IDENTIFYING FRAILTY IN CANCER SURVIVORS: PATTERNS OF CANCER FOLLOW-UP CARE AND IMPLICATIONS FOR PERSONALIZED SURVIVORSHIP MODELS

by

Sarah Marie Murnaghan

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Dalhousie University is located in Mi'kma'ki,
the ancestral and unceded territory of the Mi'kmaq.
We are all Treaty people.

Dedication

For the patients and families who touched my heart and opened my eyes to the reasons we need to strive for better.

For grammie and grampy Dickieson, my love for you both lit fire to a larger passion.

Also, for my little brother–the future is bright.

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Abstract

Improved cancer care has increased the number of survivors, straining Canada's cancer care system. As survivors age, they may become frail, resulting in complex needs better addressed through alternative care models. No research has examined health services use in frail cancer survivors or quantified frailty within a Canadian cancer survivor population.

This thesis estimated the burden of frailty amongst Nova Scotia cancer survivors diagnosed with stage I-III breast, colorectal, gynecologic, or prostate cancer between Jan 2006-Dec 2013, from the provincial Cancer Registry (n=10,176). Then, it characterized differences in survivors' patterns of follow-up care by frailty and other characteristics.

The prevalence of frailty amongst the survivor population was 17.7%. Compared to non-frail cancer survivors, frail survivors had 58% greater odds of having a high (versus low-medium) proportion of primary care provider visits (Odds Ratio 1.58, 95% CI 1.43-1.76). Future research should investigate how primary care models can best support frail survivors.

List of Abbreviations and Symbols Used

ADLs	Activities of Daily Living
AIC	Akaike's Information Criteria
APN	Advanced Practice Nurse
AYA	Adolescents and Young Adults with Cancer
AB	Alberta
BIC	Bayesian Information Criteria
BMI	Body Mass Index
BC	British Columbia
CIHI DAD	Canadian Institute for Health Information Discharge Abstracts Database
CA	Census Agglomeration
PCCF+	Census-Based Small Area Data/Postal Code Conversion File
CMA	Census Metropolitan Area
CFS	Clinical Frailty Scale
MIZ	CMA/CA Influenced Zone
CI	Confidence Interval
EFS	Edmonton Frail Scale
FRAIL	Fatigue, Resistance, Ambulation, Illness, Loss of weight (a measurement of frailty)
GLM	Generalized Linear Modelling
HR	Hazard Ratio
HDNS	Health Data Nova Scotia
IOM	Institute of Medicine

IPR	Insured Patient Registry
IQR	Interquartile Range
IRR	Incidence Rate Ratio
ICD-9/10	International Classification of Diseases, Ninth and Tenth Revisions
LPR	Licensed Provider Registry
LR	Likelihood-Ratio test
MB	Manitoba
MSI	Medical Service Insurance
NS	Nova Scotia
NSCR	Nova Scotia Cancer Registry
NSH	Nova Scotia Health
OR	Odds Ratio
OPIS	Oncology Patient Information System
ON	Ontario
ICES	Ontario's Institute for Clinical Evaluative Sciences
PCP	Primary care provider (in the context of this study, PCP refers to either a family physician, general, or community medicine practitioner)
QC	Quebec
REB	Research Ethics Board
SES	Socioeconomic status
SD	Standard Deviation
SACtype	Statistical Area Classification

TCPS 2	Tri-Council Policy Statement Ethical Conduct for Research Involving Humans
US	United States
Nd= λR	Little's Law
χ^2	Chi-squared

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Chapter 1: Introduction

Improved cancer screening and treatments have contributed to increased cancer survival (1). The aging population is a driving force for increased cancer incidence (2,3). Of those newly diagnosed, about 65% will become long-term survivors (3,4). Many cancer survivors experience lingering health issues due to their cancer and/or its treatment and require ongoing follow-up care (5). The Institute of Medicine (IOM) recommends cancer survivors receive follow-up care appointments with their health care provider to monitor for cancer recurrence and address the late and long-term effects of cancer treatment (6,7). Follow-up care in Canada has been largely oncologist-led despite evidence that alternative models of follow-up care (e.g., primary care-led, shared-care, or nurse-led) are safe and effective (8–11). Evidence for alternative care models largely comes from studies amongst survivors of breast, colorectal, or prostate cancer (8,9,12). There is a lack of evidence and consensus, particularly for survivors of other (e.g., gynecologic) and/or rare cancers (e.g., esophageal, soft tissue) regarding the appropriate follow-up pathway. Current cancer systems struggle to meet the increased demand for cancer services and deliver optimal care for newly diagnosed cancer patients and survivors (13).

Survivorship care is becoming increasingly complex as survivors are living longer, often have comorbid illness, and experience lingering health effects from cancer and its treatment. As Canada's population ages, frailty will become more common – both in the general population and in those who have survived cancer. Frailty is a vulnerable health state that leaves individuals susceptible to adverse health outcomes and reduced physical resiliency (14). Frail cancer survivors may have higher or more complex needs after

cancer treatment. Studied outside of cancer care, research has shown that health care often inadequately addresses the needs of frail people. Further, alternative care models (e.g., multidisciplinary) in other areas of care have enhanced the care of frail people (15,16).

Current data suggests our traditional models of follow-up care are not working for many survivors: cancer survivors are using more health care resources, yet there is no evidence that their needs are any better met (17,18). The current system must change as it neither meets survivors' needs nor is sustainable from a health system perspective (1). Alternative follow-up care models have been studied, prompting a recent shift to more personalized models of follow-up care. Personalized models consider the heterogeneity amongst cancer survivors by identifying subgroups best served by primary care and others that require ongoing care by their oncology teams (5,6,19,20). Thus, work must be done to better understand survivors' needs and design follow-up care models tailored to those needs. To our knowledge, no research has examined health services utilization in frail cancer survivors or studied the prevalence of frailty within a Canadian cancer survivor population.

This thesis builds upon the body of research aimed at designing more personalized models of care for cancer survivors. Chapter 2 begins with a review of the literature on cancer survivorship and frailty and concludes by identifying the knowledge gap and rationale of this thesis. Chapter 3 describes this study's objectives. The study had two main objectives. The first focused on frailty, and the second focused on health care

utilization. The two overarching objectives were first, to estimate the burden of frailty amongst NS cancer survivors and determine how frailty differs by survivor characteristics. Secondly, to identify patterns of cancer-related follow-up visits and how they differ between non-frail and frail cancer survivors, and patient characteristics.

Chapter 4 describes the methods used in this retrospective analysis of a population-based cohort. This research used a linked administrative dataset containing all those in Nova Scotia (NS) diagnosed with stage I-III breast, colorectal, gynecologic, or prostate cancer between January 01, 2006, and December 31, 2013 (n=20,901). The cohort was identified from the Nova Scotia Cancer Registry (NSCR) and linked, at the patient level, to various Health Data Nova Scotia (HDNS) databases. A survivorship cohort was identified (n=10,176). The follow-up period began 366 days after the index cancer diagnosis (i.e., the cancer diagnosed between 2006-2013) and ended on December 31, 2018. Frailty was assessed using decision rules to identify frail persons from two administrative health databases: Canadian Institute for Health Information Discharge Abstracts Database (CIHI DAD) and Medical Service Insurance (MSI) Physician Billings (14,21). The prevalence of frailty within the survivor cohort was determined. Descriptive statistics compared frail and non-frail cancer survivor characteristics. Logistic regression was used to describe variation in frailty prevalence by patient characteristics. For the study's second objective we described patterns of cancer survivor follow-up care (i.e., visit amounts and to whom) and differences between characteristics (i.e., clinical, demographic, and other characteristics). For example, we used numbers and percentages to detail visits by provider type (i.e., total, primary care, oncology, surgery) and amount. Negative binomial

regression was used to model the annual rate of all cancer-related physician visits during follow-up. Ordinal logistic regression was used to describe the proportion of all follow-up visits that were provided by primary care providers (PCPs) and how this differed by frailty and patient characteristics.

Chapter 5 includes the results of the study's analyses. Chapter 6 discusses the context of the study's results, their relation to the current body of literature, the study's strengths, limitations, and future implications. This research addresses an important gap in our understanding of health care use by a vulnerable segment of cancer survivors, which has not yet been studied, and thereby lays a foundation for designing more personalized models of follow-up care. Such knowledge provides a basis for future studies to design and test models of care to meet this subpopulation's needs best.

Chapter 2: Background

2.1 Cancer Incidence and Survivorship

Cancer broadly describes a group of diseases caused by an uncontrolled division of abnormal cells in the body. Cancer can originate in nearly any part of the human body. Cancers are generally referred to by their primary site (e.g., breast, prostate, etc.). Cancer has the propensity to affect many Canadians' lives: one in two Canadians will develop cancer at some point in their lifetime. In 2022, it was expected that 233,900 Canadians were newly diagnosed with cancer (22).

Many risk factors (e.g., age, alcohol consumption, diet, exposure to toxic substances, chronic inflammation, obesity, and tobacco use) contribute to cancer development, and these can vary by cancer (disease) site (23). When adjusted for age and population size, cancer risk has decreased (24). However, driven by the aging population and improved screening, incident cancer cases in the United States (US) are expected to rise to 79% by 2032 (13). Similarly, in Canada, given the growing and aging population, the number of cancer cases continues to increase (22). Age is a non-modifiable risk factor, meaning that health service planners and researchers should pay attention to its impact on cancer incidence as long as life expectancy increases.

From a global perspective, Canada is fortunate to have access to effective screening (e.g., colorectal cancer screening [fecal occult blood or fecal immunochemical testing for average-risk asymptomatic adults 50-74 years every two years], cervical cancer screening [papanicolau testing every three years for sexually active women aged 25-69 years] (25),

and cancer treatments (e.g., immune checkpoint inhibitors) that foster an increased life expectancy and increase cancer survival in its population (7). Canada is a leader in population-based cancer survival (26). Over the past 20 years, cancer survival has improved for most cancers (24). In the 1940s, only 25% of Canadians survived their cancer diagnoses; in 2019, the number of Canadians expected to survive long-term was 63% (3). Traditionally, cancer was considered a death sentence. Today, due to advanced treatments and improved screening, many experts believe patients treated for some types of cancers should be managed as having a chronic disease (27).

What is a cancer survivor? There are various definitions of cancer survivorship. Some consider survivorship to begin upon initial diagnosis, while others consider it to be when there are no more signs of cancer following treatment completion (7,28). Researchers use different definitions to commence monitoring of survivorship, although one-year post-diagnosis is commonly used (29–31). A long-term survivor of cancer is considered an individual five years post-diagnosis (32). Surveillance data on cancer survival in Canada are commonly presented as five-year or 10-year net survival (3,24).

This study examined cancer sites of particularly high survival, including breast, prostate, colorectal, and gynecologic cancers. There is variation in survival by cancer site. Cancers with the highest five- and 10-year net survival include thyroid, testis, and prostate (3,24). Breast, prostate, and colorectal cancer survivors combined constitute nearly half of all cancer survivors (7). The five-year net survival probabilities for breast and prostate are 80% or more, colorectal is between 50-79%, and gynecologic ranges from less than 50%

(ovarian), to between 50-79% (cervical), up to greater than 80% (uterine) (3,24). Considering their survival probabilities, it is a priority to understand and optimize the quality of life after cancer treatment in these populations (24).

After completing cancer treatment, many people describe living in a new normal versus returning to their pre-diagnosis normal. This is mainly due to the late and long-term physical and emotional effects of cancer and its treatment (33). Late effects are consequences of prior cancer treatment that manifest weeks, months (e.g., lymphoedema after axillary node removal, neuropathy after chemotherapy), or years after treatments are complete (e.g., heart disease following radiotherapy to the chest, bone loss or lung problems after chemotherapy and radiation) (7,20,34). Long-term effects include cancer therapy side effects that begin during treatment and continue after treatment completion. Many survivors live well beyond the end of treatment; therefore, late and long-term effects can significantly impact their life after cancer treatment. As a result of more complex cancer treatment combinations, late and long-term effects are becoming more common. Further, survivors may worry about the risk of secondary cancers post-treatment (e.g., breast cancer following radiotherapy for Hodgkin's lymphoma) (35). Cancer screening, diagnosis, and therapy differ by cancer site, and thus the aftermath of cancer depends on cancer site and treatment type. There are physical (e.g., fatigue, chronic pain), emotional (e.g., fear of cancer recurrence, depression, challenges in one's relationships), and practical (e.g., paying for medical bills, return to work) concerns (7). Cancer and its survival can shift relationship dynamics. Some individuals report closer intimate relationships, though this is not the case for all (36,37). The former concern

applies to both spousal relations and other family bonds, such as that between parents and adult children (38). To further describe some physical concerns, survivors may experience late effect changes in cardiovascular, endocrine, lymphatic, gastrointestinal, genitourinary, nervous, hematologic, hepatic, immune, pulmonary, or renal organ systems (7). As a result of these late and long-term effects, cancer survivors are at significant risk for morbidity, diminished quality of life, and premature mortality (5). Each survivor's challenges are uniquely influenced by their stage at diagnosis, treatment, age, genetic factors, comorbidities, and social circumstances (20). Ongoing monitoring is needed to investigate cancer recurrence and address late and long-term effects and their ramifications. This is recognized as follow-up care. The IOM strongly recommends lifelong health care for all survivors following the increased evidence of the late effects of cancer (6).

2.1.1 Guidelines for Follow-up Care

International, national, and provincial recommendations exist to guide follow-up care. Not every Canadian province has published follow-up care guidelines. NS has follow-up surveillance guidelines for breast, pancreatic, colon, and rectal cancers, which endorse follow-up by the PCP, where appropriate in partnership with the surgeon, and encourage active patient engagement in follow-up (39). Other examples include those published by the National Comprehensive Cancer Network (40–49), the American Society of Clinical Oncology (50–54), Alberta Health Services (55–67), Cancer Care Ontario (68–75), and Saskatchewan Cancer Agency (76–83) (Appendix A). Recommendations are unique to each type of cancer in terms of follow-up screening tests, examinations, and the

frequency of follow-up visits. There are also guidelines for special services, such as psychosocial oncology services (68). However, there are common elements all follow-up care should address, including preventing and managing post-treatment late and long-term effects, screening for recurrence and new primary cancers, managing non-cancer-related pre-existing chronic conditions, and addressing a survivor's preventative health needs (7,31). Follow-up care (i.e., visits) examined in the context of this study were defined as cancer-related oncology, surgery, and PCP follow-up; therefore, visits of non-cancer-related nature were excluded. The description of late and long-term effects is relatively new; thus, survivor follow-up care has primarily focused on screening for new primary cancers and monitoring for recurrence (7).

Despite guidelines, differences in follow-up care practice remain. For example, breast cancer survivors in NS have greater surgeon follow-up, while their British Columbia (BC) counterparts have greater primary care follow-up (30). Patterns of health care utilization in survivors across the country have revealed inconsistencies in care; this is likely related to the current models of cancer follow-up care (30,84–86). Health care settings and providers are important components of follow-up guidelines and play a meaningful role in the patient survivorship experience (87). Models of follow-up care (i.e., structure and delivery of follow-up care) are important for the appropriate implementation of survivorship guidelines.

2.1.2 Current Models of Cancer Survivor Follow-up Care

Existing cancer care systems were not designed or resourced considering the needs of the growing population of survivors. There are now more cancer survivors than ever before (29). The increased demand has strained the current cancer care system. In addition to treating active cancer cases, oncologists are treating survivors with late and long-term effects of cancer. As the number of cancer survivors grows, it is increasingly vital to re-evaluate cancer care organization and delivery. The traditional survivorship follow-up care model in Canada has seen patients followed by oncologists. This thesis used the overarching terms oncology and oncologist to refer to both the area of practice and practitioners, encompassing medical oncology and radiation oncology. It will be difficult, not to mention costly, for the current system to continue as is. The cost of having patients see specialists such as oncologists rather than PCPs tends to be higher (5,29). Cancer care spending is rising; in Canada, costs rose from 2.9 billion in 2005 to 7.5 billion in 2012 (88). de Oliveira et al. (2018) described this increase in cost as largely due to hospital-based care of cancer patients, including the receipt of chemotherapy and radiation. They included cancer clinic care and rehabilitation under the umbrella of hospital-based care; both of these sub-category costs also increased over the study period (88). Given the increasing cancer incidence and survival, these costs are likely to continue trending upward.

A 2018 study on medical oncologist workload in high-income countries surveyed 58 Canadian oncologists. They found the Canadian median workload per medical oncologist (175 new consults per year) aligned with Cancer Care Ontario's recommended upper

limit (160-175 new consults per year). In contrast, the median number of new patients per medical oncologist reported in other high-income countries was 125 per annum. Further, Canadian medical oncologists spent more time with each patient per day than their high-income country counterparts (89). It is crucial to consider the potential for employee burnout in oncology practitioners and its impacts on both providers and patients (90).

Efforts have been made within Canada to shift the practice of routine follow-up care to PCPs. Although, there is confusion amongst providers regarding the roles and responsibilities of follow-up care. The role of the PCP in follow-up care has been ill-defined and largely informal (91). In 2015, Choosing Wisely, a national initiative to encourage the reduction of unnecessary tests and treatments, identified the provision of follow-up care in high-cost cancer centres as one of 10 tests/treatments in cancer care not supported by evidence (92). The evidence supporting this change in practice comes from randomized controlled trials that demonstrated follow-up care by PCPs was safe, effective, and equivalent to oncologist-led follow-up care (8–10). Informed by this literature, Cancer Care Ontario created cancer survivorship guidelines for follow-up models of care. In 2017, they released a guideline stating discharge from oncologist-led care to PCP-led care was deemed a reasonable option for breast and colorectal survivors based on evidence and for prostate survivors based on the expert opinion of its similar disease trajectory to the former cancer sites (75). Their 2019 updated guideline recommended the implementation of transfer from specialist to PCP care be focused on breast and colorectal cancer site groups, with expansion to other cancer sites over time (74). In the context of this research, there is a notable lack of evidence for follow-up care

by PCPs in gynecologic survivors. However, guidelines commonly cite five years of recurrence-free follow-up as a marker for transition to PCP follow-up for some types of cervical, endometrial, and vulvar gynecologic cancer survivors (71,72,79,80,82). Studies that examined follow-up care utilization in Canada showed that despite this evidence and PCPs' expressed interest in providing follow-up care (8,10,93), utilization patterns are varied, and survivor needs are still not met (29–31,94–96).

There are at least three influential contextual points to consider upon reviewing the literature on current patterns of follow-up care; these include cancer site, study province, and provider specialty. Cancer sites examined in published studies on patterns of health care utilization in survivors within Canada include colorectal (31,94,97), breast (30,95), Hodgkin Lymphoma (98), as well as one study multi-site investigation including breast, gynecologic, prostate, and colorectal (29). The majority of the studies that examine follow-up care were done in Ontario (ON) (30,95,98–100), two included Manitoba (MB) and BC, and four were done in NS (29–31,101). Three of these focused primarily on screening/preventative measures in follow-up care (94,99,101). The evidence shows a variation in PCP use across provinces for follow-up care (100). Discharge from the oncology clinic to primary care can vary by oncology provider (29). A cohort study of colorectal cancer survivors in NS found that almost 60% of survivors continued to receive follow-up care appointments with their oncologist four years post-diagnosis. The majority of survivors engaged in follow-up visits to multiple specialist physicians (31). Hodgson et al. (2010) found that most patients had visits with both a PCP and an oncologist in years two through five after their Hodgkin's Lymphoma diagnosis. Though

many physician visits were noted, screening recommendations were not widely met (96). Similarly, a cohort study done in ON by Grunfeld et al. (2010) found that most survivors received follow-up care from their oncologist and PCP (95). Further, Kendell et al. (2017) examined physician services use across BC, MB, ON, and NS, and found that during the follow-up period (one to five years post-diagnosis) across all provinces, 65-93% of breast cancer survivors received follow-up from both oncologists and PCPs (30). Interprovincial variations were observed, with greater surgeon follow-up in NS, greater PCP follow-up in BC, and greater medical oncologist follow-up in MB (30). Overall, these results point to a lack of change from specialist to PCP-led follow-up survivor care.

There are multiple reasons why care patterns vary by provider type (i.e., PCP, oncologist, surgeon), amongst provinces, and cancer sites. Different provincial policies, initiatives, recommendations, and resources to support PCP-led follow-up care may account for some of the variation (30). Oncologists may be skeptical of PCPs' ability to provide cancer follow-up care (102,103). Additionally, PCPs may lack confidence, support, or education and feel overwhelmed by their patient load. It may also be difficult for the oncologist to transfer care back to the PCP following treatment completion after forming a therapeutic relationship (104,105). Patient preference plays a role as well. A 2017 study of prostate and melanoma cancer survivors in the Netherlands found survivors more likely to prefer a specialist (such as an oncologist) were women, older, or lower/intermediately educated. Preference for follow-up care provider (specialist versus PCP) also varies based on PCP satisfaction (106). Health visits of cancer survivors may relate to specific cancer concerns, residual mental health effects, and other chronic

conditions. It is possible that for patients with varying concerns, seeing a specialist (i.e., surgeon or oncologist) alone for follow-up does not meet all their health care needs; therefore, they also seek PCP care. Another hurdle is the lack of primary care in provinces across Canada. Adding more responsibilities to an already busy field (i.e., primary care) may impede change (107). Furthermore, some studies done amidst the efforts for change in practice may lag in capturing the actual change in practice to date (29).

2.2 Aging and Frailty

The primary risk factor for cancer is age, and thus, older people make up the majority of people who get cancer. Of all diagnosed cancers, 9 in 10 will occur in Canadians aged 50 years and older (3,24). The aging population is of particular importance for the future of cancer care, as the fastest-growing age group in Canada is those aged 65 years and above (3,24). The proportion of Canadians over the age of 65 is expected to reach 25% in 2036 (108). Paralleling this trend, the incidence of cancer is expected to rise into the 2030s. As previously described, our aging population contributes to cancer's growing burden and increased need for cancer-related services. With more and older survivors, when planning to sustain cancer care services, this population's needs must be considered and understood.

Older people tend to have a greater accumulation of health conditions to be managed. Further, as people grow older, they are more likely to experience frailty (109). Approximately 25% of Canadians over age 65 are frail, increasing to over 50% in those

older than 85 (21). Although there are various definitions of frailty, it may be described as a vulnerable health state resulting from age-related physical (e.g., weakness, muscle wasting, slow gait, decreased endurance), cognitive (e.g., dementia), and/or psychosocial (e.g., decreased autonomy with activities of daily living [ADLs], social isolation) deficits that leaves one susceptible to adverse health outcomes such as falls, hospitalization, and mortality (14,15,110). Consequently, this high risk of acute complications (e.g., infection) often delays functional rehabilitation of adverse outcomes such as disability induced by procedures or hospitalization, and increases health costs (111). Frailty is common in older individuals and those with multiple chronic conditions, but it does not require either to exist (14). Frailty may be a precursor for developing other chronic diseases, or in turn, chronic conditions may contribute to frailty (111). In contrast to terms such as comorbidity or disability, frailty has distinct implications related to health needs. As frailty includes multi-system health issues present in one person, their care and needs are increasingly complex, and their care often requires coordination amongst several providers. Frequent, intense medical monitoring to prevent acute fluctuations in health status amongst frail patients may promote more effective rehabilitation and improve prognosis (111). However, the literature on frailty within cancer survivor care is limited.

2.3 Measures of Frailty

How should frailty be measured? There are many approaches to measuring frailty. Although there is no gold standard for frailty assessment, two prominent theories that

guide frailty measurement are the phenotypic approach and the deficit accumulation approach (112).

2.3.1 Phenotypic Approach to Frailty

The phenotypic approach to frailty is a widely recognized measure of frailty in both clinical and research settings. Its criteria include grip strength, weight loss, exhaustion, walking speed, and physical activity (113). Individuals are frail if they have poor performance in any three or more criteria; those that meet two are prefrail, and those that do not perform poorly in any are non-frail. The original measurement criteria proposed by Fried et al. (2001) have evolved (114). A systematic review conducted in 2015 identified 262 variations of the frailty phenotype criteria (113). Prevalence of frailty amongst the various phenotype classifications ranged from 12.7-28.2%. Studies that use this approach are therefore limited in their comparability. Its generalizability outside of an older adult population is also limited. There are advantages of the physiologic assessment measurements used in this approach, and there are methods for mitigation of missing criterion information; however, its application to administrative data studies is limited, as the majority of administrative data do not provide the information to apply the criteria appropriately (113).

2.3.2 The Deficits Accumulation Approach to Frailty and the Frailty Index

The deficit accumulation approach focuses on the number of health deficits rather than their characteristics. Deficits may include diseases, signs, symptoms, social issues, and disabilities that collectively influence organ systems (115). This approach suggests that as

one accumulates many health deficits, slowly over time, they become frailer and are at greater risk for adverse health outcomes. It can be understood from a stochastic stance. This means there is a relationship between the number of deficits (Nd), degree of environmental stressors *(λ)*, and the ability to recover (R), written as Nd= λR (Little's Law). In one person's lifetime, generally, the trajectory of one's environmental stressors and recovery is irregular. Though, on a population level, frailty trajectories are regular and show on average an increase in the frailty index by 10-fold between the age of 20-90 years. This increase is explained by Little's Law, as environmental stress is said to be held relatively constant; thus, it is the recovery time that changes over time (115).

The deficit accumulation approach is applied through the frailty index. The number of health deficits one has, divided by the number of deficits considered, determines the frailty index. It is a score on a continuous scale from zero to one. The higher the index number, the frailer or more vulnerable to adverse health outcomes, one is (115).

The frailty index allows for variations in indices depending on what deficit data are available. Searle et al. (2008) outlined a standard procedure to create a frailty index from an existing health/aging dataset (112). None of the samples that have operationalized the frailty index have used the same deficits. Regardless, the relationship between deficit accumulation and mortality remains similar (112). This reinforces frailty as a real phenomenon and "a property of a biologically complex system" (71 p.1472). It supports that frailty can be measured in various ways and within existing datasets that might not have initially set out to measure frailty. Examples of deficit variables used in this method

include help with ADLs, self-rated health, mini-mental exam scores, body mass index (BMI), grip strength, or diagnoses such as heart attack, stroke, or diabetes (112). For the frailty index to achieve a reliable estimate of frailty, it should include a minimum of 20 and a suggested amount of 30 deficits. The deficits needed to create a frailty index are not always available in administrative data (14).

The phenotypic approach and the deficit accumulation approach aid our understanding of frailty. These algorithms to identify frailty do not work for many administrative databases. This is because some types of data, such as clinical assessment data, are not routinely found in population-based, administrative health databases (112,113,115). Some individuals may also obtain the health data needed to create a frailty index by using databases that contain International Resident Assessment Instrument data. However, these data are not gathered or accessible consistently across Canada (14,116,117). As research expands to measure frailty in other populations, such as cancer survivors, and in the context of health services research, more user-friendly measures for use in administrative data are required.

2.3.3 Rules to Identify Frailty in Administrative Data

Urquhart et al. (2017) addressed this concern by creating rules to identify frailty in administrative data (14). Before developing these rules, only one known algorithm existed to identify frail individuals within population-based administrative data (14). The earlier algorithm examined diagnostic codes from causes of death cited in death certificates (118). The weakness of the prior method is that it does not capture the

complexity of the concept of frailty because it only looks at the specific diagnoses cited on death certificates and includes medical conditions that may not adequately represent frailty (14,118). Further, its use is limited to those who are deceased (14).

While there are many clinical practice tools to screen for frailty, to gain information about frailty on a population level, frailty identification in administrative data is essential. Administrative health databases provide robust, efficient measures of population-based quality of care (119,120). Thus, the ability to identify frail individuals on a population level through administrative data allows researchers and policymakers to efficiently monitor health care utilization across the country, which may help better inform program and policy solutions to address the consequences of frailty (14).

The rules to identify frailty in administrative data create a more comprehensive approach to identify frailty in population-based administrative databases that may be applied to both those living and deceased and be used in a wide variety of settings. The advantage of these rules to identify frailty is that they consider multiple conditions that contribute to frailty, as does the deficit approach, and they can be measured and applied in most administrative health databases (14).

The rules used two sources of administrative data: hospital discharge abstracts (i.e., CIHI DAD) and physicians' claims (i.e., MSI). This method considers the concept of frailty in the context of prior frailty research and expert (geriatrician) consultation (121,122). There are three primary rules to identify frailty. One, the person is considered frail if they

are a long-term care resident. Two, the person is considered frail if they receive palliative care. Three, the person is considered frail if they meet at least two or more domain criteria (cognitive, general health status, incontinence, falls, nutritional issues, functional performance, or targeted health service utilization). Domains are derived from diagnostic codes associated with clinical frailty scales (the Edmonton Frail Scale [EFS] and the Clinical Frailty Scale [CFS]), including service utilization and several suggested events (e.g., falls, incontinence) (14,118,121,122).

These rules were created by the thesis supervisor, are published, and are being used by teams across the country, including Ontario's Institute for Clinical Evaluative Sciences (ICES), to identify frail persons in administrative databases (14,21). To date, at least three studies have been published utilizing the rules (123–125). Urquhart et al. (2017) determined that 5.1-14.7% of living persons aged 65 years and older in their study were frail, varying between provinces (BC, AB, ON, Quebec [QC], and NS) (14). This is comparable to previous literature. For example, studies using the phenotypic approach in a similar age demographic, including community-dwelling persons aged 65 years and older, estimated the prevalence of frailty ranged from 4.0-17.0% (14,126). The rules to identify frailty were used in Canada's first study to examine care for older adults with frailty using administrative data (14,21). The cohort included older persons with frailty in BC, AB, ON, QC, and NS. The study demonstrated the feasibility of using the rules to identify frailty in administrative health data across five Canadian provinces. This thesis used the rules developed by Urquhart et al. (2017) as they allow the use of administrative data, fitting for the study's focus on the health services perspective. The

rules to identify frailty are further described in the methods section of this thesis (Chapter 4).

2.4 Identifying Frailty in Non-cancer Survivor Populations/Areas of Health Care

In other (non-cancer specific) areas of care within Canada, frail people often do not receive care that meets their needs (15,16,127,128). There is a need to identify those with frailty, formulate health systems that address their needs, and pay particular attention to their care delivery. Frail individuals have complex care needs that require a unique approach to care delivery (15,16).

In 2016, Giguere et al. conducted a scoping review that described the state of health care delivery and utilization of frail individuals within Canada. They included studies of various methods ranging from qualitative inquiry to randomized trials (127). It concluded with an urgency to restructure care delivery to address the complex health issues faced by frail people appropriately. As older adults use a disproportionate amount of hospital services, their health care costs tend to be high. Reducing these costs is certainly an area of interest for decision-makers. Specifically, within NS, provincial health system decision-makers and health care providers voiced the need for improvement in information sharing, care planning, and, primarily, delivery of care. Canada has been working to improve resources and services to meet the needs of frail older adults; however, coordination of services remains a struggle and impacts both accessibility and efficiency of care (127).

Subsequently, Giguere et al. (2018) explored key stakeholders' views on the quality of care and services available to frail seniors in five Canadian provinces (BC, AB, ON, QC, NS) (15). This qualitative study examined the views of 42 frail older adults, caregivers, and administrative personnel. Stakeholders in frailty care voiced the need for more inclusion of patients and families in care planning, and more integration of care and services across settings, over time, and between providers, to meet frail seniors' needs (15). Given the number and variety of providers that may care for a frail individual, models of care are of interest. Prior research has shown outside of cancer care, that the complexity of frail peoples' needs is often best addressed within multidisciplinary teams (129). Finally, Giguere et al. (2018) called for systematic identification of frail older people to adapt health care systems to the population's needs (15).

Within the context of cancer care, studies have been conducted exploring the prevalence of frailty within newly diagnosed cancer patients and/or those receiving active treatment. Handforth et al. (2015) conducted a systematic review, establishing the prevalence of frailty and prefrailty amongst older cancer patients. With data from 20 observational studies (n=2,916), they found a median prevalence of frailty of 42%, ranging from six to 86%, and a median prevalence of prefrailty of 43%, ranging from 13-79%. Furthermore, treatment complications were more common in frail participants, including intolerance to cancer treatment (adjusted odds ratio [OR] 4.86, 95% confidence interval [CI] 2.19-10.78) and postoperative complications (adjusted 30-day hazard ratio [HR] 3.19, 95% CI 1.68-6.04) (130).

2.5 Identifying Frailty in Cancer Survivors

Frailty within the cancer survivor population is an important area for health services research as many cancer survivors are older, have comorbid conditions, and long-term health issues from their cancer treatment(s). Understanding the prevalence of frailty in cancer survivors would help discern and plan care delivery to improve the burdened cancer care system's efficiency.

The literature examining frailty in cancer survivors has grown in the last five years, yet gaps remain. A recent review published by Ness et al. (2020) discussed the prevalence of frailty in various cancer survivor populations (131). Twenty-three studies were included in the review. However, as the review also aimed to describe how frailty at diagnosis impacts cancer outcomes, some studies in the review assessed frailty status only at cancer diagnosis (131). To our knowledge, there are no studies that examine frailty in cancer survivors using solely administrative data or that estimate the prevalence of frailty amongst a Canadian cancer survivor population.

While a limited number of studies have been conducted on frailty in cancer survivors, two relevant observational studies that used self-reported survey data should be further examined. The first, a US prospective cohort study by Brown et al. (2015), quantified the prognostic value of prefrailty and frailty in an older adult non-skin-related cancer survivor population (132). They used data from the Third National Health and Nutrition Examination Survey to identify frailty using the following criteria: low BMI, slow walking speed, weakness, exhaustion, and low physical activity. Data were linked to the

National Death Index for assessment of the primary outcome, all-cause mortality. Prefrail cancer survivors (HR 1.84, 95% CI 1.28-2.65, p=0.001) and frail cancer survivors (HR 2.79, 95% CI 1.34-5.81, p=0.006) had higher risks of premature mortality than those classified as non-frail. In this study, 37.3% of participants were prefrail, and 9.1% were frail. They concluded that identifying prefrailty and frailty in older adult cancer survivors would help target cancer care and improve survival (132).

In another study, Perez-zepeda et al. (2016) examined the association between a history of cancer (i.e., self-reported cancer between 2001 and 2012) and frailty in a group of Mexican older adults (133). The nested case-control study used data from the Mexican Health and Aging Study. A 55-item frailty index was created using self-reported data. Of the 8,022 older adults with a mean age of 70.6 years of age, the prevalence of a past medical history of cancer was 3.6% (n=288). They concluded that cancer was associated with a higher frailty index, with a potentially relevant role of the time elapsed since cancer diagnosis. They found a significant association between cancer history and incident frailty amongst those recently diagnosed (i.e., less than 10 years) (OR 1.53, 95 % CI 1.04-2.26, p=0.03)]. This association remained when adjusted for age, sex, marital status, years in school, at least one negative event in the last 11 years, smoking status, cognitive decline, chemotherapy, surgery, and radiotherapy interaction (OR 1.74, 95 % CI 1.15-2.61, p=0.008). However, a significant inverse relationship was shown between those with a remote diagnosis (i.e., greater than 10 years from initial cancer diagnosis) and worsening frailty, compared to those without a cancer history (OR 0.56, 95 % CI 0.39-0.8, p=0.002); adjusted model (OR 0.61, 95 % CI 0.38-0.99, p=0.046).

The authors suggested that health professionals be aware of these associations to improve outcomes for older adults who have survived cancer. However, the study had at least two major limitations. One was their definition of a cancer survivor. They did not indicate participants' current cancer status or indicate an assessment of recurrence (133). They used cancer history and cancer survivor synonymously, classifying them into two groups: those recently diagnosed (i.e., less than 10 years) and remotely diagnosed (i.e., greater than 10 years from initial diagnosis) (n=8,022). Secondly, their analysis was inappropriate for their described study design, which may have biased their results (133). They used logistic regression, while conditional logistic regression is recommended for a nested-case control design, and did not explain any alternative appropriate analysis techniques (134).

While most studies have looked at frailty in the context of older adult survivors, the literature has also identified frailty amongst adolescents and young adult (AYA) cancer survivors. In their review, Ness and Wogksch (2020) identified eight studies examining frailty within the AYA population (131). One of those studies, a 2018 cross-sectional study conducted in the US, examined frailty in adult cancer survivors aged 15-39 years using the FRAIL (i.e., fatigue, resistance, ambulation, illness, loss of weight) questionnaire. Within their sample (n=271), 184 were at least one-year post-diagnosis. Ten percent were frail, and 21% were prefrail. They concluded a high prevalence of frailty and comorbidities exist among AYA cancer survivors, suggestive of accelerated aging (135). Furthermore, described in the 2020 review by Ness and Wogksch, although the frailty prevalence amongst adult cancer survivors was higher, ranging from 9.1-59%

(often double that of age, sex and race matched populations), the frailty prevalence amongst AYA cancer survivors was also high. Comparable to frailty found in community-dwelling older adults aged 60-80 years, the prevalence of frailty in childhood cancer survivors in their 30s and 40s ranged from 7.9-47% (131).

In addition to age, frailty in cancer survivors is associated with sex, cancer type, treatment, chronic disease, lifestyle, and access to care (131). Female cancer survivors are more likely to be frail than male cancer survivors. Treatment type also plays a role in susceptibility to frailty. Females receiving treatment affecting estrogen and males receiving androgen deprivation therapy are at increased risk. Receiving radiation to the brain, abdomen, and pelvis are also treatment-related risk factors for frailty amongst cancer survivors. Modifiable risk factors for frailty in cancer survivors include smoking, obesity, and a sedentary lifestyle (131).

These studies point to the importance of identifying frailty in cancer survivors, not only in older adults but also in survivors of all ages. However, there is a need for further studies with more robust methods to strengthen the evidence and determine the prevalence of frailty on a population scale using administrative data. Additionally, further studies in this area will expand our understanding of how frailty varies by survivor characteristics.

2.6 Future Models of Care are Personalized

The growing number of survivors, alongside increased constraints on the cancer care system, has prompted research on alternative care models for this population (136). As a new research area, the term 'personalized models of care' has not been well defined. However, it may be thought of as a way to tailor care structures and delivery to specific groups of cancer survivors with unique needs. For example, some survivors may need more specialized follow-up interventions, such as those with certain complications (e.g., lymphedema), or more support from a multidisciplinary team (i.e., physiotherapy, occupational therapy, career counselling, etc.) (6). Some survivors have severe organ dysfunction and/or are at high risk for recurrence or serious late effects (e.g., cardiovascular and pulmonary disease), causing premature mortality. Alternatively, some survivors may have fewer needs or lower risk of complications and thus, may be effectively managed by PCPs. This gradient of survivor concerns may also be influenced by other comorbid health conditions, access to health care, or psychosocial issues (5). Personalized survivor care models are a way to identify and allocate appropriate follow-up care resources to different groups of survivors by streamlining care delivery and organization (6).

Some cancer survivorship care models explored internationally include those based on provider type, cancer site, length of follow-up care, and the survivor's role in recovery (137). Models may be further categorized as nurse-led survivorship care models, risk-based pathways (i.e., stratified resource allocation based on unique survivor needs), rehabilitation-focused care models, and self-management models (137). Eleven

randomized controlled trials identified in a 2012 systematic review compared different follow-up care models; none studied needs- or risk-stratified-based care (138). Recently, the National Cancer Survivorship Initiative highlighted issues that cancer survivors face and expressed the need for care delivery to reflect those specific health concerns appropriately. One priority research area identified was the development of risk stratification tools, though it provided little details on this definition or important outcomes to address (20). Risk-based care and coordination between oncologists and PCPs have been identified as important metrics of quality cancer survivorship care (5).

Risk- and needs-based care models fall under the umbrella of personalized models of care. First, let us understand the meaning of risk- and needs-based models. Risk identification refers to events a survivor is more likely to experience in the future, while needs describe issues that are currently present (20). It is hypothesized that levels of risk may help allocate care delivery. For example, survivors at low risk for future health problems may be transitioned to their PCP soon after completion of therapy. A survivor at moderate risk could be cared for primarily by their PCP, with periodic evaluation by their oncology team. The oncology team may follow survivors at high risk for late effects yearly, such as those treated with a stem-cell transplant (6). In practice, some provinces may follow a variation of this risk-stratification through the use of survivorship clinics.

Additionally, Mittmann et al. (2019) recently found that the transition of a group of low-risk ON breast cancer survivors from oncology to PCP follow-up care was associated with fewer health care costs and similar or better patient outcomes (139). However, there

is no consistent practice or tested model of care to facilitate this transition. The assessment of both risk and need is required in the context of cancer survivorship (20). In contrast to risk, (healthcare) need is the capacity to benefit from health care (20). The level of need is a more immediate burden and consideration for health care resource use. However, the current literature does not distinguish specific items that pertain to risk versus need. Instead, they identify a list of cancer-related physical, psychological and social issues that may warrant both risk and needs assessment, including late and long-term physical effects of treatment, depression, anxiety, and financial and employment concerns (5,20).

Further, it is possible to incorporate risk- and needs-based models into a shared-care approach, as a notable aspect of quality survivorship care is having functional interfaces between each stage on the care continuum (6,137,140,141). However, before delineating and testing such models, further work must be done to identify sub-groups of survivors that require different approaches to care. There is an urgency for reliable ways to systematically assess and identify those unique needs through risk stratification and/or needs identification tools (5,6,20).

A growing body of literature suggests that identifying sub-groups of cancer survivors who require different models of care will reduce the burden on the cancer care system (5,6). Personalized models of care aim to target vulnerable high risk and/or needs patients to adequately address their concerns and create a system wherein the patient flow is improved to allow for quicker and easier access for both those identified as high risk and

those who are relatively healthy (i.e., lower risk) individuals. Ideally, this would reduce care costs by organizing care in a more efficient way (139,142).

Identifying frail cancer survivors within administrative data is one way to build upon this growing body of evidence for more personalized survivorship models. With the increasing aging population and the number of older survivors, this large group of survivors will likely require increasingly complex care. Frail survivors may have both high risk (e.g., mortality) and needs (i.e., related to multiple health problems) (132). Consequently, it is essential to understand how aging and frailty apply to future models and cancer follow-up care interventions. Due to the recent shift to encourage PCP involvement in follow-up care and the known complex needs of frail people in other areas of care, frail cancer survivors may also benefit from alternative care models, such as a shared-care approach.

Further research is needed first to determine the prevalence of frailty in cancer survivors and then examine their follow-up care usage patterns to inform improved health service planning. Understanding the trends in frail survivor follow-up care is imperative to creating future models of care that work for this population because of the complex needs of care in frail individuals. The prevalence of frail cancer survivors in NS has not been quantified, nor has their health services utilization been examined. The proposed study would be the first in Canada, if not worldwide, to do both using administrative data. Identifying frailty within the cancer survivor population is one step in gaining insight to inform future models of cancer follow-up care.

Chapter 3: Objectives

The goal of this thesis project was to build upon the body of research aimed at designing more personalized models of care for cancer survivors by identifying frail cancer survivors in NS as one subpopulation who may have differing and/or unique needs/risks after cancer treatment. Prior research outside of cancer tells us frail people are a special population with unique care needs. Our first step to address this issue in cancer care was to quantify frailty in the population. We then described patterns of follow-up care of cancer survivors to inform future model reform. The study's objectives were:

1. To estimate the burden of frailty amongst a NS cancer survivor cohort and determine how frailty differs by patient characteristics.
    1.1. To estimate the prevalence of frailty amongst a NS cancer survivor cohort and determine how it differs by clinical, demographic, and other characteristics.
    1.2. To identify frail cancer survivors' traits (i.e., demographic, clinical, and other characteristics) that differ from those of non-frail cancer survivors.
    1.3. To determine the underlying attributes (i.e., physical or cognitive impairment and health service utilization markers) for which cancer survivors are deemed frail.
2. To identify patterns of cancer-related follow-up care visits and how they differ between non-frail and frail cancer survivors, by patient characteristics, within a NS cohort.
    2.1. To determine whether frail cancer survivors have greater cancer-related follow-up care use and how this differs by patient characteristics.
    2.2. To identify the percentage of cancer survivors' follow-up visits provided by PCPs and determine how this differs by frailty and other patient characteristics.

Chapter 4: Methods

4.1 Data and Study Population

The study design was descriptive in nature and used data from a retrospective population-based dataset of NS cancer survivors. We used a Research Ethics Board (REB) approved, updated linked administrative dataset from the supervisor's prior work, containing all Nova Scotians diagnosed with invasive breast, colorectal, gynecologic, or prostate cancer between January 01, 2006, and December 31, 2013 (n=20,901). Data from the NSCR were linked, at the patient level, to data obtained from the Oncology Patient Information System (OPIS) and HDNS databases, including MSI Physician Billings, CIHI DAD, Census-Based Small Area Data/Postal Code Conversion File (PCCF+), the Licensed Provider Registry (LPR), and the Insured Patient Registry (IPR). These data provided information on patient characteristics, such as demographic and clinical characteristics, and health services use. Data from NSCR and OPIS spanned from January 01, 2006, to December 31, 2018. Data obtained from HDNS databases began two years before each individual's diagnosis date, thus starting January 01, 2004, and ending December 31, 2018. Data two years before each individual's diagnosis date was required for comorbidity case definitions. Figure 1 visually depicts study timeline information.

From this dataset, a survivor cohort was identified (n=10,176) using the following exclusion criteria: death within one year of diagnosis, stage IV and stage classified as unknown at diagnosis, evidence of metastases or new primary cancer within one year of diagnosis, previous primary cancer diagnosis (i.e., cancer history), and lack of IPR eligibility (i.e., no record of IPR eligibility, or gaps in IPR coverage greater than or equal

to 12 months). Due to our interest in cancer survivors, we included only those with stage I-III disease as the treatment and life expectancy differ for those with unknown and stage IV disease. Additionally, a minimum observation period of greater than or equal to two and a half years during follow-up time was applied. Patients observed for a short follow-up time may be misclassified as frail due to some event (e.g., death or cancer recurrence). The minimum follow-up time was put in place to balance these potential biases. Patients observed for a longer follow-up period have an increased chance for frailty identification. The maximum length of follow-up was 12 years. Survivors were censored on the evidence of a new primary cancer, cancer recurrence, loss of IPR eligibility (i.e., last date of IPR eligibility), and/or death. Data for censoring was obtained from the NSCR, OPIS, MSI Physician Billings, IPR, and CIHI DAD. Specific MSI Physician Billings and CIHI DAD procedure codes used for censoring can be found in Appendix B. Due to the linked data, the cohort included only those with a valid provincial health card number.

As frailty is not a diagnosis, frail cancer survivors were identified from the NS cancer survivor cohort using the decision rules to identify frail persons from two administrative health databases: CIHI DAD and MSI Physician Billings (14).

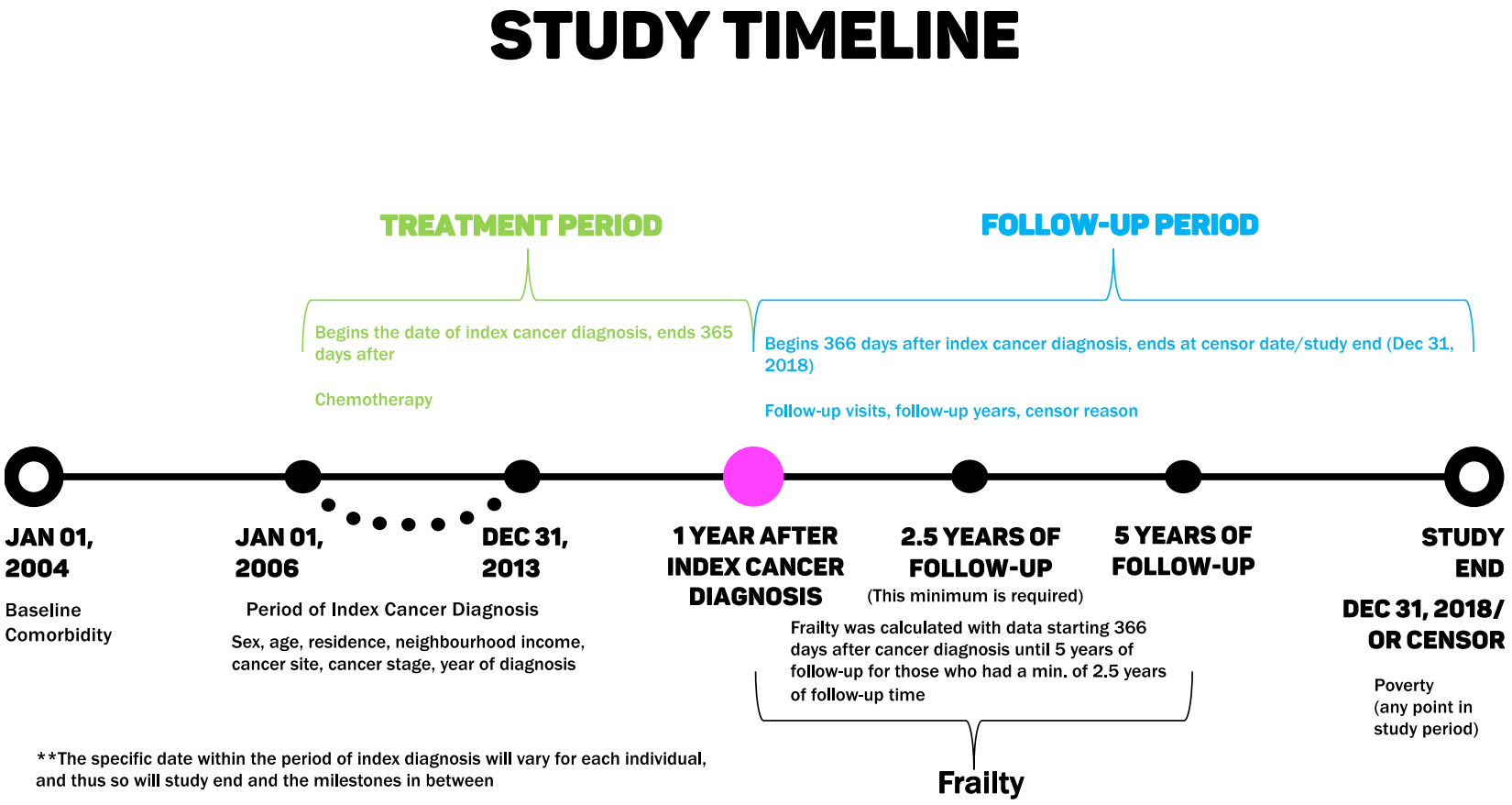

Figure 1: Study timeline.

4.2 Variables

The following describes the study's variables. All study variables were measured at the individual level except income, which was measured at the neighbourhood level.

4.2.1 Key Measures

Frailty

Frailty is the key measure for objective 1. The rules to identify frailty in administrative data were used to identify frail cancer survivors within the NS cancer survivor cohort. We used the International Classification of Diseases, Ninth and Tenth Revisions (ICD9/10) codes from CIHI DAD and MSI Physician Billings to apply the rules to identify frailty in administrative data for each survivor. These specific codes are described in previously published work (14,127).

The rules to assess frailty are based on the following three criteria. Rule 1, the person was a long-term care resident. Rule 2, the person received palliative care. Rule 3 is derived from diagnoses within the EFS, CFS, and service utilization. To be considered frail via rule 3, the individual had to meet two or more criteria listed in any one of seven domains. These domains included cognitive impairment, general health status (e.g., hospital admissions/emergency department visits), incontinence, falls, nutrition, functional performance, and targeted health service utilization (e.g., geriatrician visits). This process is described in further detail in another paper (14). In this study, frailty was categorized as a binary variable (non-frail/frail).

Frailty status was determined for patients in the NS cancer survivor cohort (n=10,176) using data collected beginning 366 days post-cancer diagnosis, ending at five years of follow-up. In reference to the observation of MSI Physician Billings and CIHI DAD ICD9/10 codes, this included at least two hospital admissions or at least two emergency department visits within any 365-day period from 366 days after the index cancer diagnosis to five years of follow-up. This is because active cancer treatment is expected during the first year post-diagnosis and may contribute to a brief deterioration in one's health state (29). Smitherman et al. (2018) used a similar one-year post-diagnosis frailty timeframe (135). Five years is commonly recognized as the end of traditional cancer follow-up, thus why we chose it as a marker for the frailty timeframe end.

Once frail cancer survivors were identified, the prevalence of frailty in the NS cancer survivor cohort was calculated. Frailty was the dependent (outcome) variable of interest in the logistic regression model run to address objective 1.2. Frailty was also used as a key clinical characteristic (independent) variable in objective 2.

Follow-up Care Visits.

The study's second objective focused on follow-up care visits. There is no specific appointment type within OPIS that identifies routine follow-up care. Therefore, Urquhart et al. (2017) made a rule to identify routine follow-up visits using cancer centre data (29) which we used in the present study. The rule uses variables within the existing dataset from NSCR and OPIS (e.g., date of diagnosis, region code, appointment type, resource use, receipt of radiotherapy). It distinguishes routine follow-up care from non-routine

follow-up care (e.g., visits to manage complex late effects or suspicion of recurrence). To determine cancer-related versus non-cancer-related follow-up care within MSI Physician Billings data, we used pre-identified ICD-9/10 billing codes known to be associated with cancer-related care (Appendix C).

Variables were created to describe follow-up care providers (i.e., PCPs, oncologists, and surgeons). Data for the provider type came from OPIS, LPR, and MSI Physician Billings. For this study, a PCP was defined as either a family physician, general, or community medicine practitioner. Additionally, where a provider was suspected to be a general practitioner with training in oncology (i.e., a PCP visit in a cancer center), they were classified as PCP. Oncology included medical and radiation oncologists. Surgeons included general surgeons, urologists, and gynecologists. Although not a surgical specialty, we included gastroenterologists in the surgical category given these specialists perform relevant procedures for colorectal cancer survivors (e.g., colonoscopies). When referring to specialists, this included oncology and surgery physicians.

Total visit count. The outcome variable for objective 2.1. A count of each individual's total cancer-related visits (i.e., PCP, oncology, surgery) during the follow-up period.

Oncology only. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person only visited an oncology provider during the follow-up period or not.

PCP only. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person only visited a PCP during the follow-up period or not.

Surgery only. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person only visited a surgeon during the follow-up period or not.

Oncology and PCP. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person visited both a PCP and an oncology provider during the follow-up period (and not surgery).

Oncology and surgery. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person visited both a surgeon and an oncology provider during the follow-up period (and not primary care).

Surgery and PCP. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person visited both a PCP and a surgeon during the follow-up period (and not oncology).

Oncology, surgery, and PCP. A variable used for objective 2.2 descriptive statistics. It is a binary variable (no/yes) indicating whether the person visited all three, PCP, surgery, and oncology providers during the follow-up period.

Proportion of cancer-related follow-up visits provided by PCPs. The outcome variable for objective 2.2. The count of each individual's visits to PCPs throughout the follow-up period divided by the count of their total cancer-related visits during the follow-up period. This was also categorized into low (i.e., ≤ the 25th percentile [≤0.30]), medium (i.e., > the 25th percentile [>0.30] and < the 75th percentile [<0.73]), and high

(i.e., ≥ the 75th percentile [≥0.73]) proportion of cancer-related follow-up visits provided by PCPs.

4.2.2 Patient Characteristics

Patient characteristics included clinical characteristics, demographics, and other characteristics. The following describes each patient variable.

Clinical Characteristics

Frailty. Frailty, as defined in objective 1 (non-frail/frail) was used in objective 2. In contrast to objective 1, in objective 2, frailty was not used as an outcome variable. Non-frail was used as the reference category in analyses.

Comorbidity. A comorbidity score was calculated based on the list of comorbid conditions developed by Elixhauser et al. (1998), excluding cancer-related comorbidities (143). The score ranges from zero to 28. This is a baseline comorbidity measure calculated over the two years prior to cancer diagnosis using ICD9/10 codes from hospital discharge records (i.e., from within CIHI DAD). Patients were divided into categories based on their number of comorbidities prior to cancer diagnosis: 0, 1, 2, ≥3, or no hospitalizations. Zero was used as the reference category in analyses.

Cancer site. The cancer site was defined as the index cancer's anatomical location (i.e., breast, colorectal, gynecologic, or prostate cancer) as recorded within the NSCR. Breast cancer was used as the reference category in analyses.

Cancer stage. Cancer stage at diagnosis was defined using the Collaborative Stage Data Collection System (i.e., stage I, II, or III) identified within the NSCR. Stage I was used as the reference category in analyses.

Chemotherapy. Receipt of chemotherapy during the treatment period (i.e., from the date of the index cancer diagnosis extending 365 days) was defined as the receipt of neoadjuvant/adjuvant chemotherapy as determined from the NSCR, OPIS, and MSI Physician Billings (e.g., procedure code for administration of IV chemotherapy). Neoadjuvant therapy is defined as treatment given prior to the main treatment, usually surgery, to shrink the tumor beforehand. Adjuvant therapy is an additional cancer treatment given after the primary treatment (144). The categorization of this variable was binary, including no indication of administration of chemotherapy during the treatment period (no), and receipt of neoadjuvant/adjuvant chemotherapy during the treatment period (yes). No chemotherapy was used as the reference category in analyses.

Year of cancer diagnosis. Year of cancer diagnosis was defined as the year an individual was diagnosed with cancer as recorded in the NSCR. Both a continuous and a categorical variable were created. Categories were years 2006-2008, 2009-2010, and 2011-2013.

Demographics

Age. Age represents the age at cancer diagnosis. This variable was created using the date of birth and date of diagnosis from the NSCR. Both a continuous and a categorical variable were created. Age categories included: ≤40, 41-50, 51-65, 66-79, and ≥80 years.

Sex. Sex was defined as male or female biological sex as recorded in the NSCR. Male sex was used as the reference category in analyses.

Residence. Urban/rural residence was defined using the patient's postal code at diagnosis and the PCCF+ file. The Statistical Area Classification (SACtype) was used to

determine whether cohort members reside in urban or rural areas based on dichotomization of the Metropolitan Influence Zone (MIZ) classification. MIZ classifies place of patient residence outside Census Metropolitan Areas (CMA) and Census Agglomerations (CA) (145). CMA is defined as an urban population of at least 100,000, and CA includes an urban population of 10,000-99,999. CMA and CA include all neighboring municipalities where 50% or more of the labor force commutes to the urban center. MIZ includes Census subdivisions outside of CMA or CA, which are categorized as strong MIZ, moderate MIZ, weak and no MIZ. Strong MIZ includes a population where 30-49% of the employed workforce commutes to CMA or CA. Moderate and weak MIZ categories include populations where less than 30% and 5%, respectively, of the employed workforce commute to CMA or CA. No MIZ represents a population where none of the employed commute to a CMA or CA, or the employed workforce includes less than 40 people. For this study, urban residence was defined as MIZ categories of CMA, CA, or strong MIZ. Rural residence was defined as MIZ categories of moderate MIZ, weak MIZ, or no MIZ (145). Urban residence was used as the reference category in analyses.

Poverty. Poverty is a proxy measure for individuals' socioeconomic status (SES), a known social determinant of health. The individual-level variables used to measure poverty were enrollment in low-income provincial drug programs, including income assistance (PIA and PIAX), NS family Pharmacare (PNSFP), Pharmacare GIS (PMSIG), and Pharmacare no co-payment (PMSIX). These were from the IPR eligibility file held by HDNS, within the variable program. Poverty was categorized as a binary variable (no/yes) to indicate poverty based on ever having been enrolled in a low-income drug

program during the study period; otherwise, they were not considered in poverty. No poverty was used as the reference category in analyses.

Neighbourhood income. Neighbourhood income represents one's median neighbourhood income at the time of cancer diagnosis. It is another proxy measure for SES, though it measures a different aspect than poverty. This income measure was reported at the neighborhood level, as individual household income is not reported in administrative health databases. The patient postal code of residence at diagnosis (from NSCR) was linked to Statistics Canada dissemination areas using the PCCF+. Dissemination areas, used as a proxy for neighbourhoods, are the smallest geographic units for which Statistics Canada reports median household income. One-hundred-and-thirty-seven (1.26%) of the study cohort were missing income data. Complete case analysis was used, and those with missing data were excluded from the study. Neighbourhood income, a continuous variable, was also categorized into quintiles representing lowest, low-middle, middle, upper-middle, and highest.

Other Characteristics

Follow-up years. A continuous variable that represents the time in years starting 366 days after the index cancer diagnosis from the NSCR, extending until the study end (i.e., December 31, 2018) or time of censoring. A corresponding categorical variable for descriptive statistics was also created. Categories were: <5 years (i.e., at minimum 2.5 years according to the study criteria, up to but not including 5 years), 5-7 years, and 8-12 years.

Censor reason. A categorical variable that represents the reason for one's end-of-study observation. Indications to censor were collected from NSCR, OPIS, MSI Physician Billings, CIHI DAD, and IPR. The initial date and reason indicating a need to censor were determined for each subject. Categories included subsequent cancer (i.e., new primary cancer), cancer recurrence, end of IPR eligibility, death, and study end (i.e., December 31, 2018).

4.3 Analysis

Prior to conducting each regression analyses, the exploratory analysis looked at the mean, median, standard deviation (SD), variance, interquartile range (IQR), boxplots, histograms, etc., of data. The distributions of outcome variables were assessed to assure alignment with the regression type and research question. Multicollinearity between covariates was assessed, including use of the variance inflation factor. Variables included in the final (adjusted/multivariate) models were informed by relevant literature and based on a combination of clinical and statistical significance. All analyses were conducted using Stata/MP 15.0.

4.3.1 Objective 1 Analysis

To address objective 1, we used cohort data from both frail and non-frail cancer survivors (n=10,176) to estimate the burden of frailty amongst the NS cancer survivor cohort, and describe how frailty differs by patient characteristics.

Objective 1.1) To estimate the prevalence of frailty amongst a NS cancer survivor cohort and determine how it differs by clinical, demographic, and other characteristics.

The prevalence of frailty in cancer survivors was calculated via proportions and then described by each characteristic (i.e., comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age, residence, poverty, income, follow-up years, and censor reason) (Table 1). The overall prevalence of frailty within the NS cancer survivor cohort, and prevalence by patient characteristics, were calculated as follows:

$$\text{prevalence of frailty in cancer survivors} = \frac{\#\ of\ people\ in\ the\ cancer\ survivor\ cohort\ identified\ as\ frail}{total\ \#\ of\ cancer\ survivors\ in\ the\ cohort} \times 100$$

Objective 1.2) To identify frail cancer survivors' traits (i.e., demographic, clinical, and other characteristics) that differ from those of non-frail cancer survivors.

First, the distribution of each trait was estimated and compared between frail and non-frail cancer survivors, including clinical characteristics (i.e., comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis), demographics (i.e., sex, age, residence, poverty, income) and other characteristics (i.e., follow-up years, censor reason). Chi-squared (χ^2) for categorical variables and t-tests for continuous variables were used to test statistical differences in the distribution between traits (Table 2).

Second, logistic regression on the binary outcome (non-frail/frail) was used to describe how frailty differs according to the patient characteristics (Table 3). Based upon frailty coding, an OR greater than one indicated higher odds of frailty, and an OR less than one indicated lower odds of frailty. Each patient characteristic variable was run in a univariate logistic model with frailty, and then selected variables were included in a multivariable model. The multivariate model allowed us to observe variations in frailty by important characteristics while adjusting for other characteristics. A priori decisions were made to include some patient characteristics in the multivariate model were based upon known importance in the literature (i.e., age, sex, comorbidity), and clinical importance (i.e., cancer site, cancer stage, chemotherapy). SES has been associated with frailty in the literature. As we had three proxy measures of SES, we included only poverty in the multivariate model as it had a large effect size in the univariate model and is measured at the individual level. Urban/rural residence was excluded as it was not significant at $p<0.20$ in the univariate model. Assumptions for logistic regression (independence of observations and errors, linearity of continuous variables, absence of multicollinearity, and lack of influential outliers) were met. Sensitivity analysis was conducted including residence in the multivariate model; it remained insignificant, and results were robust. Likelihood-Ratio (LR) tests were used to indicate the significance of categorical variables in the multivariate model. Statistical significance was set to alpha level 0.05.

Objective 1.3) To determine the underlying attributes (i.e., physical or cognitive impairment and health service utilization markers) for which survivors are deemed frail.

Descriptive statistics were used to show the number and percentage of individuals identified as frail within the NS cancer survivor cohort according to each rule to identify frailty, including markers of physical and cognitive impairment, as well as health service utilization (Table 4).

4.3.2 Objective 2 Analysis

The sum of objectives 2.1 and 2.2 address the second overarching objective: To identify patterns of cancer-related follow-up care visits and how they differ between non-frail and frail cancer survivors, by patient characteristics within a NS cohort.

Objective 2.1) To determine whether frail cancer survivors have greater cancer-related follow-up care use and how this differs by patient characteristics.

Median, 25th and 75th percentiles were first estimated, along with the IQR, for the number of total (i.e., PCP, oncology, and surgery) cancer-related visits by frailty and other patient characteristics (Table 5).

Based upon the distribution of the outcome (Appendix D), total visit count, the observation of overdispersion (mean=16.1, variance=171.9), and comparison of Akaike's Information Criteria (AIC) and Bayesian Information Criteria (BIC), we chose to use negative binomial generalized linear modelling (GLM) over Poisson regression. We modelled the annual rate of cancer-related follow-up visits, with the key independent

variable, frailty, adjusting for other patient characteristics (Table 6). An offset function in Stata was used to normalize visit exposure time (that is, the time from the beginning of the follow-up period until censoring or the end of the study, measured in years). Estimated parameters from the model are thus incidence rate ratios (IRRs), which can be interpreted as the average annual rate of total follow-up visits for the level of a variable, relative to the reference category for a variable.

Patient characteristic variables were run in univariate negative binomial GLM models with the outcome, and then selected variables were included in a multivariable model. The key independent variable of interest was frailty. A priori decisions were made to include some other patient characteristics in the multivariate model based on known importance in the literature (i.e., age, sex, comorbidity, year of cancer diagnosis), and clinical importance (i.e., cancer site, cancer stage, chemotherapy). Income, a measure of SES, was associated with routine cancer centre follow-up visits within a similar NS cancer survivor cohort (29). As we had three proxy measures of SES, we included only residence in the multivariate model as it had a more substantial effect size in the univariate model. Poverty and income were excluded as they were not significant at $p<0.20$ in their univariate models. Sensitivity analyses were conducted excluding the most extreme outliers, and removing comorbidity and age, the results remained robust. LR tests were used to indicate the significance of categorical variables in the multivariate model. Statistical significance was set to alpha level 0.05.

Objective 2.2) To identify the percentage of cancer survivors' follow-up visits provided by PCPs and determine how this differs by frailty and other patient characteristics.

First, descriptive statistics were used to describe, amongst those who had at least one visit, the percentage of all, non-frail, and frail (Table 7) cancer survivors who visited certain combinations of providers for cancer-related care during the follow-up period. Specifically, we looked at who visited specialists (i.e., only oncology, only surgery, or oncology and surgery), who visited only PCPs, and who visited both specialists and PCPs (i.e., oncology and PCP, surgery and PCP, and finally, oncology, surgery, and PCP) for cancer-related care during the follow-up period.

Based upon the distribution (Appendix E) of the continuous variable, proportion of cancer-related follow-up visits provided by PCPs, we categorized the outcome as low, medium, and high (proportion of PCP visits). Next, we described the percentage of cancer-related follow-up visits provided by PCPs for all cancer survivors (low [≤30%], medium [>30% <73%], and high [≥73%]), according to frailty and patient characteristics. We also described the proportion of cancer survivors who did not have any follow-up visits by patient characteristics (Table 8).

Each patient characteristic variable was run in a univariate multinomial model with the outcome, proportion of PCP visits (low, medium, high) (Table 9). Thus, for each patient characteristic, two models were produced. The first produced estimates of medium-high compared to low proportion of PCP visits (i.e., the odds of being in the medium-high

category compared low). The second produced estimates for being in the high category compared to low-medium (i.e., the odds of being in the high category compared to low-medium).

We used the Stata package gologit2 (146) to perform partially proportional ordinal logistic regression for multivariate analysis, as the proportional odds assumption was not met for all variables. Gologit2 with autofit allowed us to relax this assumption in instances where the assumption was not met, while applying constraints where the assumption was met, producing a final model that overarchingly did not violate the proportional odds/parallel lines assumption (Table 10). The key independent variable of interest was frailty. The multivariate partial proportional odds model allowed us to observe variations in the estimate of the proportion of visits to PCPs by frailty while adjusting for other patient characteristics. A priori decisions were made to include patient characteristics in the multivariate model based on known importance in the literature related to specialist care and/or health care use (i.e., age, sex, comorbidity, year of cancer diagnosis), and clinical importance (i.e., cancer site, cancer stage, chemotherapy). Not specific to cancer care, SES has shown an association with health care use and specialist visitation (147). As we had three proxy measures of SES, we included poverty in the multivariate model as it had a large effect size in univariate analyses and is measured at the individual level. Residence was also included based on the hypothesis that in NS there are urban and rural differences between seeing specialists or PCPs.

We investigated the appropriateness of the final model compared to regular ordinal logistic regression and a lesser constrained model using LR tests. The tests confirmed that regular ordinal logistic regression was too restrictive (LR test, $p<0.001$), and that the partial proportional odds model was not too restrictive (LR test, $p=0.1902$). Results in Table 10 can be interpreted similar to Table 9, however, where the proportional odds assumption was met, estimates in both the three left-hand and right-hand columns are the same. No influential outliers were found. Sensitivity analysis was conducted excluding comorbidity and age, the results remained robust. LR tests were used to indicate the significance of categorical variables in the multivariate model. Statistical significance was set to alpha level 0.05.

4.4 Data Access and Ethics

The proposed research used an updated existing linked administrative dataset approved by the Nova Scotia Health (NSH) REB (REB file#1022782); an amendment to the existing file was submitted and approved. A new data access request (2021-SAM-001) was submitted requesting updated and additional data for the study as a sub-study of the supervisor's original work (2016-RAU-001) and granted by HDNS. Additionally, an amendment to the NSCR/OPIS data was requested through an NSH internal data access request entitled 'Identifying frailty in cancer survivors: Patterns of cancer follow-up care and implications for personalized survivorship models (sub-study of 'Health care utilization for survivors of breast, prostate, colon, rectal, or gynecological cancers in NS'), and granted. Identifying information was not accessed, and access to person-level (de-identified) data was obtained. The linked encrypted health card numbers were

removed and replaced with unique study IDs; therefore, as per the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS 2), the study did not require individual informed consent (148). The primary ethical concern is the maintenance of confidentiality. The dataset is held on a closed HDNS server and analyses were performed within the NSH firewall. Reported results used aggregated level data with cell counts of five or greater. Per current protocols, data will be kept in a secure file behind the NSH firewall for a minimum of seven years after study completion for audit purposes. Data will be destroyed within seven years of study completion.

Chapter 5: Results

5.1 Participants Eligible for Analyses

Figure 2 outlines participants eligible for analyses. The dataset contained 20,901 Nova Scotians diagnosed with breast, prostate, colorectal, or gynecologic cancer between January 1, 2006, and December 31, 2013. Patients were excluded based on death within one year of index cancer diagnosis (n=2,608), stage IV (n=1,153) and unknown (n=490) cancer, cancer history (n=2,499), new primary cancer within one year of index cancer diagnosis (n=153), no record of IPR eligibility (n=23), gaps in IPR eligibility greater than or equal to one year (n=59), censor date before the beginning of the follow-up period (n=357), and less than two years and a half years of follow-up time (n=3,246). Further, where patient characteristic variables were missing less than 5% of data, complete case analysis was used. Participants with missing median household income (n=137) were excluded. After exclusions, the cohort included 10,176 cancer survivors. The mean age at cancer diagnosis within the cohort was 64 years (range= 7-97 years). Participants had a mean follow-up time of 7.1 years (range= 2.5-12 years). One-hundred-and-seventy-six (1.7%) of patients in the survivor cohort did not have any visits in the follow-up period; these patients were excluded only for certain analyses of objective 2.2 (Tables 7, 9 and 10), leaving 10,000 eligible patients. However, all other analyses used all 10,176 eligible cancer survivors; this difference was highlighted by using bold font in Figure 2.

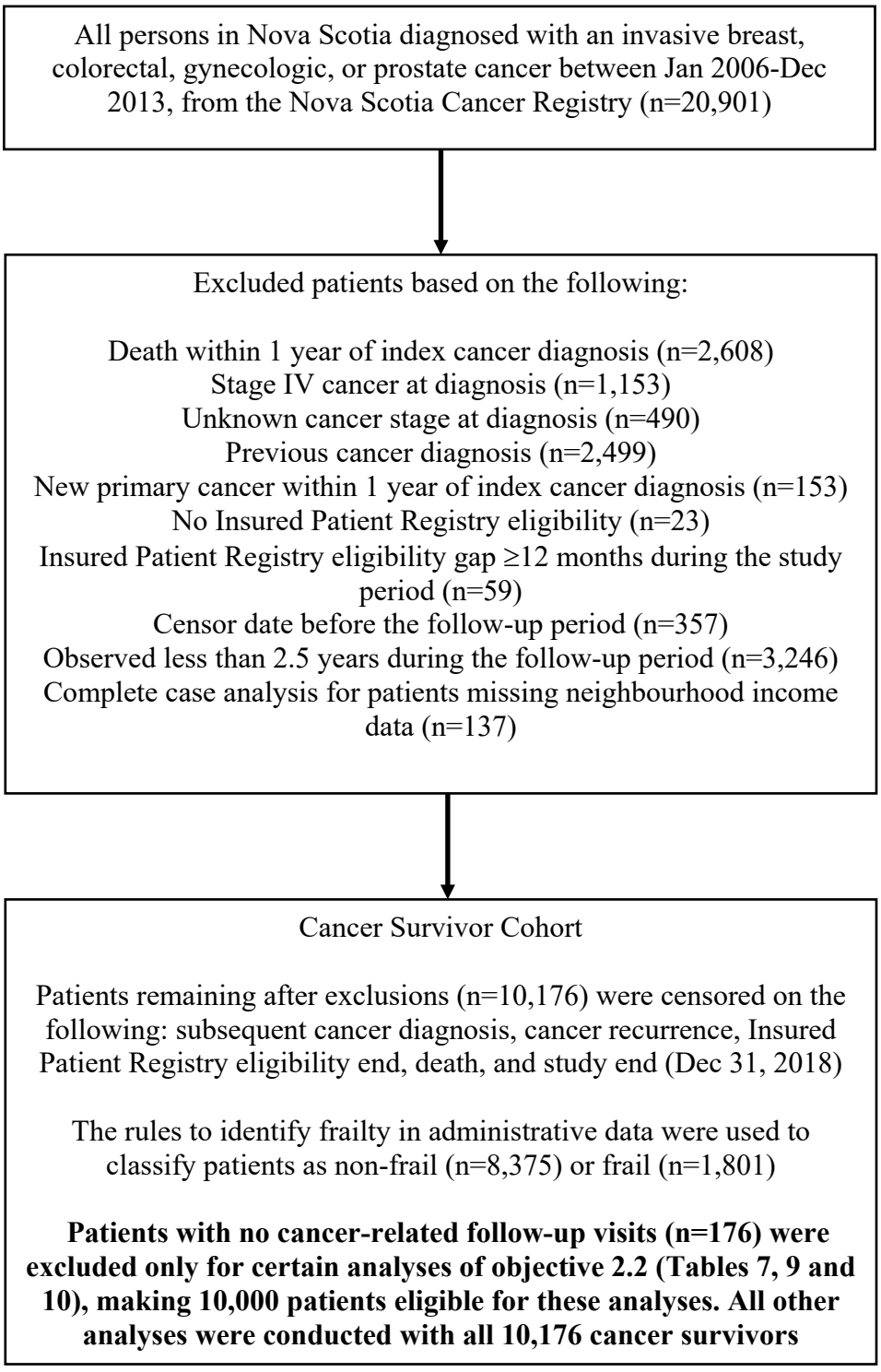

Figure 2: Flow chart of the cancer survivor cohort used for analyses.

5.2 Objective 1 Results

5.2.1 Frailty Prevalence

Overall, 10,176 cancer survivors diagnosed with stage I-III breast, colorectal, gynecologic, or prostate cancer between January 01, 2006, and December 31, 2013, were included in the NS cancer survivor study cohort (Figure 2).

Amongst this cohort (n=10,176), the prevalence of frailty observed in the first five years of follow-up, was 17.7% (n=1,801, 95% CI 16.95%-18.45%). Table 1 shows the prevalence of frailty amongst the NS cancer survivor cohort by patient characteristics. The proportion of frailty increased with the number of comorbidities. More patients with stage II (18.8%, 95% CI 17.63%-19.95%) and III (18.7%, 95% CI 16.74%-20.75%) cancer at diagnosis were frail than those diagnosed at stage I (16.2%, 95% CI 15.12%-17.37%). As expected, more females (18.8%, 95% CI 17.82%-19.90%) than males (16.3%, 95% CI 15.28%-17.43%) were frail, and frailty was higher amongst those with increased age at cancer diagnosis. Further, not surprisingly, there was evidence of socioeconomic inequality. Amongst those in poverty, 23.4% (95% CI 22.06-24.70%) were frail, compared to 14.0% (95% CI 13.15%-14.90%) of people not in poverty. A trend of lower median neighbourhood income and higher frailty compared to those with higher income was also seen. Aligning with prior knowledge, a high percentage of those censored due to death were frail (64.6%, 95% CI 61.63%-67.53%). Similarly, those who were observed for a shorter follow-up period had a higher prevalence of frailty. For further context, amongst frail cancer survivors (n=1,801), 539 (29.9%) died less than five years after being identified as frail, and 262 (14.6%) died five or more years after being

deemed frail. One thousand (55.5%) of those identified as frail did not die during the study period.

Findings for cancer site and chemotherapy were slightly more unpredictable. The proportion of frailty amongst cancer sites was lowest for gynecologic survivors (13.6%, 95% CI 11.51%-15.99%) as anticipated, however, was the highest for colorectal survivors (23.0%, 95% CI 21.23%-24.76%). Breast (17.6%, 95% CI 16.39%-18.93%) and prostate survivors (15.5%, 95% CI 14.30%-16.73%) fell in the middle. Amongst those who had chemotherapy, 11.9% (95% CI 10.38%-13.62%) were frail, while 18.8% (95% CI 17.95%-19.61%) of those with no indication of chemotherapy were frail.

5.2.2 Characteristics of Frail and Non-frail Survivors

Descriptive statistics (i.e., $\chi 2$ tests for categorical variables and t-tests for continuous variables) showed significant differences between non-frail and frail cancer survivors for all patient characteristics (i.e., comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age, residence, poverty, income, follow-up years, and censor reason), except residence (χ^2 test, p=0.364) (Table 2). There were notable differences in magnitude between the percentage of frail and non-frail cancer survivors by sex, age, poverty, neighbourhood income, and those with three or more comorbidities. Patient characteristic variables were used in univariate logistic regression models with the outcome, frailty, and results paralleled those in Table 2, with residence not significantly associated with frailty (OR 1.05, 95% CI 0.94-1.17) (Table 3).

Patient characteristics included in the multivariate logistic regression model for frailty were comorbidity, cancer site, cancer stage, chemotherapy, sex, age, and poverty (Table 3). Participants with three or more comorbidities compared to those with zero comorbidities (OR 1.96, 95% CI 1.52-2.52), older age at diagnosis (OR 1.08, 95% CI 1.07-1.08), stage II or III versus stage I cancer at diagnosis (LR test, p=0.0101), females (OR 1.35, 95% CI 1.09-1.67), and those living in poverty (OR 1.39, 95% CI 1.24-1.55) had higher odds of frailty.

Adjusted for other patient characteristics (i.e., comorbidity, cancer stage, chemotherapy, sex, age, poverty), cancer site was not significantly associated with frailty (LR test, p=0.4717). Chemotherapy was not significantly associated with frailty in the multivariate model (OR 0.91, 95% CI 0.75-1.10) (Table 3). Thus, there are differences between the summary statistics and univariate analyses compared to the *adjusted* odds of frailty for cancer site and chemotherapy.

5.2.3 Frailty Rules

Table 4 presents the results of objective 1.3, indicating the number and percentage of cancer survivors deemed frail by each frailty identification rule, for all NS cancer survivors, and by cancer site. The majority of frailty was identified through rule 3 (15.6%) related to health service use, followed by rule 1 (5.2%) indicating a person was a LTC resident, and rule 2 (2.4%) indicating receipt of palliative care. Ten-point-eight percent of cancer survivors were deemed frail through rule 3 alone. A small proportion of cancer survivors met the criteria through a combination of rules (Table 4). Within rule 3,

the most common reason for frailty was rule 3b, general health status (14.4%), which is specifically related to hospital admissions, emergency department visits, malaise/fatigue, or cachexia. This was followed by rule 3g, targeted health services use (7.7%), indicating geriatrician or in-home provider visits. Finally, 7.1% of survivors were flagged frail due to rule 3a, which represents cognitive impairment (14). Compared with the other cancer sites, colorectal cancer survivors represented the highest proportion of those identified as frail in every category except rule 3c, incontinence, which belonged to breast (4.5%). Furthermore, interestingly, colorectal cancer survivors made up the largest portion (7.4%) identified as LTC residents (rule 1).

5.3 Objective 2 Results

5.3.1 Total Cancer-related Follow-up Care

Descriptive statistics (i.e., median total visits during the follow-up period, the 25th and 75th percentiles, and IQR) described variation in visits for all patient characteristics (i.e., frailty, comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age, residence, poverty, income, follow-up years, and censor reason) (Table 5). The same variables were used in univariate logistic regression models with the outcome. Overall, results paralleled those in Table 5, with variables not significantly associated with a higher annual follow-up visit rate being poverty (IRR 1.03, 95% CI 1.00-1.06) and neighbourhood income (IRR 1.00, 95% CI 0.99-1.00) (Table 6).

Patient characteristics included in the multivariate negative binomial GLM, modelling the annual rate of cancer-related follow-up visits, were frailty, comorbidity, cancer site,

cancer stage, chemotherapy, year of cancer diagnosis, sex, age, and residence (Table 6). Cancer survivors with frailty had a higher annual cancer-related follow-up visit rate (IRR 1.28, 95% CI 1.23-1.33). Comorbidity was a significant predictor (LR test, $p<0.001$), although visits did not increase with the number of comorbidities. Compared with breast cancer survivors, survivors of colorectal cancer had lower visit use (IRR 0.76, 95% CI 0.72-0.80), as did gynecologic (OR 0.82, 95% CI 0.78-0.87). Chemotherapy received in the treatment period was associated with a 30% increase in the annual rate of follow-up visits (IRR 1.30, 95% CI 1.25-1.36). Each successive diagnosis (calendar) year was associated with a 4% increase in visits (IRR 1.04, 95% CI 1.04-1.05); this likely resulted as those with longer follow-up were diagnosed earlier in the study period. Sex was not significant in the multivariate model (IRR 1.05, 95% CI 0.99-1.12) and rural residence had an annual follow-up visit rate 8% lower than urban dwellers (IRR 0.92, 95% CI 0.90-095).

5.3.2 Proportion of Cancer-related PCP Follow-up Care

Table 7 describes the proportion of all, non-frail, and frail cancer survivors who had at least one follow-up visit and the different combination of providers they visited (i.e., oncology only, surgery only, oncology and surgery, PCP only, oncology and PCP, surgery and PCP, or oncology, surgery, and PCP). A higher proportion of frail cancer survivors (14.2%, 95% CI 12.57%-15.89%) compared with all survivors (8.2%, 95% CI 7.68-8.77%) and non-frail cancer survivors (6.9%, 95% CI 6.40%-7.51%), visited only PCPs for cancer-related follow-up. The most common combination of providers for all cancer survivors to see during the follow-up period was both surgeons and PCPs (54.3%,

95% CI 53.35%-55.31%). Twenty-four-point-one percent of cancer survivors saw all three provider types (i.e., oncologists, surgeons, and PCPs) for cancer-related care during the follow-up period.

Table 8 shows the number and percentage of cancer survivors by each patient characteristic (i.e., frailty, comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age, residence, poverty, income, follow-up years, and censor reason) whose proportion of cancer-related follow-up visits to PCPs was low (i.e., ≤30%), medium (i.e., >30% and <73%), or high (≥73%). A higher proportion of cancer survivors who were non-frail (87.3%), not hospitalized (42.8%), diagnosed later in the study period (44.0%), had prostate cancer (40.9%), were middle-aged (i.e., 51-65 years) (44.6%), males (52.3%), or not living in poverty (64.8%), had a lower proportion of their cancer-related follow-up visits to PCPs. Amongst the cancer survivor cohort, 2,485 (24.4%) were categorized as having low, 5,028 (49.4%) as medium, and 2,487 (24.4%) as having a high proportion of all cancer-related follow-up visits provided by PCPs. One-point-seven percent of the survivor cohort (n=176) did not have any follow-up visits. The majority of those with no visits were diagnosed later in the study period (52.8%), non-frail (75.0%), male (51.7%), urban dwellers (56.2%), living in poverty (53.4%), who never received chemotherapy (96.6%). The percentage of frail cancer survivors classified as low (12.7%), medium (16.1%), or high (25.3%) increased across the categories, respectively. Amongst those who were categorized as high, many were female (59.6%), diagnosed with stage I (45.8%) and/or breast cancer (40.2%). The percentage of poor

cancer survivors classified as low (35.2%), medium (37.2%), or high (47.4%) increased across the categories, respectively.

Table 9 contains results of the univariate multinomial analyses of each patient characteristic with the outcome, proportion of PCP visits (low versus medium-high, and low-medium versus high). Aligning with that described in Table 8, frailty, stage I, earlier year of diagnosis, females, and poverty were associated with a higher proportion of visits to PCPs.

Patient characteristics included in the multivariate partial proportional ordinal logistic model were frailty, comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age, residence, and poverty. Table 10 presents the ORs, 95% CIs and p-values for the estimates of low compared with medium-high proportion of PCP visits, and the estimates comparing low-medium with the high proportion of PCP visits. Where the proportional odds assumption was met (i.e., for the variables frailty, cancer stage and poverty, and for particular levels of the categorical variables comorbidity and cancer site), estimates remained the same for low (versus medium-high) and low-medium (versus high). For variables (i.e., chemotherapy, year of cancer diagnosis, sex, and age) and levels of categorical variables (i.e., comorbidity, cancer site) where the proportional odds assumption was violated, the second set of estimates were different (Table 10).

Compared to non-frail cancer survivors, frail cancer survivors had 58% greater odds of having a high proportion of PCP visits compared to low-medium, and of having a

medium-high proportion of PCP visits compared to a low proportion (OR 1.58, 95% CI 1.43-1.76). Those diagnosed at stage II or III compared to stage I had lower odds of having a medium-high or high proportion of PCP visits (OR 0.91, 95% CI 0.82-1.00 and OR 0.80, 95% CI 0.70-0.91, respectively). Comorbidity was a significant predictor (LR test, p=0.0019). Those living in poverty had 37% higher odds of having either a medium-high or high proportion of PCP visits compared to those not in poverty (OR 1.37, 95% CI 1.26-1.48). For each successive diagnosis year, the odds of having a higher proportion of visits provided by PCPs decreased; this trend held true for both medium-high (OR 0.93, 95% CI 0.91-0.95) and high (OR 0.97, 95% CI 0.95-0.99) estimates. Females compared to males had increased odds of having a greater proportion of PCP follow-up visits; this trend held true for both medium-high (OR 1.44, 95% CI 1.21-1.72) and high (OR 1.26, 95% CI 1.07-1.49) estimates.

Some trends changed considerably between multivariate analyses of the outcome by different categorization (i.e., low versus medium-high, and low-medium versus high). For example, compared to breast cancer survivors, colorectal cancer survivors had 6% lower odds of having a medium-high versus low proportion of PCP visits, although this was not significant (OR 0.94, 95% CI 0.80-1.11). However, colorectal compared to breast cancer survivors had 34% higher odds of having a high rather than low-medium amount (i.e., proportion) of PCP visits, and this finding was significant (OR 1.34, 95% CI 1.15-1.55). This may be reflective of the fact that of all breast cancer survivors (n=3,522), the majority fell into the medium category (n=1,914 [54.3%]), while 1,000 (28.4%) were categorized as high, compared to 718 (32.1%) of all colorectal cancer survivors being

categorized as high. Similarly, the finding for receipt of chemotherapy was not significant when analyzed as low versus medium-high proportion of PCP visits (OR 1.07, 95% CI 0.92-1.24). However, receipt of chemotherapy was significantly associated with 28% lower odds of having a high proportion of PCP visits (OR 0.72, 95% CI 0.62-0.84). Again, a similar trend was observed for residence, with a statistically insignificant finding for low versus medium-high proportion of PCP visits (OR 0.96, 95% CI 0.87-1.06). Yet, adjusted for other characteristics in the multivariate model, rural residents had 12% greater odds of having a high (as opposed to low-medium) proportion of PCP follow-up visits (OR 1.12, 95% CI 1.01-1.23).

5.4 Tables

5.4.1 Frailty Tables

Table 1. Prevalence of frailty in the cancer survivor cohort by patient characteristics *(Objective 1.1)*.

Variable	N Denominator	N (%) Frail	95% CI
Clinical characteristics			
Comorbidity			
0	1,304	217 (16.6)	14.66-18.78
1	3,652	685 (18.8)	17.50-20.06
2	664	197 (29.7)	26.22-33.30
≥3	491	209 (42.6)	38.15-47.08
No hospitalization	4,065	493 (12.1)	11.14-13.17
Cancer site			
Breast	3,522	621 (17.6)	16.39-18.93
Colorectal	2,234	513 (23.0)	21.23-24.76
Gynecologic	946	129 (13.6)	11.51-15.99
Prostate	3,474	538 (15.5)	14.30-16.73
Cancer stage			
I	4,228	686 (16.2)	15.12-17.37
II	4,444	834 (18.8)	17.63-19.95
III	1,504	281 (18.7)	16.74-20.75
Chemotherapy			
No	8,583	1,611 (18.8)	17.95-19.61
Yes	1,593	190 (11.9)	10.38-13.62
Year of cancer diagnosis			
2006-2008	3,760	780 (20.7)	19.46-22.08
2009-2010	2,505	482 (19.2)	17.71-20.84
2011-2013	3,911	539 (13.8)	12.72-14.90
Demographics			
Sex			
Male	4,635	757 (16.3)	15.28-17.43
Female	5,541	1,044 (18.8)	17.82-19.90
Age			
≤40 years	257	12 (4.7)	2.44-8.01
41-50 years	1,028	79 (7.7)	6.13-9.49
51-65 years	4,179	378 (9.1)	8.19-9.96
66-79 years	3,765	840 (22.3)	20.99-23.68
≥80 years	947	492 (52.0)	48.71-55.18
Residence			
Urban	6,474	1,129 (17.4)	16.52-18.39
Rural	3,702	672 (18.2)	16.92-19.43
Poverty			

Variable	N Denominator	N (%) Frail	95% CI
No	6,161	863 (14.0)	13.15-14.90
Yes	4,015	938 (23.4)	22.06-24.70
Neighbourhood income (quintiles)			
Lowest	1,977	419 (21.2)	19.41-23.06
Low-middle	2,027	381 (18.8)	17.11-20.57
Middle	2,039	353 (17.3)	15.69-19.03
Upper-middle	2,038	350 (17.2)	15.56-18.89
Highest	2,095	298 (14.2)	12.76-15.79
Other characteristics			
Follow-up years			
<5 years	2,444	549 (22.5)	20.82-24.17
5-7 years	4,099	725 (17.7)	16.53-18.89
8-12 years	3,633	527 (14.5)	13.38-15.69
Censor reason			
Study end	7,454	901 (12.1)	11.36-12.85
Subsequent cancer	719	103 (14.3)	11.85-17.10
Cancer recurrence	817	99 (12.1)	9.96-14.55
IPR end	143	24 (16.8)	11.06-23.94
Death	1,043	674 (64.6)	61.63-67.53
Total	10,176	1,801 (17.7)	16.96-18.45

CI= Confidence Interval, IPR= Insured Patient Registry.

Table 2. Patient characteristics amongst the cancer survivor cohort *(Objective 1.2)*.

Variable	Total cancer survivor cohort N (%)	Non-frail cancer survivors N (%)	Frail cancer survivors N (%)	p-value[a]
Clinical characteristics				
Comorbidity				
0	1,304 (12.8)	1,087 (13.0)	217 (12.1)	
1	3,652 (35.9)	2,967 (35.4)	685 (38.0)	
2	664 (6.5)	467 (5.6)	197 (10.9)	
≥3	491 (4.8)	282 (3.4)	209 (11.6)	
No hospitalizations	4,065 (40.0)	3,572 (42.6)	493 (27.4)	<0.001
Cancer site				
Breast	3,522 (34.6)	2,901 (34.6)	621 (34.5)	
Colorectal	2,234 (22.0)	1,721 (20.5)	513 (28.5)	
Gynecologic	946 (9.3)	817 (9.8)	129 (7.1)	
Prostate	3,474 (34.1)	2,936 (35.1)	538 (29.9)	<0.001
Cancer stage				
I	4,228 (41.5)	3,542 (42.3)	686 (38.1)	
II	4,444 (43.7)	3,610 (43.1)	834 (46.3)	

Variable	Total cancer survivor cohort N (%)	Non-frail cancer survivors N (%)	Frail cancer survivors N (%)	p-value[a]
III	1,504 (14.8)	1,223 (14.6)	281 (15.6)	0.005
Chemotherapy				
No	8,583 (84.3)	6,972 (83.2)	1,611 (89.5)	
Yes	1,593 (15.7)	1403 (16.8)	190 (10.5)	<0.001
Year of cancer diagnosis, mean (SD)	2009.5 (2.3)	2009.6 (2.3)	2009.1 (2.2)	<0.001
Demographics				
Sex				
Male	4,635 (45.5)	3,878 (46.3)	757 (42.0)	
Female	5,541 (54.5)	4,497 (53.7)	1,044 (58.0)	0.001
Age, mean (SD)	64.2 (11.6)	62.5 (11.0)	71.9 (11.3)	<0.001
Residence				
Urban	6,474 (63.6)	5,345 (63.8)	1,129 (62.7)	
Rural	3702 (36.4)	3030 (36.2)	672 (37.3)	0.364
Poverty				
No	6,161 (60.5)	5,298 (63.3)	863 (47.9)	
Yes	4,015 (39.5)	3,077 (36.7)	938 (52.1)	<0.001
Neighbourhood income ($), median IQR ($25^{th}$-$75^{th}$ percentile)	55,734 25,363 (45,259-70,622)	56,387 25,799 (45,426-71,225)	53,571 24,610 (43,543-68,153)	<0.001
Other characteristics				
Follow-up years, mean (SD)	7.1 (2.5)	7.2 (2.5)	6.6 (2.5)	<0.001
Censor reason				
Study end	7,454 (73.3)	6,553 (78.2)	901 (50.0)	
Subsequent cancer	719 (7.1)	616 (7.4)	103 (5.7)	
Cancer recurrence	817 (8.0)	718 (8.6)	99 (5.5)	
IPR end	143 (1.4)	119 (1.4)	24 (1.4)	
Death	1,043 (10.2)	369 (4.4)	674 (37.4)	<0.001
Total	10,176 (100)	8,375 (100)	1,801 (100)	

[a] t-tests for continuous variables, χ^2 test for categorical variables.

IPR= Insured Patient Registry, IQR= Interquartile Range, SD= Standard Deviation.

Table 3. Logistic regression for the association between patient characteristics and frailty *(Objective 1.2)*.

Variable	Frailty					
	Univariate			Multivariate[a]		
	OR	95% CI	p-value	OR	95% CI	p-value
Clinical characteristics						
Comorbidity (reference: 0)						<0.001[b]
1	1.16	0.98-1.37	0.089	1.00	0.83-1.20	0.978
2	2.11	1.69-2.64	<0.001	1.40	1.10-1.78	0.007
≥3	3.71	2.95-4.68	<0.001	1.96	1.52-2.52	<0.001
No hospitalizations	0.69	0.58-0.82	<0.001	0.67	0.55-0.80	<0.001
Cancer site (reference: Breast)						0.4717[b]
Colorectal	1.39	1.22-1.59	<0.001	0.90	0.74-1.08	0.244
Gynecologic	0.74	0.60-0.91	0.004	0.87	0.69-1.08	0.202
Prostate	0.86	0.75-0.97	0.016	0.89	0.68-1.16	0.372
Cancer stage (reference: Stage I)						0.0101[b]
Stage II	1.19	1.07-1.33	0.002	1.16	1.01-1.34	0.037
Stage III	1.19	1.02-1.38	0.029	1.32	1.10-1.59	0.003
Chemotherapy	0.59	0.50-0.69	<0.001	0.91	0.75-1.10	0.338
Year of cancer diagnosis*	0.91	0.89-0.93	<0.001			
Demographics						
Female sex	1.19	1.07-1.32	0.001	1.35	1.09-1.67	0.007
Age (years)*	1.09	1.08-1.09	<0.001	1.08	1.07-1.08	<0.001
Rural residence	1.05	0.94-1.17	0.364			
Poverty	1.87	1.69-2.07	<0.001	1.39	1.24-1.55	<0.001
Neighbourhood income ($)*	0.99	0.99-1.00	<0.001			
Other characteristics						
Follow-up years*	0.90	0.88-0.92	<0.001			
Censor reason (reference: Study end)						
Subsequent cancer	1.22	0.98-1.51	0.081			
Cancer recurrence	1.00	0.80-1.25	0.980			
IPR end	1.47	0.94-2.29	0.091			
Death	13.38	11.49-15.35	<0.001			

[a] Multivariate analysis adjusted for comorbidity, cancer site, cancer stage, chemotherapy, sex, age at cancer diagnosis, and poverty.

[b] Overall p-value for variables with >2 categories.

*** Continuous variable.**

CI= Confidence Interval, Insured Patient Registry= IPR, OR= Odds Ratio.

Table 4. Frailty identification amongst cancer survivors by specific rule *(Objective 1.3)*.

Frailty identification rule[a]	**Cancer site**				
	Breast N=3,552	**Colorec -tal N=2,234**	**Gynec- ologic N=946**	**Prostate N=3,474**	**Total N=10,176**
	N	**N**	**N**	**N**	**N**
	%	**%**	**%**	**%**	**%**
1. Person was a LTC resident	200	166	25	135	526
	5.7	7.4	2.6	3.9	5.2
2. Person received palliative care	59	82	16	78	235
	1.7	3.7	1.7	2.3	2.3
3. Person met at least 2 of the listed domains 3a to 3g	553	442	114	481	1,590
	15.7	19.8	12.1	13.9	15.6
3a. Cognitive impairment	244	218	37	224	723
	6.9	9.8	3.9	6.5	7.1
3b. General health status	502	411	104	448	1,465
	14.3	18.4	11.0	12.9	14.4
3c. Incontinence (urinary or fecal)	157	72	35	124	388
	4.5	3.2	3.7	3.6	3.8
3d. Falls (with hospitalization)	98	92	19	73	282
	2.8	4.1	2.0	2.1	2.8
3e. Nutrition issues	suppress	17	suppress	23	68
	suppress	0.8	suppress	0.7	0.7
3f. Functional performance	74	72	26	73	245
	2.1	3.2	2.8	2.1	2.4
3g. Targeted health services utilization	260	241	49	232	782
	7.4	10.8	5.2	6.7	7.7
Total persons identified	621	513	129	538	1,801
	17.6	23.0	13.6	15.5	17.7
Patients identified by each combination of identification rules					
Rule 1 only	49	36	6	26	117
	1.4	1.6	0.6	0.8	1.2
Rule 2 only	17	31	7	30	85
	0.5	1.4	0.7	0.9	0.8
Rule 3 only	379	286	91	338	1,094
	10.8	12.8	9.6	9.7	10.8
Rules 1 and 2	17	21	suppress	suppress	54
	0.5	0.9	suppress	suppress	0.5
Rules 1 and 3	149	126	17	108	400
	4.2	5.6	1.8	3.1	3.9
Rules 2 and 3	40	47	7	47	141
	1.1	2.1	0.7	1.4	1.4

Frailty identification rule[a]	Cancer site				
	Breast N=3,552	Colorec -tal N=2,234	Gynec- ologic N=946	Prostate N=3,474	Total N=10,176
	N	N	N	N	N
	%	%	%	%	%
Rules 1, 2, and 3	suppress	17	suppress	12	45
	suppress	0.8	suppress	0.4	0.4

[a] Patients with frailty identification by each individual rule are not mutually exclusive.

suppress Numbers suppressed due to small cell counts.

5.4.2 Health Care Use Tables

Table 5. Median number of total cancer-related follow-up visits during the follow-up period by patient characteristics *(Objective 2.1)*.

Variable	Total cancer-related follow-up visits		
	Median number visits	25th; 75th percentile	IQR
Clinical characteristics			
Frailty			
Non-frail	13	8; 21	13
Frail	14	7; 25	18
Comorbidity			
0	15	9; 23	14
1	15	9; 23	14
2	11	5.5; 19	13.5
≥3	11	5; 18	13
No hospitalizations	12	7; 19	12
Cancer site			
Breast	16	9; 24	15
Colorectal	11	6; 18	12
Gynecologic	11	7; 18	11
Prostate	13	8; 20	12
Cancer stage			
I	13	7; 20	13
II	13	8; 21	13
III	14	8; 23	15
Chemotherapy			
No	12	7; 20	13
Yes	18	11; 27	16
Year of cancer diagnosis			
2006-2008	15	9; 24	15

Variable	Total cancer-related follow-up visits		
	Median number visits	25th; 75th percentile	IQR
2009-2010	14	8; 23	15
2011-2013	11	6; 17	11
Demographics			
Sex			
Male	12	7; 20	13
Female	14	8; 22	14
Age			
≤40 years	16	10; 27	17
41-50 years	17	10; 27	17
51-65 years	13	8; 21	13
66-79 years	13	7; 21	14
≥80 years	10	4; 17	13
Residence			
Urban	14	8; 22	14
Rural	12	7; 20	13
Poverty			
No	13	8; 21	13
Yes	13	7; 21	14
Neighbourhood income (quintiles)			
Lowest	13	7; 21	14
Low-middle	12	7; 20	13
Middle	14	8; 23	15
Upper-middle	13	8; 21	13
Highest	13	8; 21	13
Other characteristics			
Follow-up years			
<5 years	10	5; 15	10
5-7 years	13	8; 20	12
8-12 years	17	10; 26	16
Censor reason			
Study end	14	8; 22	14
Subsequent cancer	12	7; 19	12
Cancer recurrence	13	8; 21	13
IPR end	9	6; 15	9
Death	10	5; 19	14
Total	13	8; 21	13

IPR= Insured Patient Registry, IQR= Interquartile Range.

Table 6. Negative binomial (GLM) regression for the association between patient characteristics and the annual rate of cancer-related follow-up visits *(Objective 2.1)*.

Variable	Annual rate of total cancer-related follow-up visits[a]					
	Univariate			Multivariate[b]		
	IRR	95% CI	p-value	IRR	95% CI	p-value
Clinical characteristics						
Frail	1.20	1.15-1.24	<0.001	1.28	1.23-1.33	<0.001
Comorbidity (reference: 0)						<0.001[c]
1	0.95	0.91-0.99	0.026	0.98	0.94-1.02	0.384
2	0.86	0.80-0.92	<0.001	0.92	0.86-0.98	0.015
≥3	0.87	0.80-0.94	<0.001	0.93	0.86-1.00	0.058
No hospitalizations	0.94	0.90-0.99	0.013	0.90	0.86-0.94	<0.001
Cancer site (reference: Breast)						<0.001[c]
Colorectal	0.77	0.74-0.80	<0.001	0.76	0.72-0.80	<0.001
Gynecologic	0.82	0.78-0.86	<0.001	0.82	0.78-0.87	<0.001
Prostate	0.85	0.82-0.88	<0.001	0.95	0.88-1.02	0.163
Cancer stage (reference: Stage I)						<0.001[c]
Stage II	1.03	1.00-1.06	0.076	1.06	1.02-1.09	0.004
Stage III	1.17	1.12-1.22	<0.001	1.18	1.13-1.24	<0.001
Chemotherapy	1.38	1.33-1.44	<0.001	1.30	1.25-1.36	<0.001
Year of cancer diagnosis*	1.03	1.02-1.03	<0.001	1.04	1.04-1.05	<0.001
Demographics						
Female sex	1.13	1.10-1.16	<0.001	1.05	0.99-1.12	0.096
Age (years)*	0.99	0.99-0.99	<0.001	0.99	0.99-0.99	<0.001
Rural residence	0.91	0.88-0.93	<0.001	0.92	0.90-0.95	<0.001
Poverty	1.03	1.00-1.06	0.028			
Neighbourhood income ($)*	1.00	0.99-1.00	0.505			
Other characteristics						
Censor reason (reference: Study end)						
Subsequent cancer	1.17	1.10-1.23	<0.001			
Cancer recurrence	1.55	1.47-1.63	<0.001			
IPR end	1.02	0.90-1.15	0.744			
Death	1.11	1.06-1.16	<0.001			

[a] Regression models were run with an offset, the log of the annual follow-up time (in years). Total cancer-related visits included oncology, primary care, and surgery follow-up visits.

[b] Multivariate analysis adjusted for frailty, comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age at cancer diagnosis, and residence.

[c] Overall p-value for variables with >2 categories.
*** Continuous variable.**
CI= Confidence Interval, GLM= Generalized Linear Model, IPR= Insured Patient Registry, IRR= Incidence Rate Ratio.

Table 7. Provider type seen by all, non-frail, and frail cancer survivors during the follow-up period *(Objective 2.2)*.

Provider type seen	Cancer survivors with visits during the follow-up period		
	All survivors N=10,000	Non-frail survivors N=8,243	Frail survivors N=1,757
	% Patients with ≥1 visit (95% CI)	% Patients with ≥1 visit (95% CI)	% Patients with ≥1 visit (95% CI)
Specialist			
Oncology only	0.5 (0.38-0.67)	0.5 (0.38-0.70)	0.5 (0.20-0.90)
Surgery only	5.7 (5.27-6.19)	6.1 (5.57-6.62)	4.0 (3.17-5.07)
Oncology and Surgery	0.8 (0.62-0.97)	0.9 (0.68-1.10)	0.3 (0.13-0.74)
PCP			
PCP only	8.2 (7.68-8.77)	6.9 (6.40-7.51)	14.2 (12.57-15.89)
Specialist and PCP			
Oncology and PCP	6.3 (0.59-0.68)	6.5 (6.00-7.10)	5.5 (4.45-6.63)
Surgery and PCP	54.3 (53.35-55.31)	54.4 (53.28-55.44)	54.2 (51.82-56.53)
Oncology, Surgery, and PCP	24.1 (23.27-24.96)	24.7 (23.77-25.65)	21.3 (19.45-23.33)

CI= Confidence Interval, PCP= Primary care provider.

Table 8. The percentage of cancer survivors' cancer-related follow-up care attributable to PCPs *(Objective 2.2)*.

Variable	% of cancer-related follow-up visits provided by PCPs			No follow-up visits
	Low (≤30%)	Medium (>30% <73%)	High (≥73%)	
	N (%)	N (%)	N (%)	N (%)
Clinical characteristics				
Frailty				
Non-frail	2,169 (87.3)	4,216 (83.9)	1,858 (74.7)	132 (75.0)
Frail	316 (12.7)	812 (16.1)	629 (25.3)	44 (25.0)
Comorbidity				
0	290 (11.7)	684 (13.6)	315 (12.7)	15 (8.5)
1	835 (33.6)	1,864 (37.1)	900 (36.2)	53 (30.1)
2	194 (7.8)	262 (5.2)	184 (7.4)	24 (13.6)
≥3	103 (4.1)	196 (3.9)	182 (7.3)	10 (5.7)

Variable	% of cancer-related follow-up visits provided by PCPs			No follow-up visits
	Low (≤30%)	Medium (>30% <73%)	High (≥73%)	
	N (%)	N (%)	N (%)	N (%)
No hospitalizations	1,063 (42.8)	2,022 (40.2)	906 (36.4)	74 (42.1)
Cancer site				
Breast	565 (22.7)	1,914 (38.1)	1,000 (40.2)	43 (24.4)
Colorectal	473 (19.0)	977 (19.4)	718 (28.9)	66 (37.5)
Gynecologic	431 (17.4)	402 (8.0)	101 (4.0)	12 (6.8)
Prostate	1,016 (40.9)	1,735 (34.5)	668 (26.9)	55 (31.3)
Cancer stage				
I	999 (40.2)	2,014 (40.1)	1,139 (45.8)	76 (43.2)
II	1,095 (44.1)	2,249 (44.7)	1,029 (41.4)	71 (40.3)
III	391 (15.7)	765 (15.2)	319 (12.8)	29 (16.5)
Chemotherapy				
No	2,140 (86.1)	4,110 (81.7)	2,163 (87.0)	170 (96.6)
Yes	345 (13.9)	918 (18.3)	324 (13.0)	6 (3.4)
Year of cancer diagnosis				
2006-2008	793 (31.9)	1,939 (38.6)	976 (39.2)	52 (29.6)
2009-2010	599 (24.1)	1,237 (24.6)	638 (25.7)	31 (17.6)
2011-2013	1,093 (44.0)	1,852 (36.8)	873 (35.1)	93 (52.8)
Demographics				
Sex				
Male	1,300 (52.3)	2,240 (44.5)	1,004 (40.4)	91 (51.7)
Female	1,185 (47.7)	2,788 (55.5)	1,483 (59.6)	85 (48.3)
Age				
≤40 years	37 (1.5)	151 (3.0)	63 (2.5)	6 (3.4)
41-50 years	192 (7.7)	575 (11.4)	249 (10.0)	12 (6.8)
51-65 years	1,107 (44.6)	2,139 (42.5)	873 (35.1)	60 (34.1)
66-79 years	969 (39.0)	1,812 (36.1)	924 (37.2)	60 (34.1)
≥80 years	180 (7.2)	351 (7.0)	378 (15.2)	38 (21.6)
Residence				
Urban	1,583 (63.7)	3,281 (65.3)	1,511 (60.8)	99 (56.2)
Rural	902 (36.3)	1,747 (34.7)	976 (39.2)	77 (43.8)
Poverty				
No	1,611 (64.8)	3,159 (62.8)	1,309 (52.6)	82 (46.6)
Yes	874 (35.2)	1,869 (37.2)	1,178 (47.4)	94 (53.4)
Neighbourhood income (quintiles)				
Lowest	438 (17.6)	950 (18.9)	551 (22.2)	38 (21.6)
Low-middle	516 (20.8)	957 (19.0)	519 (20.9)	35 (19.9)
Middle	443 (17.8)	1,069 (21.3)	491 (19.7)	36 (20.4)
Upper-middle	554 (22.3)	980 (19.5)	463 (18.6)	41 (23.3)
Highest	534 (21.5)	1,072 (21.3)	463 (18.6)	26 (14.8)
Other characteristics				

Variable	% of cancer-related follow-up visits provided by PCPs			No follow-up visits
	Low (≤30%)	Medium (>30% <73%)	High (≥73%)	
	N (%)	N (%)	N (%)	N (%)
Follow-up years				
<5 years	707 (28.4)	1,072 (21.3)	589 (23.7)	76 (43.2)
5-7 years	1,033 (41.6)	2,032 (40.4)	967 (38.9)	67 (38.1)
8-12 years	745 (30.0)	1,924 (38.3)	931 (37.4)	33 (18.7)
Censor reason				
Study end	1,799 (72.4)	3,767 (74.9)	1,780 (71.6)	108 (61.4)
Subsequent cancer	181 (7.3)	378 (7.5)	153 (6.1)	7 (4.0)
Cancer recurrence	271 (10.9)	413 (8.2)	126 (5.1)	suppress
IPR end	36 (1.4)	70 (1.4)	33 (1.3)	suppress
Death	198 (8.0)	400 (8.0)	395 (15.9)	50 (28.4)
Total	2,485 (100)	5,028 (100)	2,487 (100)	176 (100)

IPR= Insured Patient Registry, PCP= Primary care provider.
suppress Numbers suppressed due to small cell counts.

Table 9. Univariate multinomial models for the association between patient characteristics and the proportion of PCP visits (low, medium, high) *(Objective 2.2)*.

Variable	Univariate analysis[a]					
	Low (reference) vs. Medium-High PCP Visits			Low-Medium (reference) vs. High PCP Visits		
	OR	95% CI	p-value	OR	95% CI	p-value
Clinical characteristics						
Frail	1.63	1.43-1.86	<0.001	1.92	1.72-2.14	<0.001
Comorbidity (reference: 0)						
1	0.96	0.83-1.12	0.607	1.03	0.89-1.20	0.685
2	0.67	0.54-0.83	<0.001	1.25	1.01-1.54	0.042
≥3	1.07	0.83-1.37	0.625	1.88	1.50-2.35	<0.001
No hospitalizations	0.80	0.69-0.93	0.003	0.91	0.78-1.05	0.199
Cancer site (reference: Breast)						
Colorectal	0.69	0.61-0.80	<0.001	1.23	1.09-1.38	0.001
Gynecologic	0.23	0.19-0.26	<0.001	0.30	0.24-0.37	<0.001
Prostate	0.46	0.41-0.52	<0.001	0.60	0.54-0.67	<0.001
Cancer stage (reference: Stage I)						
Stage II	0.95	0.86-1.05	0.294	0.81	0.74-0.90	<0.001
Stage III	0.88	0.77-1.01	0.061	0.73	0.63-0.84	<0.001
Chemotherapy	1.23	1.08-1.40	0.002	0.74	0.65-0.85	<0.001
Year of cancer diagnosis*	0.92	0.91-0.94	<0.001	0.96	0.95-0.98	<0.001
Demographics						

Variable	Univariate analysis[a]					
	Low (reference) vs. Medium-High PCP Visits			Low-Medium (reference) vs. High PCP Visits		
	OR	95% CI	p-value	OR	95% CI	p-value
Female sex	1.44	1.32-1.58	<0.001	1.32	1.20-1.44	<0.001
Age (years)*	0.99	0.99-1.00	0.076	1.02	1.01-1.02	<0.001
Rural residence	1.00	0.91-1.10	0.954	1.19	1.08-1.30	<0.001
Poverty	1.26	1.14-1.38	<0.001	1.56	1.43-1.72	<0.001
Income ($)*	0.99	0.99-0.99	0.011	0.99	0.99-0.99	<0.001
Other characteristics						
Follow-up years*	1.09	1.07-1.11	<0.001	1.02	0.99-1.04	0.082
Censor reason (reference: Study end)						
Subsequent cancer	0.95	0.80-1.14	0.581	0.86	0.71-1.03	0.102
Cancer recurrence	0.65	0.55-0.75	<0.001	0.58	0.47-0.70	<0.001
IPR end	0.93	0.63-1.36	0.702	0.97	0.66-1.44	0.894
Death	1.30	1.10-1.54	0.002	2.07	1.80-2.37	<0.001

[a] Univariate models are presented in this table. Multivariate analysis for the same outcome can be found in Table 10.
*** Continuous variable.**
CI= Confidence Interval, OR= Odds Ratio, PCP= Primary care provider.

Table 10. Multivariate partial proportional odds for the association between patient characteristics and the proportion of PCP visits (low, medium, high) *(Objective 2.2)*.

Variable	Multivariate analysis[a]					
	Low (reference) vs. Medium-High PCP Visits			Low-Medium (reference) vs. High PCP Visits		
	OR	95% CI	p-value	OR	95% CI	p-value
Clinical characteristics						
Frail[b]	1.58	1.43-1.76	<0.001	1.58	1.43-1.76	<0.001
Comorbidity (reference: 0)			0.0019[c]			0.0019[c]
1[b]	0.95	0.83-1.07	0.388	0.95	0.83-1.07	0.388
2	0.72	0.58-0.88	0.002	0.98	0.79-1.21	0.826
≥3[b]	1.23	0.99-1.52	0.052	1.23	0.99-1.52	0.052
No hospitalizations[b]	1.00	0.89-1.14	0.954	1.00	0.89-1.14	0.954
Cancer site (reference: Breast)			<0.001[c]			<0.001[c]
Colorectal	0.94	0.80-1.11	0.453	1.34	1.15-1.55	<0.001
Gynecologic	0.22	0.19-0.26	<0.001	0.29	0.25-0.37	<0.001
Prostate[b]	0.74	0.61-0.89	0.002	0.74	0.61-0.89	0.002
Cancer stage (reference: Stage I)			0.0031[c]			0.0031[c]
Stage II[b]	0.91	0.82-1.00	0.052	0.91	0.82-1.00	0.052

Variable	Multivariate analysis[a]					
	Low (reference) vs. Medium-High PCP Visits			Low-Medium (reference) vs. High PCP Visits		
	OR	95% CI	p-value	OR	95% CI	p-value
Stage III[b]	0.80	0.70-0.91	0.001	0.80	0.70-0.91	0.001
Chemotherapy	1.07	0.92-1.24	0.356	0.72	0.62-0.84	<0.001
Year of cancer diagnosis*	0.93	0.91-0.95	<0.001	0.97	0.95-0.99	0.006
Demographics						
Female sex	1.44	1.21-1.72	<0.001	1.26	1.07-1.49	0.006
Age (years)*	0.99	0.98-0.99	<0.001	1.00	1.00-1.01	0.035
Rural residence	0.96	0.87-1.06	0.451	1.12	1.01-1.23	0.025
Poverty[b]	1.37	1.26-1.48	<0.001	1.37	1.26-1.48	<0.001
Neighbourhood income ($)*						
Other characteristics						
Follow-up years*						
Censor reason (reference: Study end) Subsequent cancer Cancer recurrence IPR end Death						

[a] Multivariate analysis adjusted for frailty, comorbidity, cancer site, cancer stage, chemotherapy, year of cancer diagnosis, sex, age at cancer diagnosis, residence, and poverty.

[b] Indicates where the proportional odds assumption was met.

[c] Overall p-value for variables with >2 categories.

*** Continuous variable.**

CI= Confidence Interval, IPR= Insured Patient Registry, OR= Odds Ratio, PCP= Primary care provider.

Chapter 6: Discussion

This study was the first to describe frailty in a cancer survivor population and examine their health services using administrative data. We found that 17.7% of breast, colorectal, gynecologic, and prostate cancer survivors in the study's NS population-based cohort were frail in their first five years of the follow-up period. Some clinical characteristics (i.e., more comorbidities and later cancer stage at diagnosis) were significantly associated with higher odds of frailty. Although, demographic characteristics were particularly important, as female sex, older age, and poverty were associated with greater odds of frailty. These findings were not surprising and are supported by prior literature.

Interestingly, when adjusted for other patient characteristics in the multivariate model, cancer site was not significantly associated with frailty. Regardless, the prevalence of frailty was highest amongst colorectal cancer survivors. Overall, the findings suggest frailty is prevalent amongst NS cancer survivors, at least within the study cohort, and highlight certain characteristics of patients who may be more susceptible to frailty. Further, frail cancer survivors had high health care usage in the follow-up period with a high proportion of visits to PCPs, which may suggest increased needs related to the late and long-term effects of cancer. From a health system planning perspective, these findings could increase awareness regarding the types of patients that may require additional support during follow-up and may benefit from a multidisciplinary model of follow-up care. There may be a need to direct adequate resources to community providers and potentially build multidisciplinary primary care teams to meet the complex needs of frail cancer survivors.

6.1 Comparing Findings to Literature

Studies that have estimated the prevalence of frailty in cancer survivor populations range from approximately 7.9-59% (149). This study found 17.7% of its cancer survivor cohort to be frail within the five-year follow-up period. One cross-sectional US survey of community-dwelling older adults 50 years and older found 16.1% of cancer survivors in their sample to be frail. Their sample included individuals who had been diagnosed with cancers of the breast, colon, prostate, or lung, lymphoma, or leukemia (150). Another cross-sectional US study, which used clinical measures and questionnaires, found that 18% of breast cancer survivors aged 53-87 years, with a mean of 5-7 years post-treatment, were frail (151). Our study was not limited to older adults; it included cancer survivors ranging from age 7-97 years. The proportion of frail cancer survivors in our study 40 years or younger was 4.7%. Frailty is not limited to older cancer survivors. Hayek et al. (2020) conducted a retrospective cohort study in the US using clinical data and questionnaires. They found frailty in childhood cancer survivors who were five or more years post-diagnosis to be three times higher compared with siblings (152). Five years is the period of typical follow-up care. This period may represent a time when needs are higher, and survivors are more vulnerable. While our study estimates frailty prevalence only within the five-year follow-up window, there are mixed findings regarding the prevalence of frailty amongst cancer survivors for longer follow-up periods. For example, one study found an inverse association between frailty and greater than 10 years elapsed since cancer diagnosis (133). Our findings reinforce the need to support cancer survivors and monitor for frailty, particularly in the five-year follow-up period.

Sociodemographic factors associated with frailty have been described in the literature. Our study demonstrated some of these expected findings, such as increased odds of frailty in the female sex, which has been previously described in the literature as related to estrogen deficiency (149,152). We also found higher odds of frailty amongst those of lower SES (i.e., poverty). While evidence is lacking specifically related to frailty in cancer survivors and SES, outside of this realm, as described in a recent systematic review, frailty is associated with lower SES (153). The associations between frailty, increasing age, and comorbidities have been well documented, including within cancer survivor populations (150,152); this study aligns with those findings.

The variation in frailty by clinical characteristics was not as conspicuous compared to its variation by demographic characteristics. Although, as expected, those with stage III cancer at diagnosis had higher odds of frailty than those with stage I. Smitherman et al. (2018) showed a similar finding (135). However, compared to breast cancer survivors, survivors of colorectal, gynecologic, and prostate had lesser odds of frailty when adjusted for other patient characteristics, though the associations were non-significant. Similarly, two studies that included survivors of various cancers did not find cancer site to be significantly associated with higher frailty (133,135). Even among studies conducted with single cancer sites, estimates of prevalence have varied. For example, amongst two studies with breast cancer survivors, one found a frailty prevalence of 5.1% (154) and the other 18% (151). Similarly, a study by Winters-Stone et al. (2017) identified a prevalence of frailty greater than 20% for prostate cancer survivors (155), contrasting with the findings of Bylow et al. (2011) who identified a frailty prevalence of less than 10% for

prostate survivors (156). Such variation suggests that using cancer site alone is likely not a great way to predict survivors who may become frail. Although descriptive data and univariate analysis showed a higher proportion of frailty amongst colorectal cancer survivors, this finding was dissolute in the multivariate model after accounting for other characteristics. It may be that other demographic factors found amongst colorectal survivors were contributing to frailty within this group.

Receipt of chemotherapy was associated with lower odds of frailty, though this finding was non-significant in the multivariate model. Within the population-based cohort, 15.7% of participants received chemotherapy during the treatment period. This number aligns with the cancer sites included in this study (e.g., chemotherapy is not standard of care for low-risk prostate cancer patients or for early stage [stage I-II], low-risk colon cancer patients); however, it is likely an underestimation of chemotherapy receipt due to missing data (i.e., no information on oral chemotherapy) (157). Some other studies have found cancer treatments to be associated with frailty (152,158), while others have not (151,159). The possible underestimation of chemotherapy and/or the particular cancer sites of survivors represented in this study may have contributed to the lack of association between chemotherapy and frailty. These findings suggest that sociodemographic factors rather than disease-specific characteristics are important for frailty identification, although those with more severe disease certainly have higher odds of frailty. Further research should be conducted to explore frailty amongst various cancer sites and treatment modalities.

Frail cancer survivors in the study's cohort were most commonly identified through rule 3 for identification of frailty in administrative data. Urquhart et al. (2017) found that rule 2 identified the largest proportion of frailty within an NS community-dwelling older adult decedent population; they were unable to calculate frailty for NS living persons due to issues with data availability (14). The health care usage that flagged frailty according to rule 3 is likely related to the late and long-term effects survivors seek care for in the follow-up period. Seven-point-one percent of cancer survivors were flagged as frail related to cognitive impairment. While the data does not contain this level of detail, it is possible this is related to 'brain or chemo' fog following cancer treatment. Related, Mandleblatt et al. (2021) described a self-reported decline in cognition as cancer survivors grew frail (160). To our knowledge, this study was the first to use these rules specifically within a cancer survivor population. Future research could use these rules amongst other Canadian cancer survivor populations.

We found that frail cancer survivors compared to non-frail cancer survivors in the study cohort had a higher annual cancer-related follow-up visit rate. This finding relates to existing literature, which states the needs of frail individuals' often go unmet (15), consequently, they continue to seek health care. Similarly, a 2019 US retrospective study of cancer patients after urologic surgery found that increasing frailty was associated with increasing health care use after surgery, including prolonged hospital stay, referrals for continuing care, and hospital re-admission (161).

This study found that each successive year of cancer diagnosis, higher stage and younger age at cancer diagnosis were significantly associated with more follow-up visits, aligning with the findings of follow-up visits examined in a similar cohort of NS cancer survivors (29). Differing from findings of this similar NS cohort of cancer survivors, neighbourhood income was not a significant predictor and rural residence was significantly associated with less follow-up visits in our study. Further, we found that compared to breast cancer survivors, survivors of gynecologic cancer had significantly less, not more visits (29). However, there were notable differences between these two cohorts that likely explain the variation. Firstly, our study used a minimum follow-up observation inclusion criterion of 2.5 years, due to our frailty assessment. Secondly, we examined not only cancer centre visits, but cancer-related visits, including those to PCP. Finally, we had a longer period of follow-up data and thus, observed visits over a longer time period.

In this study, we established that a high percentage of non-frail and frail NS cancer survivors saw both a surgeon and a PCP for follow-up care, although it was higher for those who were non-frail. Another NS study found breast cancer survivors had greater surgeon follow-up compared to other Canadian provinces (30). We also found that frail compared to non-frail cancer survivors more commonly saw only PCPs. Furthermore, frailty was associated with a higher proportion of PCP visits. Similarly, prior literature not specific to cancer care, found frailty to be associated with increased PCP use (162).

Other patient characteristics within our study cohort associated with a medium-high or a high proportion of PCP visits included female sex, poverty, breast and colorectal cancer survivors, and stage I cancer at diagnosis. Urquhart et al. (2020) examined factors associated with primary care use during follow-up care within a similar NS cancer survivor cohort (163). They found female sex significantly associated with increased annual PCP use when analyzed for all PCP visits, but not for cancer-specific PCP visits. In their study, neighbourhood income was significant at a null value. Our study found poverty was significantly associated with higher odds of a medium-high or high proportion of all cancer-related follow-up visits provided by PCPs. Urquhart et al. (2020) found stage II or III compared to stage I cancer was associated with a higher annual cancer-specific PCP visit rate. They also found that prostate cancer survivors had more cancer-specific PCP visits per year, and breast cancer survivors had more annual PCP visits for all reasons, compared to colorectal and gynecologic survivors (163). Our study found that considering all cancer-related follow-up visits, patients diagnosed with stage I cancer, or with breast or colorectal cancer, had higher odds of having a high proportion of those visits provided by PCPs. While our study found that each unit increase in the year of cancer diagnosis was associated with lower odds of a higher proportion of PCP visits, Urquhart et al. (2020) found each successive diagnosis year associated with a higher annual PCP visit rate (163). This is likely reflective of the different outcomes measured; in our study, the proportion of PCP visits, and in Urquhart et al. (2020), the annual PCP visit rate. Thus, our result likely reflects that those diagnosed later in the study period were in a more immediate follow-up period, likely still seeing specialists more often than those diagnosed earlier (i.e., where more time had passed). Patients diagnosed earlier

likely needed fewer specialist visits as time went on and/or were discharged to primary care for remaining follow-up.

6.2 Limitations

The study is not without limitations. The following discussion of the study's limitations centres around challenges using administrative data, including data availability and measurement limitations of variables.

Administrative data are not captured for research purposes. While they represent a powerful and efficient means to study healthcare utilization, there are known limitations to the use of administrative data. MSI Physician Billings data exists to pay physicians and provide accountability for their work; therefore, it is expected that these data are accurate descriptions of physicians' services rendered. However, all diagnostic codes may not have been recorded, and there is no way to tell what codes, if any, are missing. All physician visits may not be represented. Shadow billing has often been a concern with the use of physician claims data. Although we acknowledge this may have under-reported services provided, at least two recent Canadian studies, from MB and Alberta (AB), have reported high levels of accuracy in reported physician claims data (164,165). Not having a family doctor is a likely barrier to discharge from the cancer clinic. As such, those patients may be more likely to receive ongoing specialist care; this may create a high estimate of specialist care use. Our data are limited because we were unable to identify those who did not have a PCP or those who lost their PCP or specialist provider during follow-up. However, the proportion of patients in our cohort who did not have at least

one PCP visit was small (8.6%), suggesting most patients found a way to access PCP services whether or not they had a usual PCP.

We only examined cancer-related visits provided by medical oncologists, radiation oncologists, PCPs, general surgeons, obstetrician/gynecologists, gastroenterologists, and urologists. Therefore, we did not capture health services used from other specialty visits. However, this was done purposefully to achieve a narrow focus on cancer-related follow-up. We used a known set of diagnostic codes to determine cancer-related visits within MSI Physician Billings (Appendix C) and a previously used decision-rule for OPIS (29). However, we did include other cancer-related and mental health codes that represent issues commonly experienced by survivors in follow-up (e.g., depression, nausea and vomiting), though there is no way to tell if these particular codes were certainly related to a cancer diagnosis (Appendix C). Despite the possibility of overestimating cancer-related visits, the act of specifying these codes is one that few follow-up studies have done. In order to maintain a relatively narrow focus and due to feasibility, we did not explore non-cancer-related visits. Due to the complexities of care and cancer-related issues that may be addressed by other providers for frail and/or non-frail cancer survivors, it may be beneficial for future studies to explore cancer survivor patterns in non-cancer-related visits, for example, to geriatricians, other specialists, or mental health providers.

There is no gold standard to measure frailty and measuring frailty in administrative data poses some challenges. Although the rules to identify frailty have been tested and have face validity from expert geriatricians, they do not replace clinical information.

Moreover, this measure of frailty captures physical and cognitive aspects but not psychosocial factors. The rules to identify frailty thus require further validation. Further, individuals may experience varying degrees of frailty (e.g., prefrail, moderate, severe), which we were not able to delineate. However, I would argue that for population-level frailty identification, the categorization of non-frail and frail is sufficient as a starting point for health services insight. Certainly, these decision rules do identify a prevalence of frailty similar to that reported by others. Furthermore, the rules of frailty and data presented allow the reader to see in which domains an individual was deemed frail (Table 4). Additionally, the identification rules focus on specificity over sensitivity; therefore, some frail individuals may not have been identified (14).

The estimate of frailty prevalence in this study represents a period prevalence of NS breast, colorectal, gynecologic, and prostate cancer survivors diagnosed between January 01, 2006, and December 2013, during the first five years of follow-up. However, our calculation is based upon specific inclusion/exclusion criteria and does not include a group of long-term survivors in NS diagnosed before the study period who were still survivors at that time. Furthermore, it is important to note when interpreting findings, results are limited in their comparison to today's current patients, as less chemotherapy, less invasive surgeries, and more immunotherapy and targeted treatments are being utilized. Additionally, the cohort does not include those with stage IV disease. Although small numbers, this means we did not identify some stage IV patients who may have converted to curable status and had long-term survival. Therefore, the prevalence of

frailty may be underestimated, and readers should not extrapolate the findings far beyond the study cohort.

The study design does not fit the traditional definition of a retrospective cohort study or a cross-sectional study due to the follow-up data. Although a cross-sectional design is ideal for determining prevalence, this study is population-based, and thus includes NS cancer survivors of stage I-III breast, colorectal, gynecologic, and prostate cancers during the study period. For analysis purposes, data were treated as cross-sectional. Being cross-sectional, consequently, temporality between variables cannot be determined; thus, no causal inferences can be made. Finally, a critique of estimating frailty using administrative data is the overall risk for overestimation. However, I feel the study took steps to mitigate this (i.e., the rules favoured specificity over sensitivity, we used a minimum observation period, and described the proportion of those who died less than five or five or more years after becoming frail). In an effort to counteract the risk of overestimation, we may have underestimated the prevalence of frailty. However, if this is the case, the frailty prevalence of 17.7% is still a considerable proportion, given the prudent measurement.

As the measure of comorbidity used was from hospital discharge records (i.e., CIHI DAD) and no outpatient records, bias was introduced. The amount of comorbidity is likely underestimated as we are missing those with indicators of comorbidity found in outpatient records. Forty percent of individuals had no hospitalization records; thus, comorbidity results must be interpreted with caution. We removed patients with missing

data for the neighbourhood income variable (1.26%). However, complete case analysis wherein less than 5% of independent variable data is missing has been cited as having a low risk for bias when there are no clear systematic differences in those missing (166).

There are other variables or components of concepts that we may not have captured due to the nature of administrative data and/or availability within our specific datasets. For example, it would have been beneficial to observe more treatment information, such as hormone therapy, radiation, surgery, immunotherapy and targeted treatments, and drug information (e.g., oral chemotherapy). For example, codes indicating the type of surgery a patient had for treatment of their cancer would have been useful. Some surgical procedures are less invasive (e.g., polypectomy for early stage I colon cancer) compared to others (e.g., partial colectomy for stage III colon cancer). Recovering from an invasive surgery is likely more taxing on the body, and thus this information could have been particularly useful for the examination of frailty within this study. More specific cancer type information (e.g., triple-negative breast cancer) could have provided more context, especially related to health care use. Given there are racial disparities in cancer-related outcomes along the cancer care continuum (167), race would have been an important covariate to explore. However, race-based data are not available in existing administrative health data.

6.3 Strengths, Research and Policy Implications

Despite its limitations, the study has several strengths. They include the benefits of using administrative data, its novelty, the period for examination of follow-up care, the measure

of routine follow-up visits, and the rules to identify frailty within administrative data. Further, this systematic identification of frailty is useful from a health systems perspective for resource planning and future care models.

The benefit of using a population-based administrative dataset is that the study did not have to rely on self-reported data or introduce recall or selection bias associated with that type of data. Using administrative data allowed the linkage of various data sources and information, and a larger study population than would be otherwise possible. To our knowledge, this study represents the first-ever systematic identification of frailty using solely administrative data in a Canadian cancer survivor population. Given the overall prevalence of frailty (17.7%) found within the study cohort and its spread across cancer sites, it would be beneficial to ensure oncology providers are aware of this information, to prompt further clinical assessment of frailty and referrals for support amongst patients as needed, and to achieve early identification of frailty within the follow-up period. It will also be important to ensure that providers caring for this population have training in frailty care.

This study described patterns of follow-up care in a time period after Choosing Wisely Canada made recommendations (in 2015) to use PCPs where possible for survivorship follow-up care (1). Research following this recommendation is important to see if those efforts have made an impact in practice. This may prompt decision-makers to re-evaluate care pathways. Additionally, this study provides a more precise measure of follow-up visits. Unlike many prior studies, it differentiated between cancer-related and non-cancer-

related visits and included oncology and PCP follow-up visits, capturing a broader range of visits. This study shows that cancer survivors in NS are frequenting PCPs, though many continue to see specialists, oncologists, and particularly surgeons. However, frail cancer survivors do have less specialist cancer follow-up than non-frail survivors. Additionally, a higher proportion of frail cancer survivors compared to non-frail survivors visited only PCPs for cancer-related care during the follow-up period. This points to movement from specialist-led to primary-focused cancer follow-up. However, due to the volume of visits, particularly amongst frail survivors, it may point to a need for ensuring robust structures and care models equipped to care for patients with increased and complex needs. Primary care has been associated with reduced hospitalizations and increased satisfaction of care in frail patients. Primary care models tested in frail populations include, integrated care, shared care, home-based care, and family medicine speciality clinics (168). While within this study sufficient data was not available to examine the role of Advanced Practice Nurses (APNs) in follow-up care, their role in oncology care has been discussed in the literature. APNs have begun to aid in the care of older adult cancer patients across the cancer continuum. When practicing to their full scope, APNs could aid in enhancing communication across care transitions, survivorship care planning, and contribute to Comprehensive Geriatric Assessment, which would help the care team identify and manage frailty (169). Key stakeholders (i.e., decision and policy-makers, PCPs, researchers, and oncology specialists) may want to explore how community oncology care or multidisciplinary primary care models could benefit this group.

The rules to identify frailty in administrative data incorporate health service utilization in addition to physical and cognitive aspects of frailty. The rules use ICD9/10 codes and were purposefully built using only primary databases (CIHI DAD and MSI Physician Billings); thus, these data are widely available in other Canadian provinces, which makes this study easily replicable in other Canadian provinces.

6.4 Future Research Directions

This study lays a foundation on which to further investigate frailty within cancer survivors, as well as their health care use, both in the NS and Canadian contexts. Future studies should use the rules to identify frail survivors in other provinces as follow-up care practices vary by province (29).

As a large proportion of frail survivors utilized PCPs during follow-up, future studies may benefit from recruiting cancer survivors through PCP clinics for clinical frailty assessment. This could be coupled with qualitative interviews to identify what supports and interventions frail survivors would find beneficial or examine the differences in needs voiced by frail and non-frail individuals. This may also help tease out differences in needs between people with different cancer sites. Furthermore, it is unknown how information is actually being shared between providers. It would be beneficial to capture the continuity of care both in administrative data and qualitative interviews (e.g., patient perspectives of their continuity of care and transition from or between care of PCPs and specialists). Researchers should engage key stakeholders in cancer and primary care, including patients, to determine their perspectives on the model of care best suited for

frail cancer survivors, along with its potential challenges; these data could inform the selection of a care model to test within this population. The study's findings demonstrate differences between frail and non-frail cancer survivors, suggesting frailty may be useful in personalizing follow-up care. Given the complex needs frail people often have, multidisciplinary primary care teams could benefit frail survivors (e.g., social workers to aid with socioeconomic challenges, physiotherapists to rebuild muscle strength, occupational therapists to work on cognitive function, etc.). Researchers should involve oncology specialists and PCPs in planning and testing such transitions in care.

6.5 Conclusion

This study was the first to quantify frailty in a Canadian cancer survivor population. In the NS breast, colorectal, gynecologic, and prostate cancer survivor cohort, frailty was prevalent at 17.7%. While disease severity is relevant, sociodemographic factors remain particularly important for frailty assessment. Compared to non-frail survivors, frail survivors had high usage of follow-up care and a higher proportion of cancer-related follow-up visits to PCPs. SES differences amongst survivors were observed in health care use, particularly in regard to higher visit use and proportion of PCP visits. The findings suggest frail cancer survivors are being cared for by PCPs, but they require a high amount of support (visits). Moving forward, more research should be conducted with cancer survivors and key stakeholders in primary and oncology care to find and test alternative care models well suited to meet the needs of this population.

6.6 Knowledge Translation

Prior to data analysis, the initial research plan was presented in the form of a poster presentation at the Department of Community Health and Epidemiology 2020 Research Day, the 2021 Canadian Centre for Applied Research in Cancer Control conference, and the 2021 NSH Department of Medicine Research Day. I have written lay summaries to explain the research proposal to the general public for awarding funding agencies, the Maritime SPOR SUPPORT Unit, the Canadian Institutes of Health Research, and the Canadian Centre for Applied Research in Cancer Control.

Moving forward for this single study, the goal of the end-of-grant knowledge translation plan is to disseminate the findings to interested audiences. I will work with the research supervisor to identify opportunities to disseminate the research findings in summaries/abstracts and/or conferences that will reach oncology providers, researchers, and stakeholders in both cancer and frailty care. Additionally, I will prepare and submit a manuscript to a relevant cancer care journal.

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Appendix A: Follow-up Guideline Chart

The table below describes recommended models of care/provider type by cancer site according to select organizations with cancer survivor follow-up care guidelines (68,170–173).

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
Alberta Health Services	May transition early-stage survivors to family physician or nurse practitioner (56).	Follow-up care may be provided by the general practitioner, nurse practitioner, or a medical/ radiation oncologist (60).	Survivors of early stage and advanced stage recurrent/persistent cancer of the uterine cervix should initially be followed by a physician experienced in surveillance of cancer patients. After the first two years, the patient can be discharged to the primary care physician (61,62). For survivors of endometrioid carcinoma and of endometrial serous, clear cell, and carcinosarcoma, follow-up by the treating gynecologic oncologist, general oncologist, or general	No provider type recommendation found for follow-up care (58,59).

Organization	Cancer site recommendation[a]			
	Breast	Colorectal	Gynecologic	Prostate
			practitioner could be based on risk of recurrence (63,64). The algorithm for management of epithelial ovarian, fallopian tube, and primary peritoneal cancer does not specify which care provider should be responsible for follow-up (65,66). For follow-up of uterine sarcoma survivors, no provider type recommendation was found for follow-up care (57,67).	
American Society of Clinical Oncology	Early stage (i.e., tumor less than five centimeters and less than four positive nodes) may be followed solely by a primary care physician one-year post-	Recommendations for colorectal cancer survivors, stages II and III (not stage I or resected metastatic disease, both of which have minimal data to provide guidance)	No guidelines found.	May transition survivors to a primary care clinician for follow-up (54).

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
	diagnosis (52). They note a lack of evidence, but state it seems likely that history, physical and breast exams may be conducted by experienced non-physician providers (e.g., nurse practitioners, physician assistants) (51).	include transitioning survivors who have completed all treatment to community-based family physician coordinated care or institution-based nurse coordinated care (53).		
Cancer Care Ontario	Most survivors can be safely transitioned to primary care physicians (69). Community-based family physician-led, or nurse-led care within an institution are reasonable options. States hormonal therapy may still be ongoing (75).	May be discharged to community-based family physician-led. Transition to nurse-led care within an institution may be a reasonable option (70). They say although specialist follow-up is currently the most common practice, their 2019 follow-up model of care for cancer survivor guidelines	For cervical cancer survivors, follow-up by a physician experienced in surveillance of patients with cancer. May be followed by a primary care physician after five years of recurrence-free follow-up (71). For survivors of endometrial cancer, if a patient is initially followed by a specialist, they	Follow-up surveillance may be provided by the treating oncologist, urologist, family physician, nurse practitioner, or hospital-based nurses (73). Patients may still be on hormone therapy. Transition to nursing-led care within an institution is a reasonable

Organization	Cancer site recommendation[a]			
	Breast	Colorectal	Gynecologic	Prostate
		recommend primary care follow-up with specific handover pieces and supports in place from the specialist team, for survivors of all cancer types. This organization planned to implement the recommendations across ON in breast and colorectal cancer site groups and expanded to other cancer sites over time (74).	may be followed by a qualified general practitioner after three to five years of recurrence-free follow-up (72). No recommendations can be made about models of care of other gynecologic disease types based on the currently available published literature (75).	option. There is not enough data to say discharge to primary care is equivalent to specialist care, but, based on the disease trajectory, the expert opinion is that this is a reasonable option (75).
National Comprehensive Cancer Network	Shared coordination between the primary care provider, oncology and subspeciality care providers is encouraged. Transition of care to primary care provider may be done when clinically appropriate (41,49).	Care may be provided by the oncologist and the primary care provider. Roles should be clearly defined. A prescription for survivorship and transfer to the primary care physician should be written (42,43).	Unclear recommendations. Varies by specific gynecologic cancer type. But does emphasize communication and coordination with all clinicians involved in the care of survivors, including primary care clinicians. However, does	No clear recommendation. Does mention primary care as an option for patients' follow-up care (48).

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
			not specifically mention transfer of follow-up care to primary care/other (44–47).	
Nova Scotia Health Cancer Care Program	Indicates patients on routine surveillance, discharged from the cancer centre are followed-up by the primary care provider (where appropriate in partnership with the surgeon). Patients also receive a copy of the follow-up recommendations, so they are aware of the appropriate schedule. Primary care providers/surgeons can contact the patient's treating oncologist at any time for re-referral due to significant treatment-	Follow-up surveillance guidelines exist for both colon and rectal cancers (39). For both rectal and colon cancers, patients on routine surveillance, discharged from the cancer centre are followed-up by the primary care provider (where appropriate in partnership with the surgeon). Patients also receive a copy of the follow-up recommendations, so they are aware of the appropriate schedule. Primary care providers/surgeons can contact the patient's treating oncologist at any time for re-referral due to	No guidelines available.	No guidelines available.

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
	related side effects or suspected recurrence (39).	significant treatment-related side effects or suspected recurrence (39). For colon cancers, colonoscopy follow-up is to be coordinated with the attending surgeon. For rectal cancers recto sigmoidoscopy and colonoscopy are to be coordinated with the attending surgeon (39).		
Saskatchewan Cancer Agency	May transition early-stage survivors to the community physician. Although, those on adjuvant zoledronic acid or a luteinizing-hormone releasing hormone agonist require follow-up at the cancer center (77).	May transition stage I, II or low risk stage II survivors to the family doctor. High risk stage III and all stage IV, unless otherwise clinically determined are followed at the cancer centre. Radiation oncology follows those who have had definitive chemoradiotherapy (e.g., anal cancer) or long	Cervical cancer survivors are to be followed by a gynecologic oncologist for five years and then discharge to the family physician (79). Endometrial cancer survivors (stage IA and IB; endometrioid adenocarcinoma [low-risk]) are to be followed by a family physician or gynecologist	A risk-stratified approach for follow-up is described below. For survivors with localized prostate cancer and very low or low risk disease: If on active surveillance-care by urologist. If post prostatectomy, after consult with radiation oncologist can

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
		course chemoradiotherapy (e.g., rectal cancer) wherein radiation is the primary modality. Medical oncology follows those who only had chemotherapy or had chemotherapy following concurrent chemoradiotherapy (78).	for five years, then discharged from endometrial cancer follow-up (80). Endometrial cancer survivors, patients with stage IA confined to the endometrium/no myometrial invasion, to be discharged from post-op visit with no need for regular follow-up (no designated provider assigned follow-up) (80). All other endometrial cancer survivors (advanced stages, high-grade histology/ high risk) should be followed (where possible) by a gynecologic oncologist for 5 years of follow-up, then discharged if no relapse (80).	be discharged to family physician or urologist. If post external beam radiation therapy/ brachytherapy, radiation oncology to follow until resolution of toxicities and then discharge to family physician/urologist (83). For survivors in the favourable intermediate risk group: If on active surveillance- care by urologist. If post prostatectomy, after consult to radiation oncology can be discharged to family physician and or urologist. If post external beam radiation therapy /brachytherapy /androgen deprivation therapy, radiation oncology to

Organization	Cancer site recommendation[a]			
	Breast	**Colorectal**	**Gynecologic**	**Prostate**
			Ovarian cancer survivors to be followed by a gynecologic oncologist for a total of 10 years from diagnosis (82). Vulvar cancer survivors (stage I and II) no comment on a specific provider type for follow-up (82). Vulvar cancer survivors presenting with more advanced disease will be followed at the cancer center and not discharged before five years of relapse free follow-up (82).	follow until resolution of toxicities and duration of androgen deprivation therapy. Then, may be discharged to family physician and or urologist (83). For survivors with intermediate unfavourable or high-risk disease: Radiation oncology to follow post radiation therapy until resolution of toxicities and completion of androgen deprivation therapy (83).

[a] Recommendations are based on patients who have completed active treatment, have no evidence of metastatic disease, or treatment complications not already addressed by an oncologist, unless exceptions are listed. Studies with nurse-led follow-up were performed in hospital institutions, not community-based settings. As most guidelines did not define what they meant by provider type (e.g., what constitutes a primary care provider), the original verbiage used for such terms was left as stated in the guideline. Generally, those enrolled in clinical trials are expected to be followed in the cancer centre. Most guidelines state clear care direction from the discharging physician (i.e., oncology specialist) to the receiving physician (e.g., primary care provider) is required for care transition. There is a distinction between nurse coordinated care and the most responsible provider. Nurse coordinated care does not mean the nurse is the most responsible provider.

Appendix B: MSI Physician Billings/CIHI DAD Censoring Procedure Codes

The below MSI Physician Billings and CIHI DAD procedure codes represent some of the data which was used to censor individuals in the study cohort.

Cancer site	Procedures indicating cancer recurrence	
	MSI Physician Billings	**CIHI DAD**
Breast	MASG 97.12 (Unilateral) Complete Mastectomy MASG 97.13 Bilateral Complete Mastectomy MASG 97.14 (Unilateral) Extended Simple Mastectomy MASG 97.15 Bilateral Extended Simple Mastectomy MASG 97.27A Quadrant resection, lumpectomy, radical mastectomy with axillary dissection (regions required)	1.YM.89.^^ Excision total, breast 1.YM.90.^^ Excision total with reconstruction, breast 1.YM.91.^^ Excision radical, breast 1.YM.92.^^ Excision radical with reconstruction, breast
Colorectal	MASG 44.3 Segmental resection of lung (basilar) (superior) MASG 44.4 Lobectomy of lung (regions required) MASG 44.5 Complete pneumonectomy MASG 62.12 Partial hepatectomy-local excision of lesion MASG 62.2 Lobectomy of liver	1.GR.87.^^ Excision partial, lobe of lung 1.GR.89.^^ Excision total, lobe of lung 1.GR.91.^^ Excision radical, lobe of lung 1.OA.87.^^ Excision partial, liver
Gynecologic	No relevant surgical procedures	No relevant surgical procedures
Prostate	MASG 72.4A Prostatectomy with vesiculectomy includes deep lymphadenectomy MASG 72.4B Prostatectomy-radical including deep pelvic lymphadenectomy	1.QT.87.^^ Excision partial, prostate 1.QT.91.^^ Excision radical, prostate
All	VADT 13.55 Injection or infusion of cancer chemotherapeutic substance NEC	Not applicable

CIHI DAD= Canadian Institutes for Health Information Discharge Abstracts Database, MSI= Medical Services Insurance Physicians' Billings.

Appendix C: MSI Physician Billings Diagnostic Codes Cancer-related Follow-up Visits

The diagnostic codes listed below were used to identify follow-up care visits that were related to the individual's cancer diagnosis. For each cancer site, diagnosis codes considered relevant to the individual's cancer diagnosis were identified (some codes are applicable to more than one or even all sites).

Category	MSI Physician Billings diagnostic code(s)
Breast cancer	
Malignant neoplasms	174 Malignant neoplasm of female breast (includes 174.0, 174.1, 174.2, 174.3, 174.4 174.5, 174.6, 174.8, 174.9) 175 Malignant neoplasm of male breast (includes 175.0 and 175.9)
Related and benign neoplasms	195.1 Malignant neoplasm of thorax (includes: axilla, chest wall not otherwise specified) 217 Benign neoplasm of breast 238.3 Neoplasm of uncertain behaviour of breast 239.3 Neoplasm of unspecified nature of breast
Carcinoma in situ	233.0 Carcinoma in situ of breast
Other related	173.5 Unspecified malignant neoplasm of skin of trunk, except scrotum (includes: axillary fold and skin of breast) (1735.0, 173.51, 173.52, 173.59) 216.5 Benign neoplasm of skin of trunk, excluding scrotum (includes: axillary fold and skin of breast) 232.5 Carcinoma in situ of skin of trunk (includes: axillary fold and skin of breast) 451.89 Phlebitis and thrombophlebitis of other sites (includes: thrombophlebitis of breast [Mondor's disease]) 610 Benign mammary dysplasia (includes 610.0, 610.1, 610.2, 610.3, 610.4, 610.8, 610.9) 611 Other disorders of breast (includes 611.0, 611.1, 611.2, 611.3, 611.4, 611.5, 611.6, 611.7[611.71, 611.72, 611.79], 611.8[611.81, 611.82, 611.83, 611.89]) 612 Deformity and disproportion of reconstructed breast (includes 612.0, 612.1) 793.8 Abnormal radiographic or other findings of the breast (i.e., abnormal or inconclusive mammogram) (includes 793.80, 793.81, 793.82, 793.89) 879.0 Open wound of breast without mention of complication (in chapter 'internal injuries of thorax, abdomen, and pelvis') 879.1 Open wound of breast, complicated (from same chapter as above)

Category	MSI Physician Billings diagnostic code(s)
	V10.3 Personal history of malignant neoplasm of the breast V45.71Acquired absence of breast and nipple V50.41 Prophylactic removal of breast V51 Aftercare involving the use of plastic surgery (e.g., breast reconstruction) (includes V51.0, V51.8) V76.1 Special screening for malignant neoplasms of breast (includes V76.10, V76.11, V76.12, V76.19) V86 Estrogen receptor status (includes V86.0, V86.1) V87.43 Personal history of estrogen therapy
Colorectal cancer	
Malignant neoplasms	153 Malignant neoplasm of colon (includes 153.0, 153.1, 153.2, 153.3, 153.4, 153.5, 153.6, 153.7, 153.8, 153.9) 154 Malignant neoplasm of rectum, rectosigmoid junction, and anus (includes 154.0, 154.1, 154.2, 154.3, 154.8)
Related and benign neoplasms	195.2 Malignant neoplasm of abdomen (includes: intra-abdominal not otherwise specified) 211.4 Benign neoplasm of rectum and anal canal 211.9 Benign neoplasm of other and unspecified site (includes: alimentary tract, digestive system, gastrointestinal tract, intestinal tract, intestine, spleen, not otherwise specified) 235.2 Neoplasm of uncertain behavior of stomach, intestines, and rectum 239.0 Neoplasm of unspecified nature of digestive system
Carcinoma in situ	230.3 Colon (includes: appendix, cecum, ileocecal value, large intestine not otherwise specified) 230.4 Rectum 230.5 Anal canal 230.6 Anus, unspecified 230.7 Other and unspecified parts of intestine 230.9 Other and unspecified digestive organs (includes: digestive organ and gastrointestinal tract not otherwise specified, pancreas, spleen)
Other related	560 Intestinal obstruction without mention of hernia (includes 560.0, 560.1, 560.2, 560.30, 560.31, 560.32, 560.39, 560.81, 560.89, 560.9) 562 Diverticula of intestine (includes 562.00, 562.01, 562.02, 562.03, 562.10, 562.11, 562, 12, 562.13) 564 Functional digestive disorders, not elsewhere classified (includes 564.0, 564.00, 564.01, 564.02, 564.09, 564.1, 564.2, 564.3, 564.4, 564.5, 564.6, 564.7, 564.8, 564.81, 564.89, 564.9) 567 Peritonitis and retroperitoneal infections (includes 567.0, 567.1, 567.2, 567.21, 567.22, 567.23, 567.29, 567.3, 567.31, 567.38, 567.39, 567.8, 567.81, 567.82, 567.89, 567.9) 568 Other disorders of peritoneum (includes 568.0, 568.8, 568.81, 568.82, 568.89, 568.9) 569 Other disorders of intestine (includes 569.0, 569.1, 569.2, 569.3, 569.4, 569.41, 569.42, 569.43, 569.44, 569.49, 569.5, 569.6, 569.60,

Category	MSI Physician Billings diagnostic code(s)
	569.61, 569.62, 569.69, 569.7, 569.71, 569.79, 569.8, 569.81, 569.82, 569.83, 569.84, 569.85, 569.86, 569.87, 569.89, 569.9) 579.2 Blind loop syndrome (i.e., excessive intestinal bacteria, possible result of surgical complication) 579.3 Other and unspecified postsurgical non-absorption 579.8 Other specified intestinal malabsorption 579.9 Unspecified intestinal malabsorption 680.5 Infections of skin and subcutaneous tissue of the buttock (includes: anus, gluteal region) 783.9 Other symptoms concerning nutrition, metabolism, and development (i.e., hypometabolism, dehydration, disorders of electrolyte and acid-base imbalance) 787.1 Heartburn 787.2 Dysphagia (i.e., difficulty swallowing) (includes 787.20, 787.21, 787.22, 787.23, 787.24, 787.29) 787.3 Flatulence, eructation, and gas pain 787.4 Visible peristalsis 787.5 Abnormal bowel sounds (includes: absent or hyperactive bowel sounds) 787.6 Incontinence of feces (includes 7876.0, 7876.1, 7876.2, 7876.3) 787.7 Abnormal feces 787.9 Other symptoms involving digestive system (includes: diarrhea, change in bowel movements, cramping rectal pain) (includes 7879.1, 7879.9) 789 Other symptoms involving abdomen and pelvis (All 789 except 789.7 Colic (i.e., in babies) (includes 789.00,789.01, 789.02, 789.03, 789.04, 789.05, 789.06, 789.07, 789.09, 789.1, 789.2, 789.30, 789.31, 789.32, 789.33, 789.34, 789.35, 789.36, 789.37, 789.39, 789.40, 789.41, 789.42, 789.43, 789.44, 789.45, 789.46, 789.47, 789.49, 7895, 789.60, 789.61, 789.62, 789.63, 789.64, 789.65, 789.66, 789.67, 789.69, 789.9) 792.1 Abnormal findings in stool contents 793.4 Abnormal radiographic or other findings of the gastrointestinal tract 793.6 Abnormal radiographic or other findings of the abdominal area, including retroperitoneum 799.4 Cachexia V10.0 Personal history of malignant neoplasm of gastrointestinal tract (includes V10.00, V10.04, V10.05, V10.06, V10.09) V44.2 Presence of ileostomy V44.3 Presence of colostomy V44.4 Presence of other artificial opening of gastrointestinal tract V45.72 Acquired absence of small/large intestine V55.2 Encounter for aftercare or procedures related to ileostomy V55.3 Encounter for aftercare or procedures related to colostomy

Category	MSI Physician Billings diagnostic code(s)
	V55.4 Encounter for aftercare or procedures related to other artificial opening of digestive tract V76.41 Special screening for malignant neoplasms of rectum V76.5 Special screening for malignant neoplasms of intestine (includes: intestine and colon; excludes: rectum) (includes V76.50, V76.51, V76.52) E943 Adverse effects related to therapeutic use of agents primarily affecting gastrointestinal system (includes: emetics, emollients, anti-diarrheal drugs, others) (includes E943.0, E943.1, E943.2, E943.3, E943.4, E943.5, E943.6, E943.8, E943.9)
Gynecologic cancer	
Malignant neoplasm	179 Malignant neoplasm of uterus, part unspecified 180 Malignant neoplasm of cervix uteri (includes 180.0, 180.1, 180.8, 180.9) 181 Malignant neoplasm of placenta 182 Malignant neoplasm of body of uterus (includes 182.0, 182.1, 182.8) 183 Malignant neoplasm of ovary and other uterine adnexa (includes 183.0, 183.2, 183.3, 183.4, 183.5, 183.8, 183.9) 184 Malignant neoplasm of other and unspecified female genital organs (includes 184.0, 184.1, 184.2, 184.3, 184.4, 184.8, 184.9)
Related and benign neoplasm	195.3 Pelvis (includes: groin, inguinal region not otherwise specified, sacrococcygeal regions, sites overlapping within pelvis such as rectovaginal (septum) and rectovesical (septum) 218 Uterine leiomyoma (includes 218.0, 218.1, 218.2, 218.9) 219 Other benign neoplasm of uterus (includes 219.0, 219.1, 219.8, 219.9) 220 Benign neoplasm of ovary 221 Benign neoplasm of other female genital organs (includes: fallopian tubes, vagina, vulva, site NOS) (includes 221.0, 221.1, 221.2, 221.8, 221.9) 236.0 Neoplasm of uncertain behavior of uterus 236.1 Neoplasm of uncertain behavior of placenta 236.2 Neoplasm of uncertain behavior of ovary 236.3 Neoplasm of uncertain behavior of other and unspecified female genital organs 239.5 Neoplasm of unspecified nature of other genitourinary organs
Carcinoma in situ	233.1 Cervix uteri 233.2 Other and unspecified parts of uterus 233.3 Other and unspecified female genital organs (includes 233.30, 233.31, 233.32, 233.39)
Other related	614 Inflammatory disease of ovary, fallopian tube, pelvic cellular tissue, and peritoneum (includes 614.0, 614.1, 614.2, 614.3, 614.4, 614.5, 614.6, 614.7, 614.8, 614.9)

Category	MSI Physician Billings diagnostic code(s)
	615 Inflammatory diseases of uterus, except cervix (includes 615.0, 615.1, 615.9) 616 Inflammatory disease of cervix, vagina, and vulva (includes 616.0, 616.10, 616.11, 616.2, 616.3, 616.4, 616.50, 616.51, 616.8, 616.9 618 Genital prolapsed (includes 618.0, 618.1, 618.2, 618.3, 618.4, 618.5, 618.6, 618.7, 618.8, 618.9) 619 Fistula involving female genital tract (includes 619.0, 619.1, 619.2, 619.8, 619.9) 620 Noninflammatory disorders of ovary, fallopian tube, and broad ligament Includes 620.0, 620.1, 620.2, 620.3, 620.4, 620.5, 620.6, 620.7, 620.8, 620.9) 621 Disorders of uterus, not elsewhere classified (includes 621.0, 621.1, 621.2, 621.3, 621.4, 621.5, 621.6, 621.7, 621.8, 621.9) 622 Noninflammatory disorders of cervix (622.0, 622.1, 622.2, 622.3, 622.4, 622.5, 622.6, 622.7, 622.8, 622.9) 623 Noninflammatory disorders of vagina (includes 623.0, 623.1, 623.2, 623.3, 623.4, 623.5, 623.6, 623.7, 623.8, 623.9) 624 Noninflammatory disorders of vulva and perineum (includes 624.0, 624.1, 624.2, 624.3, 624.4, 624.5, 624.6, 624.8, 624.9) 625 Pain and other symptoms associated with female genital organs (includes 625.0, 625.1, 625.2, 625.3, 625.4, 625.5, 625.6, 625.7, 625.8, 625.9) 626 Disorders of menstruation and other abnormal bleeding from female genital tract (All 626 except 626.3 Puberty bleeding) (includes 626.0, 626.1, 626.2, 626.4, 626.5, 626.6, 626.7, 626.8, 626.9) 627 Menopausal and postmenopausal disorders (includes 627.0, 627.1, 627.2, 627.3, 627.4, 627.8, 627.9) 628 Infertility, female (includes 628.0, 628.1, 628.2, 628.3, 628.4, 628.8, 628.9) 629 Other disorders of female genital organs (All 629 except 629.2 Female genital mutilation status) (includes 629.0, 629.1, 629.3, 629.8, 629.9) 788 Symptoms involving the urinary system (All 788 except 788.0 renal colic) (includes 788.1, 788.20, 788.21, 788.29, 788.30, 788.31, 788.32, 788.33, 788.34, 788.35, 788.36, 788.37, 788.39, 788.41, 788.42, 788.43, 788.5, 788.61, 788.62, 788.63, 788.64, 788.65, 788.69, 788.7, 788.8, 788.9) 795.0 Abnormal Papanicolaou smear of cervix and cervical human papillomavirus (includes 795.0) 795.1 Abnormal Papanicolaou smear of vagina and vaginal human papillomavirus (includes 795.1) V10.40 Personal history of malignant neoplasm of female genital organ, unspecified V10.41 Personal history of malignant neoplasm of cervix uteri V10.42 Personal history of malignant neoplasm of other parts of uterus

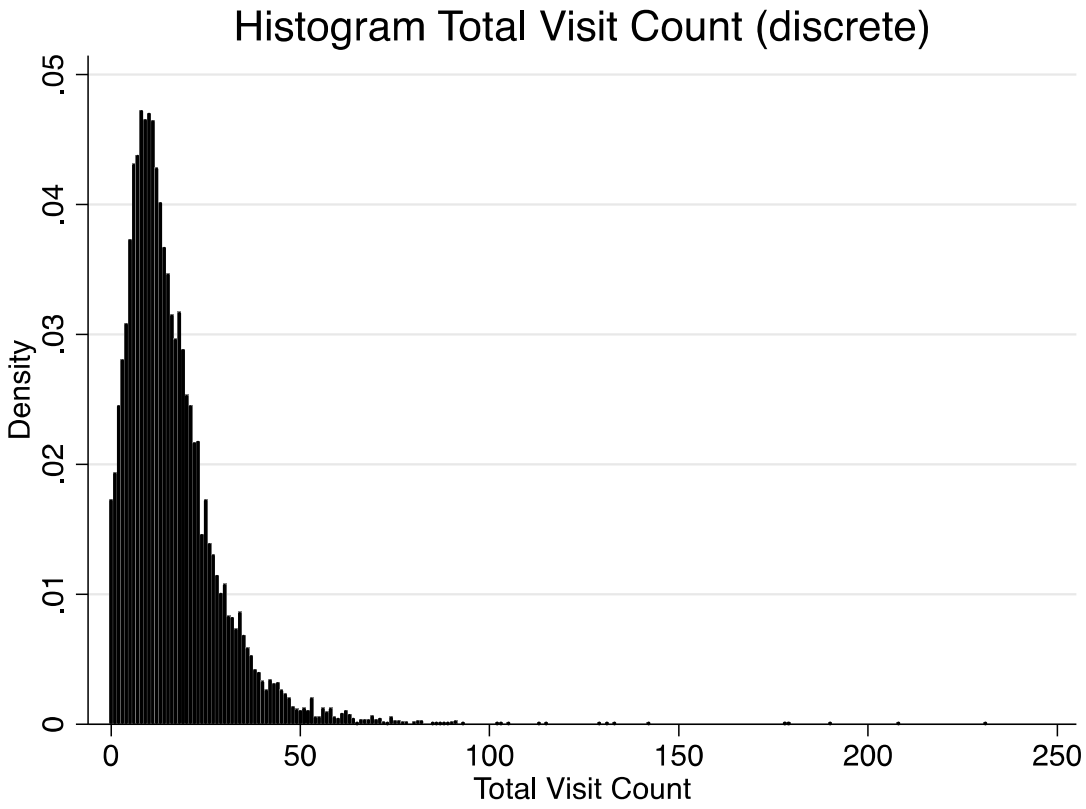
Category	MSI Physician Billings diagnostic code(s)
	V10.43 Personal history of malignant neoplasm of ovary V10.44 Personal history of malignant neoplasm of other female genital organs V45.77 Acquired absence of genital organs (excludes: cervix and uterus, genital mutilation) V47.5 Other genital problems V50.42 Prophylactic removal of ovary V72.3 Gynecological examination V76.2 Special screening for malignant neoplasms of cervix V76.46 Special screening for malignant neoplasms of ovary V76.47 Special screening for malignant neoplasms of vagina (pap smear status-post hysterectomy for non-malignant condition) V88.0 Acquired absence of cervix and uterus E932.2 Adverse effect related to therapeutic use of ovarian hormones and synthetic substitutes (includes: oral contraceptives, estrogens, estrogens and progestogens combined, progestogens)
Prostate cancer	
Malignant neoplasms	185 Malignant neoplasm of prostate
Related and benign neoplasm	195.3 Pelvis (includes: groin, inguinal region not otherwise specified, sacrococcygeal regions, sites overlapping within pelvis such as rectovaginal (septum) and rectovesical (septum) 222.2 Benign neoplasm of prostate 236.5 Neoplasm of uncertain behavior of prostate 239.5 Neoplasm of unspecified nature of other genitourinary organs
Carcinoma in situ	233.4 Prostate
Other related	600 Hyperplasia of prostate 601 Inflammatory diseases of prostate (includes 601.0, 601.1, 601.2, 601.3, 601.4, 601.8, 601.9) 602 Other disorders of prostate (includes 602.0, 602.1, 602.2, 602.3, 602.8, 602.9) 603 Hydrocele (i.e., accumulation of fluid in the spermatic cord, testis, or tunica vaginalis) (includes 603.0, 603.1, 603.8, 603.9) 604 Orchitis and epididymitis (i.e., inflammation of the testicles or epididymis) (includes 604.0, 604.90, 604.91, 604.99) 606 Infertility, male (includes 606.0, 606.1, 606.8, 606.9) 607 Disorders of the penis (includes 607.0, 607.1, 607.2, 607.3, 607.81, 607.82, 607.83, 607.84, 607.85, 607.89, 607.9) 608 Other disorders of the male genital organs (includes 608.0, 608.1, 608.20, 608.21, 608.22, 608.23, 608.24, 608.3, 608.4, 608.81, 608.82, 608.83, 608.84, 608.85, 608.86, 608.87, 608.89, 608.9) 788 Symptoms involving the urinary system (All 788 except 788.0 renal colic) (includes 788.1, 788.20, 788.21, 788.29, 788.30, 788.31, 788.32, 788.33, 788.34, 788.35, 788.36, 788.37, 788.39, 788.41, 788.42, 788.43,

Category	MSI Physician Billings diagnostic code(s)
	788.5, 788.61, 788.62, 788.63, 788.64, 788.65, 788.69, 788.7, 788.8, 788.9) 792.2 Abnormal findings in semen V10.45 Personal history of malignant neoplasm of male genital organ, unspecified V10.46 Personal history of malignant neoplasm of prostate V47.4 Other urinary problems V47.5 Other genital problems V76.44 Special screening for malignant neoplasms of prostate E932.1 Adverse effects related to therapeutic use of androgens and anabolic congeners (includes: nandrolone phenpropionate, oxymetholone, testosterone and preparations)
All cancer sites	
Malignant neoplasms	199.0 Malignant neoplasm without specification of site, disseminated 199.1 Malignant neoplasm without specification of site, other
Related and benign neoplasms	229.0 Benign neoplasm of other and unspecified sites, lymph nodes 234.9 Carcinoma in situ of other and unspecified sites, site unspecified (includes: carcinoma in situ not otherwise specified)
Other related	683 Acute lymphadenitis 780.5 Sleep disturbances (includes 780.50, 780.51, 780.52, 780.53, 780.54, 780.55, 780.56, 780.57, 780.58, 780.59) 783.0 Anorexia 783.1 Abnormal weight gain 783.2 Abnormal loss of weight and underweight 787.0 Nausea and vomiting (includes 787.01, 787.02, 787.03, 787.04) 790.0 Abnormality of red blood cells (includes: anemia, hemoglobin disorders, polycythemia) 792.9 Other nonspecific abnormal findings in body substances (includes: peritoneal, pleural, synovial, and vaginal fluids) 795.4 Other nonspecific abnormal histological findings 795.8 Abnormal tumor markers (includes: elevated tumour associated antigens and tumour specific antigens) 990 Effects of radiation, unspecified (includes: complication of radiation therapy, radiation sickness) 999.3 Other infection related to surgical or medical care (includes: infection due to port-o-cath) V15.3 Personal history of irradiation V41.7 Problems with sexual function V58.0 Encounter for aftercare or procedures related to radiotherapy V58.1 Encounter for aftercare or procedures related to chemotherapy and immunotherapy for neoplastic conditions V67.0 Follow-up examination following surgery V67.1 Follow-up examination following radiotherapy V67.2 Follow-up examination following chemotherapy (i.e., cancer chemotherapy follow-up)

Category	MSI Physician Billings diagnostic code(s)
	V87.41 Personal history of antineoplastic chemotherapy V87.42 Personal history of monoclonal drug therapy
Mental health and related	300.0 Anxiety states (includes 300.00, 300.01, 300.02, 300.09) 300.4 Dysthymic disorder (includes: anxiety depression, depression with anxiety, other types of depression) 300.5 Neurasthenia (includes: fatigue neurosis, nervous debility, psychogenic asthenia, psychogenic general fatigue) 308 Acute reaction to stress (includes 308.0, 308.1, 308.2, 308.3, 308.4, 308.9) 309 Adjustment reaction (includes 309.0, 309.1, 309.21, 309.22, 309.23, 309.24, 309.28, 309.29, 309.3, 309.4, 309.81, 309.82, 309.83, 309.89, 309.9) 311 Depressive disorder, not elsewhere classified (includes: depressive disorder not otherwise specified, depressive state not otherwise specified, depression) 799.2 Signs and symptoms involving emotional state (excludes: anxiety and depression; includes: nervousness, irritability, impulsiveness, emotional lability, demoralization and apathy, other)

MSI= Medical Services Insurance Physicians' Billings.

Appendix D: Distribution of the Total Visit Count for the Cancer Survivor Cohort



Appendix E: Distribution of the Proportion of PCP Visits (Continuous) for the Cancer Survivor Cohort