SOCIAL DETERMINANTS OF HEALTH IN UTERINE CANCER PATIENTS IN ONTARIO

SOCIAL DETERMINANTS OF HEALTH IN UTERINE CANCER PATIENTS IN ONTARIO: ASSOCIATION WITH DISEASE PRESENTATION AND OUTCOME.

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TITLE: Social Determinants of Health in Uterine Cancer Patients in Ontario: Association with Disease Presentation and Outcome.

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Lay Abstract

Conditions in the social environment in which people are born, live and work are powerful influencers of health and well-being. In fact, these circumstances have also been called Social Determinants of Health (SDH). Cancer outcomes are one of the domains impacted by SDH.

In this study, we set out to investigate the association between SDH and uterine cancer outcomes in Ontario, Canada. We guessed that SDH may influence how soon patients with symptoms seek help from their doctors, how quickly their problem is investigated and how well they are able to undergo treatment.

We used a tool called the Ontario Marginalization Index to break down Ontario's uterine cancer patient population into groups according to degree of social, financial and ethnic marginalization. We found that more marginalized patients tended to present to care with more advanced cancers, that they took longer to have surgery for their cancer and that their survival was worse. These findings suggest there is more work to be done to promote health equity in cancer care.

Abstract

Objective: Delay in diagnosis and treatment of endometrial cancer may be associated with disease progression and impact management and outcomes. Social and cultural barriers influence recognition of symptoms and self-advocacy in seeking and complying with care. Associations between social determinants of health (SDH) and disease presentation, treatment and outcomes has been shown in some healthcare systems. Our objective was to investigate these in Ontario's universal access system.

Methods: Endometrial cancer patients in Ontario diagnosed 2009-2017 were identified, and clinical, social and demographic information extracted from administrative databases. SDH were quantified using previously validated marginalization quintiles (material deprivation, residential instability and ethnic concentration). Associations between SDH, disease stage, treatment and outcome were explored using chi-square, log-rank and logistic regression.

Results: 19530 patients were identified. 73% of cancers were confined to the uterus. Stage distribution differed across marginalization quintiles ($p<0.001$) with advanced disease found more frequently in highly marginalized patients (highest vs lowest quintile): OR=1.28 (95% CI 1.14-1.45) for deprivation, OR=1.2 (95% CI 1.06-1.35) for residential instability and OR=1.3 (95% CI 1.15-1.46) for ethnic concentration (<0.0001)). Highly marginalized patients also had less timely surgery ($p<0.0001$). Overall survival was shorter in patients in high deprivation and residential instability quintiles (log rank p-value<0.0001) but not in high ethnic concentration quintiles, with HR=1.4 for deprivation ($p<0.0001$) and HR=1.53 for instability ($p<0.0001$) for the highest marginalization quintile. Survival differences persisted in more uniform cohorts of early (stage I) disease and endometrioid tumors and on multivariable analysis.

Conclusions: Marginalized populations diagnosed with uterine cancer present at more advanced stages, wait longer for surgery and have shorter overall survival. Associations of SDH with uterine cancer presentation and management in Ontario could shed light on the impact of these factors on disease trajectory, drive policies for patient advocacy and redistribution of resources and promote health equity in this population.

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Table of Contents

Tables and Figures

List of Abbreviations and Symbols

SDH – social determinants of health

SES – socioeconomic status

SEER – Surveillance, Epidemiology and End Results

ICES – Institute for Clinical and Evaluative Sciences

ICE – Index of Concentration at the Extremes

CDC – Centers for Disease Control

CCO – Cancer Care Ontario

OCR – Ontario Cancer Registry

CIHI – Canadian Institute of Health Information

DAD – Discharge Abstract Databse

ALR – Activity Level Reporting

NDFP – New Drug Funding Program

RPDB – Registered Persons Database

BMI – body mass index

OR – odds ratio

HR – hazard ratio

Declaration of Academic Achievement

Limor Helpman conceptualized this research, surveyed the existing literature, planned the analyses, interpreted the statistical outputs and wrote the manuscript.

Hsien Seow assisted with planning and interpretation and offered insightful advice throughout the process, as well as suggesting manuscript edits.

Gregory Pond assisted with statistical analysis and interpretation.

Lorraine Elit and Laura Anderson also offered valuable advice on analysis and interpretation.

Introduction

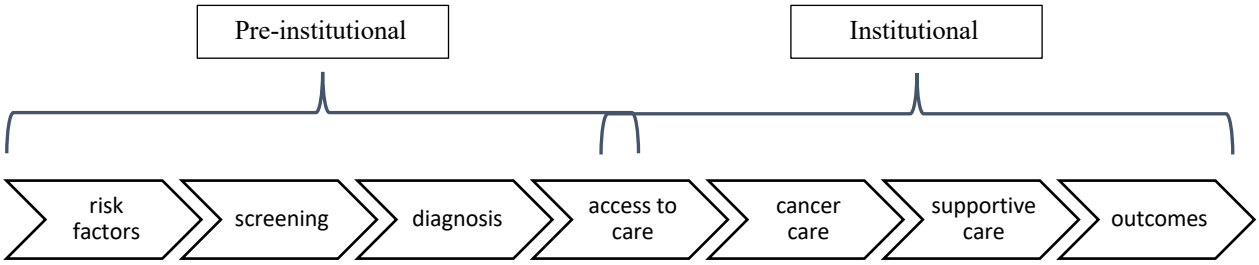
Uterine cancer is the most common gynecologic cancer in women in Canada (1), and ranks fourth among all cancers in women, as is the case in most industrialized countries. Uterine cancer incidence in Canada and the US is among the highest worldwide (2). In Ontario, over 3500 new cases were diagnosed in 2018, at an age-standardized incidence rate of 44 per 100,000 women (3).

Uterine cancer is most frequently diagnosed in post-menopausal women. It commonly presents with post-menopausal vaginal bleeding, a symptom which alerts the patient to seek help and prompts the initiation of medical investigations (4). Clinical investigation most often includes a physical examination, a pelvic ultrasound and an endometrial biopsy, which is usually performed by a gynecologist (5). Once the diagnosis of cancer is established, the patient is referred for treatment. In Ontario, provincial guidelines require that all women other than well-differentiated (Grade 1) endometrioid tumors be referred for management by a specialist at a regional cancer center (6). Treatment for uterine cancer most often begins with surgery and may be supplemented by adjuvant treatments, such as radiotherapy and/or chemotherapy (6,7).

Social determinants of health have been defined by the World Health Organization as conditions in the social environment in which people are born, live, learn, work and play, that are shaped by the distribution of resources and affect a wide range of functional quality of life outcomes, and that are powerful influencers of health and well-being (8). These social determinants include financial, educational, ethnic and cultural circumstances, social conditions and geographic locales. A landmark study assimilating US vital statistics, census and national health and community survey data over eight decades (1935-2016) demonstrated ethnic,

geographic and socioeconomic health and healthcare disparities in multiple domains (9), including overall cancer mortality. Significantly, social determinants of health are increasingly being recognized as impactful forces across the cancer care trajectory (10–13).

The cancer care pathway can be broken down to the pre-institutional phase: from prevention, through early detection, diagnosis, timely referral and access to care; and the institutional phase, including timely and appropriate surgical and oncological care, supportive care, outcomes and survivorship.



Much of the literature on association between social determinants of health and cancer presentation focuses on diseases driven by **behavioral risk factors**, such as lung, head and neck and cervical cancers (14–17). The association of social marginalization with health behaviors has been well documented both in the American (13,18) and in the Canadian (19) contexts. In one single institution study from Alabama (15), advanced stage cervical cancer was found to be associated with African American race and insurance status. A large population study using SEER data 1975-2000 as well as census, vital statistics and National Health Interview Survey data (13) demonstrated that both incidence rates and mortality for lung and cervix cancers were

higher among African Americans. Higher rates of advanced disease were also found among African Americans and among patients in living in high poverty rate census tracts.

A host of publications also links social determinants of health with poor compliance with **cancer screening** recommendations (13,20–25), which may delay early detection and explain the association found between socioeconomic and ethnic marginalization and **advanced stage at diagnosis** in screen-detectable diseases. A large epidemiological study from the US collected data on behavioral risk factors and the use of screening tests from the National health Interview Survey (13) and showed decreased screening utilization in non-Caucasians, in immigrants, in respondents with lower education and in the non-insured. The same study used census information and SEER data on cancer diagnoses and outcomes and demonstrated higher rates of advanced colorectal, prostate, breast and cervical cancers among patients living in census tracts with higher poverty rates. The National Cancer Registries Patterns of Care study (26) also found increased odds of advanced breast, colon and prostate cancers in socioeconomically marginalized patients. National SEER and American Community Survey data was used in another study to demonstrate strong associations between ethnic and financial marginalization, as measured by the geospatial Index of Concentration at the Extremes (ICE), and advanced disease stage in colorectal cancers (20). An American Cancer Society commissioned study using SEER and Cancer Registry data, CDC Behavioral Risk Factor Surveillance System data and vital statistics showed decreased use of mammography and increased odds of advanced breast cancer in racially marginalized populations (21).

No screening program is in place for endometrial cancer, and risk factors are principally associated with unopposed estrogen exposure (27,28), and do not typically include socioeconomic status (SES), smoking or sexual behavior; in fact, smoking is a protective factor

(29). In spite of this, an association between social determinants of health and uterine cancer presentation has been shown in some studies. A Danish survey-based study (30) on gynecological malignancies, including uterine cancer, demonstrated an association between diagnostic delay and rural residency. American studies using SEER data as well as National Cancer Database information have shown higher rates of advanced stage disease at diagnosis among African American women (31,32) and in low-income patients (32). Uterine cancer stage at presentation has the potential to impact management, including the extent and timing of surgery, the need for neoadjuvant treatment and the administration of postoperative radiation or chemotherapy, as well as ultimate oncologic outcome (33–36).

Many factors may cause a delay between the appearance of symptoms to diagnosis and to receipt of treatment, with progression of disease at the time of treatment. Some may be driven by **patient features**, such as timely recognition of abnormal symptoms and self-advocacy in seeking medical counsel or following up referrals (37). Social, economic, educational and cultural barriers may limit health literacy and influence the interpretation of early symptoms (30,38–42). Delay in seeking medical consultation may be driven by communication barriers (24,25,43–45) and by limited confidence in, and perceived access to, healthcare providers (46–48). Competing priorities (38) or poor self-advocacy (49) may present challenges in following referrals and in compliance with management recommendations (37).

Other factors that may play a role in treatment delay and progression of disease are **system**-driven, and may include accessibility of primary and secondary caregivers (50,51), availability of imaging facilities, and waiting times for consultations at tertiary care centers (52). In addition, **surgical wait times** can be a barrier to prompt surgical treatment, which is the cornerstone of management in most uterine cancer cases. One study using the American National

Cancer Database data from 1995-2005 included over 1.2 million cancer patients treated at 1443 institutions and demonstrated increased surgical delay for African American patients as well as patients insured through Medicaid across different disease sites (53). Among uterine cancer patients, National Cancer Database studies have also shown decreased use of minimally invasive surgical techniques in patients belonging to ethnic minorities, and in lower income patients and those without private insurance (54) as well as decreased rates of timely surgery for uterine cancers among ethnically, socially and financially marginalized patients (36).

Finally, multiple publications have demonstrated associations between SDH and **cancer outcomes** across many disease sites (13,14,16,17,21,26,55–66). Data on uterine cancer, specifically, also indicates a link between social marginalization and compromised outcomes: a Detroit-area population study demonstrated an association between higher household income and Caucasian ethnicity and decreased risk of death from uterine cancer (32). A SEER study focusing on race and ethnicity showed that uterine cancer survival for African American women was significantly worse, even when stratified by disease stage and grade (67). And a Danish study using national cancer registry data found that low educational level was associated with excess endometrial cancer mortality (57).

The majority of publications describing the association of social determinants of health (SDH) with cancer outcomes originate in the United States, where health insurance is not universal and socioeconomic factors directly drive access to and quality of care. Ontario's population is in many ways comparable to the US population, but its healthcare system is publicly funded and universally accessible. Nevertheless, disparities in cancer diagnosis and outcome for marginalized patients have been demonstrated for some cancer types in Ontario (59,63,68–70). These have not thus far included gynecological cancers.

Investigating the association of SDH with uterine cancer presentation and outcomes in Ontario's universal access healthcare system could shed light on the indirect impact of these patient factors on disease trajectory, and present opportunities for improved patient education and advocacy, redistribution of resources and health equity promotion.

Research Question

Are social determinants of health associated with disease stage at presentation, access to care and oncological outcomes in women diagnosed with uterine cancer in Ontario between 2009-2017?

Specific objectives: Among women diagnosed with uterine cancer in Ontario in 2009-2017,

1. To describe patient and disease characteristics, treatment and outcomes grouped by SDH as reflected in the Ontario marginalization scores.
2. To evaluate associations between SDH and disease stage at presentation.
3. To evaluate the association between SDH and treatment delay (time from biopsy to surgery).
4. To evaluate associations between SDH and secondary outcomes including adjuvant treatment and survival.

Hypothesis

Ontarian women in marginalized communities diagnosed with endometrial cancer may present with more advanced disease and experience longer delays in therapy. This could impact their risk of requiring adjuvant treatment and overall oncologic outcome. The mediators of such a putative association are multifactorial, and could include poor health literacy, self-advocacy and objective and healthcare utilization, among other factors.

Study design, methods and procedures

This study was designed as a population-based retrospective cohort study of uterine cancer patients in the province of Ontario. Women with uterine cancer diagnosed 2009-2017 were identified from the Ontario Cancer Registry, which has undergone rigorous quality control as part of a global cancer surveillance project (71), has met quality criteria for inclusion in publications from the International Association of Cancer Registries (IACR) and the International Agency for Research in Cancer (World Health Organization) and has been found to be comparable to the US SEER (Surveillance, Epidemiology and End Results) program and the National Program of Cancer Registries in terms of completeness of follow up information and accuracy of survival estimates (72). The timeframe chosen was selected to reflect a period in which stage information was systematically entered in the OCR, and was cut off to allow for latency in reporting. All endometrial cancer histologies were included, but uterine sarcomas were excluded because of their distinct clinical behavior. Populations excluded from ICES databases – namely, patients covered by federally funded healthcare, including institutionalized persons, members of the Canadian Armed Forces and indigenous people living on Reserves -were not included in the study population.

ICES (Institute of Clinical and Evaluative Sciences) (73) algorithms were used to extract and link information from Ontario's administrative databases. Demographic data, including date of birth and death was available from the Ontario Registered Person Database. Exposure variables, including marginalization scores, income quintiles and rurality scores, are neighborhood-based and assessed using conversion software from Statistics Canada to match individuals' postal codes to small geographical units (Census Tracts and Dissemination Area).

Studies comparing health outcome associations using geographical unit sizes of these magnitudes (2500–8000 people vs. 125–440 households or dwellings) as area-level indicators of socioeconomic status have shown that results are similar for both (74).

The Ontario adaptation of the Canadian Marginalization Index has been previously validated for health research in Ontario and includes material deprivation, residential instability, dependency and ethnic concentration indices (19). This population health research tool has been validated for stability over time and in different geographical areas, and has also been shown to be consistently associated with health behaviors as captured in the Canadian Community Health Survey, as well as health outcomes across a spectrum of diseases. Where most health equity research assesses unidimensional exposure variables such as income, insurance status or race, this marginalization index is multifaceted and was created to reflect four domains of marginalization: The residential instability index reflects housing instability, size of family units (proportion of dependents) and number of residents per dwelling among others. The material deprivation index includes education, income, proportion of single-parent households, government support and unemployment. The ethnic concentration index reflects the proportion of recent immigrants (< 5 years) and those who self-identify as a minority. The dependency index reflects the proportion of seniors and active labor force participation and was designed to capture life-cycle marginalization. Since uterine cancer is most prevalent in women in their 60s and 70s and is uncommon in young women, age-dependent marginalization was not felt to be an appropriate stratifier in the uterine cancer population. The Marginalization Index can be used as a summary measure of the domains assessed, or each domain can be assessed separately.

Immigration Status was extracted from the Citizenship and Immigration Canada permanent resident databases (75), which contain records for every permanent legal immigrant who landed in Canada since 1985 onward and are available and linkable through ICES.

The modified Charlson-Deyo comorbidity score was calculated based on diagnoses registered for patients during hospital admissions in the year preceding surgery (76,77).

Cancer diagnoses and histologies as well as stage information is collected by Cancer Care Ontario (CCO) in the Ontario Cancer Registry. CCO collects stage data based on the staging criteria of the American Joint Committee on Cancer or the Collaborative Stage initiative. For cases with more than one valid stage value, a resolved "best stage" is derived based on a pre-specified algorithm. Stage information has been entered in the OCR since 2009.

Dates of procedures and treatments were extracted from the Ontario Health Insurance Plan databases, used for documenting and billing all healthcare interactions by providers, and from the Discharge Abstract Database maintained by the Canadian Institute of Health Information (CIHI). Receipt of adjuvant treatments was collected from the Activity Level Reporting database (ALR) and New Drug Funding Program database (NDFP). Death was extracted from the Canadian Vital Statistics Death Database and the Registered Persons Database (RPDB).

Data Analysis:

Descriptive statistics were used to summarize patient, tumor and treatment characteristics as well as outcomes. Linear transformations and categorization of non-normal data were applied as necessary for statistical purposes.

The primary outcome was defined as disease stage at presentation and dichotomized into stage 1 versus 2-4 for the purpose of analyses. Logistic regression analysis was used to investigate factors associated with the outcome, in both univariate and multivariate analyses.

Forward stepwise selection was used to construct the multivariable regression model. In light of collinearity and overlap between some of the marginalization domains (such as material deprivation and residential instability) a summary marginalization score (modified to exclude dependency) was used for all multivariable analyses. An alternative strategy could have been performing multivariable analyses separately for each marginalization index, to include non-SDH confounders and enable assessment of the separate marginalization domains in a multivariable model.

Secondary time-to-event outcomes, including time from diagnosis to surgery and overall survival were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazards regression methods was used to explore factors associated with these secondary outcomes. Confidence intervals were constructed for statistics of interest. All tests and confidence intervals were two-sided and defined at the $\alpha=0.05$ level of significance.

Ethical Considerations

ICES uses strict de-identification tools to protect the privacy of individuals. Information is extracted and linked through unique encoded identifiers. Data linkage occurs at a centralized site, and only de-identified data or results of statistical analysis are uploaded onto an electronic platform available to researchers. The study was evaluated and approved by the Hamilton Health Sciences integrated Research Ethics Board.

Results

19,530 women diagnosed with endometrial cancers between 2009-2017 were identified. Demographic, clinical and surgical data is presented in Table 1.

In 5874 women (30%), stage information was missing. Of patients with known cancer stage, 9988 (73%) were diagnosed with stage I disease. 73% of endometrial cancers were of endometrioid histology, and 9% were of serous histology. Grade information was poorly captured in the OCR with about 90% rate of missing information and was not used for the purpose of this analysis.

20% of patients were morbidly obese with a BMI of 40 and above. Charlson comorbidity scores were only available in 36% of the patient population. 64% of patients had no admissions in the year preceding their surgery. 70% of patients lived in large urban centers. 88% were Canadian born, and only 1.3% were new immigrants who had lived in Canada less than five years.

Table 1A (n=19530) – descriptive statistics, entire cohort

Characteristic		Value
Age	Mean ± SD	63.63 ± 11.27
	Median (IQR)	63 (56-71)
Cancer stage	Missing	5,874 (30.1%)
	1	9,988 (51.1%)
	2	1,265 (6.5%)
	3	1,575 (8.1%)
	4	828 (4.2%)
Neighbourhood Income Quintile	Missing	42 (0.2%)
	1	3,684 (18.9%)
	2	4,064 (20.8%)
	3	3,893 (19.9%)
	4	3,850 (19.7%)
	5	3,997 (20.5%)
RIO score* categories	Missing	153 (0.8%)
	0-9 (Large Urban)	13,588 (69.6%)
	10-40 (Small Urban)	4,318 (22.1%)
	>40 (Rural)	1,471 (7.5%)
Charlson-Deyo Index	Missing	12,516 (64.1%)
	0	5,352 (27.4%)
	1	1,030 (5.3%)
	2	347 (1.8%)
	3+	285 (1.5%)
BMI > 40	No	15,616 (80.0%)
	Yes	3,914 (20.0%)
Dependency Quintile	Missing	85 (0.4%)
	1	3,452 (17.7%)
	2	3,465 (17.7%)
	3	3,664 (18.8%)
	4	3,812 (19.5%)
	5	5,052 (25.9%)
Deprivation Quintile	Missing	85 (0.4%)
	1	3,779 (19.3%)
	2	3,872 (19.8%)
	3	3,939 (20.2%)
	4	3,973 (20.3%)
	5	3,882 (19.9%)

Characteristic		Value
Ethnic Concentration Quintile	Missing	85 (0.4%)
	1	3,793 (19.4%)
	2	3,756 (19.2%)
	3	3,715 (19.0%)
	4	3,787 (19.4%)
	5	4,394 (22.5%)
Instability Quintile	Missing	85 (0.4%)
	1	3,513 (18.0%)
	2	3,634 (18.6%)
	3	3,743 (19.2%)
	4	3,849 (19.7%)
	5	4,706 (24.1%)
Immigration status	Born in Canada	17,260 (88.4%)
	>10 y resident	1,738 (8.9%)
	5-10 y resident	271 (1.4%)
	<5 y resident	261 (1.3%)
Histology	Endometrioid adenoca	14,188 (72.6%)
	Serous adenoca	1,730 (8.9%)
	Clear cell	285 (1.5%)
	Mixed type 1/2	1,348 (6.9%)
	Carcinosarcoma	774 (4.0%)
	Undifferentiated	307 (1.6%)
	Other	880 (4.5%)
	Missing	18 (0.1%)

* RIO = Rurality Index of Ontario

Surgery occurred in 18051 (92%) endometrial cancer patients (Table 1B). 53% of patients having surgery underwent the procedure at an academic center. Patients underwent surgery with a general gynecologist in 11961 cases (66%) and with a gyn oncologist in 4086 cases (23%). Median time from biopsy to surgery was 49 days (IQR, 26-73).

Table 1B (n=18,048) –descriptive statistics, patients who had a hysterectomy

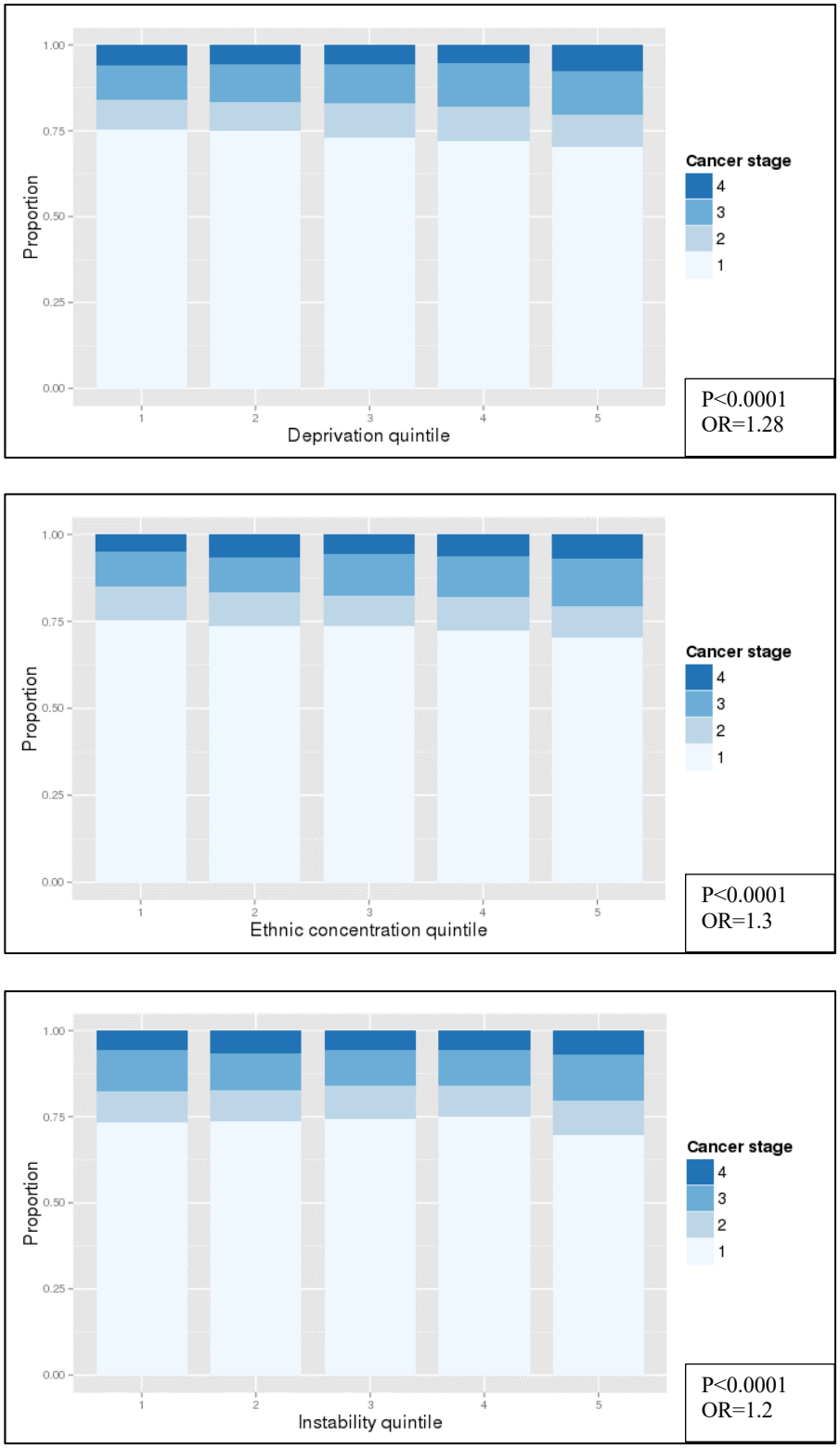
Characteristic		Value
Time from biopsy to surgery (days)	Mean ± SD	59.48 ± 96.54
	100% Max	2826
	99%	333
	95%	134
	90%	103
	75% Q3	**73**
	50% Median	**49**
	25% Q1	**26**
	10%	0
	5%	0
	1%	0
Surgery location	Academic centre	9438 (52.29%)
	Community/small hospital	8469 (46.92%)
	Missing	141 (0.78%)
Surgeon	OB/GYN	11,959 (66.26%)
	Gynecologic Oncology	4086 (22.64%)
	General Surgery	95 (0.53%)
	Other	1145 (6.34%)
	Missing	763 (4.23%)
Adjuvant Treatment	Yes	7302 (40.46%)
Recurrence	Yes	2657 (14.72%)
	Min, Max time to	273, 3401
	Mean ± SD time to	772.3 (606.27)
	Median IQR time to	530 (322-1009)

Characteristics of the study population stratified by marginalization quintile are presented in the appendix (Appendix 1).

Associations between SDH and disease stage

Figure 1 depicts stage distribution of endometrial cancer patients stratified by marginalization quintile. Patients in the highest marginalization quintiles of all domains were diagnosed with advanced disease (stages II-IV) more frequently than patients in the lowest quintiles: 30% vs. 25% for material deprivation, OR=1.28 (CI, 1.14-1.45); 30% vs. 25% for ethnic concentration, OR=1.3 (CI, 1.15-1.46); 30% vs. 27% for residential instability, OR=1.2 (CI, 1.06-1.35); $p<0.001$ for all. In an exploratory analysis dichotomizing stage at presentation as early (stage I-II) vs. advanced (stage III-IV), differences between marginalization quintiles were equally significant ($p<0.001$ for all). Details of stage distribution dichotomized by both models are shown in the Appendix (Appendix 2).

Figure 1. Stage distribution by marginalization quintile.



*OR of advanced stage disease in highly marginalized patients (quintile 5) compared to non-marginalized patients (quintile 1).

Because of the high rates of missing stage information, a sensitivity analysis was performed on a subset of patients diagnosed in 2009-2013, when stage information was more complete (88% complete stage information overall). This confirmed a persistent association between cancer stage and marginalization indices in the material deprivation, residential instability and ethnic concentration domains during this timeframe:

Proportion of patients missing stage information

Index year	Count	%
2009	479	27.4
2010	386	18.9
2011	147	6.8
2012	147	6.4
2013	165	7.5
2014	1099	47.8
2015	1081	44.2
2016	1144	43.8
2017	1226	71.1

Sensitivity analysis: Chi-sq test of association between cancer stage and marginalization index

Index	Chi-sq val.	p-value
Dependency	8.1735	0.771
Deprivation	24.274	0.019
Ethnic concentration	23.6633	0.023
Instability	21.0911	0.049

On univariable regression analysis, patient factors associated with increased odds of advanced stage at presentation included age, low neighborhood income, urban residency, increased Charlson-Deyo comorbidity index, and increased marginalization (material deprivation, residential instability and ethnic concentration domains) (Table 2). Obesity was protective. Disease histology was strongly associated with disease stage at presentation with odds ratios of 2.4-12.2 for different histological subtypes.

Table 2: Univariate analysis: associations with advanced (II-IV) stage at presentation

n=13,656		OR (95% CI)	p value
Age	Age	1.02 (1.02, 1.02)	<.0001
Neighbourhood Income Quintile (ref=5)	1	1.24 (1.1, 1.4)	0.0005
	2	1.25 (1.11, 1.4)	0.0002
	3	0.97 (0.86, 1.1)	0.662
	4	1.1 (0.97, 1.24)	0.1224
RIO score (ref=large urban)	Small Urban	0.92 (0.84, 1.01)	0.0776
	Rural	0.8 (0.68, 0.93)	0.003
Charlson comorbidity Index (ref=0)	1	1.06 (0.88, 1.27)	0.5598
	2	1.19 (0.88, 1.6)	0.2588
	3+	1.44 (1.06, 1.96)	0.0199
	Missing	1.14 (1.04, 1.24)	0.0043
BMI > 40	Yes	0.54 (0.48, 0.6)	<.0001
Deprivation Quintile (ref=1 i.e. least marginalized)	2	1.02 (0.9, 1.16)	0.738
	3	1.12 (0.99, 1.27)	0.0694
	4	1.18 (1.05, 1.34)	0.0062
	5	1.28 (1.14, 1.45)	<.0001
Ethnic Concentration Quintile (ref=1 i.e. least marginalized)	2	1.1 (0.97, 1.24)	0.13
	3	1.1 (0.97, 1.24)	0.1442
	4	1.17 (1.04, 1.32)	0.0117
	5	1.3 (1.15, 1.46)	<.0001
Instability Quintile (ref=1 i.e. least marginalized)	2	0.99 (0.87, 1.12)	0.8209
	3	0.96 (0.84, 1.09)	0.4987
	4	0.91 (0.8, 1.04)	0.1568
	5	1.2 (1.06, 1.35)	0.0029
Immigrant status (ref=CA-born)	>10 y resident	1.13 (0.98, 1.3)	0.0815
	5-10 y resident	1.18 (0.85, 1.65)	0.318
	<5 y resident	1.15 (0.83, 1.59)	0.4045
Histology (ref=endometrioid adenoca)	Serous adenoca	5.5 (4.86, 6.22)	<.0001
	Clear cell	5.3 (4.01, 7)	<.0001
	Mixed type 1/2	2.37 (2.06, 2.72)	<.0001
	Carcinosarcoma	6.79 (5.69, 8.11)	<.0001
	Undifferentiated	12.22 (8.49, 17.61)	<.0001

Stepwise multivariable regression analyses were performed to investigate the association of patient and disease factors found on univariable analysis with advanced stage at presentation. Exploratory analyses are presented in Appendix 3. In light of collinearity and overlap between some of the exposure variables assessed (such as neighborhood income, urban residency, material deprivation and residential instability) an analysis incorporating age, obesity, the modified Charlson-Deyo comorbidity index and a summary marginalization score (modified to exclude dependency) was selected. These factors, as well as disease histology, remained significantly associated with advanced disease at presentation (Table 3). The odds of presenting with advanced disease was found to be 1.1/quintile for patients in increasingly marginalized communities.

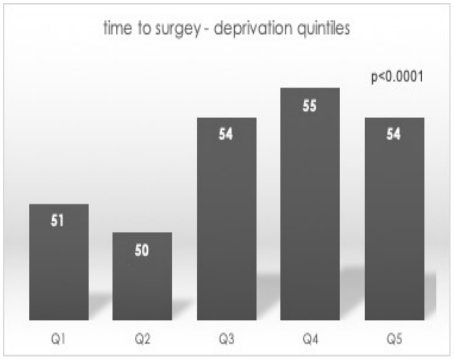
Table 3: Multivariable regression analysis: associations with advanced (II-IV) stage at presentation

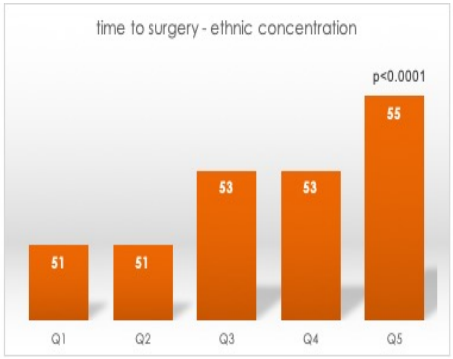
n=13,656		**OR (95% CI)**	**p value**
Age	Age	1.01 (1, 1.01)	0.0004
Charlson Index (ref=0)	1	1.07 (0.87, 1.3)	0.5245
	2	1.09 (0.79, 1.5)	0.6004
	3+	1.3 (0.93, 1.81)	0.1236
	Missing	1.14 (1.03, 1.25)	0.0075
BMI > 40	Yes	0.67 (0.6, 0.75)	<.0001
Modified Marginalization Summary Score	/quintile	1.1 (1.05, 1.14)	<.0001
Histology (ref=endometrioid)	Serous adenoca	5.01 (4.42, 5.68)	<.0001
	Clear cell	4.65 (3.51, 6.15)	<.0001
	Mixed type 1/2	2.29 (1.99, 2.63)	<.0001
	Carcinosarcoma	6.17 (5.16, 7.37)	<.0001
	Undifferentiated	11.33 (7.85, 16.36)	<.0001

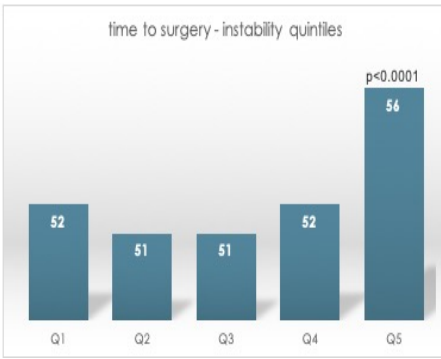
Associations between SDH and treatment

Delay to surgery was quantified as time from endometrial biopsy for diagnosis of cancer, to hysterectomy. Median times from biopsy to surgery by marginalization quintiles are depicted in Figure 2. Patients in the highest marginalization quintiles (most marginalized communities) had longer delays to surgery than patients in the lowest quintiles: median, 54 vs. 51 days for material deprivation, 55 vs. 51 days for ethnic concentration and 56 vs. 52 days for residential instability ($p<0.0001$ for all comparisons).

Figure 2: time to surgery, stratified by marginalization quintile

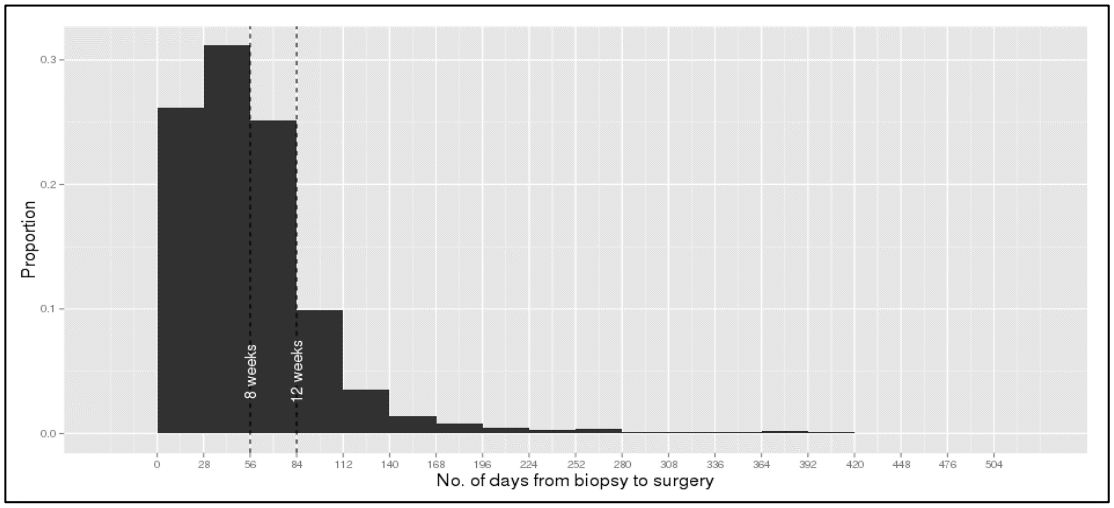






The majority of patients had surgery within 12 weeks of diagnostic biopsy (Figure 3).

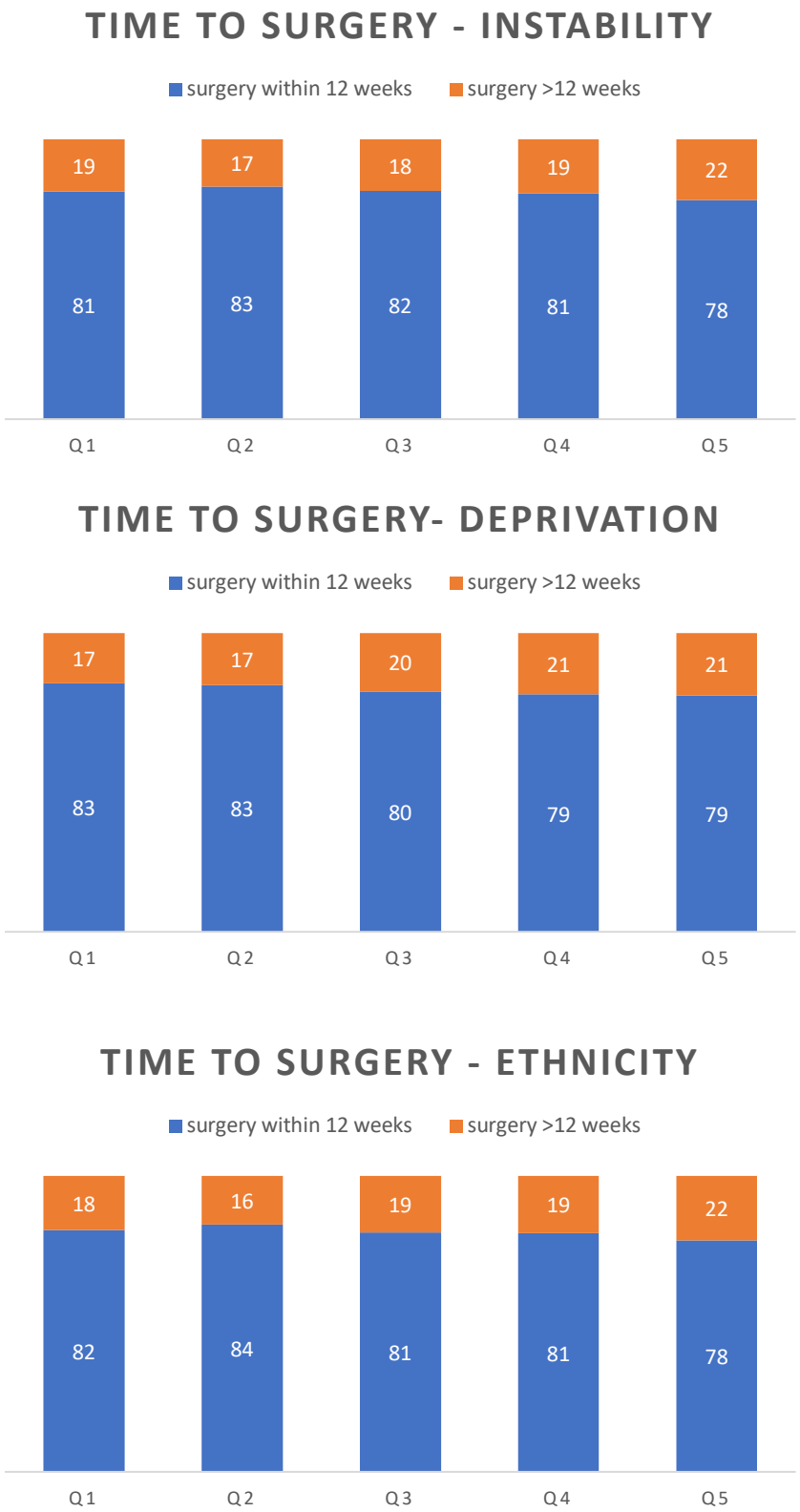
Figure 3: time from biopsy to surgery, among patients who had a hysterectomy



CCO guidelines require that surgery for most malignant neoplasms be completed within 4 weeks of diagnosis to be considered timely (78). Unfortunately, under 30% of the study cohort received surgery within this timeframe. Under 60% of the study cohort received surgery within an eight week window of diagnosis, and a lower proportion of patients in highly marginalized communities had surgery within the 8-week window (56% vs. 59% for material deprivation deprivation, p=0.04; 55% vs. 59% for ethnic concentration, p=0.007; 54% vs. 58% for residential instability, p=0.005).

A previous publication on surgery for uterine cancer in Ontario demonstrated decreased survival for women receiving surgery later than 12 weeks of diagnosis (35). This time window was therefore considered most clinically significant. When dichotomized for surgery within 12 weeks of diagnosis, a lower proportion of patients in highly marginalized communities were observed to receive timely surgery (79% vs. 83% for material deprivation, p<0.001, 78% vs. 82% for ethnic concentration, p=0.002, 78% vs. 81% for residential instability, p=0.01) (Figure 4).

Figure 4: surgery within 12 weeks, stratified by marginalization quintile (shown in %)



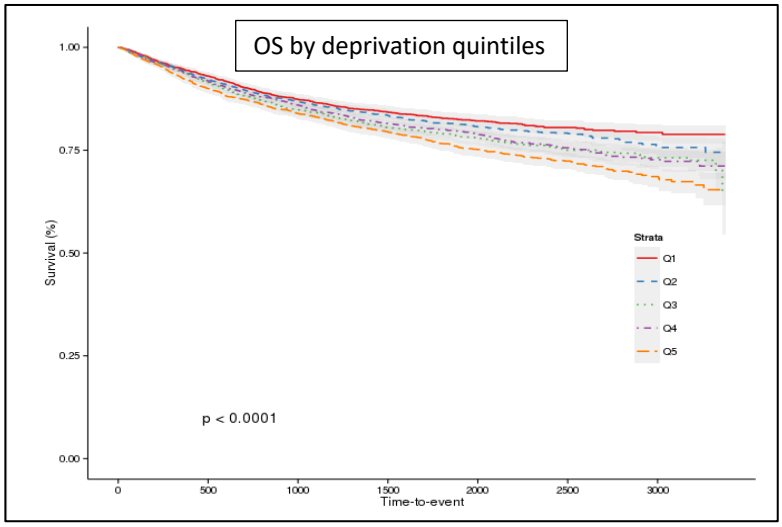
Of patients undergoing surgery for stage I disease, a higher proportion of patients in the most highly marginalized communities for residential instability required adjuvant treatment – 773 (34%) in the highest quintile vs. 480 (29%) in the lowest quintile (p=0.038). A difference in the receipt of adjuvant treatment was not found for patients in high material deprivation and ethnic concentration quintiles.

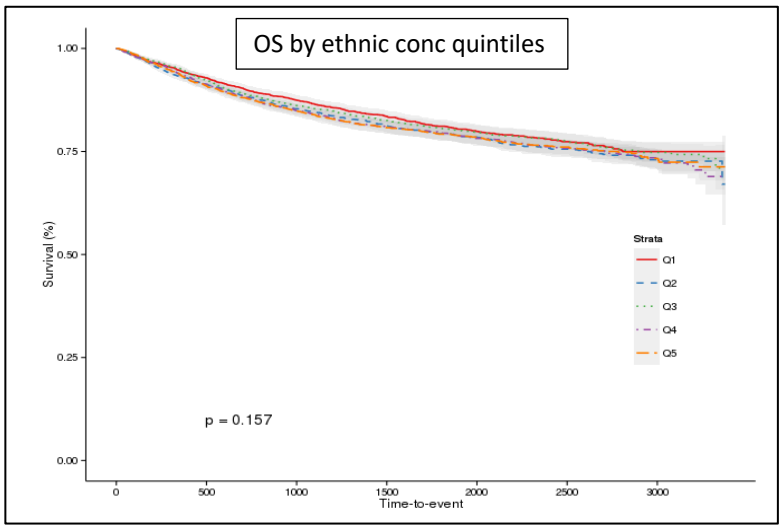
Associations between SDH and overall survival.

Median follow-up time was 43 months (IQR, 21-73). 5-year overall survival was 81% for the entire cohort.

Overall survival was modeled using the Kaplan-Meier method (Figure 5). When comparing patients across marginalization quintiles in the different domains using the log-rank test, significant survival differences were demonstrated between quintiles for the material deprivation and the residential instability domains ($p<0.0001$), though not for the ethnic concentration domain. Since an association was found between marginalization and advanced disease at presentation, and since disease stage is considered one of the important drivers of oncological outcome, a sub-analysis of patients presenting with stage I disease (N=9988) was performed. A significant survival difference between marginalization quintiles in the material deprivation and the residential instability domains held within this subpopulation of early disease, as well ($p<0.0001$).

Figure 5: Overall survival – Kaplan Meier curves by marginalization quintile (total cohort)





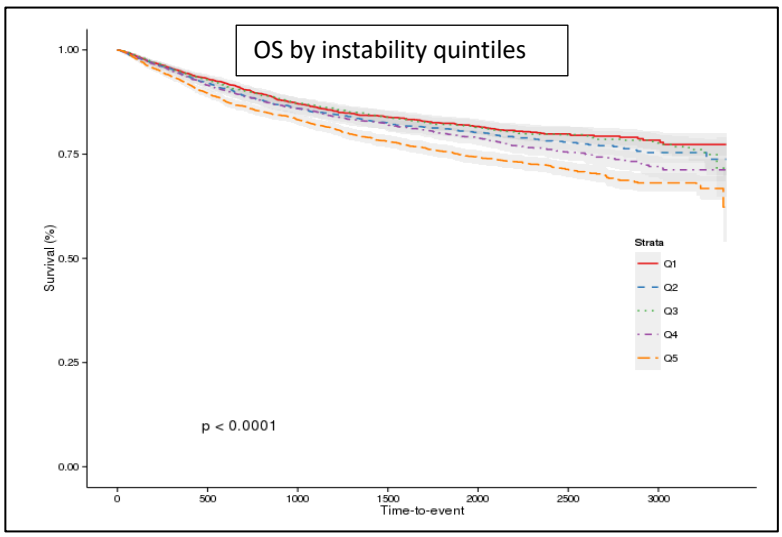
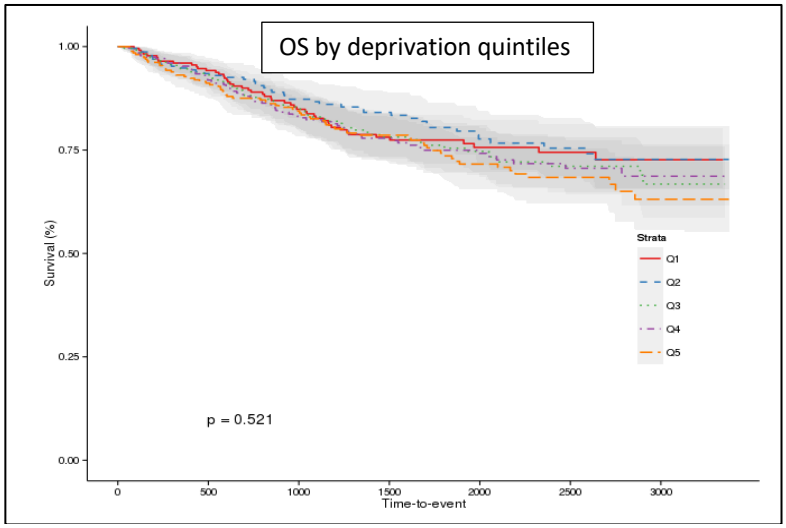
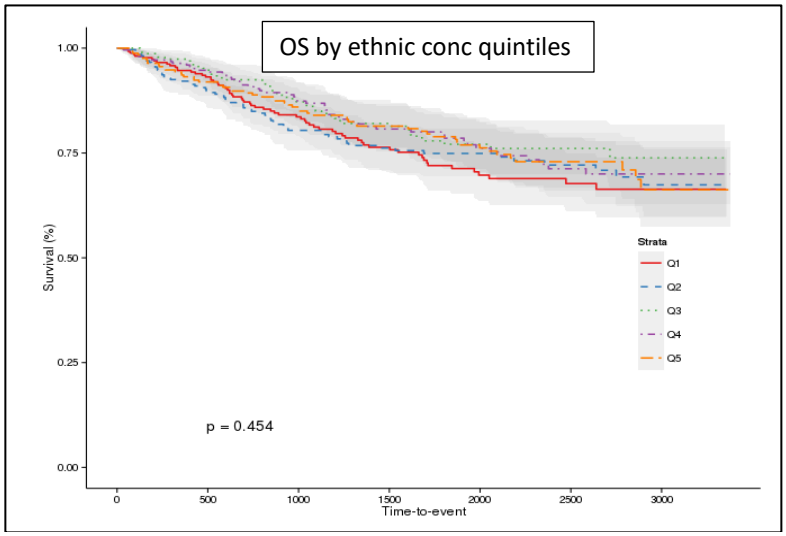
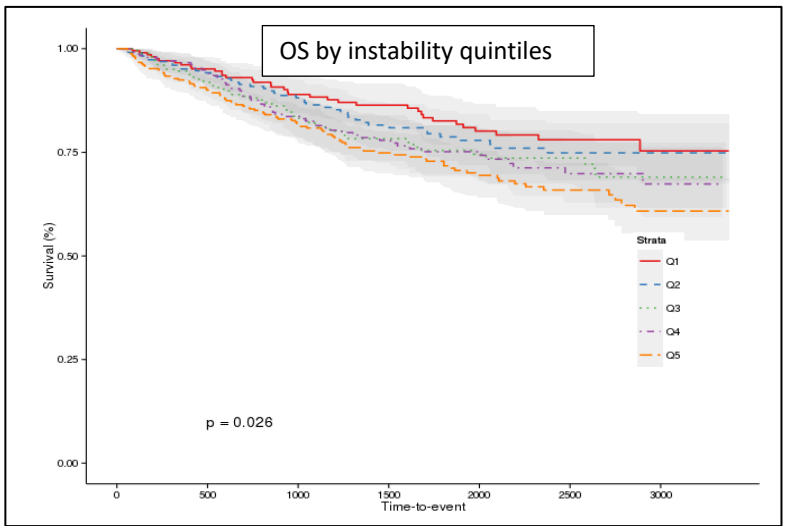


Figure 6: Overall survival – Kaplan Meier curves by marginalization quintile (stage I disease)







Cox proportional modeling was used to quantify associations between patient and disease factors and the risk of death. Results are presented in Table 4. Predictably, advanced disease stage and high risk histological subtypes were found to be associated with increased hazard ratio of death. Advanced patient age and increased Charlson comorbidity score were also associated with increased risk. Morbid obesity (BMI>40) and being an immigrant were both found to be associated with decreased risk of death in this uterine cancer population.

Exposure variables in the SDH realm demonstrated the anticipated associations: decreasing neighborhood income quintile and increasing neighborhood marginalization were shown to be associated with increased hazard ratio of death, trending up with increased marginalization. Hazard ratio for death was 1.4 for patients in the highest material deprivation quintile ($p<0.0001$) and 1.53 for patients in the highest residential instability quintile ($p<0.0001$).

Table 4. Cox univariate regression analysis: associations between covariates and time to death.

		Hazard Ratio	p value
Age		1.066	<.0001
Stage (ref= Stage 1)	2	2.384	<.0001
	3	5.67	<.0001
	4	22.777	<.0001
Neighbourhood Income Quintile (ref=5)	1	1.396	<.0001
	2	1.357	<.0001
	3	1.174	0.003
	4	1.134	0.021
RIO score (ref=large urban)	Small Urban	0.979	0.6026
	Rural	0.895	0.0906
Charlson Index (ref=0)	1	1.577	<.0001
	2	2.395	<.0001
	3+	3.563	<.0001
	Missing	0.914	0.0191

		Hazard Ratio	p value
BMI > 40	Yes	0.456	<.0001
Deprivation Quintile (ref=1 i.e. least marginalized)	2	1.076	0.1893
	3	1.24	<.0001
	4	1.233	0.0001
	5	1.401	<.0001
Ethnic Concentration Quintile (ref=1 i.e. least marginalized)	2	1.075	0.1718
	3	0.969	0.5635
	4	1.036	0.5109
	5	1.081	0.1262
Instability Quintile (ref=1 i.e. least marginalized)	2	1.08	0.1871
	3	1.055	0.3572
	4	1.248	<.0001
	5	1.534	<.0001
Immigrant status (ref=CA-born)	>10 y resident	0.808	0.0009
	5-10 y resident	0.601	0.0031
	<5 y resident	0.576	0.0022
Histology (ref=endometrioid adenoca)	Serous adenoca	5.255	<.0001
	Clear cell	4.3	<.0001
	Mixed type 1/2	2.219	<.0001
	Carcinosarcoma	7.521	<.0001
	Undifferentiated	13.535	<.0001
	Other	4.345	<.0001

Stepwise multivariable regression analyses were performed to investigate the association of patient and disease factors found on univariable analysis with increased risk of death. Exploratory analyses are presented in Appendix 4. In light of collinearity and overlap between some of the exposure variables assessed (such as neighborhood income, urban residency, material deprivation and residential instability), as described for stage distribution analyses, an analysis incorporating age, obesity, the modified Charlson-Deyo comorbidity index and a summary marginalization score (modified to exclude dependency) was selected. These factors,

as well as disease stage and histology, remained significantly associated with an increased hazard ratio of death (Table 5). The hazard ratio of death was found to increase x1.05/quintile (or HR=1.22 for the highest marginalization quintile compared to the lowest) (p<0.001).

Table 5. Cox multivariable regression analysis: associations between covariates and time to death.

		Hazard Ratio (CI)	p value
Year of Diagnosis	/ year	0.96 (0.94, 0.97)	<0.001
Age Groups	/ age group	1.34 (1.31, 1.36)	<0.001
Charlson Score	0	0.87 (0.80, 0.95)	<0.001
	1-2	0.96 (0.88, 1.04)	
	3-4	1.34 (1.17, 1.53)	
	5+	2.16 (1.81, 2.58)	
	No Admission‡	Reference	
Prior Cancer	Yes vs No	1.30 (1.15, 1.47)	<0.001
BMI	>40 vs ≤40	0.93 (0.84, 1.03)	0.17
Histology (ref=endometrioid)	Serous Adeno	2.41 (2.20, 2.65)	<0.001
	Clear Cell	2.06 (1.69, 2.51)	
	Mixed Type ½	1.77 (1.58, 1.99)	
	Carcinosarcoma	3.59 (3.22, 4.01)	
	Undifferentiated	7.11 (6.11, 8.26)	
	Other/Missing	3.07 (2.72, 3.46)	
Stage (ref=stage 1)	2	1.88 (1.65, 2.14)	<0.001
	3	3.54 (3.21, 3.92)	
	4	10.23 (9.19, 11.39)	
	Unknown	2.28 (2.09, 2.49)	
Modified Marginalization Score	/ quintile	1.05 (1.03, 1.08)	<0.001

Endometrioid endometrial cancers

Since disease histology is an important driver of presentation and outcome, exploratory analyses were also undertaken of a sub-cohort of endometrial cancer patients with endometrioid

histology. 14,188 women diagnosed with endometrioid endometrial cancers between 2009-2017 were identified.

In this subgroup again, patients in the highest marginalization quintiles had increased odds of being diagnosed with advanced disease at presentation (stages II-IV) than patients in the lowest quintiles: OR=1.26 for deprivation (CI, 1.07-1.48, p=0.0045); OR=1.19 for ethnic concentration (CI, 1.01-1.39, p=0.035); OR=1.31 for instability (CI, 1.12-1.54, p=0.0007). In a multivariable regression analysis of endometrioid cancer cases including age, obesity, and the Charlson comorbidity index, a summary marginalization score remained significantly associated with advanced disease at presentation (Table E1).

Table E1: Multivariable logistic regression analysis of associations between covariates and advanced stage at presentation (stages II-IV vs. I), endometrioid cohort (n=9997)

		OR (95% CI)	p value
Age	Age at index date	1 (1, 1.01)	0.0903
Charlson Index (ref=0)	1	1.18 (0.92, 1.52)	0.1819
	2	1.32 (0.89, 1.97)	0.1696
	3+	1.39 (0.91, 2.14)	0.1273
	Missing	1.21 (1.08, 1.37)	0.0016
BMI > 40	Yes	0.68 (0.59, 0.77)	<.0001
Modified Marginalization Summary Score	/quintile	1.12 (1.06, 1.18)	<.0001

Cox modeling of overall survival among this subgroup demonstrated an increased hazard ratio of death in patients across marginalization quintiles in the material deprivation and residential instability domains (but not in the ethnic concentration domain), with the risk of death increasing with marginalization (Table E2). Hazard ratio for death was 1.62 for the highest deprivation quintile ($p<0.0001$) and 1.88 for the highest instability quintile ($p<0.0001$).

Table E2. Associations between covariates and time to death, endometrioid cohort (n=14188).

		Hazard Ratio	p value
Age		1.075	<.0001
Cancer stage (ref= Stage 1)	2	1.827	<.0001
	3	4.48	<.0001
	4	21.609	<.0001
Neighbourhood Income Quintile (ref=5)	1	1.574	<.0001
	2	1.448	<.0001
	3	1.299	0.002
	4	1.187	0.0466
RIO score (ref=large urban)	Small Urban	1.032	0.6082
	Rural	0.956	0.6489
Charlson Index (ref=0)	1	1.692	<.0001
	2	3.342	<.0001
	3+	4.804	<.0001
	Missing	0.87	0.0194
BMI > 40	Yes	0.613	<.0001
Deprivation Quintile (ref=1 i.e. least marginalized)	2	1.22	0.0233
	3	1.307	0.0021
	4	1.315	0.0015
	5	1.624	<.0001
Ethnic Concentration Quintile (ref=1 i.e. least marginalized)	2	0.934	0.3824
	3	0.883	0.1205
	4	0.926	0.3334
	5	0.826	0.0159
Instability Quintile (ref=1 i.e. least marginalized)	2	1.233	0.0264
	3	1.187	0.0669
	4	1.519	<.0001
	5	1.881	<.0001
Immigrant status (ref=CA-born)	>10 y resident	0.636	<.0001
	5-10 y resident	0.427	0.0073
	<5 y resident	0.432	0.0082

Discussion

The association of social determinants of health (SDH) such as education, income, employment, housing, and ethnicity with a spectrum of health outcomes is well documented (9,19). Cancer presentation and outcomes, in particular, have been shown to be associated with social determinants of health in a variety of settings and across multiple disease sites (14–17,20,21,30,38,56,58,59,62–70,79–82).

A large proportion of the data on health inequities originates in the United States, where a financially complex healthcare system presents unique challenges. Nevertheless, despite its universal healthcare system, Canada is not immune to health disparities (83). Although some comparative research suggests that Canadian cancer patients living in under-privileged communities are less disadvantaged than comparable patients in the American system (84), Canadian population-based research demonstrates inequities in cancer outcomes across several disease sites (59,63,68,69).

Disparities in cancer incidence rates (13,57,79,85) in marginalized populations have been linked to adverse health behaviors (18), such as smoking, diet, substance misuse and unprotected intercourse. Gaps in cancer screening (13,22,23,86–88) in these populations have been used to explain higher rates of advanced stage diagnoses (13,15,20,21,26,30,32,66). However, the impact of social marginalization on cancer outcomes is likely more complex and pervasive. Since uterine cancer is not associated with typical behavioral risk factors, and since no screening program is in place for early detection, assessing uterine cancer outcomes in Ontario's universal healthcare system through the SDH lens presents an opportunity to neutralize some common confounders.

Social determinants of health constitute a complex interplay of social, cultural and financial factors that combine to influence the entire trajectory of health and healthcare (89). In the cancer care pathway, these factors impact risk and prevention, screening and early detection, diagnosis, treatment, outcomes and survivorship (13). Delay in presentation to care and in diagnosis may be driven by availability of services in the community and access issues (38,51), but also by patient-centric factors in healthcare utilization, including as gaps in health literacy and early symptom recognition (30,38–42), communication barriers (24,25,43–45), lack of confidence and trust in healthcare providers and institutions (46–48), competing priorities (38) in patients struggling with basic income and housing issues, or poor self-advocacy (49). These delays are difficult to assess at the population level, but they may translate into advanced disease stage at presentation for treatment. Indeed, our data demonstrates a disparity in stage distribution among uterine cancer patients in Ontario, with higher rates of advanced disease diagnosed in more marginalized patients (Figure 1, Tables 2 and 3). Moreover, even within stage I patients who constituted the majority of the patient population, we found that marginalized patients with a higher instability score more frequently required adjuvant treatment (773 (34%) vs. 480 (29%), highest vs. lowest quintile (p=0.038)), which may also be a surrogate marker of delayed presentation for treatment. Although disease histology was certainly the strongest driver of disease stage, marginalization score was independently associated with the odds of presenting with advanced disease on multivariate analysis, as well as on a sub-analysis of a more homogeneous group of endometrioid uterine cancers (Table E1). Interestingly, obesity was a protective factor associated with decreased odds of advanced disease. This in itself is not surprising, since obesity is a risk factor for estrogen-dependent tumors (27,28,90,91) which are primarily well differentiated and carry a better prognosis. However, as obesity has consistently

been linked to social marginalization (92), their association could actually mitigate the impact of SDH on stage distribution in this disease.

Once a diagnosis of endometrial cancer is made, the patient's trajectory through the healthcare system is easier to quantify. Delay in surgical treatment was represented in this study by the time from endometrial biopsy to surgery, and was found to be significantly longer for marginalized patients on all three scores (Figures 2,4). This finding is consistent with a previous publication reporting consistent associations between socioeconomic marginalization and surgical delay across a spectrum of malignancies (53). Categorization of surgical delay within an 8-week and within a 12-week window also showed significantly lower rates of timely surgery for marginalized patients across categories. A previous Ontario population-based study demonstrated that a delay in treatment of uterine cancer beyond 12 weeks adversely impacts overall survival (35), and a US National Cancer Database study found adverse survival in women receiving surgery more than 6 weeks from diagnosis (36), highlighting the significance of this finding.

Treatment delays and/or suboptimal management of marginalized cancer patients have been documented in other settings and disease sites; this includes both surgical treatment (14,17,31,36,38,53,54,64,84,93,94) and non-surgical anti-neoplastic treatment (95–99). Adjuvant treatment delays and variations were not analyzed in this study, and would be difficult to assess with administrative data given the variability in treatment plans and schedules depending on disease features and provider preferences. Certainly, marginalized patients may find adherence to treatment and surveillance challenging as these entail multiple cancer center visits, transportation costs and missed work days. An analysis of health-related quality of life (HRQOL) in ovarian cancer patients in a large randomized clinical trial demonstrated that insurance status, as a

surrogate of deprivation, correlated with HRQOL on multiple indices (100). The "financial toxicity" of cancer diagnosis and treatment has been linked with several important outcomes, including symptom burden and HRQOL as well as compliance with treatment (100–104). One US national random-sample survey found that 62% of bankruptcies filed in 2007 were medical (105); and financial insolvency has even been shown to be linked to early cancer mortality (60).

Finally, the association of social determinants of health with survival outcomes was assessed. Unlike American epidemiological data (13,61,64,80,89,106,107), we did not find an association between ethnic marginalization and overall survival despite a skewed disease stage distribution at diagnosis. The ethnic concentration index reflects the concentration of ethnic minorities and immigrants in the community. We postulate that the healthy immigrant effect may partially counterbalance the effects of social, cultural and financial marginalization often associated with ethnic concentration (108). In support of this, recent immigration to Canada (within 5 or 10 years) was, in fact, found to be associated with improved overall survival (Table 4).

Overall survival was found to be negatively associated with increased marginalization, as reflected in the material deprivation and residential instability scores. This is consistent with previous findings on associations between uterine cancer outcomes and marginalization (32,57,67). It is likely that this association is compounded by other factors associated with SDH, including adverse health behaviors, stress, and chronic diseases and their sequelae. In fact, previous studies have shown that the presence of comorbid conditions adversely affects survival in endometrial cancer patients (109); a large SEER study that included over 33,00 patients with endometrial cancer demonstrated that the leading causes of death in this population were actually cardiovascular disease and other non-malignant etiologies (110). Since competing causes of

death may confound the interpretation of overall survival data in this disease site, analysis of recurrence rates and disease-specific survival could have ideally facilitated a cleaner assessment of the impact of SDH on disease outcomes. However, recurrences are not collected on the Ontario Cancer Registry and secondary causes of death are not dependendably documented in death certificates, making cancer-specific mortality capture from administrative databases inherently inaccurate. Despite this limitation, a multivariable regression analysis that included the Charlson-Deyo index does support the independent contribution of marginalization to adverse overall survival outcomes.

Strengths and Limitations

This is a robust population-based study, that includes a large sample of patients and with access to a broad spectrum of information on socio-demographic, clinical and pathological information through administrative databases that have been previously validated. The focus on uterine cancer in Ontario's universally accessible healthcare system facilitates an unbiased assessment of the association between social determinants of health and disease trajectory. Finally, the quality of the Ontario Cancer Registry (71,72), the ability to link detailed patient data through the Institute of Clinical and Evaluative Sciences (ICES) (73) and the development of validated Canadian measures of marginalization (19) provide a unique opportunity to evaluate associations between complex social, educational, financial and cultural barriers and cancer presentation and outcomes.

However, there are limitations to this study design which should be acknowledged. Many exposure variables, including marginalization indices, are based on neighborhood or community characteristics, which may create misclassification bias when assessing an individual patient; however in this situation the bias would tend to the null hypothesis, strengthening the validity of

our findings. Certain information was missing in a large proportion of patients, creating a potential information bias. Charlson-Deyo scores, for example, are calculated based on a history of admissions. Although the assumption is generally that a missing Charlson score indicates a low morbidity profile, patients may avoid admissions for a variety of reasons. 12,516 patients (64% of our patient population) had no admissions in the year preceding surgery; it is reassuring however that missing Charlson scores were evenly distributed among marginalization quintiles (see Appendix 1). In 5874 women (30%), stage information was missing. This was particularly high in 2014-2018, when budget cuts forced Cancer Care Ontario (CCO) to narrow its stage collection focus to breast, colon, lung and cervical cancers. Missing stage information was evenly distributed between marginalization quintiles (see Appendix 1); moreover, in a sensitivity analysis including years when stage information was more complete, the association between increased marginalization and advanced disease stage at presentation persisted. These findings mitigate the risk that cases missing stage information may have biased our findings. Finally, multiple confounders were considered and controlled for in multivariable analyses. These include age, which is associated with both marginalization and disease prognosis and may also influence referral decisions and the extent and duration of medical investigations prior to surgery; medical comorbidities, which are associated with social determinants of health and may impact overall survival; obesity, which is associated with SDH and found to be protective in our analysis, possibly diluting the associations between marginalization and disease outcomes; and disease histology, which may be associated with age and ethnicity and is a strong driver of presentation and outcome.

Impact and significance

National and international organizations, including the WHO (111) and the American Cancer Society (10) place increasing emphasis on the inclusion of health equity objectives into national cancer control programs and policies. In fact, Ontario's Cancer Plan IV (2015-2019) (11) incorporates health equity as a goal to "ensure health equity for all Ontarians across the cancer care system". This is becoming increasingly important as social disparities in Canada widen.

Elucidating some of the mediators of social health disparities in Ontario could focus public health interventions and healthcare system modifications to promote health equity in cancer care. Opportunities to reduce disparities in cancer outcomes exist across the entire disease trajectory, from prevention through early detection, access to care and healthcare utilization, treatment and survivorship. Some examples include:

1. Addressing modifiable risk factors for uterine cancer, such as obesity.
2. Community health support projects (40,48,112,113) targeting marginalized communities and emphasizing education and recognition of early cancer symptoms, as well as programs and online tools (114) for pro-active health screening.
3. Continuing education projects for primary healthcare practitioners and community gynecologists, to heighten awareness of symptoms, to highlight the need for proactive history taking and to reinforce active follow up on cancer investigations and consultation referrals in at-risk patients.
4. Evaluation and improvement of workflow patterns from patient referral to completion of treatment, both at the institutional and at the provincial level.
5. Development and implementation of screening tools (115,116) for social determinants of health at regional cancer centers to inform distribution of resources, institution of patient navigation (48,117) tools and referral to socio-oncology resources.

In conclusion, this study supports an association of social determinants of health with uterine cancer presentation, treatment and outcomes in Ontario and highlights an important aspect of health disparity. Our findings are thought provoking and disturbing, but leave some gaps in framing the health equity problem. Further analyses should be geared towards identifying targetable events in the cancer care trajectory that are impacted by SDH, as well as assessing the efficacy of interventions and modifications at the community- and institution-level in moving toward a more health-equitable society.

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APPENDIX 1: study population categorized by marginalization quintile

		Q1	Q2	Q3	Q4	Q5
	N	3937	4413	4435	3776	3667
Demographic Information						
Age Groups	18-39	64 (1.6)	76 (1.7)	82 (1.9)	84 (2.2)	72 (2.0)
	40-44	91 (2.3)	121 (2.7)	81 (1.8)	88 (2.3)	78 (2.1)
	45-49	217 (5.5)	198 (4.5)	196 (4.4)	155 (4.1)	158 (4.3)
	50-54	513 (13.0)	527 (11.9)	472 (10.6)	370 (9.8)	352 (9.6)
	54-59	767 (19.5)	718 (16.3)	703 (15.9)	604 (16.0)	517 (14.1)
	60-64	757 (19.2)	841 (19.1)	839 (18.9)	673 (17.8)	599 (16.3)
	65-69	626 (15.9)	771 (17.5)	787 (17.8)	627 (16.6)	617 (16.8)
	70-74	447 (11.4)	519 (11.8)	501 (11.3)	437 (11.6)	440 (12.0)
	75-79	236 (6.0)	337 (7.6)	369 (8.3)	327 (8.7)	342 (9.3)
	80+	220 (5.6)	305 (6.9)	405 (9.1)	411 (10.9)	492 (13.4)
Year of Diagnosis	2009	300 (7.6)	352 (8.0)	425 (9.6)	344 (9.1)	327 (8.9)
	2010	365 (9.3)	414 (9.4)	488 (11.0)	358 (9.5)	390 (10.6)
	2011	387 (9.8)	452 (10.2)	470 (10.6)	409 (10.8)	414 (11.3)
	2012	395 (10.0)	513 (11.6)	514 (11.6)	412 (10.9)	441 (12.0)
	2013	406 (10.3)	466 (10.6)	517 (11.7)	427 (11.3)	392 (10.7)
	2014	491 (12.5)	538 (12.2)	494 (11.1)	372 (9.9)	383 (10.4)
	2015	536 (13.6)	526 (11.9)	472 (10.6)	482 (12.8)	422 (11.5)
	2016	521 (13.2)	591 (13.4)	519 (11.7)	497 (13.2)	455 (12.4)
	2017	536 (13.6)	561 (12.7)	536 (12.1)	475 (12.6)	443 (12.1)
Charlson Score	0	1013 (25.7)	1044 (23.7)	1024 (23.1)	866 (22.9)	803 (21.9)
	1-2	861 (21.9)	983 (22.3)	1046 (23.6)	899 (23.8)	903 (24.6)
	3-4	128 (3.3)	185 (4.2)	208 (4.7)	195 (5.2)	202 (5.5)
	5+	37 (0.9)	45 (1.0)	51 (1.2)	48 (1.3)	52 (1.4)
	No Admission‡	1898 (48.2)	2156 (48.9)	2106 (47.5)	1768 (46.8)	1707 (46.6)
Social Determinants of Health Information						
Income Quintile	1	33 (0.8)	125 (2.8)	430 (9.7)	1082 (28.7)	2113 (57.7)
	2	171 (4.3)	549 (12.5)	1186 (26.8)	1321 (35.0)	975 (26.6)
	3	554 (14.1)	1142 (25.9)	1267 (28.6)	768 (20.4)	318 (8.6)
	4	1292 (32.8)	1297 (29.4)	895 (20.2)	362 (9.6)	165 (4.5)
	5	1887 (47.9)	1297 (29.4)	654 (14.8)	240 (6.4)	90 (2.5)
Rural	N (%) Yes	590 (15.0)	669 (15.2)	701 (15.8)	417 (11.0)	91 (2.5)
Distance to Nearest RCC	Median (IQR)	16.1 (8.5, 32.2)	13.1 (6.0, 41.8)	10.9 (5.0, 49.4)	7.9 (4.3, 42.6)	6.5 (3.9, 12.1)
RIO Score	0	985 (25.0)	1396 (31.6)	1734 (39.1)	1982 (52.5)	2421 (66.0)
	1-39	2641 (67.1)	2516 (57.0)	2132 (48.1)	1427 (37.8)	1162 (31.7)
	40-79	268 (6.8)	449 (10.2)	502 (11.3)	315 (8.3)	77 (2.1)
	80+	28 (0.7)	27 (0.6)	37 (0.8)	NR	NR
	Unknown	15 (0.4)	25 (0.6)	30 (0.7)	NR	NR
Dependency Quintile	1	1241 (31.5)	983 (22.3)	497 (11.2)	560 (14.8)	306 (8.3)
	2	1185 (30.1)	771 (17.5)	763 (17.2)	467 (12.4)	432 (11.8)
	3	1043 (26.5)	776 (17.6)	764 (17.2)	640 (17.0)	525 (14.3)
	4	417 (10.6)	1163 (26.4)	941 (21.2)	794 (21.0)	675 (18.4)
	5	51 (1.3)	720 (16.3)	1470 (33.2)	1315 (34.8)	1729 (47.2)
Deprivation Quintile	1	2122 (53.9)	1188 (26.9)	555 (12.5)	NR	NR
	2	1341 (34.1)	1370 (31.0)	998 (22.5)	NR	NR
	3	409 (10.4)	1254 (28.4)	1297 (29.2)	876 (23.2)	262 (7.1)
	4	58 (1.5)	525 (11.9)	1168 (26.3)	1343 (35.6)	970 (26.5)
	5	7 (0.2)	76 (1.7)	417 (9.4)	1180 (31.3)	2347 (64.0)

Ethnicity Quintile	1	910 (23.1)	1073 (24.3)	1076 (24.3)	678 (18.0)	176 (4.8)
	2	939 (23.9)	984 (22.3)	1028 (23.2)	617 (16.3)	383 (10.4)
	3	1061 (27.0)	885 (20.1)	839 (18.9)	589 (15.6)	511 (13.9)
	4	823 (20.9)	668 (15.1)	780 (17.6)	770 (20.4)	879 (24.0)
	5	204 (5.2)	803 (18.2)	712 (16.1)	1122 (29.7)	1718 (46.9)
Instability Quintile	1	1903 (48.3)	989 (22.4)	538 (12.1)	187 (5.0)	9 (0.3)
	2	1487 (37.8)	1294 (29.3)	577 (13.0)	307 (8.1)	76 (2.1)
	3	474 (12.0)	1412 (32.0)	1266 (28.6)	600 (15.9)	200 (5.5)
	4	67 (1.7)	566 (12.8)	1414 (31.9)	1382 (36.6)	602 (16.4)
	5	6 (0.2)	152 (3.4)	640 (14.4)	1300 (34.4)	2780 (75.8)
Cancer Information						
Histology	Endometrioid	2992 (76.0)	3276 (74.2)	3205 (72.3)	2749 (72.8)	2577 (70.3)
Best Stage	1	2102 (53.4)	2324 (53.7)	2379 (53.6)	1872 (49.6)	1831 (49.9)
	2	246 (6.3)	281 (6.4)	302 (6.8)	229 (6.1)	255 (7.0)
	3	284 (7.2)	341 (7.7)	335 (7.6)	333 (8.8)	345 (9.4)
	4	151 (3.8)	174 (3.9)	187 (4.2)	162 (4.3)	185 (5.0)
	Unknown	1154 (29.3)	1293 (29.3)	1232 (27.8)	1180 (31.3)	1051 (28.7)
Prior Cancer Within 5 Years of Diagnosis	N (%) Yes	206 (5.2)	222 (5.0)	202 (4.6)	183 (4.9)	175 (4.8)
Multiple Cancers on Day of Diagnosis	N (%) Yes	19 (0.5)	21 (0.5)	22 (0.5)	13 (0.3)	18 (0.5)
Surgical Information						
Days, Diagnosis to Surgery	No Surgery	277 (7.0)	334 (7.6)	385 (8.7)	387 (10.3)	388 (10.6)
	Same Day	719 (18.3)	768 (17.4)	762 (17.2)	586 (15.5)	560 (15.3)
	≤180 Days	2840 (72.1)	3194 (72.4)	3159 (71.2)	2690 (71.2)	2589 (70.6)
	>180 Days	76 (1.9)	89 (2.0)	104 (2.3)	90 (2.4)	102 (2.8)
Minimally Invasive Surgeries	N (%) Yes	1374 (37.5)	1565 (38.4)	1408 (34.8)	1308 (38.6)	1204 (36.7)
Surgeon Type	Gyn Oncologist	1502 (41.0)	1668 (40.9)	1633 (40.3)	1354 (40.0)	1358 (41.4)
	General Gynecologist	1908 (52.1)	2088 (51.2)	2111 (52.1)	1778 (52.5)	1626 (49.6)
	Other	141 (3.9)	171 (4.2)	157 (3.9)	119 (3.5)	124 (3.8)
	Unknown	109 (3.0)	152 (3.7)	149 (3.7)	138 (4.1)	171 (5.2)
Hospital Type for Surgery	Community	1868 (51.0)	2119 (52.0)	2065 (51.0)	1770 (52.2)	1564 (47.7)
	Small	NR	39 (1.0)	19 (0.5)	19 (0.6)	NR
	Teaching	1458 (39.8)	1554 (38.1)	1591 (39.3)	1296 (38.2)	1369 (41.8)
	Other	NR	52 (1.3)	59 (1.5)	48 (1.4)	NR
	Unknown	261 (7.1)	315 (7.7)	316 (7.8)	256 (7.6)	292 (8.9)

APPENDIX 2: Stage distribution and association with marginalization quintile : two dichotomization models.

Chi-sq for Early (stage I) vs Advanced (Stage II-IV)						p value
Dependency						0.1616
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1	1680 (74%)	1719 (72%)	1917 (74%)	1928 (72%)	2698 (73%)	
2 or 3 or 4	593 (26%)	653 (28%)	660 (26%)	765 (28%)	987 (27%)	
Deprivation						<0.001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1	1977 (75%)	2037 (75%)	1968 (73%)	2014 (72%)	1946 (70%)	
2 or 3 or 4	649 (25%)	683 (25%)	724 (27%)	783 (28%)	819 (30%)	
Ethnic Concentration						<0.001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1	2073 (75%)	2053 (74%)	1948 (74%)	1898 (72%)	1970 (70%)	
2 or 3 or 4	675 (25%)	734 (26%)	695 (26%)	723 (28%)	831 (30%)	
Instability						<0.0001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1	1686 (73%)	1871 (74%)	2001 (74%)	2045 (75%)	2339 (70%)	
2 or 3 or 4	610 (27%)	667 (26%)	693 (26%)	675 (25%)	1013 (30%)	

Chi-sq for Early (stage I-II) vs Advanced (Stage III-IV)						p value
Dependency						0.1242
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1 or 2	1884 (83%)	1936 (82%)	2132 (83%)	2181 (81%)	3069 (83%)	
3 or 4	389 (17%)	436 (18%)	445 (17%)	512 (19%)	616 (17%)	
Deprivation						<0.001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1 or 2	2203 (84%)	2269 (83%)	2232 (83%)	2290 (82%)	2208 (80%)	
3 or 4	423 (16%)	451 (17%)	460 (17%)	507 (18%)	557 (20%)	
Ethnic Concentration						<0.0001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1 or 2	2336 (85%)	2320 (83%)	2179 (82%)	2147 (82%)	2220 (79%)	
3 or 4	412 (15%)	467 (17%)	464 (18%)	474 (18%)	581 (21%)	
Instability						<0.0001
Stage	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
1 or 2	1892 (82%)	2096 (83%)	2261 (84%)	2282 (84%)	2671 (80%)	
3 or 4	404 (18%)	442 (17%)	433 (16%)	438 (16%)	681 (20%)	

APPENDIX 3: Exploratory multivariable regression analyses of associations with advanced disease at presentation.

Parameter	Level	OR (95% CI)	StdErr	Wald ChiSq	ProbChiSq
Intercept			0.1736	159.61	<.0001
Age	Age	1.01 (1, 1.01)	0.00202	12.35	0.0004
Neighbourhood Income Quintile (ref=5)	1	1.14 (0.94, 1.38)	0.0965	1.8084	0.1787
	2	1.21 (1.03, 1.42)	0.0808	5.6357	0.0176
	3	0.96 (0.83, 1.12)	0.0746	0.2454	0.6203
	4	1.11 (0.97, 1.27)	0.0681	2.4402	0.1183
RIO score (ref=large urban)	Small Urban	1.07 (0.95, 1.2)	0.0615	1.1462	0.2843
	Rural	0.93 (0.76, 1.12)	0.0977	0.616	0.4325
Charlson Index (ref=0)	1	1.08 (0.88, 1.32)	0.1024	0.5277	0.4676
	2	1.08 (0.78, 1.49)	0.1639	0.2161	0.642
	3+	1.33 (0.95, 1.85)	0.1695	2.8012	0.0942
	Missing	1.15 (1.04, 1.26)	0.0482	8.0595	0.0045
BMI > 40	Yes	0.67 (0.6, 0.75)	0.0577	48.9012	<.0001
Dependency Quintile (ref=1 i.e. least marginalized)	2	1.07 (0.93, 1.23)	0.072	0.9116	0.3397
	3	1 (0.86, 1.15)	0.073	0.0039	0.9503
	4	1.09 (0.94, 1.26)	0.0736	1.2862	0.2567
	5	1 (0.87, 1.16)	0.0737	0.0003	0.9858
Deprivation Quintile (ref=1 i.e. least marginalized)	2	1.02 (0.89, 1.17)	0.0701	0.0806	0.7765
	3	1.07 (0.92, 1.24)	0.0756	0.8106	0.368
	4	1.12 (0.95, 1.32)	0.0833	1.9671	0.1608
	5	1.18 (0.97, 1.43)	0.0975	2.8298	0.0925
Ethnic Concentration Quintile (ref=1 i.e. least marginalized)	2	1.1 (0.96, 1.26)	0.0698	1.8867	0.1696
	3	1.1 (0.95, 1.29)	0.0782	1.5805	0.2087
	4	1.07 (0.9, 1.26)	0.0837	0.575	0.4483
	5	1.02 (0.85, 1.21)	0.09	0.0361	0.8494
Instability Quintile (ref=1 i.e. least marginalized)	2	1 (0.87, 1.15)	0.0722	0.002	0.9643
	3	0.98 (0.85, 1.14)	0.0736	0.0467	0.8289
	4	0.88 (0.76, 1.02)	0.0755	2.7426	0.0977
	5	1.08 (0.93, 1.25)	0.0759	1.05	0.3055
Immigrant status (ref=CA-born)	>10 y resident	1.08 (0.93, 1.27)	0.0797	1.0125	0.3143
	5-10 y resident	1.2 (0.84, 1.72)	0.1828	1.0102	0.3148
	<5 y resident	1.14 (0.8, 1.63)	0.1811	0.5542	0.4566
Histology group (ref=endometrioid adenoca)	Undifferentiated	11.26 (7.79, 16.28)	0.188	165.9004	<.0001
	Other	3.42 (2.83, 4.14)	0.0975	159.1065	<.0001
	Clear cell	4.59 (3.46, 6.1)	0.1446	111.1517	<.0001
	Mixed type 1/2	2.29 (1.99, 2.63)	0.0713	134.3457	<.0001
	Serous adenoca	5.03 (4.43, 5.71)	0.0647	622.4792	<.0001
	Carcinosarcoma	6.22 (5.19, 7.44)	0.0917	397.3712	<.0001

Income quintile, RIO, immigration status removed

Parameter	Level	OR (95% CI)	StdErr	Wald ChiSq	ProbChiSq
Intercept			0.1615	168.10	<.0001
Age	Age	1.01 (1, 1.01)	0.00199	10.83	0.0010
Charlson Index (ref=0)	1	1.07 (0.87, 1.3)	0.102	0.4094	0.5223
	2	1.07 (0.77, 1.47)	0.1639	0.1488	0.6997
	3+	1.31 (0.94, 1.83)	0.169	2.5697	0.1089
	Missing	1.14 (1.04, 1.25)	0.048	7.437	0.0064
BMI > 40	Yes	0.67 (0.6, 0.75)	0.0572	49.6197	<.0001
Dependency Quintile (ref=1 i.e. least marginalized)	2	1.07 (0.93, 1.23)	0.0718	0.8521	0.3559
	3	1 (0.86, 1.15)	0.0727	0.0021	0.9633
	4	1.08 (0.94, 1.25)	0.0733	1.1586	0.2818
	5	0.99 (0.86, 1.14)	0.0733	0.0132	0.9086
Deprivation Quintile (ref=1 i.e. least marginalized)	2	1.04 (0.91, 1.19)	0.0681	0.3174	0.5732
	3	1.1 (0.96, 1.26)	0.0693	1.9797	0.1594
	4	1.2 (1.04, 1.38)	0.0716	6.2855	0.0122
	5	1.29 (1.11, 1.5)	0.0777	10.8079	0.001
Ethnic Concentration Quintile (ref=1 i.e. least marginalized)	2	1.1 (0.96, 1.25)	0.0668	1.9786	0.1595
	3	1.08 (0.95, 1.24)	0.0695	1.3288	0.249
	4	1.05 (0.92, 1.2)	0.0698	0.4995	0.4797
	5	1.02 (0.88, 1.17)	0.0738	0.0493	0.8243
Instability Quintile (ref=1 i.e. least marginalized)	2	1 (0.87, 1.15)	0.0717	0.0007	0.9787
	3	0.98 (0.85, 1.13)	0.0727	0.0637	0.8007
	4	0.9 (0.78, 1.04)	0.0739	1.9288	0.1649
	5	1.11 (0.96, 1.28)	0.0726	1.9836	0.159
Histology group (ref=endometrioid adenoca)	Undifferentiated	11.38 (7.88, 16.44)	0.1876	168.0467	<.0001
	Other	3.41 (2.82, 4.13)	0.0971	159.9405	<.0001
	Clear cell	4.68 (3.53, 6.2)	0.1437	115.4184	<.0001
	Mixed type 1/2	2.29 (1.99, 2.63)	0.0709	136.578	<.0001
	Serous adenoca	5.04 (4.45, 5.72)	0.0644	630.7076	<.0001
	Carcinosarcoma	6.19 (5.18, 7.41)	0.0914	397.8945	<.0001

Income quintile, RIO, immigration status removed and summary marginalization index used

Parameter	Level	OR (95% CI)	StdErr	Wald ChiSq	ProbChiSq
Intercept			0.1518	210.90	<.0001
Age	Age	1.01 (1, 1.01)	0.00196	9.98	0.0016
Charlson Index (ref=0)	1	1.07 (0.88, 1.31)	0.1018	0.44	0.5071
	2	1.09 (0.79, 1.51)	0.1634	0.3004	0.5836
	3+	1.3 (0.93, 1.81)	0.169	2.393	0.1219
	Missing	1.14 (1.04, 1.25)	0.0479	7.3465	0.0067
BMI > 40	Yes	0.67 (0.6, 0.75)	0.057	48.6142	<.0001
Marginalization Summary Score	/quintile	1.11 (1.05, 1.17)	0.0268	15.1858	<.0001
Histology group (ref=endometrioid adenoca)	Undifferentiated	11.3 (7.83, 16.32)	0.1874	167.4764	<.0001
	Other	3.43 (2.83, 4.14)	0.0969	161.416	<.0001
	Clear cell	4.66 (3.51, 6.17)	0.1434	114.9847	<.0001
	Mixed type 1/2	2.29 (2, 2.63)	0.0707	137.9715	<.0001
	Serous adenoca	5.04 (4.45, 5.72)	0.064	638.8506	<.0001
	Carcinosarcoma	6.18 (5.17, 7.39)	0.0912	398.9681	<.0001

Income quintile, RIO, immigration status removed and modified summary marginalization index (excluding dependency) used

Parameter	Level	OR (95% CI)	StdErr	Wald ChiSq	ProbChiSq
Intercept			0.1491	218.75	<.0001
Age	Age	1.01 (1, 1.01)	0.00195	12.47	0.0004
Charlson Index (ref=0)	1	1.07 (0.87, 1.3)	0.1019	0.405	0.5245
	2	1.09 (0.79, 1.5)	0.1634	0.2744	0.6004
	3+	1.3 (0.93, 1.81)	0.1691	2.3712	0.1236
	Missing	1.14 (1.03, 1.25)	0.0479	7.1553	0.0075
BMI > 40	Yes	0.67 (0.6, 0.75)	0.057	48.1739	<.0001
Modified Marginalization Summary Score	/quintile	1.1 (1.05, 1.14)	0.0215	18.2866	<.0001
Histology group (ref=endometrioid adenoca)	Undifferentiated	11.33 (7.85, 16.36)	0.1874	167.7597	<.0001
	Other	3.42 (2.83, 4.14)	0.0969	161.2849	<.0001
	Clear cell	4.65 (3.51, 6.15)	0.1434	114.6579	<.0001
	Mixed type 1/2	2.29 (1.99, 2.63)	0.0707	136.8835	<.0001
	Serous adenoca	5.01 (4.42, 5.68)	0.0641	633.4772	<.0001
	Carcinosarcoma	6.17 (5.16, 7.37)	0.0912	397.7133	<.0001

APPENDIX 4: Exploratory Cox multivariable regression analyses of associations with overall survival.

Factor	N	Comparison	Hazards Ratio (95% CI)	p-value
Year of Diagnosis	20228	/ year	0.97 (0.96, 0.99)	<0.001
Age Groups	20228	/ age group	1.41 (1.38, 1.43)	<0.001
Known Charlson Score	20228	0 1-2 3-4 5+ No Admission‡	0.90 (0.83, 0.98) 1.00 (0.92, 1.08) 1.61 (1.41, 1.83) 4.78 (4.02, 5.68) Reference	<0.001
Prior Cancer	20228	Yes vs No	1.94 (1.73, 2.18)	<0.001
Income Quintile	20213	/ quintile	0.93 (0.91, 0.96)	<0.001
Rural	20228	Yes vs No	0.98 (0.89, 1.08)	0.67
Distance to Nearest RCC	20039	Log-transform	0.99 (0.96, 1.01)	0.27
RIO Score (exclude unk)	20131	/ group	0.95 (0.91, 1.00)	0.054
LHIN	20228	By LHIN		0.008
ICD-O-3 Code	20228	C541 vs other	0.27 (0.24, 0.31)	<0.001
Morphology	20228	83803 vs other	0.21 (0.20, 0.23)	<0.001
Best Stage	20228	1 2 3 4 Unknown	0.40 (0.36, 0.43) 0.93 (0.81, 1.05) 2.12 (1.92, 2.33) 8.11 (7.36, 8.94) Reference	<0.001
Dependency Quintile	20228	/ quintile	1.08 (1.06, 1.11)	<0.001
Deprivation Quintile	20228	/ quintile	1.08 (1.05, 1.10)	<0.001
Ethnicity Quintile	20228	/ quintile	1.01 (0.99, 1.03)	0.41
Instability Quintile	20228	/ quintile	1.11 (1.08, 1.13)	<0.001
Summary Score Quintile	20228	/ quintile	1.13 (1.10, 1.16)	<0.001
BMI	20228	>40 vs ≤40	0.54 (0.48, 0.59)	<0.001
Histology	20228	Endometrial Endo Carcinosarcoma Clear Cell Mixed Type ½ Other/Missing Serous Adeno Undifferentiated	Reference 7.33 (6.60, 8.15) 4.23 (3.48, 5.15) 2.30 (2.05, 2.58) 4.91 (4.36, 5.52) 5.26 (4.82, 5.74) 13.45 (11.62, 15.57)	<0.001
Modified Marginalization Quintile (no dependency)	20228	/ quintile	1.09 (1.07, 1.12)	<0.001
Multivariable Model 1 (using individual marginalization scores)				
Year of Diagnosis	19931	/ year	0.95 (0.94, 0.97)	<0.001
Age Groups		/ age group	1.34 (1.31, 1.36)	<0.001
Known Charlson Score		0 1-2 3-4 5+ No Admission‡	0.87 (0.80, 0.95) 0.96 (0.89, 1.05) 1.35 (1.18, 1.55) 2.14 (1.79, 2.57) Reference	<0.001
Prior Cancer		Yes vs No	1.31 (1.17, 1.48)	<0.001
Income Quintile		/ quintile	0.97 (0.94, 1.00)	0.079
Rural		Yes vs No	1.08 (0.96, 1.22)	0.22
Distance to Nearest RCC		Log-transform	1.01 (0.98, 1.05)	0.47

RIO Score (exclude unk)		/ group	0.97 (0.90, 1.04)	0.40
BMI		>40 vs ≤40	0.92 (0.82, 1.02)	0.10
Histology		Endometrial Endo	Reference	<0.001
		Carcinosarcoma	3.69 (3.30, 4.13)	
		Clear Cell	2.08 (1.70, 2.54)	
		Mixed Type ½	1.78 (1.58, 2.00)	
		Other/Missing	3.05 (2.70, 3.44)	
		Serous Adeno	2.46 (2.24, 2.70)	
		Undifferentiated	7.08 (6.09, 8.24)	
Best Stage		1	Reference	<0.001
		2	1.88 (1.65, 2.14)	
		3	3.57 (3.22, 3.95)	
		4	10.21 (9.17, 11.37)	
		Unknown	2.30 (2.10, 2.51)	
Dependency Quintile		/ quintile	0.98 (0.95, 1.00)	0.055
Deprivation Quintile		/ quintile	1.00 (0.97, 1.04)	0.82
Ethnicity Quintile		/ quintile	1.00 (0.96, 1.03)	0.77
Instability Quintile		/ quintile	1.06 (1.03, 1.09)	<0.001
Multivariable Model 2 (using summary marginalization score)				
Year of Diagnosis	19931	/ year	0.96 (0.94, 0.97)	<0.001
Age Groups		/ age group	1.33 (1.31, 1.36)	<0.001
Known Charlson Score		0	0.87 (0.80, 0.95)	<0.001
		1-2	0.96 (0.88, 1.04)	
		3-4	1.34 (1.17, 1.53)	
		5+	2.16 (1.80, 2.58)	
		No Admission‡	Reference	
Prior Cancer		Yes vs No	1.32 (1.17, 1.49)	<0.001
Income Quintile		/ quintile	0.96 (0.94, 0.99)	0.007
Rural		Yes vs No	1.07 (0.95, 1.21)	0.28
Distance to Nearest RCC		Log-transform	1.01 (0.98, 1.05)	0.54
RIO Score (exclude unk)		/ group	0.98 (0.91, 1.05)	0.51
BMI		>40 vs ≤40	0.92 (0.83, 1.02)	0.12
Histology		Endometrial Endo	Reference	<0.001
		Carcinosarcoma	3.67 (3.29, 4.10)	
		Clear Cell	2.06 (1.68, 2.52)	
		Mixed Type ½	1.78 (1.59, 2.00)	
		Other/Missing	3.06 (2.71, 3.46)	
		Serous Adeno	2.43 (2.21, 2.67)	
		Undifferentiated	7.06 (6.07, 8.21)	
Best Stage		1	Reference	<0.001
		2	1.88 (1.65, 2.14)	
		3	3.56 (3.22, 3.94)	
		4	10.15 (9.11, 11.30)	
		Unknown	2.29 (2.09, 2.50)	
Summary Score Quintile		/ quintile	1.03 (1.01, 1.06)	0.045
Multivariable Model 3 (using modified marginalization score)				
Year of Diagnosis	19931	/ year	0.95 (0.94, 0.97)	<0.001
Age Groups		/ age group	1.34 (1.31, 1.36)	<0.001
Known Charlson Score		0	0.87 (0.80, 0.95)	<0.001
		1-2	0.96 (0.88, 1.04)	
		3-4	1.34 (1.17, 1.53)	
		5+		

		No Admission‡	2.17 (1.81, 2.59) Reference	
Prior Cancer		Yes vs No	1.32 (1.17, 1.49)	<0.001
Income Quintile		/ quintile	0.96 (0.93, 0.99)	0.009
Rural		Yes vs No	1.08 (0.95, 1.22)	0.24
Distance to Nearest RCC		Log-transform	1.01 (0.98, 1.05)	0.44
RIO Score (exclude unk)		/ group	0.97 (0.90, 1.05)	0.46
BMI		>40 vs ≤40	0.92 (0.83, 1.02)	0.12
Histology		Endometrial Endo Carcinosarcoma Clear Cell Mixed Type ½ Other/Missing Serous Adeno Undifferentiated	Reference 3.66 (3.28, 4.09) 2.06 (1.68, 2.51) 1.78 (1.59, 2.00) 3.06 (2.71, 3.46) 2.43 (2.21, 2.67) 7.04 (6.05, 8.19)	<0.001
Best Stage		1 2 3 4 Unknown	Reference 1.88 (1.65, 2.14) 3.56 (3.22, 3.94) 10.14 (9.11, 11.30) 2.28 (2.09, 2.49)	<0.001
Modified Score Quintile		/ quintile	1.03 (0.99, 1.06)	0.13
Multivariable Model 4 (using modified marginalization score, drop RIO, rurality, distance, income quintile)				
Year of Diagnosis	20228	/ year	0.96 (0.94, 0.97)	<0.001
Age Groups		/ age group	1.34 (1.31, 1.36)	<0.001
Known Charlson Score		0 1-2 3-4 5+ No Admission‡	0.87 (0.80, 0.95) 0.96 (0.88, 1.04) 1.34 (1.17, 1.53) 2.16 (1.81, 2.58) Reference	<0.001
Prior Cancer		Yes vs No	1.30 (1.15, 1.47)	<0.001
BMI		>40 vs ≤40	0.93 (0.84, 1.03)	0.17
Histology		Endometrial Endo Carcinosarcoma Clear Cell Mixed Type ½ Other/Missing Serous Adeno Undifferentiated	Reference 3.59 (3.22, 4.01) 2.06 (1.69, 2.51) 1.77 (1.58, 1.99) 3.07 (2.72, 3.46) 2.41 (2.20, 2.65) 7.11 (6.11, 8.26)	<0.001
Best Stage		1 2 3 4 Unknown	Reference 1.88 (1.65, 2.14) 3.54 (3.21, 3.92) 10.23 (9.19, 11.39) 2.28 (2.09, 2.49)	<0.001
Modified Score Quintile		/ quintile	1.05 (1.03, 1.08)	<0.001