 3.65)
Newfoundland & Labrador	-	1.59 (0.55, 4.56)	-	1.40 (0.54, 3.61)
Prince Edward Island	-	2.16 (0.21, 22.59)	-	1.17 (0.18, 7.64)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=9.02$**	-	-
Part time	-	2.23 (0.48, 10.26)	-	1.71 (0.49, 6.03)
Unemployed/Sick	-	3.82 (0.96, 15.21)*	-	2.39 (0.67, 8.50)
Retired	-	0.30 (0.07, 1.31)	-	0.74 (0.28, 1.92)
Full time	-	1.0 Reference	-	1.0 Reference

		OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Multimorbidity		-	*$X^2(1)=0.003$*	-	-
	Yes	-	0.97 (0.38, 2.48)	-	1.01 (0.47, 2.18)
	No	-	1.0 Reference	-	1.0 Reference

Notes:

[MI]Multiple Imputation

X^2 Wald Chi-square value

* significant at $p<0.05$

** significant at $p<0.01$

*** significant at $p<0.001$

Table 5 Logistic Regression analysis predicting current depressive symptoms by fitting a lifetime history of a PCa diagnosis and the individual association of modifiable lifestyle factors (diet, PA, sleep, alcohol, and smoking) among men residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, and multimorbidity.

	No depression vs. depressive symptoms			
	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Model	**$X^2(2)=7.27$***	**$X^2(16)=41.58$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=6.02$***	*$X^2(1)=4.12$**	-	-
Yes	2.10 (1.16, 3.79)**	2.42 (1.03, 5.69)*	1.37 (0.86, 2.19)	1.30 (0.73, 2.30)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Diet	*$X^2(1)=1.68$*	*$X^2(1)=2.42$*	-	-
Insufficient intake	1.47 (0.82, 2.62)	1.73 (0.87, 3.45)	1.33 (0.82, 2.15)	1.36 (0.81, 2.23)
Sufficient intake	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=2.90$*	-	-
	-	0.96 (0.93, 1.01)	-	0.98 (0.95, 1.01)
Ethnicity	-	*$X^2(1)=0.35$*	-	-
Non-White	-	0.62 (0.12, 3.10)	-	0.61 (0.20, 1.93)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.95$*	-	-
High school or less	-	0.80 (0.33, 1.95)	-	0.81 (0.38, 1.71)
College or trade level	-	1.21 (0.60, 2.46)	-	1.23 (0.64, 2.37)
University level or higher	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Income	-	*$X^2(2)=5.25$*	-	-
CAD ≤$49,999	-	2.83 (1.12, 7.15)*	-	2.31 (0.94, 5.71)
CAD $50,000 – 99,999	-	1.25 (0.60, 2.59)	-	1.06 (0.53, 2.12)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=2.76$*	-	-
Non-Married	-	2.07 (0.88, 4.87)	-	1.52 (0.75, 3.07)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=3.07$*	-	-
New Brunswick	-	0.66 (0.32, 1.38)	-	0.94 (0.54, 1.63)
Newfoundland & Labrador	-	0.49 (0.19, 1.23)	-	0.67 (0.30, 1.53)
Prince Edward Island	-	1.39 (0.24, 7.99)	-	0.70 (0.13, 3.80)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=6.24$*	-	-
Part time	-	1.64 (0.50, 5.37)	-	1.33 (0.48, 3.68)
Unemployed/Sick	-	1.44 (0.39, 5.32)	-	1.47 (0.52, 4.18)
Retired	-	0.37 (0.14, 1.01)*	-	0.66 (0.32, 1.39)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=2.23$*	-	-
Yes	-	1.71 (0.85, 3.44)	-	1.46 (0.84, 2.51)
No	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Model	**$X^2(3)=23.87$*****	**$X^2(17)=46.49$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=5.96$***	*$X^2(1)=3.44$*	-	-
Yes	2.35 (1.19, 4.69)**	2.58 (0.95, 6.99)	1.40 (0.86, 2.28)	1.32 (0.74, 2.38)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Physical Activity	*$X^2(2)=18.03$****	*$X^2(2)=18.38$****	-	-
Low	3.35 (1.51, 7.44)**	4.72 (1.75, 12.74)**	2.96 (1.11, 7.87)*	3.37 (1.06, 10.74)*
Medium	0.78 (0.33, 1.83)	0.84 (0.30, 2.35)	0.76 (0.34, 1.72)	0.95 (0.36, 2.49)
High	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=2.47$*	-	-
	-	0.96 (0.91,1.01)	-	0.98 (0.95, 1.02)
Ethnicity	-	*$X^2(1)=0.002$*	-	-
Non-White	-	0.97 (0.19, 5.03)	-	0.70 (0.23, 2.15)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.56$*	-	-
High school or less	-	1.05 (0.35, 3.11)	-	0.89 (0.41, 1.94)
College or trade level	-	1.36 (0.59, 3.17)	-	1.24 (0.62, 2.52)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=2.28$*	-	-
CAD ≤$49,999	-	1.88 (0.57, 6.17)	-	2.53 (0.91, 7.00)
CAD $50,000 – 99,999	-	0.79 (0.33, 1.90)	-	1.13 (0.57, 2.27)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Marital Status	-	*$X^2(1)=2.84$*	-	-
Non-Married	-	2.42 (0.87, 6.78)	-	1.34 (0.65, 2.77)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=3.06$*	-	-
New Brunswick	-	0.55 (0.23, 1.32)	-	0.93 (0.53, 1.64)
Newfoundland & Labrador	-	0.45 (0.16, 1.28)	-	0.67 (0.29, 1.55)
Prince Edward Island	-	0.98 (0.13, 7.10)	-	0.72 (0.13, 4.17)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=5.37$*	-	-
Part time	-	3.51 (0.92, 13.30)	-	1.46 (0.49, 4.32)
Unemployed/Sick	-	1.25 (0.23, 6.91)	-	1.35 (0.45, 4.03)
Retired	-	0.61 (0.17, 2.15)	-	0.71 (0.32, 1.57)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=0.54$*	-	-
Yes	-	1.39 (0.57, 3.33)	-	1.37 (0.79, 2.36)
No	-	1.0 Reference	-	1.0 Reference
Model	**$X^2(2)=15.39$*****	**$X^2(16)=42.16$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=6.88$***	*$X^2(1)=4.56$**	-	-
Yes	2.23 (1.23, 4.07)**	2.56 (1.08, 6.07)*	1.40 (0.88, 2.23)	1.33 (0.75, 2.36)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Sleep	*$X^2(1)=9.08$***	*$X^2(1)=3.81$**	-	-
Not recommended sleep	2.28 (1.33, 3.89)**	1.90 (1.00, 3.63)	1.59 (1.00, 2.53)*	1.39 (0.82, 2.34)
Recommended sleep	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=2.33$*	-	-
	-	0.97 (0.93, 1.01)	-	0.98 (0.95, 1.01)
Ethnicity	-	*$X^2(1)=0.27$*	-	-
Non-White	-	0.65 (0.12, 3.36)	-	0.66 (0.21, 2.09)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=0.91$*	-	-
High school or less	-	0.83 (0.33, 2.06)	-	0.83 (0.39, 1.73)
College or trade level	-	1.25 (0.61, 2.57)	-	1.27 (0.65, 2.49)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=4.13$*	-	-
CAD ≤$49,999	-	2.47 (0.96, 6.37)	-	2.15 (0.86, 5.41)
CAD $50,000 – 99,999	-	1.10 (0.52, 2.32)	-	1.00 (0.50, 2.01)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=1.84$*	-	-
Non-Married	-	1.82 (0.77, 4.31)	-	1.51 (0.75, 3.05)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Region	-	*$X^2(3)=1.89$*	-	-
New Brunswick	-	0.68 (0.32, 1.44)	-	1.01 (0.58, 1.78)
Newfoundland & Labrador	-	0.56 (0.22, 1.45)	-	0.75 (0.33, 1.72)
Prince Edward Island	-	1.03 (0.17, 6.24)	-	0.77 (0.14, 4.15)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=5.84$*	-	-
Part time	-	1.52 (0.44, 5.20)	-	1.38 (0.49, 3.86)
Unemployed/Sick	-	1.70 (0.46, 6.22)	-	1.53 (0.54, 4.38)
Retired	-	0.39 (0.14, 1.09)	-	0.68 (0.32, 1.45)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=2.07$*	-	-
Yes	-	1.69 (0.83, 3.43)	-	1.44 (0.83, 2.50)
No	-	1.0 Reference	-	1.0 Reference
Model	**$X^2(4)=17.10$****	**$X^2(18)=48.50$*****	**-**	**-**
Lifetime History of PCa diagnosis	*$X^2(1)=8.79$***	*$X^2(1)=6.02$***	-	-
Yes	2.54 (1.37, 4.70)**	3.08 (1.25, 7.57)**	1.43 (0.90, 2.28)	1.46 (0.84, 2.54)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Alcohol Use	*$X^2(3)=10.86$***	*$X^2(3)=7.76$**	-	-
Habitual drinker	0.47 (0.19, 1.16)	0.50 (0.16, 1.61)	0.62 (0.26, 1.48)	0.88 (0.31, 2.55)
Regular drinker	0.50 (0.21, 1.18)	0.62 (0.20, 1.89)	0.67 (0.29, 1.53)	0.96 (0.34, 2.70)
Occasional drinker	1.30 (0.58, 2.93)	1.61 (0.58, 4.49)	1.61 (0.59, 4.41)	1.34 (0.52, 3.45)
Abstainers	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Age	-	*$X^2(1)=2.15$*	-	-
	-	0.97 (0.93, 1.01)	-	0.98 (0.94, 1.01)
Ethnicity	-	*$X^2(1)=0.12$*	-	-
Non-White	-	0.75 (0.15, 3.87)	-	0.58 (0.18, 1.85)
White	-	1.0 Reference	-	1.0 Reference
Education	-	*$X^2(2)=1.68$*	-	-
High school or less	-	1.82 (0.74, 4.53)	-	1.58 (0.75, 3.33)
College or trade level	-	1.51 (0.58, 3.93)	-	1.31 (0.60, 2.86)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=3.69$*	-	-
CAD ≤$49,999	-	0.39 (0.16, 0.96)*	-	0.44 (0.18, 1.09)
CAD $50,000 – 99,999	-	0.43 (0.15, 1.18)	-	0.44 (0.17, 1.12)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=2.54$*	-	-
Non-Married	-	2.06 (0.85, 4.98)	-	1.48 (0.73, 3.04)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=1.90$*	-	-
New Brunswick	-	2.01 (0.21, 19.27)	-	1.89 (0.23, 15.35)
Newfoundland & Labrador	-	1.39 (0.14, 13.70)	-	1.84 (0.22, 15.09)
Prince Edward Island	-	1.13 (0.11, 12.15)	-	1.36 (0.18, 10.24)
Nova Scotia	-	1.0 Reference	-	1.0 Reference

		OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Working Status		-	*$X^2(3)=6.62$*	-	-
	Part time	-	0.70 (0.19, 2.65)	-	0.75 (0.25, 2.20)
	Unemployed/Sick	-	0.27 (0.06, 1.24)	-	0.52 (0.15, 1.78)
	Retired	-	1.51 (0.28, 8.00)	-	1.03 (0.24, 4.36)
	Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity		-	*$X^2(1)=1.20$*	-	-
	Yes	-	1.50 (0.73, 3.11)	-	1.23 (1.01, 1.51)
	No	-	1.0 Reference	-	1.0 Reference
Model		**$X^2(3)=9.49$***	**$X^2(17)=42.90$*****	**-**	**-**
Lifetime History of PCa diagnosis		*$X^2(1)=5.42$**	*$X^2(1)=3.41$*	-	-
	Yes	2.04 (1.12, 3.73)*	2.25 (0.95, 5.32)	1.35 (0.84, 2.17)	1.27 (0.71, 2.27)
	No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Smoking Use		*$X^2(2)=4.80$*	*$X^2(2)=3.31$*	-	-
	Current smoker	2.37 (1.09, 5.15)*	2.51 (0.92, 6.81)	2.04 (1.05, 3.96)	1.72 (0.78, 3.82)
	Former smoker	1.19 (0.67, 2.11)	1.37 (0.69, 2.74)	1.14 (0.65, 1.98)	1.27 (0.68, 2.36)
	Never smoked	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age		-	*$X^2(1)=2.22$*	-	-
		-	0.97 (0.93, 1.01)	-	0.98 (0.95, 1.01)
Ethnicity		-	*$X^2(1)=0.23$*	-	-
	Non-White	-	0.68 (0.14, 3.37)	-	0.62 (0.20, 1.92)
	White	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Education	-	*$X^2(2)=0.99$*	-	-
High school or less	-	0.70 (0.28, 1.74)	-	0.75 (0.35, 1.58)
College or trade level	-	1.08 (0.53, 2.23)	-	1.18 (0.61, 2.27)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=5.21$*	-	-
CAD ≤$49,999	-	2.74 (1.08, 6.92)*	-	2.25 (0.90, 5.58)
CAD $50,000 – 99,999	-	1.17 (0.56, 2.45)	-	1.03 (0.51, 2.06)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=1.82$*	-	-
Non-Married	-	1.80 (0.77, 4.22)	-	1.48 (0.73, 2.97)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(3)=3.50$*	-	-
New Brunswick	-	0.67 (0.32, 1.40)	-	0.93 (0.53, 1.62)
Newfoundland & Labrador	-	0.43 (0.17, 1.11)	-	0.65 (0.29, 1.47)
Prince Edward Island	-	1.16 (0.19, 6.92)	-	0.64 (0.12, 3.44)
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=5.98$*	-	-
Part time	-	1.49 (0.43, 5.17)	-	1.32 (0.46, 3.78)
Unemployed/Sick	-	1.22 (0.32, 4.58)	-	1.34 (0.47, 3.83)
Retired	-	0.35 (0.13, 0.95)*	-	0.65 (0.31, 1.38)
Full time	-	1.0 Reference	-	1.0 Reference

		OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Multimorbidity		-	*$X^2(1)=3.50$*	-	-
	Yes	-	1.99 (0.97, 4.11)	-	1.51 (0.87, 2.63)
	No	-	1.0 Reference	-	1.0 Reference

Notes:

[MI]Multiple Imputation

X^2 Wald Chi-square value

* significant at $p<0.05$

** significant at $p<0.01$

*** significant at $p<0.001$

Table 6 Logistic Regression analysis predicting current anxiety symptoms by fitting treatment modality among men who reported a lifetime history of a PCa diagnosis from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, multimorbidity and survivorship time.

	No anxiety vs. anxiety symptoms			
	n=63 OR (95% CI)	n=56 (95% CI) aOR	n=139 OR_{MI} (95% CI)	n=126 aOR_{MI} (95% CI)
Model	**$X^2(2)=1.32$**	**$X^2(15)=24.40$***	**-**	**-**
Treatment Modality	*$X^2(2)=1.28$*	*$X^2(2)=0.32$*	-	-
Radiation Therapy	2.36 (0.50, 11.19)	1.99 (0.16, 24.74)	1.68 (0.41, 6.832)	2.30 (0.24, 21.77)
2 or more combined treatments	1.86 (0.40, 8.58)	1.72 (0.15, 20.28)	1.64 (0.43, 6.21)	1.63 (0.18, 15.03)
Surgery	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=0.31$*	-	-
	-	1.08 (0.83, 1.41)	-	0.98 (0.79, 1.23)
Ethnicity[a]	-	-	-	-
Education	-	*$X^2(2)=1.14$*	-	-
High school or less	-	0.20 (0.005, 7.63)	-	0.34 (0.20, 5.82)
College or trade level	-	1.20 (0.12, 12.03)	-	0.78 (0.09, 6.62)
University level or higher	-	1.0 Reference	-	1.0 Reference
Income	-	*$X^2(2)=3.50$*	-	-
CAD ≤$49,999	-	56.35 (0.66, 4789.65)	-	3.74 (0.21, 66.78)
CAD $50,000 – 99,999	-	1.31 (0.12, 14.88)	-	0.56 (0.03, 9.63)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Marital Status	-	*$X^2(1)=1.80$*	-	-
Non-Married	-	10.24 (0.34, 308.26)	-	1.42 (0.09, 23.73)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(2)=3.45$*	-	-
New Brunswick	-	2.14 (0.06, 72.52)	-	1.40 (0.10, 20.30)
Newfoundland & Labrador	-	11.24 (0.28, 455.18)	-	1.95 (0.14, 27.59)
Prince Edward Island[b]	-	-	-	-
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=2.88$*	-	-
Part time	-	1.47 (0.004, 557.40)	-	5.53 (0.22, 141.13)
Unemployed/Sick	-	0.12 (0.001, 13.29)	-	2.93 (0.05, 167.11)
Retired	-	0.03 (0.00, 3.79)	-	1.05 (0.06, 19.35)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=0.08$*	-	-
Yes	-	1.5 (0.09, 24.05)	-	2.81 (0.26, 30.31)
No	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Survivorship Time	-	*$X^2(1)=1.56$*	-	-
	-	0.75 (0.48, 1.18)	-	0.93 (0.66, 1.31)

Notes:

[MI]Multiple Imputation

X^2 Wald Chi-square value

[a] Ethnicity excluded from model due to collinearity

[b] No participants from PEI

* significant at $p<0.05$

Table 7 Logistic Regression analysis predicting current depressive symptoms by fitting treatment modality among men who reported a lifetime history of a PCa diagnosis from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, multimorbidity, and survivorship time.

	No depression vs. depressive symptoms			
	n=63 OR (95% CI)	n=56 (95% CI) aOR	n=139 OR_{MI} (95% CI)	n=126 aOR_{MI} (95% CI)
Model	**$X^2(2)=1.33$**	**$X^2(15)=18.49$**	**-**	**-**
Treatment Modality	*$X^2(2)=1.34$*	*$X^2(2)=0.72$*	-	-
Radiation Therapy	2.19 (0.58, 8.33)	2.03 (0.36, 11.33)	1.57 (0.47, 5.22)	2.03 (0.41, 10.18)
2 or more combined treatments	1.26 (0.33, 4.80)	1.77 (0.28, 11.32)	1.37 (0.44, 4.31)	1.07 (0.20, 5.71)
Surgery	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	-	*$X^2(1)=2.67$*	-	-
	-	1.21 (0.96, 1.52)	-	1.05 (0.89, 1.24)
Ethnicity[a]	-	-	-	-
Education	-	*$X^2(2)=0.84$*	-	-
High school or less	-	0.51 (0.06, 4.41)	-	0.29 (0.03, 2.94)
College or trade level	-	1.43 (0.26, 7.82)	-	0.83 (0.16, 4.31)
University level or higher	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Income	-	*$X^2(2)=3.50$*	-	-
CAD ≤$49,999	-	13.85 (0.77, 248.15)	-	3.43 (0.44, 26.55)
CAD $50,000 – 99,999	-	1.46 (0.26, 8.21)	-	0.84 (0.12, 5.67)
CAD ≥$100,000	-	1.0 Reference	-	1.0 Reference
Marital Status	-	*$X^2(1)=4.36$**	-	-
Non-Married	-	18.44 (1.20, 284.55)*	-	3.71 (0.29, 47.83)
Married or living with a partner	-	1.0 Reference	-	1.0 Reference
Region	-	*$X^2(2)=1.55$*	-	-
New Brunswick	-	5.60 (0.37, 84.45)	-	2.18 (0.27, 17.66)
Newfoundland & Labrador	-	4.66 (0.27, 79.05)	-	0.91 (0.06, 12.87)
Prince Edward Island[b]	-	-	-	-
Nova Scotia	-	1.0 Reference	-	1.0 Reference
Working Status	-	*$X^2(3)=2.17$*	-	-
Part time	-	0.49 (0.01, 20.39)	-	1.51 (0.09, 26.09)
Unemployed/Sick	-	0.14 (0.004, 4.94)	-	1.03 (0.07, 14.87)
Retired	-	0.15 (0.01, 2.19)	-	0.68 (0.10, 4.74)
Full time	-	1.0 Reference	-	1.0 Reference
Multimorbidity	-	*$X^2(1)=1.14$*	-	-
Yes	-	0.36 (0.06, 1.06)	-	0.82 (0.17, 3.89)
No	-	1.0 Reference	-	1.0 Reference

	OR (95% CI)	aOR (95% CI)	OR_{MI} (95% CI)	aOR_{MI} (95% CI)
Survivorship Time	-	*$X^2(1)=2.70$*	-	-
	-	0.76 (0.55, 1.06)	-	0.95 (0.75, 1.21)

Notes:

[MI]Multiple Imputation

X^2 Wald Chi-square value

[a] Ethnicity excluded from model due to collinearity

[b] No participants from PEI

* significant at $p<0.05$

Chapter 6 Discussion

In this study between a lifetime history of a PCa diagnosis and mental health outcomes among a matched sample of Atlantic Canadian men, we observed a significant association between a lifetime history of a PCa diagnosis and screening positive for current depressive symptoms. We also found that among the modifiable lifestyle factors tested in the association between a lifetime history of a PCa diagnosis and screening positive for current depressive symptoms, PA and smoking significantly contributed to the models. The association between a lifetime history of a PCa diagnosis and screening positive for current anxiety symptoms was not significant. When controlled for in the models, diet, PA, sleep and smoking resulted in a significant association between a lifetime history of a PCa diagnosis and a positive screening for current anxiety symptoms. Finally, we observed that treatment modality was not statistically significantly associated with screening positive for current anxiety or depressive symptoms among individuals with a lifetime history of a PCa diagnosis.

6.1 Mental Health & PCa

In objective one we hypothesized that the association between a lifetime history of a PCa diagnosis and screening positive for current anxiety and depressive symptoms would be statistically significant compared to men without a lifetime history of a PCa diagnosis. Lifetime history of a PCa diagnosis was statistically significantly associated with current depressive symptoms in the current study, in line with previous research (Fervaha et al., 2019; Ilie et al., 2020b; Moodie et al., 2019; Watts et al., 2014). In contrast with previous research findings, however, we did not observe a statistically significant association

between a lifetime history of a PCa diagnosis and current anxiety symptoms. A recent cross-sectional study in Atlantic Canada found that based on a subsample of 6,585 men aged 45-69, individuals with a lifetime history of a PCa diagnosis had two times higher odds of screening positive for both current anxiety and depressive symptoms compared to men who never had a history of a cancer diagnosis (Ilie et al., 2020b). Results from a Canadian wide cross-sectional study (n=25,183) found comparable results (Moodie et al., 2019). However, compared to our study, these studies had much larger sample sizes (Ilie et al., 2020b; Moodie et al., 2019). The control groups also differ between studies. Ilie et al. (2020b) compared individuals with a presence of a lifetime history of a PCa diagnosis to individuals without a cancer diagnosis and to individuals with other types of cancer diagnoses. In contrast, Moodie et al. (2019) utilized the same control group as our study and compared men with a lifetime history of a PCa diagnosis to men without a lifetime history of a PCa diagnosis. Similar to our study, Ilie et al. (2020b) and Moodie et al. (2019) both controlled for age, education, ethnicity, income, marital status, and province of residence. These studies differ from each other as Ilie et al. (2020b) also controlled for survivorship time, while Moodie et al. (2019) controlled for multimorbidity. In addition to these eight covariates, our study also controlled for working status.

Our findings add to the existing literature by providing further support that a lifetime history of a PCa diagnosis is associated with screening positive for current depressive symptoms. Our study also expands the literature by utilizing a matched design and by controlling for additional covariates, such as working status and multimorbidity. There currently exists limited research in the association between a lifetime history of a PCa diagnosis for both anxiety and depression. Therefore, future studies are warranted.

The association between PCa and mental health outcomes (anxiety and depression) may also be influenced by the social construct of masculinity in relation to mental health outcomes among men. The traditional definition of masculinity is characterized as restrictive emotions, stoicism, self-reliance (Pleck, 1995). Conformity to these traditional masculine roles may be associated with poor mental health symptoms, reluctance to agree to psychological evaluation, and difficulties admitting emotional distress (Addis & Mahalik, 2003; Matthew & Elterman, 2014; Seidler et al., 2016). Due to the treatment side effects, men with a lifetime history of a PCa diagnosis may have an additional risk of being associated with poor mental health symptoms due to the social construct of masculinity. These side effects include erectile dysfunction and gynecomastia, which can disrupt a man's perceived masculinity and may lead to increased symptoms of poor mental health. The current literature on sex and gender in men with a lifetime history of a PCa diagnosis is sparse (Kiss & Meryn, 2001). Therefore, future studies should consider using a sex and gender-based analysis in order to improve intervention and health policies for all men with a lifetime history of a PCa diagnosis who are experiencing poor mental health.

6.2 Mental Health & Modifiable Lifestyle Factors

Objective two results demonstrate that modifiable lifestyle factors significantly contribute to the association between a lifetime history of a PCa diagnosis and current mental health symptoms.

6.2.1 Diet

Diet was a significant contributor to the association between a lifetime history of a PCa diagnosis and screening positive for current anxiety symptoms. These findings are inconsistent with results from a cross-sectional study by Blanchard et al. (2004) which

found that diet (≥ 5 servings of fruit and vegetables) was not significantly associated with mental health among 316 individuals with a cancer diagnosis. This study, however, measured health-related quality of life as a measure of mental health rather than specifically examining mental health outcomes (e.g., anxiety or depression). The population of this study encompassed multiple cancer types (breast, colorectal, and PCa) and did not focus solely on individuals with a PCa diagnosis (Blanchard et al., 2004). It also did not include a control group (e.g., individuals without a history of a cancer diagnosis).

As previously reported (Chapter 2 above), the relationship between diet and mental health has not been thoroughly examined among individuals with a cancer diagnosis, specifically men with a PCa diagnosis (Blanchard et al., 2004). However, extensive research in the general population does show that increased frequency of fruit and vegetable intake is associated with decreases in anxiety and depressive symptoms (McMartin et al., 2013). Although studies show that simple indicators, such as fruit and vegetable intake, are good predictors of diet quality, future research should include comprehensive diet monitoring utilizing validated diet quality questionnaires (Garriguet, 2009). As the literature is limited regarding diet and mental health outcomes among individuals with a cancer diagnosis, specifically a PCa diagnosis, our findings address this gap in the literature and highlight the need for continued research in this area.

6.2.2 Physical Activity

When PA was controlled for in the logistic model, we found that a lifetime history of a PCa diagnosis became statistically significantly associated with screening positive for current anxiety symptoms but was no longer significantly associated with screening

positive for current depressive symptoms. The literature review illustrated that the understanding of the association between PA and depression and anxiety is inconsistent, and our study is no exception to these findings. Our study complements a special report from Campbell et al. (2019) which reviewed meta-analyses, systematic reviews, and randomized control trials and found strong evidence that PA was associated with decreased anxiety and depression symptoms among individuals with a cancer diagnosis. Strong evidence was quantified as having a substantial number of randomized control trials (≥5), an aggregate sample size (n>150), and the beneficial effect of PA was observed consistently across studies (Campbell et al., 2019). In addition, our research is consistent with findings that PA is significantly associated with decreased depression symptoms in men with a PCa diagnosis (Bock et al., 2017). In contrast to these reported findings, a meta-analysis reviewed 13 randomized control trials in a PCa specific population and concluded that there was no significant association between PA and anxiety and depression (Vashistha et al., 2016).

Although our study complements the findings from Campbell et al. (2019) and Bock et al. (2017), we differ in sample characteristics and methodology. For instance, Campbell et al. (2019) included any cancer type that met the a-priori guidelines for selection of study and did not look at a PCa specific population. In the Bock et al. (2017) study they did not include anxiety as an outcome variable and measured depression using a single item validated question rather than a complete questionnaire, such as the PHQ-9. Therefore, future research is needed to further examine the association between a lifetime history of a PCa diagnosis and anxiety and depression in order to improve comparison across studies.

The contradictory results between studies may also be due to differences in PA regimens and instruments used to measure PA across studies. Our study utilized IPAQ which is a validated tool for measuring PA, but self-report tools often overestimate activity levels compared to accelerometers (Prince et al., 2008). Despite our efforts to mitigate this effect, future studies should consider examining PA with supervised exercises. Inconsistencies between the limited studies that examine PA and mental health among men with a PCa diagnosis indicate that further research is necessary to determine the contribution of PA in the association between a lifetime history of a PCa diagnosis and mental health.

6.2.3 Sleep

Results of our study suggest that sleep significantly contributes to the association between a lifetime history of a PCa diagnosis and screening positive for current anxiety but not depressive symptoms. This finding is consistent with Maguire et al. (2019) who investigated the association between sleep and anxiety and observed that poor sleep is significantly associated with increased anxiety symptoms among men with a lifetime history of a PCa diagnosis. However, two previous cross-sectional studies by Dirksen et al. (2009) and Maguire et al. (2019) found that poor sleep leads to significant increase in depressive symptoms among men with a lifetime history of a PCa diagnosis. In contrast to our study, these studies defined sleep problems as insomnia with validated questionnaires, whereas our study relied on self-reported data that only looked at sleep duration (Dirksen et al., 2009; Maguire et al., 2019). As these studies specifically examined insomnia it is difficult to determine whether sleep problems that are not clinically diagnosed disorders, such as sleep duration, impact the mental well-being in men with a lifetime history of a

PCa diagnosis. The current study contributes to the existing literature by focusing on both anxiety and depression in the PCa population.

A potential mechanism for the association between sleep and mental health symptoms in the PCa population may include treatment modality. Previous cross-sectional studies have shown that men who select ADT as a treatment modality have increases in hot flashes and night sweats, while men treated with radiation therapy have reported higher levels of insomnia severity compared to their counterparts (Dirksen et al., 2009; Hervouet et al., 2005). The side effects that disrupt sleep in the PCa population may differ by treatment modality and thus may be associated with a different impact on mental health. As such, it is important to include treatment modality as a control variable when investigating the contribution of sleep on the association between a lifetime history of a PCa diagnosis and mental health.

6.2.4 Substance Use

Results of our study indicate that smoking significantly contributes to the association between a lifetime history of a PCa diagnosis and anxiety and depression symptoms, while alcohol consumption does not contribute to the association between a lifetime history of a PCa diagnosis and depression or anxiety symptoms. Typically, previous research has combined smoking and alcohol consumption in one model, thus making it difficult to compare findings of our study on the individual contribution of smoking and alcohol consumption on the association between a lifetime history of a PCa diagnosis and mental health outcomes (anxiety and depression). Among the general population, Stranges et al. (2014) found that individuals who smoked heavily and were

non-drinkers or heavy drinkers had higher odds of screening positive for poor mental health (anxiety and depression) compared to those who never smoked and moderately drank. Stranges et al. (2014) measured mental health with the Warwick-Edinburgh Mental Well-being Scale. This study simultaneously included smoking, alcohol consumption, and fruit and vegetable intake in their model, thus limiting our ability to compare our study's findings with the results they obtained.

To the best of our knowledge only one study examined the contribution of substance use on the association between a lifetime history of a PCa diagnosis and mental health outcomes (Bock et al., 2017). This longitudinal study only included depression in the model and found that men who consumed low alcohol and were non-smokers had decreased depressed mood compared to individuals with high alcohol intake and were current smokers before RP; however, this association was not statistically significant long-term (Bock et al., 2017). Additionally, Bock et al. (2017) used a single-item questionnaire to measure depression; therefore, it is difficult to compare our findings to this study. Our current study contributes to the literature by examining the association between a lifetime history of a PCa diagnosis and mental health while individually controlling for the contribution of substance use (smoking and alcohol).

6.3 Mental Health & PCa Treatment Modality

The final objective evaluated in this thesis examined the association of treatment modality and mental health outcomes (anxiety and depression) among men with a lifetime history of a PCa diagnosis. We found no statistically significant association between

treatment modality and mental health (anxiety and depression) in the subpopulation of men with a lifetime history of a PCa diagnosis.

Previous studies examining treatment modality in PCa and mental health are conflicting. Our findings complement Donovan et al. (2016) which found no differences in anxiety and depression across RP, radiation therapy and active surveillance therapies (Donovan et al., 2016). In contrast, Ravi et al. (2014) found a significant difference between active surveillance, RP, and radiation therapy on mental health outcomes (anxiety and depression) (Ravi et al., 2014). However, our treatment modality variable was not comparable to these two studies as the categories were defined differently. Our study categorized treatment modality as RP, radiation therapy and a combination of treatment modalities (due to count sizes of other treatment modalities being too small to compare to other cells). Our results also did not corroborate the conclusions of two other studies that found that men treated with radiation therapy had higher odds of screening positive for poor mental health compared to men treated with non-radiation therapies (e.g., RP or hormone therapy) (Hervouet et al., 2005; Ilie et al., 2020a). Again, these differences may be due to how treatment modality was defined. Hervouet et al. (2005) categorized treatment modality as radiation (EBRT, brachytherapy) and RP, while Ilie et al. (2020a) also included hormonal therapy (Hervouet et al., 2005; Ilie et al., 2020a).

The differences in results between studies may also be due in part to differences in mental health outcomes as well as how the outcomes (anxiety, depression, psychological distress) were measured. For instance, Ravi et al. (2014) used variations of the Short Form Health Survey, Ilie et al. (2020a) used the Kessler Psychological Distress scale,

Donovan et al. (2016) and Hervouet et al. (2005) used the Hospital Anxiety and Depression Scale, and our study used the GAD-7 and PHQ-9. No previous studies have examined external validity across instruments described above, thus future research on this topic is warranted.

Future studies should continue to examine the association between treatment modality and mental health outcomes (anxiety and depression) among men with a lifetime history of a PCa diagnosis, while also examining the contribution of potential side effects. For instance, the complications of concern with RP are incontinence and erectile dysfunction, with 42% of men reporting incontinence and 30-35% reporting potency rates 24 months after surgery (Keyes et al., 2013). Complications associated with radiation therapy, specifically brachytherapy, include difficulty starting urination and bleeding from the rectum. However, in comparison to surgical options there are fewer urinary and sexual dysfunctions but more rectal dysfunctions (Heidenreich et al., 2014; Keyes et al., 2013). ADT is an effective treatment modality for PCa but it is accompanied by numerous side effects, such as increased erectile dysfunction, hot flashes, fatigue, mood swings, and gynecomastia (breast growth) (Canadian Cancer Society, 2019).

6.4 Sensitivity Analysis

It is important to note that the findings for objectives one and two should be interpreted with caution as sensitivity analyses comparing results from the original data to pooled MI data revealed that none of these associations remained statistically significant. Sensitivity analyses comparing results from the original data to pooled MI data on the association between treatment modality and mental health outcomes remained consistent.

6.5 Limitations & Strengths

This work is not without its limitations. As this study is cross-sectional in design, we are only able to determine the association between two or more predictors with the outcomes of interest, and not causation; therefore, we will only be able to identify the associations between a lifetime history of a PCa diagnosis and mental health outcomes. Data from longitudinal studies and randomized control trials should be considered in order to determine if a lifetime history of a PCa diagnosis leads to poor mental health.

There are several potential biases due to the retrospective and self-reported measures of the study, such as recall bias and social desirability bias. Recall bias may not be of great concern regarding our mental health outcomes, as questions on GAD-7 and PHQ-9 surveys only ask participants to reflect on their mental health for the previous two weeks. Social desirability bias is of particular concern among the outcome variables, anxiety and depression. Although the use of validated questionnaires, such as GAD-7 and PHQ-9, reduce the influence of social desirability bias, we recommend that future studies should consider including a clinical interview to further mitigate these biases. This data also lacks heterogeneity, which may limit the generalisability of the results to populations outside of Atlantic Canada. Our sub-sample of men is highly selective, as the majority of men are white, well educated, married or are living with a partner, and have moderate to high income. These factors may limit our ability to generalize to all men with a lifetime history of a PCa diagnosis outside the Atlantic region. Additionally, as this study employed propensity score matching, it is only representative of a PCa specific-population and not the general population.

There is a difference in response rate between the core questionnaire and the Atlantic Canada supplementary questionnaire. The information for the exposure variables, PCa diagnosis and treatment modality, is from the core questionnaire and has a 100% response rate, while the information for the outcome variables, anxiety and depression, is from the supplementary questionnaire and has a 68% response rate. The difference in response rate may result in non-response bias. In particular, it is possible that the mental health outcome is underestimated in this sample as individuals with poor mental health may not have been able to complete the survey because of negative side effects associated with poor mental health (i.e. inability to concentrate).

Lastly and most importantly, the use of propensity scores in the methodological approach resulted in significant missing data specific to the outcome variables, anxiety (45.1%) and depression (44.8%). To address this issue, we employed a sensitivity analysis that compared the difference between the use of the original dataset and the pooled MI dataset. This sensitivity analysis showed that our model was not robust and as a result our conclusions may be biased. Therefore, there is a need for future research to examine the possible source of inconsistency.

Despite these potential limitations, this study also has several methodological strengths. The survey is a representative sample of Atlantic Canada and is also a sub study of the nationwide CanPath, thus allowing for potential comparisons across provinces throughout Canada. The Atlantic PATH database is a longitudinal study that will follow participants for the next 30 years. As this pilot study utilized data from the first cycle of the Atlantic PATH survey (2009-2015), future studies could examine follow-up data to assess longitudinal changes in mental health outcomes among men with a lifetime history

of a PCa diagnosis. Information gathered from longitudinal studies will allow researchers to assess causation between the relationship of a lifetime history of a PCa diagnosis and mental health outcomes. It could also explore the patterns of change and the dynamics of an individual's behaviour.

The Atlantic PATH database has a breadth of information available, which allowed for the inclusion of multiple important, modifiable lifestyle factors that are not routinely collected together. In doing so, we were able to capture an in-depth picture of an individual's entire lifestyle rather than that being broken down into components. This work can then expand knowledge to create holistic interventions that can impact an individual's entire lifestyle. This study also provides a baseline measurement for future longitudinal studies that can examine causation between modifiable lifestyle factors and mental health outcomes among men with a lifetime history of a PCa diagnosis.

Data collected from this survey also included a question regarding time of diagnosis, which allowed for the calculation and control of survivorship time among individuals with a lifetime history of a PCa diagnosis. By including survivorship time, we were able to ensure that our findings were not biased due to differences in time of diagnosis, as studies show that men in different stages in their PCa journey may experience different mental health outcomes (European Association of Urology, 2019; Watts et al., 2014). Studies, such as the Canadian Longitudinal Study on Aging, are not able to include survivorship time as a covariate due to lack of information regarding the time of diagnosis. The Atlantic PATH database also collected information that includes several important sociodemographic variables which were included in the calculation of propensity scores. The use of propensity scores controls for confounding variables in the analyses by ensuring

the sample is matched based on similar characteristics, thus allowing for a clearer interpretation of the findings (Chen & Moskowitz, 2016). However, studies also show that propensity score matching may not be ideal, as it can lead to increased covariate imbalance regardless of decreased distance in propensity score between matched units (Ripollone et al., 2018). In studies with a small sample size, the inclusion of propensity scores can result in a decrease in precision of the estimated exposure effect and only a small decrease in biases (Brookhart et al., 2006). Therefore, despite the possible strengths of using propensity scores, caution should be taken when interpreting the results as the use of propensity scores may be a limitation in this study.

Recently, there have been numerous studies that have examined the association between a lifetime history of a PCa diagnosis and mental health outcomes (Fervaha et al., 2019; Ilie et al., 2020b; Moodie et al., 2019). This pilot study provided further evidence on the association between a lifetime history of a PCa diagnosis and mental health outcomes. It has also provided baseline data on the contribution of modifiable lifestyle factors on the association between a lifetime history of a PCa diagnosis and mental health outcomes.

6.6 Implications & Recommendations

The results from this study add to the growing knowledge of men with a lifetime history of a PCa diagnosis and their quality of life in Atlantic Canada. This has several important implications. Firstly, this study provides further evidence of poor mental health among men with a lifetime history of a PCa diagnosis in Atlantic Canada. We also addressed important modifiable lifestyle factors that contribute to the association between a lifetime history of a PCa diagnosis and mental health outcomes. These findings highlight the need for further support from multidisciplinary healthcare teams to improve overall

mental wellbeing throughout the cancer continuum, including post-diagnosis. Secondly, this study can be used to further inform patient empowerment programs. For instance, the Prostate Cancer Patient Empowerment Program (PC-PEP) is a holistic program that aims to provide programming to improve the challenges that men with a PCa diagnosis have throughout their PCa journey. Programming from PC-PEP includes support groups, PA regimens, meditation, and other activities. The results from this study can provide further support for current patient empowerment programs and identifies opportunities for improvement, such as how to cope with sleeping problems and education on the harms of substance use. Additionally, these results can also be used to educate men with a lifetime history of a PCa diagnosis on how to improve general mental health through balanced diet, regular PA, meeting sleep recommendations, and the effects of substance use.

Throughout sections 6.2 and 6.3, we have listed recommendations and next steps for future studies for each objective and each modifiable lifestyle factor. The following recommendations pertain to the entire study. Atlantic PATH is a multicenter prospective cohort and is a regional contributor to the CanPath database. As data for this study was derived from the first cycle (2009-2015) of Atlantic PATH study, it is important for future research to re-examine the association between a lifetime history of a PCa diagnosis and mental health outcomes (anxiety and depression) to assess longitudinal changes. We also recommended that findings for this study should be compared to baseline results of other provinces in the CanPath database.

As previously discussed, the Ilie et al. (2020b) study examined prevalence of PCa in Atlantic Canada and examined the association between a lifetime history of a PCa diagnosis and mental health (anxiety and depression). This study compared individuals

with a presence of a lifetime history of a PCa diagnosis to individuals without a cancer diagnosis and to individuals with other types of cancer diagnoses. Future research using our study's data should re-examine the contribution of modifiable lifestyle factors on the association between a lifetime history of a PCa diagnosis and mental health outcomes (anxiety and depression) and include additional comparison groups, such as individuals with a history of another cancer diagnosis excluding PCa.

In reference to objective two, three studies included several modifiable lifestyle factors simultaneously in their models. Blanchard et al. (2004) include PA, diet and smoking; Stranges et al. (2014) included smoking, alcohol and diet; and Bock et al. (2017) included smoking, drinking and PA. We recommend that future studies should examine the contribution of multiple modifiable lifestyle factors in one model on the association between a lifetime history of a PCa diagnosis and mental health outcomes (anxiety and depression). Furthermore, this study has provided baseline information on the contribution of modifiable lifestyle factors on the association between a lifetime history of a PCa diagnosis and mental health outcomes. This provides the foundation to study and clarify causal pathways on the role and contribution of modifiable lifestyle factors and mental health outcomes among men with a lifetime history of a PCa diagnosis.

The results from this study also indicate possible mediating, moderating, and suppressor variables. The contribution of PA and smoking resulted in a change between the association of a lifetime history of a PCa diagnosis and depression from significant to non-significant. These findings suggest that PA and smoking may be possible mediating or moderating variables. Additionally, the contribution of diet, PA, sleep and smoking resulted in a change between the association of a lifetime history of a PCa diagnosis and

anxiety from non-significant to significant. This change indicates that diet, PA, sleep and smoking may be possible suppressor variables. We recommend future studies conduct further statistical analyses to determine if the mentioned variables are mediating, moderating, or suppressing the association between a lifetime history of a PCa diagnosis and depression and anxiety.

This study has provided several important implications for clinicians. Our study observed a significant association between a lifetime history of a PCa diagnosis and screening positive for current depressive symptoms but not for anxiety symptoms. A possible explanation as to why depression emerged may be due to the type of treatment modality selected and the side effects on individual experiences. For instance, if participants are experiencing severe side effects (sexual, urinary and bowel dysfunction) due to treatment modality selection, the changes in quality of life may be more disruptive to mental health. Additionally, the average survivorship time in this population was 4.5 years and it is possible that participants are no longer experiencing anxiety regarding concerns of a PCa diagnosis and possible relapse. Future studies should examine causation on the association between a lifetime history of a PCa diagnosis and mental health outcomes to further clarify these results. Knowledge gained from this work and future research may inform clinicians on interventions that can address specific male coping behaviours and can ensure stronger emotional supports are delivered to fully meet the needs of men with a lifetime history of a PCa diagnosis.

6.7 Conclusion

In conclusion, data from this propensity-score matched sample of men in Atlantic Canada indicated that those with a lifetime history of a PCa diagnosis have higher odds of

screening positive for current depressive symptoms compared to men without a lifetime history of a PCa diagnosis. These findings were not significant when initially examining the association between a lifetime history of a PCa diagnosis and current anxiety symptoms. Our results identified important modifiable lifestyle factors that contributed to our main investigation. We also identified that there is no statistically significant association between treatment modalities and mental health among men with a lifetime history of a PCa diagnosis. This research can have implications related to care of PCa survivors, by informing new interventions and care plans that acknowledge and address mental health concerns among these men with a lifetime history of a PCa diagnosis.

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Appendix A

Table 8 Complex Logistic Regression analysis using cluster variance estimators to predict depression symptoms by lifetime history of a PCa diagnosis among men residing in Atlantic Canada from the baseline cycle of the Atlantic PATH database (2009-2015). Adjusted odds ratios were controlled for by age, ethnicity, education, income, marital status, region, working status, and multimorbidity.

		No depression vs. mild, moderate, moderately severe or severe depressive symptoms
		n=338[a]
		OR (95% CI)
Model		**$X^2(15)=41.85$*** **
Lifetime History of PCa Diagnosis		
Yes		2.05 (1.12, 3.78)*
	aOR	2.39 (0.94, 6.08)*
No		1.0 Reference
Age		0.97 (0.93, 1.01)
Ethnicity		
Non-White		0.72 (0.11, 4.58)
White		1.0 Reference
Education		
High School or less		0.84 (0.37, 1.93)
College or trade level		1.29 (0.62, 2.71)
University level or higher		1.0 Reference
Income		
CAD ≤$49,999		2.93 (1.24, 6.93)**
CAD $50,000 – 99,999		1.25 (0.58, 2.71)
CAD ≥$100,000		1.0 Reference
Marital Status		
Non-Married		1.89 (0.84, 4.25)
Married or living with a partner		1.0 Reference
Region		
New Brunswick		0.65 (0.32, 1.33)
Newfoundland and Labrador		0.49 (0.20, 1.21)
Prince Edward Island		1.10 (0.17, 7.16)
Nova Scotia		1.0 Reference
Working Status		
Part time		1.58 (0.52, 4.82)
Unemployed/Sick		1.37 (0.32, 5.82)
Retired		0.34 (0.13, 0.88)*
Full time		1.0 Reference

		OR (95% CI)
Multimorbidity		
	Yes	1.69 (0.78, 3.66)
	No	1.0 Reference

Notes:
X^2 Wald Chi-square value
* significant at $p<0.05$
** significant at $p<0.01$
*** significant at $p<0.001$