












Sexual health outcomes after colorectal cancer diagnosis in females: a population-based cohort study

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Abstract

Background: Colorectal cancer (CRC) affects a growing number of females. Our objective was to evaluate the impact of CRC on sexual health outcomes among females, while controlling for age.

Methods: We conducted a cohort study using administrative health data from the province of British Columbia (BC) including linked health visits and cancer registry from 1985 to 2017. The cohort included females with CRC ($n = 25\,402$; mean age [SD]: 69.0 [13.1]) and matched controls without CRC ($n = 254\,020$; 69.0 [13.1]) in a 1:10 ratio by age, further stratified by age groups (≤ 39 years and ≥ 40 years). Multivariable Cox regression models assessed the associations between CRC and 5 sexual health outcomes (dyspareunia, pelvic inflammatory disease, endometriosis, abnormal bleeding, and premature ovarian failure), adjusting for covariates. Sensitivity analyses focused on females with CRC to explore associations between sociodemographic and cancer-related factors and sexual health outcomes. Tests were 2-sided (statistical significance $P < .05$).

Results: Females with CRC had higher risks of dyspareunia (HR 1.67; 95% CI = 1.62 to 1.73), pelvic inflammatory disease (HR 3.42; 95% CI = 3.07 to 3.81), and endometriosis (HR 1.95; 95% CI = 1.69 to 2.25) compared to controls. In the ≥ 40 -year group, these associations persisted, while in the ≤ 39 -year group, endometriosis was not associated with CRC, but premature ovarian failure was (HR 1.75; 95% CI = 1.40 to 2.19). In sensitivity analyses, we also observed associations with cancer treatments (surgery, chemotherapy, radiation) and sexual health outcomes.

Conclusions: This population-based study identified associations between CRC and adverse sexual health outcomes among female patients, highlighting the need for targeted interventions and support.

Introduction

In Canada, colorectal cancer (CRC) is the fourth most common cancer diagnosed among females, with approximately 10 500 new cases in 2023.¹ Evidence over the past decade highlights the rising risk of early age-onset colorectal cancer (EAO-CRC), including among adolescents and young adults (AYA) aged 15 to 39.² The Global Burden of Disease Study reported a global increase in AYA-CRC cases from 37 285 in 1990 to 76 090 in 2019.³ Five-year relative survival rates for CRC among AYAs (colon: 72.8%; rectal: 70.9%) compared to adults >40 (colon: 64.8%; rectal: 67.9%)

suggest the need for lifelong health support, particularly for sexual health, given that CRC involves the pelvic region.⁴

Sexual health, as defined by the World Health Organization, is “a state of physical, emotional, mental, and social well-being in all matters relating to sexuality.”⁵ This is particularly relevant for female CRC patients, who may experience issues such as premature ovarian failure, vaginal dryness, reduced libido, body image concerns, and poorer mental health.⁶ In 2019, Canty et al. conducted a systematic review of the impact of CRC on female sexual function with included studies largely based on self-report.⁷ In their

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2024 systematic review, Feier identified 5 studies on CRC and sexual functioning.⁸ To highlight included studies, Sanford et al. found that CRC patients ≤ 40 years faced greater intimate life impacts than those ≥ 40 (OR 3.04; 95% CI = 1.14 to 8.11).⁹ The REACCT Collaborative study also utilized self-report data and reported sexual dysfunction in 6% of 1425 EAO rectal cancer participants.¹⁰ Current evidence on CRC and sexual health is limited to self-reported data and lacks comparison to cancer-free individuals, hindering analyses of associations or specific sexual health outcomes (eg, premature ovarian failure, endometriosis, dyspareunia). The objective of this study was to leverage administrative health data to evaluate sexual health outcomes in females diagnosed with CRC compared to those without CRC.

Methods

Data source and source population

We used Population Data British Columbia (BC), a longitudinal, deidentified data resource covering all 5.4 million residents of BC, Canada. Holdings include the Medical Services Plan (MSP) for outpatient visits, the Discharge Abstract Database (DAD) for inpatient visits, the Consolidation File for demographics, and the Vital Statistics File for deaths since 1985, as well as PharmaNet for dispensed medications since 1996. We also linked this information to the BC Cancer Registry,¹¹ which includes details on cancer diagnosis and treatments since 1985.

The source population included patients diagnosed with CRC between January 1, 1985, and December 31, 2017, as identified in the BC Cancer Registry using International Classification of Diseases for Oncology (ICD-O), Third Edition codes: C18.3, C18.0, C18.2 (right colon); C18.6, C18.7, C18.5, C19 (left colon); C18.4 (transverse colon); C20, C21.8 (rectum); and C18.9, C18.1, C18.8 (unspecified). The index date was defined as the diagnosis date. Each CRC patient was age- and sex-matched to 10 cancer-free controls (Figure 1). To examine sexual health outcomes, from this source population, we drew a cohort of females with CRC ($n = 25\ 402$) and without CRC ($n = 254\ 020$).

Outcomes

We examined 5 outcomes: 4 on gynecological health (related to reproductive organ function) and 1 on broader sexual health, recognizing that gynecologic outcomes are a subset of sexual health outcomes.⁵ Using MSP, DAD, and PharmaNet data, we examined these 5 outcomes (yes vs no) as relevant to the age group in question: (1) Dyspareunia, defined by genital pain experienced before, during, or after intercourse¹² (ICD-9 625.X, 789.0X, or ICD-10 N94.X; and pelvic pain ICD-10 R10.2X, R10.3X)¹³; (2) Abnormal bleeding, defined as irregularities in the menstrual cycle involving frequency, regularity, duration, and volume of flow outside of pregnancy¹⁴ (ICD-9 626.X¹⁵ or ICD-10 N91.X, N92.X, N93.X¹⁶); (3) Pelvic inflammatory disease, an inflammation of the female upper genital tract, typically due to an infection¹⁷ (ICD-9 614.X, 615.X, or ICD-10 N70.X, N71.X, N73.0X-N73.5X, N73.8X-N73.9X)¹⁸; (4) Endometriosis, a chronic condition characterized by implantation of endometrial tissue outside of the uterine cavity¹⁹ (ICD-9 617.X or ICD-10 N80.0X-N80.6X and N80.8X-N80.9X)¹³; and (5) Premature ovarian failure, defined as menopause (ie, absent period for 12 months) in females < 40 years of age²⁰ (analysis was only completed in those ≤ 39 years old; ICD-9 627.X²¹ or ICD-10 codes E28.3X, E894,²² and at least 1 prescription for hormone replacement therapy [HRT] formulations including estrogen, estrogen alone, and progestin, in vaginal, topical, and transdermal form [Anatomical Therapeutic Chemical Classification 3

G03A, G03C, G03D, and Anatomical Therapeutic Chemical Classification 4 L02AA]).²¹

Covariates

Demographic factors considered were age, neighborhood income quintile (Quintile of Adjusted Income per Person Equivalent, QAIPE; 1-5: a measure of area-based income adjusted for household size), and residence type (urban vs rural, determined using Census Metropolitan Area/Census Agglomeration data).²³ We also evaluated comorbidities, including the Charlson-Romano comorbidity index (a weighted score of comorbidities affecting patient outcomes)^{24,25} and inflammatory bowel disease.²⁶ Additionally, we assessed health care encounters, focusing on hospital visits and frequency of physician visits.²³ Finally, we considered CRC characteristics, including cancer site (left, transverse, unspecified, right colon, and rectum) and treatment types (surgery, chemotherapy, radiation). Treatment types were treated as separate (eg, discrete) variables. Non-cancer covariates were measured from 1 to 0 years prior to the index date, while cancer covariates were assessed after the index date.

Statistical analysis

As gender is not recorded in BC's administrative databases, we analyzed individuals assigned female at birth, based on MSP data. We used univariate and multivariable Cox regression models to evaluate the association between CRC diagnosis and each sexual health outcome. Individuals were followed until sexual health outcome, death, migration out of the province, or end of the study period (ie, data availability), whichever came first. Models were computed for the overall study cohort and stratified by age (≤ 39 years and ≥ 40 years) with the cut-off aligning with our interest in AYA cancer outcomes. Multivariable models adjusted for age (entered as a continuous variable and scaled in 10-year increments), neighborhood income quintile (quintiles 1-4 vs quintile 5), residence type (rural vs urban), healthcare encounters (hospitalization: yes vs no), number of doctor visits, the Charlson-Romano comorbidity index, and inflammatory bowel disease (yes vs no). All statistical tests were 2-sided, with statistical significance defined as $P < .05$. Sensitivity analyses were conducted among individuals with CRC to assess associations between cancer characteristics (site and treatment) and each sexual health outcome. All analyses were performed using SAS statistical software v9.4.²⁷

Study conduct

This study was approved by the University of British Columbia (H17-03530). Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through the Data Stewards or their designated service providers. All datasets listed above were used in this study. You can find further information regarding these datasets by visiting the Population Data BC project webpage at: https://my.popdata.bc.ca/project_listings/18-088/collection_approval_dates. All inferences, opinions, and conclusions drawn in this publication are those of the author(s), and do not reflect the opinions or policies of the Data Steward(s).

Results

The study cohort included 25 402 females with CRC (mean age 69.0 [SD: 13.1]) and 254 020 females without CRC (69.0 [13.1]) ($P = .9765$) (Table 1). Females with CRC had a higher proportion of comorbid inflammatory bowel disease (1.9% vs 0.4%; $P < .0001$). They also had more doctor visits in the year prior (15.1 vs 10.9; $P < .0001$) and a higher rate of hospitalization (55.2% vs 20.7%;

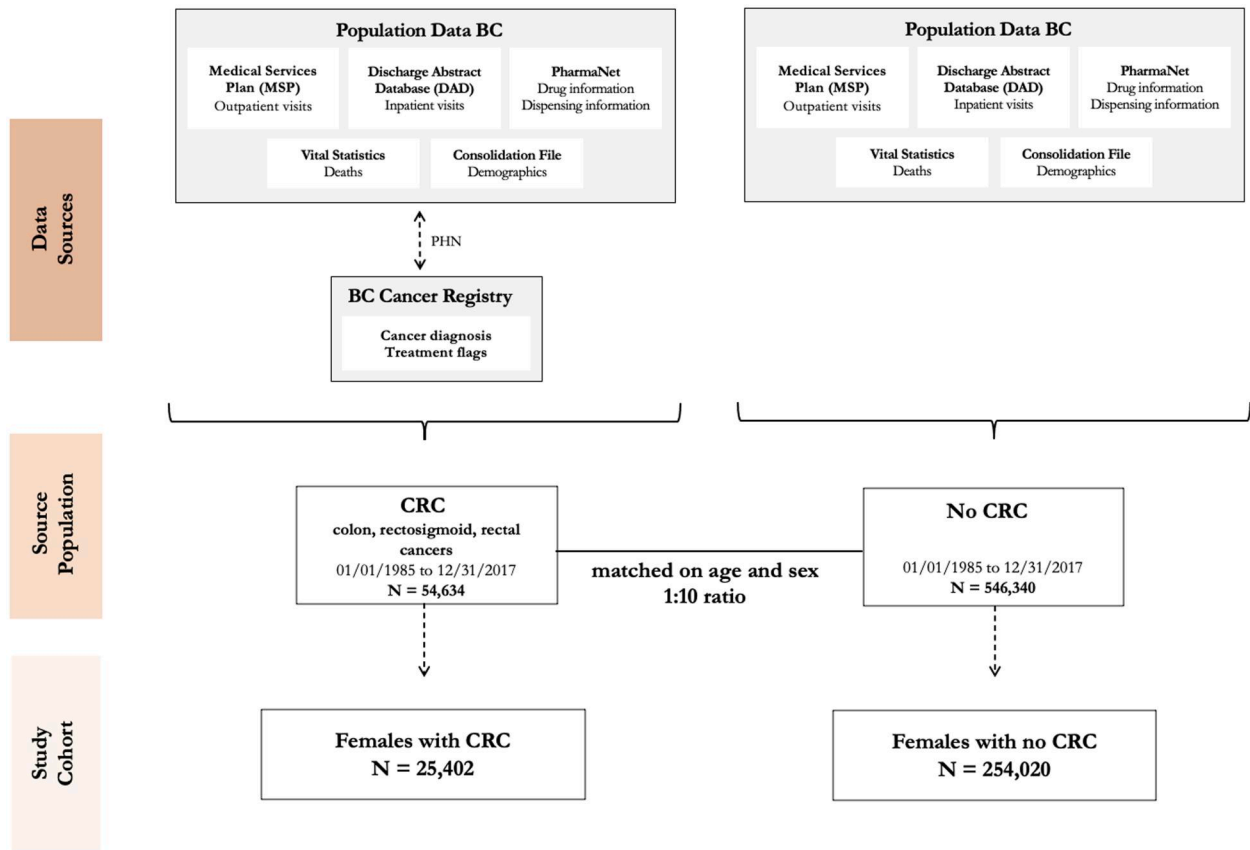


Figure 1. Flow of data sources and linkages, source populations, and study cohort (dashed arrows indicating linkages between databases using PHNs which are then de-identified). Abbreviations: CRC = colorectal cancer; PHN = personal health number.

Table 1. Characteristics of study cohort of females with CRC and without CRC (matched on age and sex).

Characteristic	CRC (n = 25 402)	No CRC (n = 254 020)	P ^a
Demographic factors			
Age, mean (SD)	69.0 (13.1)	69.0 (13.1)	.9765
Neighborhood income, n (%)			<.001
Quintile 1 (Low)	5601 (22.1)	56 855 (22.4)	
Quintile 2	4892 (19.3)	51 458 (20.3)	
Quintile 3	5985 (23.5)	53 655 (21.1)	
Quintile 4	4424 (17.4)	45 818 (18.0)	
Quintile 5 (High)	4527 (17.8)	46 234 (18.2)	
Residence, n (%)			.1121
Urban	22 021 (86.7)	221 103 (87.0)	
Rural	3381 (13.3)	32 917 (13.0)	
Healthcare utilization			
Doctor visits, mean (SD)	15.1 (12.7)	10.9 (11.5)	<.001
Hospitalization, n (%)	14 018 (55.2)	52 592 (20.7)	<.001
Comorbidities			
Charlson-Romano comorbidity index, mean (SD)	1.0 (2.2)	0.1 (0.6)	<.001
Inflammatory bowel disease, n (%)	478 (1.9)	1121 (0.4)	<.001
CRC characteristics			
Cancer site, n (%)			
Left colon	10 106 (39.8)	–	–
Rectum	7312 (28.8)	–	–
Right colon	4532 (17.8)	–	–
Transverse colon	1732 (6.8)	–	–
Unspecified	1729 (6.8)	–	–
Treatment			
Surgery, n (%)	10 903 (42.9)	–	–
Chemotherapy, n (%)	9006 (35.5)	–	–
Radiation, n (%)	4763 (18.8)	–	–

^a t-test for numerical variables and chi-squared test for categorical variables; P <.05 for statistical significance.

$P < .0001$). Among females with CRC, the most common cancer sites were the left colon (39.8%) and rectum (28.8%), while the most frequent treatments were surgery (42.9%) and chemotherapy (35.5%).

Evaluation of sexual health outcomes

Table 2 summarizes the univariate and multivariable Cox regression models assessing the association between CRC and sexual health outcomes in females. Age-stratified analyses (≤ 39 and ≥ 40 years) are shown in Tables 3 and 4. Tables S1–S3 present sensitivity analyses among females with CRC, evaluating the associations between cancer-related variables and sexual health outcomes.

Dyspareunia

The median follow-up time for dyspareunia was 3.3 years for females with CRC and 7.5 years for those without. Among those with CRC 19.71% experienced dyspareunia and among those without CRC, 16.41%. In the multivariable model, females with CRC had a 67% higher risk of dyspareunia compared to those without (HR 1.67; 95% CI = 1.62 to 1.73) (Table 2). The association persisted in age-stratified models: females ≤ 39 years (HR 1.90; 95% CI = 1.58 to 2.28) (Table 3) and females ≥ 40 years (HR 1.67; 95% CI = 1.61 to 1.73) (Table 4). Sensitivity analysis among females with CRC showed increased risk of dyspareunia with surgery (HR 1.23; 95% CI = 1.14 to 1.33), chemotherapy (HR 1.25; 95% CI = 1.16 to 1.34), and radiation (HR 1.24; 95% CI = 1.12 to 1.37) (Table S1).

Abnormal bleeding

For abnormal bleeding, the median follow-up was 3.8 years for females with CRC and 7.9 years for those without. Abnormal bleeding was observed in 5.71% of individuals with CRC and 7.82% without CRC. In the multivariable Cox model for all ages, CRC was not associated with abnormal bleeding (HR 1.01; 95% CI = 0.95 to 1.08) (Table 2). However, age-stratified analysis showed a negative association between CRC and abnormal bleeding for females ≤ 39 years (HR 0.74; 95% CI = 0.59 to 0.93) (Table 3). No association was observed for females ≥ 40 years (HR 1.04; 95% CI = 0.97 to 1.11) (Table 4). In sensitivity analysis among females of all ages with CRC, we found that chemotherapy is positively associated with abnormal bleeding (HR 1.24; 95% CI = 1.09 to 1.41) (Table S1).

Pelvic inflammatory disease

The median follow-up time for pelvic inflammatory disease was 4.0 years for females with CRC and 8.2 years for those without. Among those with CRC 1.96% experienced pelvic inflammatory disease outcome and among those without CRC, 0.73%. The multivariable model showed a higher risk of pelvic inflammatory disease among females with CRC compared to those without (HR 3.42; 95% CI = 3.07 to 3.81) (Table 2). Age-stratified analysis revealed attenuated risk for females ≤ 39 years (HR 1.67; 95% CI = 1.08 to 2.57) (Table 3), while the risk remained strong for those ≥ 40 years (HR 3.66; 95% CI = 3.27 to 4.09) (Table 4). Sensitivity analysis among females with CRC showed an increased risk by 80% for left colon CRC (HR 1.80; 95% CI = 1.26 to 2.56) and 121% for rectal CRC (HR 2.21; 95% CI = 1.52 to 3.23). Radiation treatment also increased the risk by 56% (HR 1.56; 95% CI = 1.21 to 2.02) (Table S1).

Endometriosis

The median follow-up time for endometriosis was 4.0 years for females with CRC and 8.2 years for those without. Endometriosis

was observed in 0.95% for individuals with CRC and 0.70% for individuals without CRC. In the multivariable analysis, CRC was associated with a higher risk of endometriosis among females of all ages (HR 1.95; 95% CI = 1.69 to 2.25) (Table 2). In age-stratified analysis, no association was found for females ≤ 39 years (HR 1.21; 95% CI = 0.78 to 1.89) (Table 3), while the association remained statistically significant for those ≥ 40 years (HR 2.07; 95% CI = 1.78 to 2.40) (Table 4). Sensitivity analysis among females with CRC indicated that surgery increased the risk of endometriosis by 80% (HR 1.80; 95% CI = 1.32 to 2.45) (Table S1).

Premature ovarian failure

The median follow-up time for premature ovarian failure was 3.2 years for females with CRC and 6.3 years for those without. In the multivariable model, females ≤ 39 years old with CRC had a higher risk of premature ovarian failure compared to those without CRC (HR 1.75; 95% CI = 1.40 to 2.19) (Table 3). Sensitivity analysis among females ≤ 39 years with CRC showed a 164% increased risk of premature ovarian failure in those who received chemotherapy (HR 2.64; 95% CI = 1.65 to 4.22) (Table S2).

Discussion

Using population-based administrative health data for a cohort of females with and without CRC, our evaluation of sexual health outcomes over all ages, those ≤ 39 years, and those ≥ 40 years old revealed several key findings. For dyspareunia, females with CRC had a higher risk compared to those without CRC, which persisted for both younger and older females. In contrast, abnormal bleeding in all ages and those ≥ 40 years showed no association with CRC, but a decreased risk was observed in females ≤ 39 years. Pelvic inflammatory disease was strongly associated with CRC, with the increase in risk weakened for females ≤ 39 years and remaining high for those ≥ 40 years. We also noted that endometriosis risk was elevated in females with CRC, particularly among those ≥ 40 years. Lastly, premature ovarian failure was notably associated with CRC in females ≤ 39 years. We also found associations between sexual health outcomes and cancer characteristics when conducting sensitivity analyses among CRC females. Altogether, these findings indicate an intricate relationship between CRC and sexual health outcomes, as well as impacts of cancer-related variables.

To our knowledge, this is the first population-based analytic study to evaluate the association between CRC and sexual health outcomes among females. Indeed, prior studies on CRC and sexual health have largely been descriptive cross-sectional studies involving individuals with CRC,⁸ which limits the findings to the burden of outcomes rather than risk. Our study also expands the understanding of sexual health outcomes by focusing on clinically diagnosed outcomes, as opposed to prior studies that evaluated outcomes based on self-reports and surveys (eg, sexual dysfunction).

Individuals ≥ 40 years faced higher risks of pelvic inflammatory disease and endometriosis, while dyspareunia risk was similar across age groups compared to cancer-free comparators. Abnormal bleeding was inversely associated with CRC only in those ≤ 39 years. Generally, age was inversely linked to risk across outcomes. Younger females may have better baseline sexual health due to hormonal factors, potentially mitigating CRC's impact. However, they might be more susceptible to treatment effects due to higher sexual activity²⁸ and psychosocial factors like intimacy and body image concerns.²⁹ Our study also suggests a detection bias, as those with more health care interactions 1

Table 2. Hazard ratios and 95% confidence intervals from Cox regression models on the association between CRC and sexual health outcomes among females (all ages).

	Dyspareunia (N ^a = 38 043)	Abnormal bleeding (N ^a = 16 965)	Pelvic inflammatory disease (N ^a = 2287)	Endometriosis (N ^a = 1969)
CRC, n (%) ^b	3904 (19.71)	1139 (5.71)	481 (1.96)	234 (0.95)
No CRC, n (%) ^b	34 139 (16.41)	15 826 (7.82)	1806 (0.73)	1735 (0.70)
Univariable models				
CRC (vs no)	1.83 (1.77 to 1.89) ^c	1.04 (0.98 to 1.11)	3.76 (3.40 to 4.16) ^c	1.88 (1.64 to 2.16) ^c
Multivariable models				
CRC (vs no)	1.67 (1.62 to 1.73) ^c	1.01 (0.95 to 1.08)	3.42 (3.07 to 3.81) ^c	1.95 (1.69 to 2.25) ^c
Age ^d	0.88 (0.87 to 0.88) ^c	0.50 (0.49 to 0.50) ^c	0.64 (0.62 to 0.66) ^c	0.48 (0.46 to 0.49) ^c
Neighborhood income				
Quintile 1 vs 5 ^e	1.02 (0.99 to 1.06)	0.92 (0.88 to 0.97) ^c	1.13 (0.99 to 1.29)	0.86 (0.74 to 0.99) ^c
Quintile 2 vs 5 ^e	1.03 (1.00 to 1.07)	0.97 (0.92 to 1.01)	1.10 (0.96 to 1.25)	0.96 (0.83 to 1.10)
Quintile 3 vs 5 ^e	1.01 (0.98 to 1.04)	0.90 (0.86 to 0.94) ^c	1.11 (0.97 to 1.27)	0.96 (0.84 to 1.11)
Quintile 4 vs 5 ^e	1.03 (1.00 to 1.07)	0.99 (0.94 to 1.04)	1.09 (0.95 to 1.25)	1.06 (0.93 to 1.22)
Rural (vs urban)	1.15 (1.11 to 1.18) ^c	0.85 (0.81 to 0.89) ^c	1.04 (0.92 to 1.17)	1.25 (1.11 to 1.41) ^c
Number of doctors' visits ^d	1.02 (1.02 to 1.02) ^c	1.01 (1.01 to 1.01) ^c	1.01 (1.01 to 1.01) ^c	1.01 (1.01 to 1.01)
Hospitalization (vs no)	1.09 (1.06 to 1.12) ^c	0.97 (0.92 to 1.01)	1.21 (1.09 to 1.34) ^c	0.91 (0.81 to 1.04)
Charlson-Romano comorbidity index ^d	0.99 (0.97 to 1.00)	0.96 (0.93 to 0.99) ^c	0.97 (0.92 to 1.02)	0.91 (0.84 to 0.99) ^c
Inflammatory bowel disease (vs no)	1.44 (1.27 to 1.64) ^c	1.23 (1.01 to 1.50) ^c	1.30 (0.89 to 1.91)	0.56 (0.29 to 1.08)

Covariates were assessed -1 to 0 years from index date.

- ^a Total sample size of CRC and no CRC females of all ages with the outcome;
- ^b Incidence expressed as a proportion and calculated as the number of individuals with the outcome/number of individuals at risk for outcome within group (ie, CRC or no CRC); CRC = colorectal cancer;
- ^c Statistically significant difference from the referent group;
- ^d Modelled as a continuous variable and scaled in 10-year increments;
- ^e Reference category is highest neighborhood income quintile.

Table 3. Hazard ratios and 95% confidence intervals from Cox regression models on the association between CRC and sexual health outcomes among females (≤39 years).

	Dyspareunia (N ^a = 1468)	Abnormal bleeding (N ^a = 1521)	Pelvic inflammatory disease (N ^a = 243)	Endometriosis (N ^a = 314)	Premature ovarian failure (N ^a = 944)
CRC, n (%) ^b	143 (39.61)	89 (38.84)	25 (5.05)	23 (4.43)	98 (31.82)
No CRC, n (%) ^b	1325 (35.34)	1432 (59.79)	218 (4.33)	291 (5.74)	846 (28.76)
Univariable models					
CRC (vs no)	1.98 (1.67 to 2.36) ^c	0.74 (0.60 to 0.92) ^c	1.70 (1.13 to 2.58) ^c	1.15 (0.75 to 1.76)	1.65 (1.34 to 2.04) ^c
Multivariable models					
CRC (vs no)	1.90 (1.58 to 2.28) ^c	0.74 (0.59 to 0.93) ^c	1.67 (1.08 to 2.57) ^c	1.21 (0.78 to 1.89)	1.75 (1.40 to 2.19) ^c
Age ^d	0.84 (0.76 to 0.94) ^c	0.81 (0.73 to 0.90) ^c	0.60 (0.47 to 0.76) ^c	0.83 (0.66 to 1.04)	0.66 (0.57 to 0.75) ^c
Neighborhood income					
Quintile 1 vs 5 ^e	1.23 (1.04 to 1.46) ^c	0.97 (0.83 to 1.14)	1.06 (0.71 to 1.59)	1.10 (0.77 to 1.56)	1.14 (0.93 to 1.41)
Quintile 2 vs 5 ^e	1.12 (0.95 to 1.33)	0.93 (0.79 to 1.10)	0.94 (0.62 to 1.43)	0.78 (0.53 to 1.15)	1.02 (0.82 to 1.26)
Quintile 3 vs 5 ^e	0.97 (0.82 to 1.16)	1.00 (0.85 to 1.17)	1.02 (0.68 to 1.55)	1.01 (0.70 to 1.46)	1.14 (0.92 to 1.41)
Quintile 4 vs 5 ^e	1.01 (0.85 to 1.21)	0.86 (0.73 to 1.02)	0.95 (0.62 to 1.46)	1.15 (0.80 to 1.65)	1.10 (0.88 to 1.37)
Rural (vs urban)	1.02 (0.87 to 1.19)	0.89 (0.76 to 1.04)	1.17 (0.81 to 1.70)	1.35 (0.99 to 1.84)	0.87 (0.71 to 1.06)
Number of doctors' visits ^d	1.01 (1.01 to 1.01) ^c	1.00 (1.00 to 1.01)	1.00 (0.99 to 1.01)	1.00 (1.00 to 1.01)	1.01 (1.00 to 1.01)
Hospitalization (vs no)	1.07 (0.93 to 1.23)	1.06 (0.92 to 1.22)	1.39 (1.01 to 1.90) ^c	1.03 (0.77 to 1.39)	0.89 (0.75 to 1.05)
Charlson-Romano comorbidity index ^d	1.10 (1.01 to 1.18) ^c	0.97 (0.86 to 1.08)	0.92 (0.72 to 1.18)	0.91 (0.71 to 1.18)	0.99 (0.89 to 1.10)
Inflammatory bowel disease (vs no)	1.43 (0.92 to 2.22)	0.97 (0.59 to 1.60)	0.52 (0.13 to 2.11)	0.66 (0.21 to 2.10)	0.83 (0.42 to 1.61)

Covariates were assessed -1 to 0 years from index date.

- ^a Total sample size of CRC and no CRC females ≤39 years old with the outcome;
- ^b Incidence expressed as a proportion and calculated as the number of individuals with the outcome/number of individuals at risk for outcome within group (ie, CRC or no CRC); CRC = colorectal cancer;
- ^c Statistically significant difference from the referent group;
- ^d Modelled as a continuous variable and scaled in 10-year increments;
- ^e Reference category is highest neighborhood income quintile.

year prior to CRC diagnosis were more likely to be diagnosed with sexual health issues after CRC diagnosis. Specifically, all evaluated outcomes in individuals ≥40 years were positively linked to health care encounters, compared to only 2 of 5 outcomes in those ≤39 years. This is expected, as older individuals typically engage more with the health care system, increasing diagnosis opportunities.³⁰ In contrast, younger females may face underdiagnosis due to less frequent health care access. Therefore, it is crucial to consider health care encounter patterns when

assessing CRC's impact on sexual health, as increased health care exposure may indicate a higher likelihood of diagnosis rather than an actual increase in risk.

In sensitivity analyses, our study also identified associations between cancer treatment types and sexual health outcomes investigated. The biological mechanisms underlying these effects warrant discussion. Chemotherapy and surgery can alter hormone production; chemotherapy may affect sexual organs,³¹ while surgery can induce menopause through the removal of

Table 4. Hazard ratios and 95% confidence intervals from Cox regression models on the association between CRC and sexual health outcomes among females (≥ 40 years).

	Dyspareunia (N ^a = 36 575)	Abnormal bleeding (N ^a = 15 444)	Pelvic inflammatory disease (N ^a = 2044)	Endometriosis (N ^a = 1655)
CRC, n (%) ^b	3761 (19.34)	1050 (5.34)	456 (1.89)	211 (0.88)
No CRC, n (%) ^b	32 814 (16.07)	14 394 (7.19)	1588 (0.65)	1444 (0.60)
Univariable models				
CRC (vs no)	1.83 (1.76 to 1.89) ^c	1.06 (0.99 to 1.13)	4.04 (3.64 to 4.48) ^c	2.02 (1.75 to 2.33)
Multivariable models				
CRC (vs no)	1.67 (1.61 to 1.73) ^c	1.04 (0.97 to 1.11)	3.66 (3.27 to 4.09) ^c	2.07 (1.78 to 2.40) ^c
Age ^d	0.89 (0.88 to 0.90) ^c	0.48 (0.48 to 0.49) ^c	0.66 (0.64 to 0.69) ^c	0.43 (0.42 to 0.45) ^c
Neighborhood income				
Quintile 1 vs 5 ^e	1.01 (0.98 to 1.04)	0.92 (0.88 to 0.97) ^c	1.12 (0.97 to 1.29)	0.83 (0.71 to 0.97)
Quintile 2 vs 5 ^e	1.03 (0.99 to 1.06)	0.97 (0.92 to 1.02)	1.11 (0.96 to 1.27)	1.00 (0.86 to 1.16)
Quintile 3 vs 5 ^e	1.01 (0.98 to 1.04)	0.89 (0.84 to 0.93) ^c	1.11 (0.97 to 1.28)	0.96 (0.82 to 1.12)
Quintile 4 vs 5 ^e	1.03 (1.00 to 1.07)	1.00 (0.95 to 1.05)	1.10 (0.95 to 1.27)	1.05 (0.90 to 1.22)
Rural (vs urban)	1.15 (1.12 to 1.19) ^c	0.84 (0.81 to 0.89) ^c	1.03 (0.91 to 1.17)	1.24 (1.08 to 1.41) ^c
Number of doctors' visits ^d	1.02 (1.02 to 1.02) ^c	1.01 (1.01 to 1.01) ^c	1.01 (1.01 to 1.02) ^c	1.01 (1.01 to 1.02) ^c
Hospitalization (vs no)	1.09 (1.06 to 1.12) ^c	0.96 (0.92 to 1.01)	1.17 (1.05 to 1.31) ^c	0.91 (0.79 to 1.04)
Charlson-Romano comorbidity index ^d	0.98 (0.97 to 1.00)	0.96 (0.93 to 0.99) ^c	0.97 (0.92 to 1.02)	0.91 (0.83 to 1.00)
Inflammatory bowel disease (vs no)	1.43 (1.25 to 1.64) ^c	1.32 (1.06 to 1.64) ^c	1.58 (1.06 to 2.36) ^c	0.55 (0.24 to 1.22)

Covariates were assessed -1 to 0 years from index date.

^a Total sample size of CRC and no CRC females ≥ 40 years old with the outcome;

^b Incidence expressed as a proportion and calculated as the number of individuals with the outcome/number of individuals at risk for outcome within group (ie, CRC or no CRC); CRC = colorectal cancer;

^c Statistically significant difference from the referent group;

^d Modelled as a continuous variable and scaled in 10-year increments;

^e Reference category is highest neighborhood income quintile.

reproductive organs,³¹ leading to premature ovarian failure and an increased risk of endometriosis due to hormonal disruptions.³² Radiation can damage tissue and scar the vaginal canal, while chemotherapy may decrease vaginal lubrication and elasticity, contributing to dyspareunia.^{31,33} Additionally, since chemotherapy suppresses the immune system and radiation and surgery can compromise natural infection barriers, patients become more vulnerable to infections that cause pelvic inflammatory disease.³⁴ Nonetheless, given the restricted nature of our sensitivity analyses (eg, among individuals with CRC only) and resultant small sample sizes, future studies with larger sample sizes of individuals with CRC are warranted to fully evaluate the impact of cancer treatment on sexual health outcomes.

Sexual health impacts should be addressed during treatment planning. In 2018, Sutsunbuloglu and Vural's study in Turkey found that 79% of 100 patients, including 84 with CRC, were not informed about sexual side effects, and 83% were unaware of treatment options.³⁵ In 2019, Almont et al. surveyed CRC patients in France and reported that only 11% of female patients recalled having discussions about sexual health with their medical team.³⁶ Finally, a 2023 Canadian study by Oveisi et al. highlighted unmet sexual health needs among 15 female pelvic cancer patients, attributing this to inadequate provider training and limited resources.³⁷ They called for better provider training, counseling, support groups, targeted research, and improved access to specialized sexual health care.

It is important to address both the strengths and limitations of this study. We used a robust provincial dataset that links Population Data BC, which includes demographic and clinical information, with the BC Cancer Registry, known for its high quality due to annual reviews by the North American Association of Central Cancer Registries. However, administrative health databases have challenges, such as variability in data entry and oversight. These databases also lack information on gender diversity and sexual orientation, which may affect health care access and sexual health outcomes. We were not able to consider stage given lack of sufficient data on CRC disease stage in the

administrative databases. We were also not able to capture osteomies, which may be associated with sexual health challenges. Additionally, certain sexual health outcomes may not be accurately captured due to limitations in ICD coding and potential underreporting if individuals do not seek care.³⁸ It is likely we missed outcomes for cohort members not pursuing treatment. CRC patients may indeed be more inclined to access health care due to their cancer history and regular follow-ups. Lastly, our study identified associations, so causation cannot be established; while CRC may increase the risk of these outcomes, the opposite may also be true.

This study provides valuable insights into sexual health outcomes for females with CRC using population-based data. We found higher risks of dyspareunia, pelvic inflammatory disease, endometriosis, and premature ovarian failure in female CRC patients. Critically, we found variations in risk when stratifying analyses according to age (eg, ≤ 39 years and ≥ 40 years), which suggest the complex link between CRC and sexual health. Future research focusing on the development of interventions and supports to reduce sexual health impacts in females with CRC are warranted.

Author contributions

Niki Oveisi (Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing—original draft, Writing—review and editing), Eric C. Sayre (Formal analysis, Methodology, Writing—review and editing), Lori Anne Brotto (Conceptualization, Supervision, Writing—review and editing), Vicki Cheng (Writing—review and editing), Vienna Cheng (Writing—review and editing), Sharlene Gill (Conceptualization, Writing—review and editing), Gillian E. Hanley (Conceptualization, Supervision, Writing—review and editing), Helen McTaggart-Cowan (Conceptualization, Supervision, Writing—review and editing), Stuart Peacock (Conceptualization, Supervision, Writing—review and editing), Meera Rayar (Conceptualization, Supervision, Writing—review and editing), Amirtha Srikanthan (Conceptualization, Writing—review

and editing), Dani Taylor (Writing—review and editing), Mikaela Barnes (Writing—review and editing), and Mary De Vera (Conceptualization, Methodology, Project administration, Supervision, Writing—original draft, Writing—review and editing).

Supplementary material

Supplementary material is available at JNCI: Journal of the National Cancer Institute online.

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Conflicts of interest

None exist.

Data availability

Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through the Data Stewards or their designated service providers. The following data sets were used in this study: Medical Services Plan, Discharge Abstract Database, Consolidation File, Vital Statistics File, PharmaNet, and British Columbia Cancer Registry. You can find further information regarding these datasets by visiting the PopData project webpage at: https://my.popdata.bc.ca/project_listings/18-088/collection_approval_dates. All inferences, opinions, and conclusions drawn in this publication are those of the author(s), and do not reflect the opinions or policies of the Data Steward(s).

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