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April 1, 2016

Preventive Health Service Use Among Ovarian Cancer Survivors

by
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Master of Science in Public Health
Health Policy and Management

A thesis submitted to the faculty of the Rollins School of Public Health at Emory University in partial fulfillment of the requirements for the Master of Science in Public Health in the Department of Health Policy and Management.

Atlanta, Georgia
2016

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B. S., Economics
Northeastern University
2014

Thesis Committee Chair: Joseph Lipscomb, PhD

An abstract of
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Abstract

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Previous studies have examined preventive health service utilization differences between cancer survivors and non-cancer controls and have found mixed results. No previous research has examined preventive health services among ovarian cancer survivors, who have different survival outcomes and experiences than cancer survivors examined in past studies. This study examined elderly ovarian cancer survivors' adherence to evidence-based guidelines regarding post-treatment receipt of flu vaccinations, screening mammography and bone density tests. The study included women with ovarian cancer diagnosed from 2001-2010, who were age 66 or older. Ovarian cancer survivors were matched to non-cancer controls on age, race and state from a 5% random Medicare Beneficiary file. Logistic regression models were used to compare the likelihood of receipt of preventive health services for cancer survivors compared to controls. Results showed that cancer survivors were more likely to be adherent to flu vaccine and mammography, but no differences were found for bone density test adherence. Racial and socio-economic disparities were identified: blacks were less likely to be adherent to all three preventive health services when compared to white counterparts, and those with state Medicaid Buy-in were less likely to be adherent compared to those without state Medicaid Buy-in. Adherence to guidelines by cancer survivors was not substantially influenced by their rate of receipt of cancer surveillance visits or by their intensity of interaction with the health care system, as indexed by the overall physician visit rate. Similarly, among controls the magnitude of health system interaction on adherence was small. After controlling for all measureable factors, substantial differences remained between survivors and controls for two of the three measures. Therefore, differences in adherence are likely attributable to differences between the groups on unmeasured variables. An important avenue to explore these differences is patient-reported on factors influencing attitudes towards using preventive services, along with barriers and facilitators to toward use of healthcare. This could be helpful in enhancing understanding of ovarian cancer survivors' attitudes toward cancer and non-cancer care following initial cancer therapy. Survivorship Care Plans, as advocated by major cancer organizations, should emphasize preventive health services, in addition to surveillance for cancer recurrence.

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CHAPTER I: INTRODUCTION

In 2005, the Institute of Medicine (IOM) report *From Cancer Patient to Cancer Survivor: Lost in Transition* [1] recommended that every cancer patient should be given a survivorship care plan (SCP) that includes guidelines to monitor and maintain health beyond treatment. The SCP is a tool aimed to facilitate transition of care from oncologists to primary care providers (PCP) and improve quality of care [1]. The American College of Surgeons (ACoS) has reinforced these recommendations with their 2012 standard requiring all accredited cancer centers to provide survivorship care plans to all of their patients by January 1, 2019 [2]. Enforcing this SCP provision as a quality of care metric calls attention to the utility of these plans for providers and patients.

Different groups have developed templates for SCPs including the American Society of Clinical Oncology (ASCO) SCP Template [2], LIVESTRONG Care Plan[3], and *Journey Forward* [4]. The core components of a SCP as recommended by ASCO include a treatment summary and follow-up care plan [2]. These core components include cancer treatment details and expected long-term side effects, need for cancer screening for early detection of new primaries and preventive testing and examinations [2].

Additionally, professional groups have created more specialized SCPs for specific cancers. The Society for Gynecologic Oncology (SGO) has developed a SCP for ovarian cancer, including the core components ASCO has emphasized, with additional detailed symptoms that may occur post treatment and a timeline for surveillance recommendations [5]. SGO has also developed a Self Care Plan (Table 1), which identifies healthy behaviors and preventive screenings that should be maintained through

survivorship [6]. Table 1 shows that the SGO recommends screening for breast cancer and osteoporosis, while also referring to the American Cancer Society and CDC guidelines, but does not provide specific guidelines for ovarian cancer survivors [6]. A recent study of SCPs piloted with gynecologic cancer patients found similar patient-related outcomes when comparing the quality of care for patients who received SCPs and those who did not [7]. The researchers concluded that further investigation into the usefulness of SCPs and components of SCPs could lead to improved quality for cancer survivors [7].

The Advisory Committee on Immunization Practices (ACIP) and United States Preventive Services Task Force (USPSTF) recommend preventive health services (PHS) for adults including influenza immunizations [8], screening for early detection of breast cancer [9] and osteoporosis [10]. Preventive screenings were chosen based on what was previously used in research [11-21]. The seminal paper that examined PHS among cancer survivors utilizing SEER-Medicare data chose the screenings based on relevance to breast cancer survivorship and those that were feasible to assess from the given data [16]. Researchers chose services from the list of quality metrics included in the Health Plan Employer Data and Information Set (HEDIS) and assessed the following: influenza vaccination, lipid testing, cervical and colon screening and bone densitometry [17]. We selected three screenings from the previous researchers' focus for this study because of their feasibility and representativeness of different preventive health categories, and include the following: influenza vaccination, mammography and bone densitometry. Although this study will not focus on breast cancer survivors as the original study, there

have been many other studies that used these screenings as quality indicators in different cancer populations [11-21].

This study will investigate the current state of the provision of selected preventive screenings, categorized as cancer screenings, health maintenance screenings and vaccinations, for ovarian cancer survivors to understand whether increased emphasis should be placed on general health screenings among standard SCPs. If for instance, the study finds that ovarian cancer survivors are not adherent to the recommendation of yearly flu vaccinations but that they are adherent to mammography, then we would suggest flu vaccines are important to emphasize in the SCP to protect the immune-comprised ovarian cancer survivors.

This study population will include elderly ovarian cancer survivors. The focus on the older age range is in part due to the rich information that is included in the Surveillance, Epidemiology and End-Results (SEER)-Medicare data set, which includes only Medicare beneficiaries age 65+. SEER-Medicare data reflects a linkage of two large population-based sources of data that contains registry-derived information about Medicare beneficiaries including the clinical, demographic and cause of death information for persons with cancer and the Medicare claims for covered health services starting from Medicare eligibility until death [22]. Furthermore, there is a high burden of these preventable diseases on the elderly population, as detailed in Chapter 2. The motivation for studying ovarian cancer survivors is the absence of research regarding what is needed and useful in a SCP and the general lack of published information on ovarian cancer survivorship. As the number of ovarian cancer survivors grows [23], it is imperative to provide them with the resources they need to ensure health maintenance.

The Centers for Disease Control and Prevention (CDC) and the IOM, recently convened an expert panel to summarize the state of research on ovarian cancer research. In their March 2016 report, the experts acknowledge that much of the survivorship research that is relevant for women with ovarian cancer has focused on other cancer types or general gynecologic cancer [24]. Further, they found that most research on ovarian cancer survivors does not distinguish between the needs of different age groups, racial and ethnic groups and those diagnosed at different stages [24].

This study also aims to describe rates of adherence of ovarian cancer survivors relative to matched controls from the Medicare Beneficiary 5% Random Sample; the methodology is detailed in Chapter 3. If ovarian cancer survivors are doing poorly overall, but well compared with matched controls, then we suggest that emphasis should be placed on these PHS in the general elderly population, not just in SCP.

Previous research suggests that there may be differences in care that cancer survivors receive post-treatment by providers, by time since diagnosis and by minority groups. Some theories propose that oncologists may focus on cancer specific surveillance and not give as much attention to routine health maintenance as a primary care physician might. Other theories posit that due to the increased number of visits survivors have with their oncology specialists, there may be lack of communication between the specialist and the primary care physician regarding the delineation of provision of health care services. Moreover, the increased interaction with the healthcare system for cancer survivors may increase the likelihood of getting PHS.

To date, no known studies have examined PHS use among ovarian cancer survivors to determine whether they are receiving appropriate care compared to the

general elderly population. Ex ante, there is insufficient evidence to hypothesize one way or another because of conflicting possibilities and evidence, as detailed further in Chapters 2 and 3. Rather, this research will investigate what the data are telling us, in order to inform the future of SCP in the ovarian cancer survivorship population.

Table 1. Society for Gynecologic Oncology's Self Care Plan

Recommendation [6]	Frequency	Comments									
<p>Breast Cancer Screening</p> <p>For more information, see the ACS document <i>Breast Cancer: Early Detection</i>.</p> <p>www.cancer.org/ssLINK/breast-cancer-early-detection-toc</p>	<ul style="list-style-type: none"> Yearly mammograms starting at age 40, and continuing for as long as a woman is in good health Clinical breast exam (CBE), performed by a health care professional, every three years for women in their 20s and 30s, and every year for women 40 and over. A monthly breast self-exam (BSE) is a good way to monitor breast health. Women should know how their breasts normally look and feel, and report any change promptly to their health care provider 	<p>The ACS recommends that some women – because of their family history, a genetic tendency, or certain other factors – be screened with Magnetic Resonance Imaging (MRI) in addition to mammograms. The number of women who fall into this category is small (less than 2 percent of all U.S. women). Talk with your doctor about your personal history and whether you should have additional tests at an earlier age.</p>									
<p>Keep your bones healthy.</p> <p>For more information visit www.niams.nih.gov/Health.../Bone/Bone_Health/bone_health_for_life</p> <p>For the FRAX (Fracture Risk Assessment) tool, visit: www.shef.ac.uk/FRAX, to estimate 10-year risk for fractures</p>	<ul style="list-style-type: none"> Ask your primary care provider about screening for osteoporosis beginning at age 65 or at a younger age if your bone fracture risk is increased The 10-year risk for osteoporotic fractures can be calculated for individuals using the FRAX tool and could help to guide screening decisions for women younger than 65 years. Maximize your bone health by eating healthy, getting enough calcium and vitamin D, and exercising regularly 	<p>Certain cancer treatments, such as chemotherapy or hormonal therapy, can cause bone loss. In addition, after menopause, women can lose up to 20 percent of their bone density. The good news is that women can maximize their bone density by eating healthy, getting enough calcium and vitamin D, and exercising regularly.</p> <table border="1" data-bbox="1270 1195 1780 1421"> <thead> <tr> <th>Age (years)</th> <th>Calcium per day</th> <th>Vitamin D per day</th> </tr> </thead> <tbody> <tr> <td>19 to 49</td> <td>1000 milligrams</td> <td>600 units</td> </tr> <tr> <td>50 or over</td> <td>1200 milligrams</td> <td>800 units</td> </tr> </tbody> </table>	Age (years)	Calcium per day	Vitamin D per day	19 to 49	1000 milligrams	600 units	50 or over	1200 milligrams	800 units
Age (years)	Calcium per day	Vitamin D per day									
19 to 49	1000 milligrams	600 units									
50 or over	1200 milligrams	800 units									

<p>Have regular check-ups by a healthcare professional.</p> <p>For more information about health screening tests for women and men visit the U.S. Department of Health and Human Services. http://www.cdc.gov/vaccines/recs/schedulesadult-schedule.htm</p>	<ul style="list-style-type: none"> • Keep up-to-date on general health screening tests, including cholesterol, blood pressure and glucose (blood sugar) levels. • Get an annual influenza vaccine (flu shot). • Get vaccination with the pneumococcal vaccine, which prevents a type of pneumonia, and re-vaccinated as determined by your health care team • Don't forget dental and eye health! 	<ul style="list-style-type: none"> • The American Optometric Association recommends adults have their eyes examined every two years until age 60, then annually. People who wear glasses or corrective lenses or are at high risk for eye problems (i.e. diabetics, family history of eye disease) should be seen more frequently • The American Dental Association recommends adults see their dentist at least once a year.
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CHAPTER II: LITERATURE REVIEW

This study investigates PHS for ovarian cancer survivors. In this chapter, we summarize ovarian cancer prevalence, treatment and the psychosocial survivorship issues of ovarian cancer survivors. Next, we emphasize the importance of PHS for elderly and the national guidelines and recommendations. Building upon the recommendations, we review previous studies examining previous PHS in cancer survivors of other types of cancers.

Ovarian Cancer

Cancer occurs when cells grow out of control within someone's body [25].

Ovarian cancer is cancer that begins in the ovaries [25]. Ovaries, which are reproductive glands in women, consist of three main types of cells that develop into different types of tumors: stromal, germ and epithelial [25]. The most common ovarian tumor is epithelial tumors (~90%), which start in cells that cover the outer surface of the ovary [25].

Epithelial ovarian tumors, or carcinomas, can be further broken down into different types: serous, mucinous, endometrioid, and clear cell [25]. In addition to the cell subtypes, epithelial carcinomas are given grades and stages that describe the aggressiveness of the cancer and how far the tumor has spread [25]. The typical pathway for an epithelial tumor is to spread to the lining and organs of the pelvis and abdomen through a process termed shedding [25]. Approximately 20,000 women are diagnosed with epithelial ovarian cancer each year, of which half are women aged 63 and older [25].

There are many risk and protective factors for ovarian cancer including age, obesity, reproductive history, birth control, gynecologic surgery, fertility drugs, androgens, estrogen therapy, hormone therapy and family history of ovarian, breast or

colorectal cancer [25]. Demographic characteristics including older age and higher body mass index have a higher risk of developing cancer [25]. Ovarian cancer risk factors include many reproductive links; women who have been pregnant and carried the baby to term before age 26 have a lower risk, while those who have never carried a pregnancy to term or have after age 35 have a high risk [25]. Further, studies have found birth control pills and an injectable hormonal contraceptive are protective, as well as a tubal ligation and hysterectomy [25]. There is also a hereditary component to risk of ovarian cancer including family history of ovarian, breast or colorectal cancer; 5 to 10% of ovarian cancers are caused by mutations in BRCA1 and BRCA2 [25]. Unlike many cancers, smoking and alcohol use are not risk factors for ovarian cancer [25].

Many women with ovarian cancer do not have symptoms, leaving the tumor to go untreated until progression to advanced stage, which for many years gave ovarian cancer the name, *silent killer* [26]. However, there has been much controversy over the phrase as timely diagnosis is key to long-term survival, and medical specialists argue that if you know what to look for you will have a faster diagnosis [27]. For some women ovarian cancer causes signs and symptoms that may alert a woman to see her gynecologist including, but not limited to bloating, pelvic or abdominal pain, trouble eating, urinary urgency, fatigue and upset stomach [25]. The USPSTF recommends against routine screening for ovarian cancer in women who are asymptomatic and who do not have the known genetic mutations [28]. Although the screening tests for ovarian cancer are not recommended, there are two that have been studied: transvaginal ultrasound (TVUS) and cancer antigen-125 (CA-125) blood test [25]. TVUS looks at the uterus, fallopian tubes and ovaries using an ultrasound wand to find tumors in the ovary, although most found

using this method are not cancer [25]. The alternative method is testing for CA-125, a protein present at high levels in some women with ovarian cancer, but there are other conditions that also cause these elevations [25].

Ovarian Cancer Survivors

The typical treatment for ovarian cancer using the improved technology described above includes primary debulking surgery and chemotherapy [29]. Women on average stay in the hospital for three to seven days following surgery and can resume daily activities within four to six weeks [29]. The next step following surgery is chemotherapy, which typically involves three to six cycles of a combination of two or more drugs given intravenously every three to four weeks [29]. Even after intensive first-line therapy, the risk of cancer recurrence is approximately 70%, which is very high compared to most major cancers [30]. About 40%-50% who achieve remission after first-line therapy, have recurrence within 3 years [31].

At stage I, the cancer is contained within the ovary or fallopian tubes and at stage II the cancer has spread to other organs within the pelvis area like the uterus or bladder [25]. As previously mentioned, there are no effective screening methods for ovarian cancer and only 1/5th of cases are diagnosed at stages I or II [32], where 5-year survival rates are 90% and 70%, respectively [33]. At stage III, ovarian cancer is characterized by spread beyond the pelvis to the lining of the abdomen or to lymph nodes in the back of the abdomen; at stage IV the cancer has metastasized [25]. For those diagnosed at stage III and IV, 5-year survival rates are approximately 39% and 17%, respectively [33]. Due to advances in treatment and technology, relative survival rates have improved by 50% from 1975 to 2011 for stage I ovarian cancer [23].

A recent longitudinal study of epithelial ovarian cancer survivors, diagnosed from 1994 to 2011 in California, found that 58% of women diagnosed between ages 65 and 74 survived longer than 2 years, compared with 33% of women diagnosed at 75 or older [34]. The study also found that 30% of ovarian cancer survivors lived 10 years or longer [34]. The authors point to improved surgical techniques and use of concomitant intraperitoneal (IP) and intravenous (IV) adjuvant chemotherapy for possible explanations for long-term survival [34].

Despite low survival rates and high recurrence rates, there are an estimated 200,000 ovarian cancer survivors living today [35]. Many studies [26, 36-43] have attempted to understand the health-related quality of life for ovarian cancer survivors and found a high prevalence of fear of diagnostic testing (30% [39]), recurrence (20-45% [36, 39, 43]) and post-traumatic stress disorder (PTSD) (20% [39]). Overall, cancer survivors live with uncertainty and anxiety, reflecting in part an underlying fear of recurrence and the perception of being at risk [38]. One study identified PTSD prevalence in ovarian cancer survivors as determined by experiences of symptoms including arousal symptoms and avoidance symptoms [39]. For individuals diagnosed with later stage epithelial ovarian cancer, 29% had met the criteria for PTSD compared to 14% of survivors with stage I [39].

Unique to ovarian cancer survivors is fear of recurrence specific to a cancer marker, known as the “CA-125 obsession” [38]. This obsession refers to survivors who take periodic CA-125 blood tests and stress over their CA-125 level because it is used as a sign of recurrence [38]. One study used mixed methods to examine self-reported anxiety and emotional stress of women following surgery after ovarian cancer diagnosis

[44]. Quantitatively, the investigators found there was no significant relationship between CA-125 levels and distress, but qualitatively they found low knowledge of what a low or high level of CA-125 means for their health and high levels of anxiety associated with the number [44]. Study investigators suggest that nurses need to further educate their patients on what CA-125 levels are and their utility in understanding their cancer [44]. This CA-125 obsession may influence an ovarian cancer survivor's propensity to visit their health care providers, and may be more focused on cancer surveillance than other PHS.

The importance of preventive health services

PHS including influenza immunizations [8], screening for early detection of breast cancer [9] and osteoporosis [10] are recommended by the USPSTF and ACIP. SGO has also reinforced the recommendations of regular mammography and bone density tests in their toolkit developed for survivors of gynecologic cancers [5]. Further, Medicare incentivizes these preventive services by having zero cost-sharing for beneficiaries [45]. The recommendations for mammography and bone density tests are given a grade of B, which under the Patient Protection and Affordable Care Act (ACA) must be covered at zero cost under private health plans [46]. Thus, it will be useful to keep in mind that there are no financial barriers to the receipt of services, for either the ovarian cancer survivors or the non-cancer controls. Further, because the ACA provisions reach to the under-65 population, the difference in insurance coverage from Medicare to the under 65 would not be expected to have a differential effect in terms of the results of this study.

Preventive health services for cancer survivors

Although no studies have focused on ovarian cancer survivors, a number of studies have examined PHS among survivors of other types of cancers (e.g., breast,

colorectal, prostate, uterine). These studies examined patterns within the United States using claims and survey data, and internationally in the United Kingdom using survey data. We will review studies for particular PHS: immunizations, mammography and bone density tests.

In 2011, the Centers for Disease Control and Prevention (CDC) released a report, *Enhancing Use of Clinical Preventive Services Among Older Adults – Closing the Gap* [8], calling attention to low utilization of PHS among Medicare beneficiaries. The National Commission on Preventive Priorities identified 25 clinical preventive services that have the biggest population health impact and are the most cost-effective [8]. Among these 25 are influenza immunizations, screening for breast cancer, and screening for osteoporosis [8].

Influenza immunizations among the elderly have been shown to reduce hospitalizations, thereby reducing costs, and to avert deaths [8]. Furthermore, of the deaths and hospitalizations that are attributed to the flu, the majority of the burden falls among those 65 years or older, 85% and 63% respectively [8]. Despite the importance of influenza immunizations, only about two-thirds of older adults receive the vaccine, and among female Medicare FFS beneficiaries the coverage was as low as 50% [47]. Studies that examined influenza vaccination rates for cancer survivors compared to elderly with no history of cancer have found mixed results. While the majority of studies reported that cancer survivors, including breast, colorectal and prostate cancer, were more likely than non-cancer controls to receive an influenza vaccine [11, 16, 48], one study found that breast cancer survivors were less likely [17] and two found no significant differences among uterine and breast cancer survivors [13, 21].

Among women 65 and older, breast cancer screening is particularly important, as half of new cases and more than 60% of deaths from breast cancer are in this older age group [8]. Data from 2011 showed that about 80% of older women had gotten a mammography in the last two years [8] and the coverage was about 65% in the female Medicare FFS population [47]. However, it should be noted that the national coverage data is noted to overestimate rates of mammography because of the sampling method, the social desirability bias and because both diagnostic and screening mammography are captured [49]. Strategies to increase mammography have included making the mammography appointments when women are getting their influenza vaccination [8]. These screenings are especially important to ovarian cancer survivors, who have an increased risk of breast cancer compared to women with no history of cancer [50]. Many studies examining receipt of mammography among cancer survivors who are not breast cancer survivors have found them more likely to have mammography compared to matched non-cancer controls [12, 13, 15-18, 21]. Studies from the United Kingdom and community health centers in the United States reported non-significant differences in mammography use between cancer survivors and non-cancer controls [11, 14]. The characteristics of the studies' patient population and their providers may differ from those found in the SEER-Medicare dataset due to the fragmented healthcare delivery system in the US [11, 14].

The USPSTF also encourages elderly women to get general PHS including osteoporosis screenings [10, 51]. Among female Medicare FFS beneficiaries, 53% received density tests [47], and about 71% of female elderly receive bone density tests nationally[8]. These screenings are particularly important for ovarian cancer survivors

who have higher incidence of comorbidities including hypertension, osteoarthritis and cerebrovascular disease than cancer-free women 66 and older [52]. Screening for osteoporosis includes hip scans and bone density tests and is associated with decreased hip fractures that approximately 40% of women experience in their life [8]. Similar to the research on cancer screenings noted just above, studies that examined receipt of bone density tests among cancer survivors and individuals with no history of cancer found mixed results. Four studies [11, 16] using SEER-Medicare data and a UK primary care research database found breast, colorectal and prostate cancer survivors were more likely to have a bone density test compared with non-cancer individuals. Two studies using SEER-Medicare data found competing results: breast cancer survivors were less likely to receive bone density tests compared to demographically similar individuals without cancer [17], while there was no significant differences between uterine cancer survivors and women without cancer [21].

Preventive Health Services for Ovarian Cancer Survivors

Although many studies have examined PHS use in cancer survivor populations, none have focused on ovarian cancer survivors specifically. One study using the National Health Interview Survey (NHIS) aggregated ovarian cancer survivors' data (n=267) with other female cancer survivors (e.g. breast, cervix, colon, uterus, melanoma, other (n=4970)) [12]), and found that female cancer survivors had higher levels mammography utilization compared to women without cancer [12]. These findings are similar to those from previous studies that found breast cancer survivors are more likely to get any PHS [13, 14, 16]. Ovarian cancer survivors comprised a small portion of the study population, so it is not clear how well the NHIS study results apply to the ovarian cancer survivors.

The findings of previous studies [11-21] examining PHS use among cancer survivors have not been consistent across different types of cancers. Further, ovarian cancer is different than the cancer survivors that have been studied, including the higher threat of recurrence, whose receipt of PHS has not been previously examined. Thus, these mixed results cannot readily be generalized to the population of ovarian cancer survivors. This literature review has explored the unique psychosocial issues and sequelae that ovarian cancer survivors have that may change an individual's interaction with the healthcare system. Although we cannot conduct a direct comparison, we expect ovarian cancer survivors' propensity to adhere to guidelines to be different from what has been seen in studies of breast and colorectal cancer survivors, due in part to these psychosocial issues that differentially affect ovarian survivors.

This literature review has led us to understand the complexities of ovarian cancer sequelae and survivorship that make them a unique population to examine. We have also seen from past literature assessing preventive health guideline adherence that there are some differences in adherence between cancer survivors and non-cancer controls, and across types of preventive health measures. The present study seeks to understand the role ovarian cancer survivorship has on PHS adherence.

CHAPTER III: METHODOLOGY

Study Aims and Research Questions

Following the methods of previous studies, we will examine the propensity of these survivors to adhere to selected evidence-based PHS recommendations and compare their propensity to matched non-cancer controls. Ultimately, we want to know and

understand if cancer survivors are receiving recommended PHS, and controls are ancillary to answering this question as they provide a referent group against which we can compare background adherence.

The study will address the following Aims:

Aim 1: To examine whether ovarian cancer survivors are adherent to PHS recommendations when compared to non-cancer controls, after adjusting for predisposing, enabling and need characteristics.

Aim 2: To understand what factors determine variations in adherence by ovarian cancer survivors.

Aim 2 will aid in making policy recommendations. By investigating if there are differences among cancer survivors and non-cancer survivors, the results may reveal what areas or underserved subpopulations our efforts should be focused on in terms of improving preventive health service adherence. Policy recommendations may be aimed at designing and implementing survivorship care plans or targeting specific interventions for any subgroup that may be less likely to be adherent to guidelines. A priori, we have no hypotheses on what factors may be different, given the previous findings from studies reviewed.

Institutional Review Board: Emory University

An exemption was received on 9/1/2015 since this study uses secondary data that are completely de-identified with respects to patients and providers.

Data Source

This study will use a SEER-Medicare linked data set including all ovarian cancer patients age 66 and over diagnosed from 2001 to 2010, and followed through 2013.

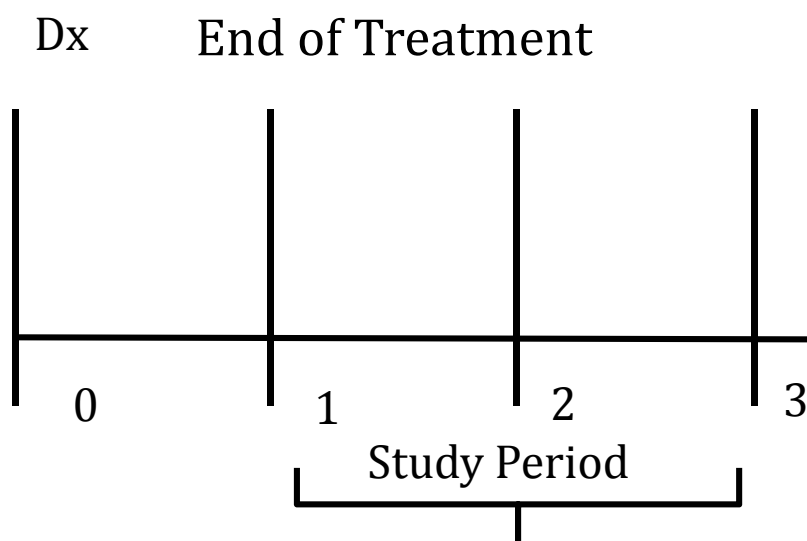
Background

This analysis will use multiple years (2001-2013) of data from SEER-Medicare for individuals with ovarian cancer and a 5% sample of Medicare beneficiaries without cancer living in regions with a SEER registry [22]. The ongoing SEER-Medicare database was created by a partnership of the National Cancer Institute (NCI), the SEER registries, and the Centers for Medicare and Medicaid Services (CMS) [53]. This database, created by NCI and CMS, has a 93% rate of linking individuals in the SEER registries to the Medicare enrollment file [54]. SEER-Medicare data are longitudinal and include Medicare claims for services starting from the time when beneficiaries are first eligible for Medicare until they discontinue eligibility or die [53]. The Medicare files include Medicare Provider Analysis and Review, Physician (Carrier), Outpatient and Hospice claims [55]. The database includes claims only for fee-for-service (FFS) Medicare beneficiaries and are not necessarily generalizable to Medicare Advantage beneficiaries [53].

The SEER registry system has nearly complete information [56] on patients' demographic and clinical cancer characteristics including the age and stage at diagnosis [53]. The dataset created for this analysis includes information from all of the SEER registries, which collectively provide representation of racial/ethnic minorities and cover about 26% of the US elderly population [56]. These SEER registries include: Georgia (Atlanta, Rural and Greater Georgia), Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Los Angeles, San Jose-Monterey, Greater California, Seattle-Puget Sound, Utah, Alaska, Kentucky, Louisiana, and New Jersey [57].

Study Sample Identification

Figure 1. Each of the models for PHS will have a 2-year time frame



The primary cancer-directed treatment for ovarian typically takes about one year [29], so no PHS will be assessed in the first years after diagnosis. Receipt of PHS in accordance with guidelines will begin in year 1 and extend to year 3, as shown in Figure 1, labelled 'Study Period.' In order to keep the follow-up time consistent for the entire sample, the analysis will only include ovarian cancer survivors and non-cancer controls meeting inclusion and exclusion criteria through the study period.

To be included in the study, individuals had to be enrolled in both Medicare Part A and Part B, be age 66 or older, and have ovarian cancer as their primary and only cancer. Individuals were excluded if they were enrolled in a health maintenance organization because claims are not available for them. Individuals were excluded based on the restriction of age, 66 and older, and for not having a diagnosis month or for having a second primary cancer. This decision regarding age was made to ensure that all individuals had been enrolled in Medicare for at least a year so that comorbidities could

be assessed. Following previous literature, individuals who did have a second primary were also excluded [16, 17] to ensure that only diagnoses of ovarian cancer occurred in the population. Other cancer diagnoses may change an individual's behavior with the healthcare system or outlook of receiving preventive health services. Secondary analysis was conducted to assess whether this decision would bias the adherence rates because in excluding women who go on to get breast cancer we may be biasing the actual number of women getting mammography. Secondary analysis showed that when including women who had secondary cancers the adherence to mammography was similar.

Others excluded included those without continuous enrollment in FFS Medicare, those with non-epithelial ovarian cancer, those diagnosed at stage IV and those that we could not follow through the full study period for reasons of hospice or death. Those who were not continuously enrolled in FFS Medicare during the study window were excluded because claims would not have been available to assess PHS utilization accurately. Individuals who were diagnosed with other kinds of ovarian cancer other than epithelial or were stage IV were excluded. Only epithelial ovarian cancer was included because about 90% of ovarian cancers are epithelial and other types of ovarian cancer may have different treatment or survivor sequelae [30]. Due to lower 5-year survival and higher rates of recurrence, those with stage IV were excluded. Finally, we included only those available for the full study period so that each individual had the same opportunity to receive the preventive health services and were not enrolled in hospice or died. Figure 2 shows the criteria applied and the final sample size is 2,437.

The control group was matched to the ovarian patients on age, race, state and number of years of follow-up available in the dataset [58] as detailed in Figure 3.

Eligible beneficiaries were selected from the Medicare 5% sample, which included about 430,000 individuals who had never had cancer. Once matched to a cancer individual, a pseudo-diagnosis (i.e., the diagnosis date of the matching case) was given to the control in order to ensure that the control entered the study at the same time as the survivor.

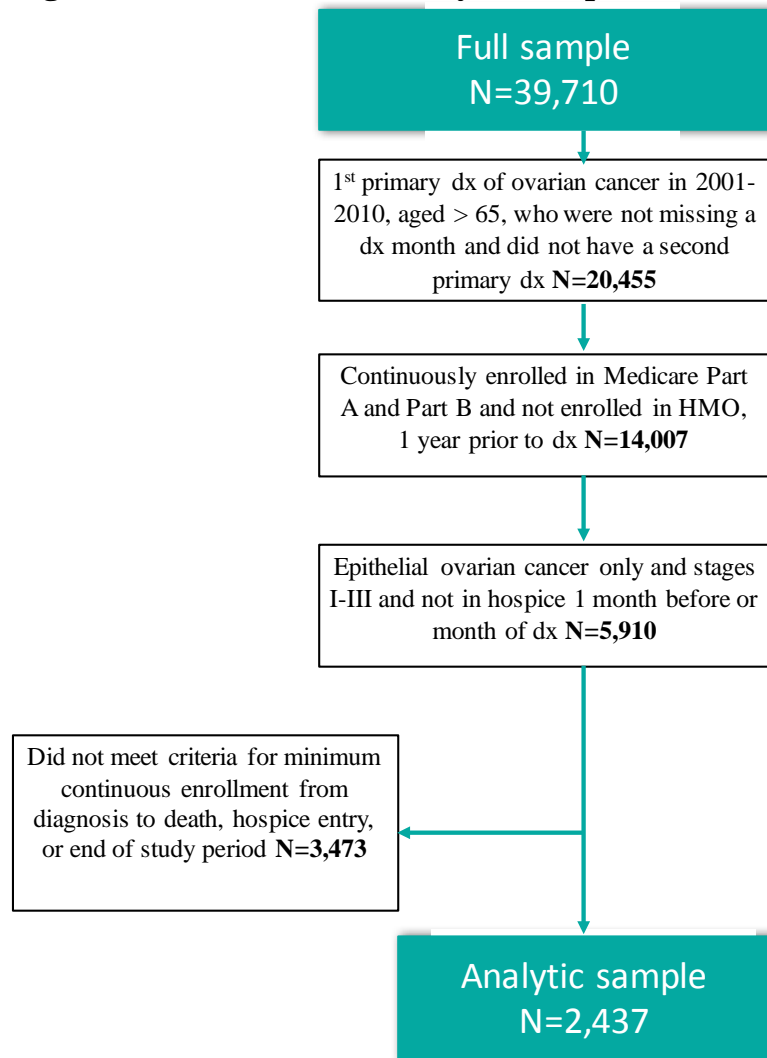
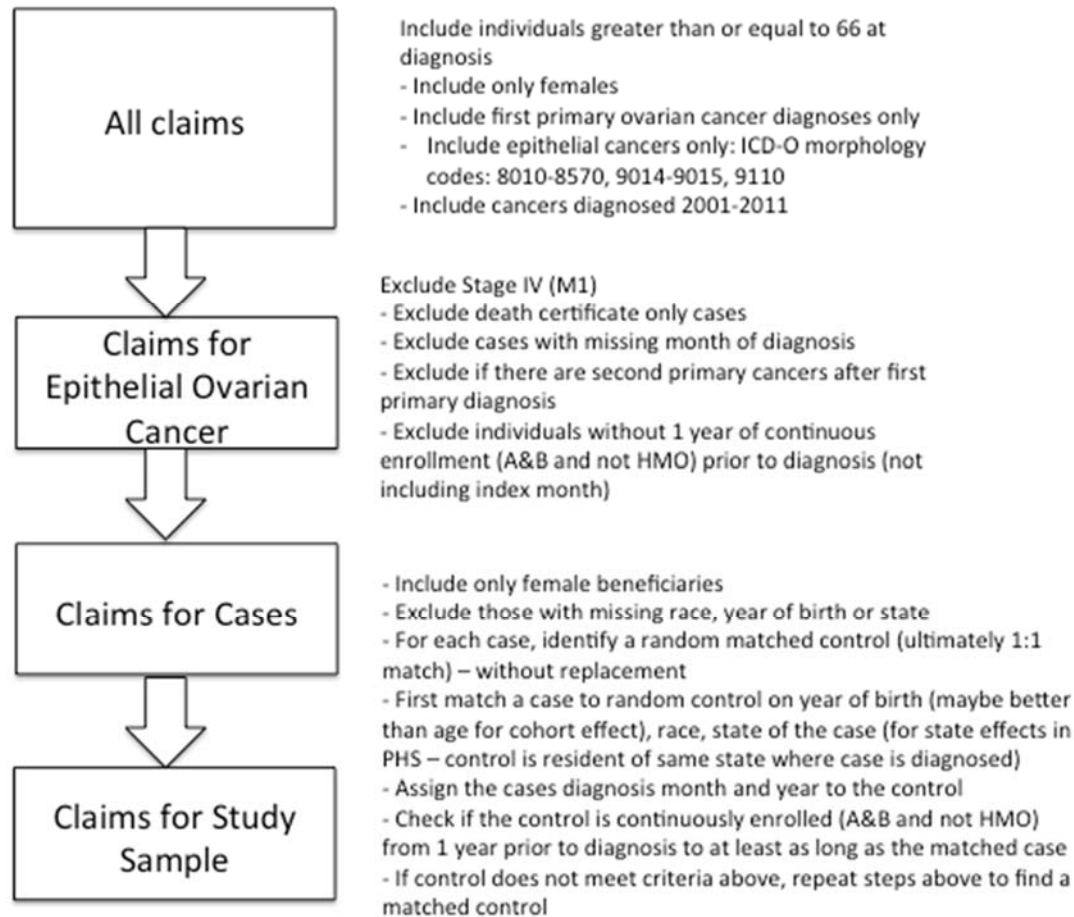
Figure 2. Flow Chart for Analytic Sample

Figure 3. Flow Chart for cases and matching controls



Conceptual Framework

This framework for analysis of ovarian cancer survivorship and PHS utilization (Figure 4) draws on the Andersen and Aday behavioral model of health services use [59] and the economic theory of demand [60]. The Andersen and Aday model includes three categories of factors that influence utilization of care: predisposing, enabling and need [59]. Predisposing characteristics include those that influence the propensity to use health care, such as demographic factors (age and race/ethnicity). Enabling characteristics affect the ability to access health care, including socioeconomic status (SES) and urbanicity. Need characteristics are measures of health status that influence demand for health care and include evaluated and perceived health status indicators, such as the presence of comorbidities and psychosocial distress. Economic theory [60] informs the physician and patient mechanisms through which these predisposing, need and enabling characteristics may influence PHS use, including cancer-directed care [61, 62] and intensity of interaction with the health care system. Economic theory says we have trade-offs in what goods we consume; as you increase your visits focused on cancer surveillance you may have a lower likelihood of getting visits that focus on PHS. Increased intensity of system interaction is a mechanism driven by opportunity cost theory; the more often you visit the doctor, the lower the incremental cost of getting other PHS.

Figure 4. Conceptual Framework

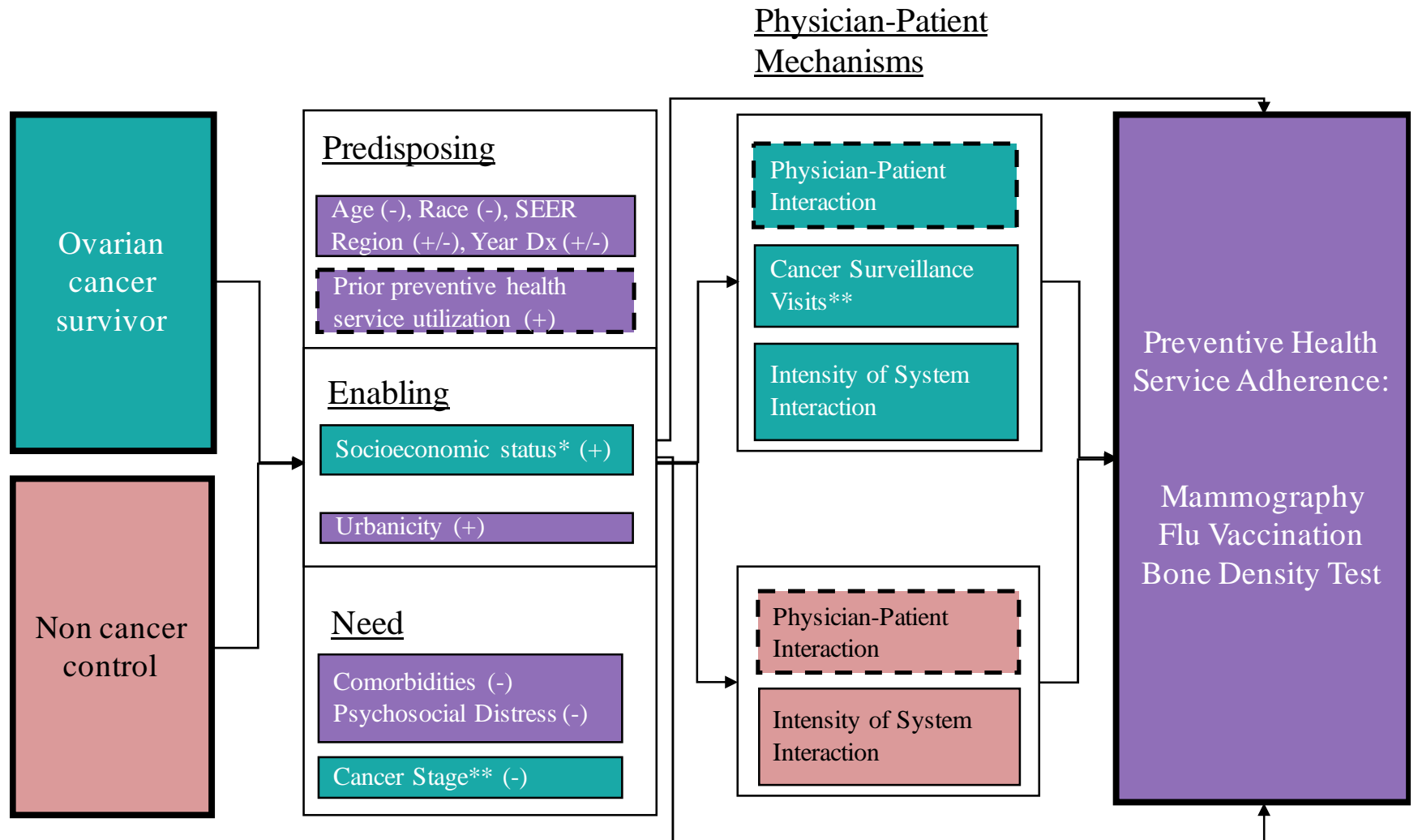
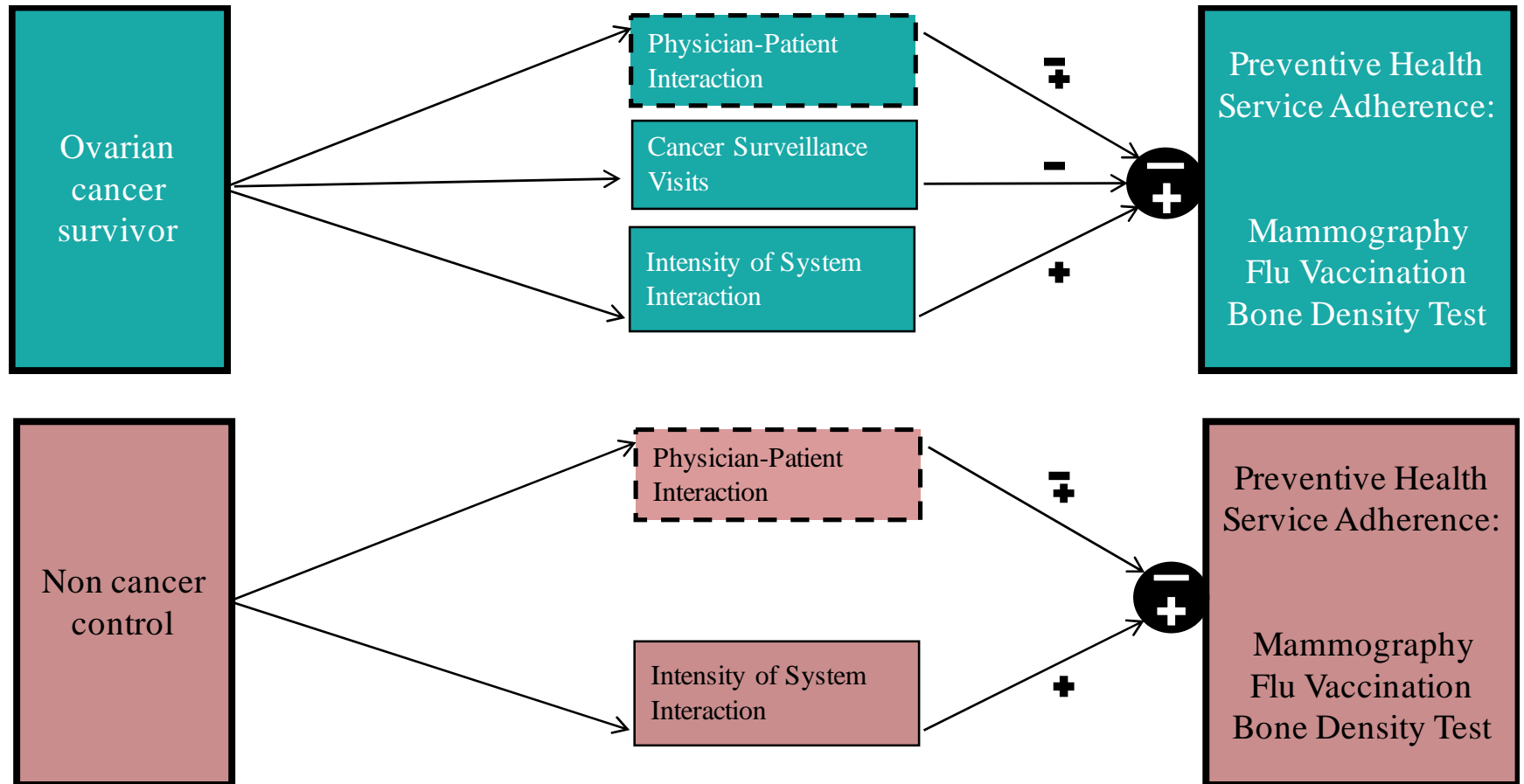


Figure 5. Focal Relationship



Focal Relationship

As noted, this study has two aims to examine: to examine the difference between ovarian cancer survivors and controls in adherence to PHS recommendations, and to investigate factors influencing adherence within both groups.

The relationship between ovarian cancer survivorship and receipt of PHS is influenced by predisposing, enabling and need characteristics, along with mechanisms that arise from the provider-patient interaction [63]. Patient mechanisms include characteristics of individual health care use such as intensity of interaction with the health system [63] and ovarian cancer surveillance. Intensity of interaction with the health care system can be thought to capture contacts with healthcare professionals that would recommend PHS and thus are likely to positively influence adherence. Intensity of interaction with the health care system is measured by outpatient visits, as these would be the type of visits where preventive health services are provided. Inpatient visits are not included in intensity of interaction because they are unlikely to facilitate the receipt of a preventive health service. Further, inpatient visits are likely to be heavily weighted towards the cancer patients and would not be representative of both groups. On the other hand, cancer surveillance visits may specifically work against this mechanism, as more interaction with the system directed to cancer surveillance could result in less focus on PHS. Cancer surveillance visits are measured by a visit that has a CA-125 test, a CT or PET scan. Unmeasured variables include the actual interaction between the patient and the physician, and are hypothesized to have either a negative or a positive influence on PHS receipt depending on each individual's interaction. Due to the conflicting directions and previous mixed findings as outlined in the literature review, there is insufficient evidence to hypothesize whether the net sum of these forces will be positive or negative.

This analysis considers the impact of ovarian cancer survivorship on the receipt of PHS, which is defined here in three different categories: vaccinations, cancer screenings, and health maintenance screenings. Cancer and general health screening recommendations for elderly women are published by the USPSTF [9, 64], while vaccination recommendations are published by the ACIP [65]. This study's cancer and general health screenings include mammography screening for breast cancer and bone density tests to detect osteoporosis, and also includes influenza vaccination.

Confounders and their association with constructs in the focal relationship

The individual-level confounders of the focal relationship are categorized as predisposing, enabling, and need related characteristics (Figure 4).

Predisposing characteristics

There are many predisposing characteristics, including demographics such as age and race, that could independently influence PHS use and thus confound the relationship between ovarian cancer survivorship and the hypothesized mechanisms. Age is defined as age at diagnosis, and it is hypothesized that the younger the individual the more likely they are to receive recommended PHS [18, 19, 48].

Race is defined as a social category referring to social groups that often share cultural heritage and ancestry [66]. Blacks have been shown to have less PHS use [67], so minorities are hypothesized to be less likely to receive recommended PHS.

Receipt of PHS prior to the cancer diagnosis is hypothesized to be positively correlated with the receipt of recommended PHS [68, 69], but is unmeasured in this study.

Both year of cancer diagnosis and region variables are characterized as predisposing as there is no a priori reason to expect temporal or regional differences.

Enabling characteristics

The individual enabling characteristics that could confound the relationship between ovarian cancer survivorship and use of PHS include socio-economic status (SES) and urbanicity. SES status is defined as one's access to financial, social, cultural, and human resources [70]. Urbanicity is defined as the effect of residing in urban areas at any given time [71].

Need characteristics

There are many need characteristics that could confound the relationship between ovarian cancer survivorship and PHS, including comorbidities, cancer stage at diagnosis, age at diagnosis, and psychosocial distress. The presence of comorbidities is hypothesized to be associated with a higher likelihood of receiving recommended PHS [16, 19, 48].

Based on previous literature, the lower a woman's cancer stage at diagnosis, which is determined based on the growth of the tumor [72], the lower the probability of PHS adherence. Women who are diagnosed with cancer at a younger age [73] are more likely to receive recommended PHS than women diagnosed at an older age.

Psychosocial distress is defined as having an unpleasant experience of a psychological and social nature that interferes with the ability to cope with cancer treatment and survivorship; this may include feelings of vulnerability, sadness, anxiety and panic [74]. Psychosocial distress may be negatively associated with preventive health services use [37, 39, 43].

Measures

Dependent Variable: *PHS Use*. The three preventive health services will be measured by dichotomous variables for adherence to the specific types of PHS, based on the

USPSTF and ACIP recommendations. More specifically, indicator variables will be created for adherence to recommendations for the following PHS (Table 3): breast cancer screening, osteoporosis screening and influenza vaccinations.

Focal Independent Variable:

Ovarian cancer survivor: An indicator for whether the individual is an ovarian cancer survivor will be used to determine the impact of being a survivor on adherence to PHS.

Predisposing characteristics.

Predisposing characteristics that influence the focal relationship between survivors and PHS include demographics such as age and race. Age will be measured using age at diagnosis. Race will be captured by three mutually exclusive categories: white, black and other using information from the Social Security application form as recorded in the Medicare enrollment database [75].

Table 2. Measurement of Adherence to PHS Recommendations

PHS	Adherent to Recommendation	Non-Adherent to Recommendation
Breast cancer screening (for women 65-74 years old) [9]	Receipt of mammography within the last two years.	No mammography.
Osteoporosis screening [10]	Receipt of bone density test within the last two years.	No receipt of bone mass measurement test.
Influenza vaccination [65]	Receipt of two influenza vaccination within the last two years.	No receipt of influenza vaccination within the last year.

Enabling characteristics. Enabling confounders that are hypothesized to impact the relationship between ovarian cancer survivors and adherence to PHS include SES status and urbanicity. SES will be measured using individual- and population-level variables for income and education. Individual income will be approximated by state Medicaid Buy-In (SBI) status, measured as an indicator variable for whether a woman was recorded in the Medicare enrollment database to have any state buy-in coverage during the year [18]. An area-based measure of income will be determined based on census tract median income. Urbanicity will be measured using a variable based on the Rural/Urban Continuum Codes (RUCA) from the United States Department of Agriculture [76] that have been recoded by SEER into six categories: Big Metro, Metro, Urban, Less Urban, Rural and Unknown. Due to sample size limitations, the categories Urban, Less Urban, Rural, and Unknown will be grouped together.

Need characteristics. Need characteristics exogenous to the relationship of ovarian cancer survivorship and PHS include measures of health status: comorbidities, cancer stage and psychosocial distress. Comorbidities will be measured by a modified version of the Charlson comorbidity index using inpatient, outpatient and carrier Medicare claims [77-80] (excluding any tumor or metastatic solid tumor, and leukemia/lymphoma [81]), and will be used to categorize women who have zero, one, or two or more comorbidities. Cancer stage at diagnosis will be measured by the Federal International Gynecologic Oncology classification into three groups: Stage I, Stage II, and Stage III. Psychosocial distress will be approximated by mental health illness as measured by an indicator variable using ICD-9-CM diagnosis codes to identify women with anxiety or depression: 311, 296.90, 399.00, 296.21, 296.22, 296.30, 309, 300.02, 293.83.

Comorbidities and psychosocial distress variables will be static in this study for simplification purposes and be measured prior to diagnosis.

Table 3. Exogenous variables measurement and hypotheses

Construct	Measure	Hypothesized relationship with the dependent variable
Race/Ethnicity	Women will be classified into three racial groups: <ul style="list-style-type: none"> - White - Black - Other 	Minorities are less likely than white, to be adherent to PHS recommendations.
Previous PHS Use	Not Measured	Women with prior history of PHS use are more likely to be adherent to PHS recommendations.
Comorbidities	Charlson Comorbidity Index will be categorized in three groups: <ul style="list-style-type: none"> - 0 comorbidities - 1 comorbidity - 2 or more comorbidities 	Women with more comorbidities are more likely to adhere to PHS recommendations.
Age at Diagnosis	Continuous variable of age at diagnosis as recorded in the SEER registry. For women with no history of cancer, age at diagnosis will be the matched case's age at diagnosis.	Women who were diagnosed at an older age are less likely to be adherent to PHS recommendations than women diagnosed at a younger age.
Cancer Stage at Diagnosis	Stage will be classified into three categories: <ul style="list-style-type: none"> - I - II - III 	Women diagnosed with ovarian cancer at a higher stage are less likely to adhere to PHS recommendations due to a greater propensity to receive cancer related services and lower life expectancy.
Psychosocial Distress	Mental Health illness: if any diagnosis code during follow-up time with a mood, anxiety or depressive disorder No Mental health illness: if not diagnosed with any mood, anxiety or depressive disorder	Women with psychosocial distress are less likely to adhere to PHS recommendations.

SES		
Income	SBI: Individual who had any SBI coverage in a given year No SBI: Individual who had no SBI coverage in a given year.	Women with SBI coverage will be more likely to adhere to PHS recommendations.
	The unadjusted median income by census tract will be used.	Women with higher income are more likely to adhere to PHS recommendations.
Urbanicity	Urbanicity will be classified into 3 categories at the census tract level: <ul style="list-style-type: none"> - Big Metro - Metro/Urban - Rural/Less Rural 	Women in urban areas are more likely to be adherent to PHS recommendations than women in non-urban areas

Analytic Strategy

Logistic regression models will be used to estimate the probability of ovarian cancer survivors receiving appropriate PHS (influenza vaccinations, mammography, bone density test). Each PHS will be regressed on a set of mechanism variables and covariates that are predicted to influence adherence. Table 5 shows the indicators used in the regressions.

Separate models will be specified to address Aims 1 and 2, respectively. First, a set of pooled logistic regressions will be run to determine the propensity to meet guidelines for ovarian cancer survivors compared to non-cancer controls for each PHS (influenza immunization, mammography, osteoporosis screening) using covariates that are measurable among both cancer and non-cancer populations. The difference between the two groups (adjusting for other factors) will be captured by an indicator variable identifying ovarian cancer survivors versus those with no history of cancer.

Then, individual models will be run for cancer and non-cancer controls, using the best set of variable available in each case. While the majority of the variables we can measure for non-cancer individuals overlap with the ovarian cancer survivors, we cannot

measure median income (due to data availability) or cancer-specific variables, such as stage and cancer surveillance visits.

All data cleaning, formatting, manipulation and analyses were conducted in SAS version 9.4 and Stata version 14.1. The output of each logistic model was transformed into marginal effects to show the magnitude of the impact of a change in predictor variable levels on the likelihood of receiving PHS. For example, in the pooled model the marginal effect for ovarian cancer survivor indicator will tell us compared to the non-cancer controls how many percentage points (pp) more, or less, likely ovarian cancer survivors are to be adherent to PHS guidelines. The c statistic of concordance will also be reported to show the internal predictive power of the models.

Table 5. Variables being used in models

	Pooled Model	Cancer Model	Control Model
Mechanisms			
Intensity of Interaction with Healthcare system		X	X
Cancer Surveillance		X	
Control Variables			
Age	X	X	X
Race	X	X	X
Region	X	X	X
Year of Diagnosis	X	X	X
Urbanicity	X	X	X
Charlson Comorbidity Index	X	X	X
Psychosocial Distress	X	X	X
Medicaid State Buy-in	X	X	X
Cancer Stage		X	

Median Income		X	
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As indicated in table 5, the mechanisms that we previously hypothesized to be important in explaining adherence to PHS will only be used in the individual models. Although we can use intensity of interaction with the healthcare system in both models, we will not be using it in the pooled model. If we were to use it in the pooled model, we would be accounting for the mechanisms available for non-cancer controls but we would still have to omit cancer surveillance visits because they are only available for ovarian cancer survivors. Due to the hypothesis that, taken all together, the forces that influence PHSs for both ovarian cancer survivors and non-cancer controls could be positive or negative. If the intensity of visits variable was included, the indicator variable for ovarian cancer survivors would pick up some unknown effect from cancer surveillance visits and what difference exists between the two groups. Thus, it isn't possible to hypothesize what omitting cancer surveillance visits for cancer survivors would have on the pooled model. Rather than underspecifying these mechanisms in the pooled model, we decided to not include any mechanisms in the pooled model and let the difference be captured only by the indicator for ovarian cancer survivors. Then we will explore our hypothesized mechanisms further within the individual models, which will help us understand the unique relationship the mechanisms have on adherence for each group of cancer survivors and controls.

Aim 1. Pooled Models

An indicator will be used in equations 1 – 3 indicating the difference between ovarian cancer survivors and non-cancer controls.

Pooled Model using common covariates

1. $\log\left[\frac{P(\text{Flu Vaccine in 1 year}=\text{Yes})}{P(\text{Flu Vaccine in 1 year}=\text{No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Year of Diagnosis}) + \beta_8 (\text{SEER Region}) + \beta_9 (\text{Ovarian Cancer Survivor})$
2. $\log\left[\frac{P(\text{Mammography in 2 years}=\text{Yes})}{P(\text{Mammography in 2 years}=\text{No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Year of Diagnosis}) + \beta_8 (\text{SEER Region}) + \beta_9 (\text{Ovarian Cancer Survivor})$
3. $\log\left[\frac{P(\text{Bone Densitometry in 2 years}=\text{Yes})}{P(\text{Bone Densitometry in 2 years}=\text{No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Year of Diagnosis}) + \beta_8 (\text{SEER Region}) + \beta_9 (\text{Ovarian Cancer Survivor})$

Aim 2. Individual Models

The cancer model will describe what factors influence adherence to guidelines for ovarian cancer survivors.

Cancer model using best available covariates

4. $\log\left[\frac{P(2 \text{ Flu Vaccine in 2 years}=\text{Yes})}{P(2 \text{ Flu Vaccine in 2 years}=\text{No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Cancer Surveillance Visits}) + \beta_9 (\text{Year of Diagnosis}) + \beta_{10} (\text{SEER Region})$
5. $\log\left[\frac{P(\text{Mammography in 2 years}=\text{Yes})}{P(\text{Mammography in 2 years}=\text{No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Cancer Surveillance Visits}) + \beta_9 (\text{Year of Diagnosis}) + \beta_{10} (\text{SEER Region})$

$$6. \log\left[\frac{P(\text{Bone Density in 2 years=Yes})}{P(\text{Bone Density in 2 years=No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Cancer Surveillance Visits}) + \beta_9 (\text{Year of Diagnosis}) + \beta_{10} (\text{SEER Region})$$

Non-cancer model using the best available covariates

The non-cancer model will describe what factors influence adherence to guidelines for non-cancer controls and we will compare whether these are different for the other models.

$$7. \log\left[\frac{P(\text{2 Flu Vaccine in 2 years=Yes})}{P(\text{2 Flu Vaccine in 2 years=No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Year of Diagnosis}) + \beta_9 (\text{SEER Region})$$

$$8. \log\left[\frac{P(\text{Mammography in 2 years=Yes})}{P(\text{Mammography in 2 years=No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Year of Diagnosis}) + \beta_9 (\text{SEER Region})$$

$$9. \log\left[\frac{P(\text{Bone Density in 2 years=Yes})}{P(\text{Bone Density in 2 years=No})}\right] = \beta_0 + \beta_1 (\text{Age}) + \beta_2 (\text{Race}) + \beta_3 (\text{SBI}) + \beta_4 (\text{Urbanicity}) + \beta_5 (\text{Psychosocial Distress}) + \beta_6 (\text{Charlson Comorbidity Index}) + \beta_7 (\text{Number of Outpatient Visits}) + \beta_8 (\text{Year of Diagnosis}) + \beta_9 (\text{SEER Region})$$

CHAPTER IV: Results

Descriptive Statistics

The descriptive statistics for ovarian cancer survivors in the analytic sample are shown in Table 6. The average age of patients was 74, and the majority were white and

diagnosed in stage III. Geographically, a large portion of patients were from California and resided in counties classified as Big Metro. About 1/5th of the patients had Medicaid State Buy-In (SBI), an indicator of whether the state paid for any of their Medicare premiums, and the average of the median income of the census tract was almost \$33,000.

Table 6. Descriptive statistics: Analytic Sample

Characteristics	Cases (N=2,437)	
	No.	%
Age, years		
Mean	74.6	
SD	5.8	
Race		
White	2,195	90
Black	118	5
Other	124	5
Stage		
I	741	30
II	360	15
III	1,279	52
Year of Diagnosis		
2001	227	9.3
2002	222	9.1
2003	235	9.6
2004	252	10.4
2005	264	10.8
2006	256	10.5
2007	210	8.6
2008	249	10.2
2009	256	10.5
2010	266	10.9
Charlson Comorbidity Index (CCI)		
0	1,757	72
1	484	20
2+	196	8
SEER Registry site		
Connecticut	137	5.6
Detroit	132	6

Hawaii	19	0.8
Iowa	154	6.5
New Mexico	59	2.5
Seattle	156	6.5
Utah	50	2
Kentucky	174	7
Louisiana	139	5.7
New Jersey	362	15
Georgia	284	12
California	771	31
Urbanicity		
Big Metro	1,343	45
Metro	461	19
Less Urban/Rural	397	16
Socioeconomic status		
Medicaid State Buy-in	361	15
Median Income (Census Tract)		
Q1	377	15
Q2	406	17
Q3	434	18
Q4	444	18
Q5	478	20

Flu vaccine: Table 7 shows the unadjusted adherence rates to flu guidelines for cases and controls. Overall, the ovarian cancer survivors were more adherent to flu vaccination guidelines, 65% compared to 60%, respectively. For those who were white, cases were more adherent to guidelines than the controls. Individuals with psychosocial distress did not have different adherence to flu guidelines between cases and controls. This is unexpected, particularly for those defined as having psychosocial distress, as we expected those with psychosocial distress to be more focused on their mental health than on adherence to preventive health guidelines. This result could be due to the measurement of psychosocial distress of diagnosis and anxiety, which could impact both cases and controls equally. However, the measurement may not be getting at the direct

psychosocial issues of fear of recurrence that ovarian cancer survivors often experience. It is also worth noting that urbanicity differences are not found across big metropolitan, metropolitan and rural/less urban areas for cancer survivors. This finding suggests that those who live in rural/less urban areas make multiple appointments for their health and their cancer surveillance facilitates other health care services, so their proximity to healthcare services does not impede adherence.

Table 7. Unadjusted adherence rates to *flu vaccine* guidelines for ovarian cancer survivors and controls

Flu	Case	Control	P value
Overall	65%	60%	0.000
White	69%	63%	0.000
Black	52%	45%	0.30
Buy-in	53%	52%	0.81
No Buy-in	70%	64%	0.0001
Big Metro	68%	61%	0.0008
Metro	68%	63%	0.08
Rural	68%	60%	0.026
CCI =0	66%	58%	0.000
CCI =1	69%	71%	0.44
CCI 2+	76%	65%	0.009
Psychosocial Distress	72%	69%	0.65
No Psychosocial Distress	67%	61%	0.000

Mammography: Table 8 shows patterns for adherence to mammography by selected groups that are generally similar to those reported in Table 7. We see that ovarian cancer survivors had higher adherence to mammography at 46% compared to 40% for controls. Among those who were white, cases had a higher adherence to mammography. Among those with SBI, there was no significant difference between cases and controls.

Table 8. Unadjusted adherence rates to mammography guidelines for ovarian cancer survivors and controls

Mammography	Case	Control	P value
Overall	46%	40%	0.001
White	47%	40%	0.0002
Black	36%	24%	0.085
Buy-in	36%	33%	0.52
No Buy-in	47%	41%	0.0003
Big Metro	46%	40%	0.007
Metro	44%	40%	0.212
Rural	49%	37%	0.003
CCI =0	48%	39%	0.0000
CCI =1	45%	45%	0.93
CCI 2+	35%	37%	0.70
Psychosocial Distress	41%	40%	0.92
No Psychosocial Distress	46%	40%	0.001

Bone Density: Table 9 shows a particularly low adherence to bone density guidelines compared to flu vaccinations and screening mammography, and no differences

between cases and controls overall. These low rates may be due to reimbursement issues for bone density tests. In 2007, reimbursement was decreased for this service, and in 2010 the ACA provided coverage for them as a preventive health service but only for women with specific risk factors [82].

Table 9. Unadjusted adherence rates to *bone density* guidelines between ovarian cancer survivors and controls

Bone Density	Case	Control	P value
Overall	29%	30%	0.53
White	30%	30%	0.77
Black	14%	14%	1.00
Buy-in	20%	20%	0.88
No Buy-in	31%	32%	0.24
Big Metro	30%	30%	0.81
Metro	30%	33%	0.26
Rural	30%	26%	0.10
CCI =0	29%	30%	0.77
CCI =1	30%	31%	0.81
CCI 2+	22%	28%	0.22
Psychosocial Distress	26%	34%	0.11
No Psychosocial Distress	29%	29%	0.81

Logistic Results

The following three tables will address whether there is a difference between ovarian cancer survivors and controls in adherence to PHS guidelines, after adjusting for

other factors. Results are reported as marginal effects (ME), with standard errors (SE), and the overall predictive strength of the model is indicated by c-statistics.

Flu Vaccine Logistic Results

Pooled Model

Ovarian cancer survivors are 5 pp more likely to be adherent to flu vaccine guidelines than non-cancer controls. Blacks compared to whites were 15 pp less likely to be adherent to flu vaccine guidelines. Individuals with comorbidities are more likely to be adherent to flu vaccine guidelines compared to those with no comorbidities. Individuals with SBI were 15 percentage points less likely to be adherent to flu vaccine guidelines.

Cancer survivors

The results of the logistic regression, assessing adherence to flu vaccination guidelines among cancer survivors only, do not suggest that either the mechanism of cancer surveillance or the intensity of interaction with the healthcare system has a clinically significant impact on adherence to flu vaccine guidelines for ovarian cancer survivors. Although there is a statistically significant effect found for cancer surveillance, the marginal effects are very small, with a 0.3 pp difference.

Compared to whites, black individuals were less likely to be adherent to flu vaccine guidelines by 12 pp. Further, compared to individuals with no comorbidities, those with one comorbidity were 5 pp less likely and those with two or more comorbidities were 13 pp less likely to be adherent. Socioeconomic status was a strong predictor of adherence. Compared to individuals in quintile 1 (lowest), there was a gradient of increasing likelihood to be adherent: quintile 2 was 5 pp more likely, quintile 3 was 6 pp more likely, quintile 4 was 7 pp more likely and the highest quintile was 11 pp more likely. Individuals with SBI status were 14 pp less likely to be adherent to flu

vaccine guidelines, suggesting that although dual-eligible individuals have coverage they may face barriers to accessing health care.

Controls

Similar to the results for ovarian cancer survivors, for the controls the impact of the variable indexing interaction with the healthcare system was statistically significant, but the marginal effect was small in magnitude. Compared to whites, blacks were 14 pp less likely to be adherent to flu vaccine guidelines. We found an unexpected direction of effect for the variable representing psychosocial distress; they were 7 pp more likely to be adherent to flu vaccine guidelines than those with no psychosocial distress. A negative relationship was identified for those with SBI, as they were found to be 14 pp less likely to be adherent to guidelines than those without SBI.

Table 10. Do ovarian cancer survivors have different adherence to flu vaccine guidelines when compared to non-cancer controls?

Flu Vaccine Adherence	Pooled N=4,874		Cancer N=2,434		Non-cancer N=2,376	
	ME	SE	ME	SE	ME	SE
Ovarian cancer survivors	0.05***	0.01				
Cancer Surveillance Intensity of Interaction with Healthcare System			0.003***	0.001		
Age at diagnosis	0.006***	0.00	0.01***	0.002	0.007***	0.002
Race						
White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Black	-0.15***	0.04	-0.12**	0.05	-0.14***	0.05
Other	0.02	0.03	0.02	0.05	0.08*	0.04
Charlson Comorbidity Index						

0	Ref.		Ref.		Ref.	Ref.
1	0.08***	0.02	0.05**	0.02	0.11***	0.02
2+	0.09***	0.02	0.13***	0.03	0.05	0.03
Psychosocial Distress	0.05*	0.02	0.02	0.04	0.07*	0.04
Cancer Stage						
I			0.03	0.02		
II			0.06**	0.03		
III			Ref.	Ref.		
Median Income						
Quintile 1			Ref.	Ref.		
Quintile 2			0.05*	0.03		
Quintile 3			0.06**	0.03		
Quintile 4			0.07**	0.03		
Quintile 5			0.11***	0.03		
Medicaid Buy-in	-0.15***	0.02	-0.14***	0.03	-0.14***	0.02
C statistic	63%		65%		63%	
† adjusted for urbanicity, year of diagnosis, SEER Region, * p < 0.1, ** p < 0.05, *** p < 0.01						

Mammography Logistic Results

Pooled Model

Table 11 shows that ovarian cancer survivors were 4 pp more likely to be adherent to mammography guidelines compared to non-cancer controls. The sample size is smaller in Table 11, compared to Table 10, due to the age restriction of mammography guidelines. Blacks compared to whites were 13 pp less likely to be adherent to mammography guidelines. Individuals with one comorbidity compared to those with no comorbidities were 7 pp more likely to be adherent to mammography guidelines, but there was no significant difference between individuals with 2 or more comorbidities and individuals with none. With more 2 or more comorbidities, the patient's health status may be such that it is actually reducing the likelihood of getting PHS, notwithstanding

that the individual is interacting with the system quite a bit. Individuals with SBI were 14 pp more likely to be adherent to mammography guidelines.

Cancer survivors

Column 2 shows the cancer survivors' adherence to mammography. Both hypothesized mechanisms were not significant, and cancer surveillance was in the unexpected direction. For each additional year in the age at diagnosis, the survivor was found to be 11 pp less likely to be adherent. Socioeconomic status was a strong predictor of adherence, but did not have an increasing gradient as with flu vaccination. Compared to individuals in quintile 1, quintile 2 was 10 pp more likely, quintile 3 was 14 pp more likely, quintile 4 was 12 pp more likely and the highest quintile was 12 pp more likely to adhere to guidelines. Individuals with SBI status were 9 pp less likely to be adherent to flu vaccine guidelines, suggesting that although dual-eligible individuals have coverage they may face barriers to accessing health care.

Controls

Column 3 shows the adherence to mammography guidelines for non-cancer individuals. Intensity of Interaction with the Healthcare System had a positive and significant effect but was small in magnitude. Similar to ovarian cancer cases, age at diagnosis was a significant predictor of mammography, with each additional year of age associated with a 7 pp reduction in the probability of adherence. Psychosocial distress had a negative but not significant effect on adherence. Those with SBI were 12 pp less likely to be adherent to mammography guidelines when compared to those without SBI, consistent with what was found for flu vaccinations.

Table 11. Do ovarian cancer survivors have different adherence to mammography guidelines when compared to non-cancer controls?

Mammography Adherence Variables	Pooled N=3,565		Cancer N=1,842		Non-cancer N=1,669	
	ME	SE	ME	SE	ME	SE
Ovarian cancer survivors	0.09***	-0.02				
Cancer Surveillance Intensity of Interaction with Healthcare System			0.001	0.001		
Age at diagnosis	-0.09***	0.004	-0.11***	0.004	-0.07***	0.003
Race						
White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Black	-0.13***	0.04	-0.07	0.06	-0.17***	0.05
Other	0.07	0.05	0.04	0.07	0.12*	0.07
Charlson Comorbidity Index						
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1	0.08***	0.03	0.05	0.04	0.10***	0.04
2+	0.03	0.04	-0.05	0.06	0.06	0.05
Psychosocial Distress	-0.03	0.04	-0.05	0.05	-0.05	0.05
Cancer Stage						
I			0.09**	0.04		
II			0.04	0.05		
III			Ref.	Ref.		
Median Income						
Quintile 1			Ref.	Ref.		
Quintile 2			0.10**	0.05		
Quintile 3			0.14**	0.05		
Quintile 4			0.12**	0.05		
Quintile 5			0.12**	0.05		
Medicaid Buy-in	-0.11***	0.02	-0.09**	0.04	-0.12**	0.03
C statistic	59%		86%		73%	

† adjusted for urbanicity, year of diagnosis, SEER Region, * p < 0.1, ** p < 0.05, *** p < 0.01

Bone Density Logistic Results

Pooled Model

Results in column 1 of Table 12 show a negative but non-significant difference between ovarian cancer survivors and non-cancer controls' adherence to bone density screening. Blacks when compared to whites were 14 pp less likely to be adherent to bone density guidelines. Those with SBI compared to those without were 11 pp less likely to be adherent to bone density guidelines.

Cancer survivors

The second column shows the results for ovarian cancer survivors' adherence to bone density guidelines. The proposed mechanisms for ovarian cancer survivors are found to have no significant impact on adherence. Compared to whites, black individuals were 14 pp less likely to be adherent to bone density guidelines. Compared to women diagnosed at stage III, those diagnosed at stage I were 9 pp more likely to be adherent to guidelines. As with the other two PHS services, the likelihood of bone density testing was negatively associated with the woman's SBI status; those with SBI were 9 pp less likely to be adherent.

Controls

Bone density guideline adherence for non-cancer controls is shown in column 3. One additional visit to the healthcare system increased the likelihood of adherence to bone density guidelines by 2 pp, which was significant statistically but very small in magnitude. The negative findings for minorities found for flu vaccine guidelines are also evident here. Compared to those who are white, black controls are 14 pp less likely to be

adherent to guidelines. In line with other analyses, SBI individuals were 13 pp less likely to be adherent to bone density guidelines.

Table 12. Do ovarian cancer survivors have different adherence to bone density guidelines when compared to non-cancer controls?

Bone Density Test Adherence Variables	Pooled N=4,874		Cancer N=2,434		Non-cancer N=2,376	
	ME	SE	ME	SE	ME	SE
Ovarian cancer survivors	-0.01	0.01				
Cancer Surveillance Intensity of Interaction with Healthcare System			0.00002	0.002		
Age at diagnosis	0.01***	0.001	-0.01***	0.001	0.002***	0.0007
Race						
White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Black	-0.14***	0.03	-0.14***	0.04	-0.14***	0.04
Other	-0.01	0.03	-0.07*	0.04	0.07	0.05
Charlson Comorbidity Index						
0						
1	0.03	0.02	0.03	0.02	0.004	0.02
2+	-0.01	0.02	-0.04	0.03	-0.02	0.03
Psychosocial Distress	0.02	0.03	-0.02	0.04	0.06	0.04
Cancer Stage						
I			0.09***	0.02		
II			0.02	0.03		
III			Ref.	Ref.		
Median Income						
Quintile 1			Ref.	Ref.		
Quintile 2			0.03	0.03		
Quintile 3			0.05	0.03		
Quintile 4			0.03	0.03		
Quintile 5			0.08**	0.03		

Medicaid Buy-in	-0.11*** 0.02	-0.09*** 0.03	-0.13*** 0.02
C statistic	60%	63%	63%
† adjusted for urbanicity, year of diagnosis, SEER Region, * p < 0.1, ** p < 0.05, *** p < 0.01			

Pooled Results

Overall, we found that there are differences between ovarian cancer survivors' and non-cancer controls' adherence to PHS guidelines for flu vaccine and mammography but not for bone density tests. There were no statistically significant interesting results for temporal or regional trends (not shown). Blacks compared to whites are less likely to be adherent to all three PHS guidelines. Those with SBI compared to those without SBI are less likely to be adherent. Comorbidities may positively influence receipt of flu vaccine and mammography but not adherence to bone density guidelines. Finally, there were findings of urbanicity (not shown) or psychosocial distress.

Cancer Model Results

Overall, our hypothesized mechanisms, involving cancer surveillance and intensity of interaction with the health care system, were not significant factors explaining adherence to PHS. Cancer surveillance was statistically significant only for flu vaccine adherence but had a very small magnitude. The surveillance measure was found positive throughout the models, contrary to expectations. The intensity measure was positive, as expected, for two measures, but in an unexpected direction for bone density tests. We find that median income had a significant impact on adherence to flu vaccine and mammography adherence; those who lived in a census tract with higher median income were more likely to be adherent to guidelines. Overall, we found a consistent negative relationship between blacks' adherence to PHS compared to whites. We also

consistently found a negative relationship for adherence to guidelines for those with SBI compared to those without SBI. Psychosocial distress was not a statistically significant predictor for any PHS and had an unexpected direction of effect for flu vaccinations. Similar to the pooled models, no interesting temporal or regional trends were found.

Non-cancer Model Results

Overall, for non-cancer controls the intensity of interaction variable was positively associated with receipt of all PHS but the magnitude was very small. Age at diagnosis was a positive factor for adherence to flu vaccine but had a negative impact on adherence to mammography and bone density tests. As was the case in the pooled and cancer models, receipt of PHS was significantly lower for blacks than whites. Similar to what was found in the cancer model, there was a positive relationship between having comorbidities and adherence to PHS. Psychosocial distress had a positive association with adherence to flu vaccine and bone density guidelines but a negative association for mammography. There were no significant results for urbanicity, regional or temporal trends.

CHAPTER V: DISCUSSION

Key Findings

Ovarian cancer survivors are more likely to be adherent to both flu vaccination and mammography guideline adherence but less likely to be adherent to bone density guidelines, compared to non-cancer controls. Overall, adherence to bone density guidelines for both ovarian cancer survivors and non-cancer controls is low. The low bone densitometry rates are similar to findings from Snyder et al. 2008 and Earle and Neville 2005, which reported bone density rates of 10% and 5.7% among women who

survived colorectal cancer and breast cancer, respectively [17, 83]. The low provision of bone density tests could be due to reimbursement cuts made in 2008 [82]. Alternative suggestions from expert opinion suggest that bone density screenings are often not able to be performed in cancer centers and have to be referred out, so second appointments need to be made which logistically may be more difficult.

The hypothesized mechanisms did not have magnitudes that were large, suggesting that although interaction with the healthcare system may be important, at the margin the number of times you see your doctor is not the main driver for adherence to PHS guidelines. Similarly, when exploring how cancer surveillance impacted adherence to guidelines for ovarian cancer survivors only, we found that the effect was small and in the unexpected direction. This suggests that the evident differences in PHS adherence between ovarian cancer survivors and non-cancer controls in the pooled models may be attributable to factors, likely unmeasured here, that go well beyond the extent to which the patient interacts with the healthcare system. There may be something inherent in being an ovarian cancer survivor that is driving the difference in adherence.

Further, there are negative significant differences throughout all three models for blacks compared to whites and those with SBI compared to those without SBI. For all measures, median income has a positive impact of adherence for cancer survivors.

Policy Implications

The findings of this study supports the importance of emphasizing PHS in SCP, since adherence is far from complete, especially for bone density guidelines. By emphasizing PHS on a SCP, survivors will be able to understand what is needed to maintain their health and prevent other diseases. Although all three PHS studied are

included in SGO's Self Care Plan, the plan could be designed to emphasize stronger recommendations of these services.

Furthermore, there may be an opportunity for decreasing racial and socioeconomic disparities for PHS. Our study reveals significant black-white differences in adherence among both ovarian cancer survivors and non-cancer controls; these findings are similar to previous studies of disparities in ovarian cancer treatment adherence [58, 84]. Additionally, when comparing the unadjusted rates of guideline adherence between ovarian cancer survivors and non-cancer controls, we found that overall PHS adherence is not high among the women older than 65. Community outreach and mobile screening could be used to reach underserved populations that may not have the means to go to the doctor's office for preventive health screenings, and this could increase rates overall.

Limitations

Our study has several limitations. Although SEER-Medicare data is helpful for getting longitudinal views of persons, it only has claims for FFS beneficiaries and those age 65 and over. This greatly limits our ability to draw conclusions about Medicare beneficiaries who are in Medicare Managed Care or ovarian cancer survivors who are under age 66. Although we can observe these individuals after diagnosis of cancer if they are in Medicare FFS Parts A and B, we have no understanding of their health service patterns prior to entering Medicare. These service patterns are likely to be important predictors of when a person will seek care after their cancer diagnosis.

Additionally, patient reports on factors influencing receipt of care could not be captured in this study. This information is important to understanding an individual's perception of their own health status. The mechanisms proposed in this study did not

explain adherence to PHS guidelines, which suggest there may be something inherent to being an ovarian cancer survivor that influences adherence. The complicated sequelae of interacting with the healthcare system post-treatment for ovarian cancer survivors cannot be fully understood through cancer registry and insurance claims data alone.

Recommendations for Future Studies

Future studies could focus on the SGO's guidelines for PHS as outlined in their self-care plan, which recommended yearly mammography. Adherence to SGO guidelines could be compared to adherence to the USPSTF guidelines. This could also allow us to draw conclusions about the use of the current SGO self-care plan, which could inform future directions for future SCP design and provision.

Previous studies [58, 84, 85] found differences in adherence to guidelines due to provider specialty and temporal differences in adherence farther away from cancer treatment. Following a smaller group of survivors for a longer time and taking advantage of rich longitudinal data could also help us understand how ovarian cancer survivorship influences PHS adherence further from diagnosis. Data on provider characteristics, for both oncologists and general practitioners, could yield insights into the relationship between physician specialty and the provision of PHS consistent with guidelines. Future studies using provider characteristics would give better insight into what role the survivorship care plans could have for ovarian cancer survivors' PHS use.

Other studies have also found treatment disparities due to not receiving recommended care from gynecologic oncologists [86, 87]. Future studies could investigate whether women who are not receiving recommended treatment for their

ovarian cancer are also not receiving preventive health services in the post-treatment period.

To strengthen our understanding of why ovarian cancer survivors are more likely to be adherent to mammography and flu vaccination guidelines, surveys could be distributed after treatment to ascertain their perceptions of how survivorship has impacted them. The National Health Service of England recently published a summary on their response to a Patient Reported Outcomes Measures (PROM) pilot for gynecologic cancer that could be adapted to create one for the SEER registries [88]. The Functional Assessment of Cancer Therapy for Ovarian Cancer (FACT-O) instrument could also be adapted to assess well-being in survivorship [89]. Combining findings from studies using patient reported data and findings from studies using SEER-Medicare could provide a better picture of how to support, encourage and facilitate ovarian cancer survivors to receive guideline-recommended PHS. These PHS are recommended because they bring positive health benefits to elderly women by decreasing risk of adverse health events from reasons other than ovarian cancer.

CHAPTER VI: CONCLUSION

This is the first study to assess adherence to PHS guidelines among ovarian cancer survivors, a group with unique cancer survivorship issues. This study showed that being an ovarian cancer survivor was positively associated with adherence to guidelines for flu vaccination and mammography in comparison with non-cancer controls.

Additionally, this study found racial and socio-economic disparities for PHS guideline adherence, which follows previous disparities found in ovarian cancer

treatment [90-92]. These persistent disparities suggest that future research and efforts should be dedicated to decreasing disparities along the ovarian cancer continuum (from diagnosis to survivorship), but also within the general elderly population.

More research is needed on ovarian cancer survivors and their experiences with the healthcare system post-treatment in order to better understand their needs for healthcare that is not directly related to their cancer surveillance. Future research should include patient reported data to understand how ovarian cancer survivorship changes women's interaction with the healthcare system and the decision making process of receiving preventive health services. We found no large impact of the mechanisms that we hypothesized to influence the PHS adherence, intensity of interaction with the healthcare system and cancer surveillance visits. We suggest using provider characteristics and patient reported data in future research to better understand the unmeasured patient-provider interaction that influences PHS use.

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