Examining the Impact of a Cancer Diagnosis on Non-Fatal Self-Injury: A Matched Cohort Study

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Abstract

Purpose: Psychological distress following a cancer diagnosis potentially increases the risk of intentional, non-fatal self-injury (NFSI). The purpose of this work is to evaluate and compare NFSI rates among individuals in Ontario diagnosed with cancer against matched controls with no history of cancer.

Methods: Adults in Ontario diagnosed with cancer from 2007-2019 were matched to two controls with no history of cancer, based on age and sex. The absolute and relative difference in NFSI rates were calculated in the 5 years prior to and after the index date (date of cancer diagnosis/dummy date for controls). Crude difference in differences methods and adjusted Poisson regression-based analyses were used to examine if the change in NFSI rates before and after index differed between cancer patients and controls.

Results: The cohort included 803,740 persons with cancer and 1,607,480 matched controls. In the first year after diagnosis, individuals with cancer had a 1.17-fold increase in NFSI rates (95% CI: 1.03, 1.33) compared to matched controls, after accounting for pre-existing differences in rates of NFSI and other clinical characteristics between the groups. Rates of NFSI remained elevated in the cancer group by 1.09-fold for up to five years after diagnosis (95% CI: 0.99, 1.21).

Conclusions: In this study, NFSI incidence was higher in individuals diagnosed with cancer, with the greatest impact observed in the first year after diagnosis. This work highlights the need for robust and accessible psychosocial oncology programs to support mental health along the cancer journey.

Introduction

Following a cancer diagnosis, individuals are often faced with real risks of death and disability.[1-3] In times of prolonged stress, individuals are particularly susceptible to depressive symptoms or severe manifestations of mental illness, including self-injury or suicide.[4,5] In Canada, rates of death by suicide are 1.3 times higher for individuals with cancer than in the general population.[5] In other countries, suicide rates have been reported to be up to 4.4 times higher than in the general population. [6 - 8] While a significant amount of work has focused on suicide risk among those diagnosed with cancer, [9] broader manifestations of mental illness such as non-fatal self-injury have not been as well studied. We recently established that 3 in 1000 patients will experience a non-fatal self-injury event after their cancer diagnosis.[10] However, how this compares with the general population is unknown. Identifying whether individuals diagnosed with cancer are at an increased risk for non-fatal self-injury is important in devising and funding supportive care programs for cancer patients.

Given this, we sought to compare the rate of non-fatal self-injury among individuals in Ontario diagnosed with cancer against matched controls with no history of cancer.

Methods

A matched cohort study examined under a difference-in-differences framework was conducted using population-based routinely collected administrative data. All databases used in this study were linked using unique encoded identifiers and analyzed at ICES. Studies conducted at ICES using administrative data fall under section 45 of the Personal Health Information Protection Act of Ontario, and do not require research ethics board approval. This study was reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11]

2.1 Data Sources

The Ontario Cancer Registry (OCR) is a provincial database of individuals diagnosed with cancer and is estimated to capture more than 95% of all diagnoses in Ontario.[12] The Registered Persons Database (RPDB) contains demographic information for all individuals that are eligible for the Ontario Health Insurance Plan (OHIP).[13] The Discharge Abstract Database (DAD) contains patient level data including clinical data, demographic data, and administrative data for acute, rehab, chronic, and day surgery institutions in Ontario.[14] The National Ambulatory Care Reporting System (NACRS) captures information on patient visits to hospitals and community based ambulatory care. The Ontario Mental Health Reporting System (OMHRS) contains information from participating hospitals in Ontario that report on patients' psychiatric diagnoses or usage of mental health services. The Ontario Marginalization Index (ON-MARG) is a geographically based index that quantifies the degree of marginalization across Ontario based on Canadian census data.[15]

2.2 Study Cohort

Individuals 18 years or older diagnosed with cancer between January 1, 2007 and March 31, 2019, as identified in the OCR using ICD-O.3 codes,[16] were selected for potential inclusion in the study. Individuals were subsequently excluded if they had more than one cancer diagnosis on the same day, if their date of last contact was missing, if they died prior to their cancer diagnosis, if they were OHIP ineligible on the date of diagnosis, or if their OHIP eligibility lapsed for a period of greater than 90 days in the 5 years prior to diagnosis.

Two control individuals without a cancer history were selected for each individual with cancer, based on a hard match of age and sex. For individuals with cancer, their index date was the date of cancer diagnosis. Individuals in the control group were assigned the same index date as the matched cancer patient. Information was collected for up to 5 years prior to the index date.

Individuals were then followed from the index date until their date of death, the date of their last contact with the health care system, or up to March 31, 2020, whichever occurred first.

2.3 Covariates

All covariates were measured at the index date. Age and sex were categorical variables. Rurality was dichotomized as rural or urban using the Rurality index of Ontario.[17] Material deprivation, a measure of socioeconomic status, was categorized into quintiles with the fifth quintile representing the highest level of deprivation (most deprived).[15] Prior usage of mental health services in the five years prior to the index date was categorized as: no mental health service use, inpatient psychiatric care, outpatient psychiatric care, or other mental health usage, as previously described. [18, 19] The presence of comorbidities in the two years prior to the index date was captured using a modified version of the Elixhauser comorbidity index that excluded cancer diagnoses and was dichotomized as low (0-3) or high (≥4). [20, 21] For individuals with cancer, cancer stage, cancer type, and year of diagnosis (grouped by 2-year intervals) were reported. Cancer stage was reported as per the American Joint Committee on Cancer seventh edition.[22]

2.4 Outcome

The outcome of interest was the rate of non-fatal self-injury. Based on prior work, non-fatal self-injury incidence was defined as an emergency department visit for self-injury (including physical injury or self-poisoning) of intentional (ICD 10- CA codes X61-X84) or undetermined intent (ICD-10-CA codes Y10–Y19, Y28).[23-26]

2.5 Statistical Analysis

The distributions of baseline characteristics were compared between cancer patients and corresponding matched controls. Between-group comparisons of proportions were performed

using weighted standardized differences. [27] A significant imbalance was defined as a weighted standardized difference of ≥ 0.10.[27]

A crude difference-in-difference (DID) analysis comparing absolute rates of non-fatal self-injury, and an adjusted Poisson regression-based analysis were employed. For both approaches, the rate of non-fatal self-injury in the cancer group and the control group were calculated in the first year after the index date (year 0-1) and compared to the rate in the 5 years prior to the index date. Rates in years 0-5 and 1-5 were also calculated and compared to pre-index rates of non-fatal self-injury.

The recorded date of diagnosis for an individual is not necessarily the date that they become aware of their cancer diagnosis or the date that they begin to experience symptoms associated with their diagnosis. In fact, individuals may enter the healthcare system with cancer-related symptoms up to 1 year before they receive a diagnosis, this is referred to as the peri-diagnostic period.[28] For this reason, there is the potential that any non-fatal self-injury events that occur in the year before diagnosis may not be reflective of the baseline rate of self-injury but may instead be related to the cancer diagnosis. To ensure that we captured a true pre-index rate of non-fatal self-injury that was unaffected by the cancer experience, we repeated our analyses excluding the peri-diagnostic period, allowing for a 6-month peri-diagnostic period, by excluding all non-fatal self-injury events and follow-up time in the 6-months immediately preceding the index date. This was repeated allowing for a 12-month peri-diagnostic period.

For the crude analysis, the difference in rates (cancer rate minus control rate) and relative rates (cancer rate divided by control rate) were calculated. The crude DID was then calculated by subtracting the difference obtained in the pre-index period from the difference obtained in the post-index period. The ratio of relative rates was calculated by dividing the relative rate of non-fatal self-injury post-index by the relative rate pre-index.

For the regression-based analysis, we implemented a Poisson regression model utilizing generalized estimating equations to account for the matched design. The univariable analysis modelled the outcome rate and included 3 necessary covariates: exposure (cancer or control), period (pre- or post-index), and an interaction between exposure and period. The multivariable model included any measured covariates that demonstrated imbalance between the cancer and control groups at index. Statistical significance was determined at the $p<0.05$ level, using two-sided tests. All analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC, USA) and R Studio 12.1 (R Foundation, Vienna, Austria).

Results

The final study cohort included 803,740 individuals with cancer and 1,607,480 matched controls (Figure 1). Over the entire study period, there were 6,708 non-fatal self-injury events in the cancer group and 13,070 in the control group. The mean follow-up time among cancer patients was 2,596 days (minimum to maximum: 1 to 4,838 days).

In the 5 years before the index date, there were 9.37 events per 10,000 person-years of follow-up time among individuals with cancer and 8.64 events per 10,000 person-years among controls (RR: 1.08; 95% CI: 1.04, 1.13). In years 0-1 after the index date, there were 10.40 events per 10,000 person-years among individuals with cancer and 8.24 events per 10,000 person-years among controls (RR: 1.26; 95% CI: 1.15, 1.38) (Table 2). The adjusted ratio of relative rates obtained from the regression model was 1.17 (95% CI: 1.03, 1.33) indicating that after accounting for pre-existing differences in rates of non-fatal self-injury between the two groups, rates in the cancer group remained 1.17 times higher after diagnosis compared to the control group (Figure 2). When the analysis was repeated excluding the peri-diagnostic period (assuming a 6-month peri-diagnostic period) we observed a 1.20-fold (95% CI: 1.05, 1.37) increase in non-fatal self-injury

in the cancer group compared to the control group. Assuming a 12-month peri-diagnostic period, we observed a 1.21-fold (95% CI: 1.06, 1.39) increase. The DID of non-fatal self-injury between the cancer and control group in years 1-5 after index was lower compared to years 0-1 (RR: 1.07; 95% CI: 0.95, 1.21) (Figure 3).

Discussion

In this population-based difference-in-differences study, non-fatal self-injury rates were compared between individuals with and without cancer who were matched on demographic characteristics. Individuals with cancer were 1.17 times more likely to experience non-fatal self-injury in the first year following a diagnosis compared to individuals without cancer. While the risk decreases after the first year, rates of self-injury remained elevated by 1.09 times in the 5 years after diagnosis.

While non-fatal self-injury is recognized as a crucial repercussion of critical illness or other traumatic events, such as major burns, it has not been examined in cancer patients.[29, 30] The critical illness literature identified different sets of risk factors for self-injury in different clinical groups.[30] These results suggest that risk factors for self-injury may be context-specific, supporting the need for cancer-specific research to identify risk factors for self-injury among individuals with cancer. The increased rate of non-fatal self-injury following cancer diagnosis observed in this study, particularly in the first year after diagnosis, mirrors trends in suicide following cancer diagnosis.[5-7] Though this study assessed rates of non-fatal self-injury which may include self-injury with suicidal intent as well as self-injury without suicidal intent, these two behaviours have overlapping risk factors such as depression, anxiety, and hopelessness, related to cancer-associated poor mental health.[31 - 33] This work adds to the existing literature on mental illness among individuals with cancer by reporting on non-fatal self-injury as a target outcome for potentially severe manifestations of poor mental health.

When we exclude the peri-diagnostic period from the analysis, we observe a greater difference-in-differences of non-fatal self-injury rates (as represented by the ratio of relative rates) between the two groups. The difference is even greater when we assume a 12-month peri-diagnostic period compared to a 6-month peri-diagnostic period. The peri-diagnostic period is a noted time of distress,[34] creating the potential for increased non-fatal self-injury. By counting these events as part of the "pre" diagnosis period it is possible that we artificially inflate the pre-index rates of non-fatal self-injury in the cancer group, thereby decreasing the observed difference-in-differences measurement.

Recognizing that individuals with cancer have an increased risk for self-injury compared to the general population confirms that cancer patients require additional support and resources to manage poor mental health throughout the continuum of their care. Our prior work has identified that younger age, certain cancer subsites (including head and neck cancers), history of severe psychiatric illness, and prior self-injury were independently associated with risk of non-fatal self-injury. [10] Furthermore, these exposures act synergistically, placing young adults with a prior mental health history at the greatest risk of non-fatal self-injury. Such high-risk patients should be carefully counselled and offered supportive mental health resources throughout their cancer journey. Caring for a patient's psychological wellbeing improves their quality of life, makes them more likely to adhere to medical recommendations, and can also reduce the burden on the health care system by decreasing health care utilization.[35, 36]

One limitation of the study is that we likely underestimate the true incidence of self-injury by only counting non-fatal self-injury events that result in emergency department visits. However, collecting self-injury events from emergency department data has been shown to be an effective method to capture self-injury incidence[37] and, as we use the same methods of data collection for

both the cancer and control groups, our comparisons remain valid. Another limitation of this study is that we did not account for rates of self-injury by cancer type or stage. Rates of self-injury are likely to vary due to different symptom burden and prognoses associated with different cancer types and cancer stages.[10] However, as the purpose of this work was to assess the effect of cancer diagnosis on rates of self-injury, this fell beyond the scope of the current study. The primary strength of this study lies in the cohort and study design which maximizes the ability for causal inference. We adjusted for potential confounders resulting in two comparable groups and accounted for pre-existing differences among the population. The longitudinal data, unique to our datasets, allowed us to capture non-fatal self-injury rates for all individuals diagnosed with cancer in Ontario over a period of 12 years and allowed us to follow these individuals for up to 13 years after diagnosis. As our study takes place within a universal healthcare system, loss of information due to insurance status and loss to follow-up is minimal.

Conclusion

Individuals diagnosed with cancer are at increased risk for non-fatal self-injury compared to those without cancer. This risk is greatest during the first year but remains elevated for up to five years after diagnosis. Non-fatal self-injury is an important outcome of cancer-related mental health that must be considered when devising supportive care programs for cancer patients. The findings from this study reinforce the need to provide robust and accessible psychosocial oncology programs to support mental health along the cancer journey, particularly in the first year after diagnosis, and highlight non-fatal self-injury as an important target outcome for potentially severe manifestations of poor mental health.

Acknowledgement

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References

1. Carlson LE, Angen M, Cullum J, et al. High levels of untreated distress and fatigue in cancer patients. *Br J Cancer.* 2004; 90(12), 2297-2304. doi:10.1038/sj.bjc.6601887.

2. Albrecht TA, Rosenzweig M. Management of cancer-related distress in patients with a hematologic malignancy. *J Hosp Palliat Nurs.* 2012; 14(7), 462-468. doi:10.1097/njh.0b013e318268d04e.

3. Frost MH, Suman VJ, Rummans, T. A., et al. Physical, psychological and social well-being of women with breast cancer: the influence of disease phase. *Psycho-Oncology*. 2000; 9(3), 221-231. doi:10.1002/1099-1611(200005/06)9:3<221::aid-pon456>3.0.co;2-t.

4. Lo C, Zimmermann C, Rydall A, et al. Longitudinal study of depressive symptoms in patients with metastatic gastrointestinal and lung cancer. *J Clin Oncol.* 2010; 28(18), 3084-3089. doi:10.1200/jco.2009.26.9712

5. Klaassen Z, Wallis CJ, Chandrasekar T, et al. Cancer diagnosis and risk of suicide after accounting for prediagnosis psychiatric care: a matched-cohort study of patients with incident solid-organ malignancies. *Cancer*. 2019; 125(16):2886-2895. doi: 10.1002/cncr.32146. Epub 2019 Apr 25. PMID: 31021430.

6. Misono S, Weiss NS, Fann JR, Redman M, Yueh B. Incidence of suicide in persons with cancer. *J Clin Oncol.* 2008; *26*(29), 4731-4738. doi:10.1200/jco.2007.13.8941.

7. Zaorsky NG, Zhang Y, Tuanquin L, Bluethmann SM, Park HS, Chinchilli VM. Suicide among cancer patients. *Nat Commun.* 2019;10(1):207. doi: 10.1038/s41467-018-08170-1. Erratum in: Nat Commun. 2020 Jan 31;11(1):718. PMID: 30643135; PMCID: PMC6331593.

8. Henson KE, Brock R, Charnock J, Wickramasinghe B, Will O, Pitman A. Risk of suicide after cancer diagnosis in England. JAMA Psychiatry. 2019;76(1):51-60. doi: 10.1001/jamapsychiatry.2018.3181. PMID: 30476945; PMCID: PMC6583458.

9. Anguiano L, Mayer DK, Piven ML, Rosenstein D. a literature review of suicide in cancer patients. *Cancer Nurs*. 2012; 35(4):E14-26. doi: 10.1097/NCC.0b013e31822fc76c. PMID: 21946906.

10. Noel CW, Eskander A, Sutradhar R, et al. Incidence and factors associated with non-fatal self-injury after a diagnosis of cancer. *JAMA Netw Open.* 2021;4(9):e2126822. doi:10.1001/jamanetworkopen.2021.26822.

11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573-577. doi:10.7326/0003-4819-147-8- 200710160-00010

12. Robles SC, Marrett LD, Clarke EA, Risch HA. An application of capture-recapture methods to the estimation of completeness of cancer registration. *J Clin Epidemiol*. 1988;41(5):495-501. doi: 10.1016/0895-4356(88)90052-2. PMID: 3367181.

13. Iron K, Zagorski B, Sykora K, Manuel D. Living and dying in Ontario: An opportunity for improved health information. Toronto: Institute for Clinical Evaluative Sciences; 2008.

14. Juurlink D, Preyra C, Croxford R, et al. Canadian Institute for Health Information discharge abstract database: A validation study. Toronto, ON, Canada: Institute for Clinical Evaluative Sciences; 2006.

15. Matheson FI, Dunn JR, Smith KL, Moineddin R, Glazier RH. Development of the Canadian Marginalization Index: A new tool for the study of inequality. *Can J Public Health.* 2012;103(8)(suppl 2):S12-S16.

16. World Health Organization. (2010). ICD-10 International Statistical Classification of Diseases and Health Related Problems. 10th Revision.

17. Kralj B. Measuring "rurality" for purposes of health-care planning: An empirical measure for Ontario. *On Med Rev.* 2000;67(9):33-52.

18. Mahar A. The impact of a severe psychiatric illness on a cancer diagnosis, treatment, and survival. Ph.D. Thesis. Queen's University. Kingston, Ontario, Canada.

19. Mahar AL, Kurdyak P, Hanna TP, Coburn NG, Groome PA. The effect of a severe psychiatric illness on colorectal cancer treatment and survival: A population-based retrospective cohort study. *Plos One,* 2020; *15*(7). doi:10.1371/journal.pone.0235409

20. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005 Nov;43(11):1130-9. doi: 10.1097/01.mlr.0000182534.19832.83. PMID: 16224307.

21. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care.* 2009 Jun;47(6):626-33. doi: 10.1097/MLR.0b013e31819432e5. PMID: 19433995.

22. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol.* 2010;17(6):1471-1474. doi:10.1245/s10434-010-0985-4

23. Bethell J, Rhodes AE. Identifying deliberate self-harm in emergency department data. *Health Rep.* 2009;20(2):35.

24. Mahar AL, Cramm H, Aiken AB, et al. A retrospective cohort study comparing non-fatal self-harm emergency department visits between Canadian veterans living in Ontario and matched civilians. International review of psychiatry. 2019;31(1):25-33.

25. Butler A, Adair C, Jones W, Kurdyak P, Vigod S, Smith M. Towards quality mental health services in Canada: a comparison of performance indicators across 5 provinces. Vancouver BC: Centre for Applied Research in Mental Health & Addiction (CARMHA). 2017;

26. Chartier M. Mental illness among adult Manitobans. Manitoba Centre for Health Policy; 2018

27. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat Simul Comput.* 2009;38:1228-1234.

28. Neal RD, Din NU, Hamilton W, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: analysis of data from the UK General Practice Research Database. *Br J Cancer.* 2014 Feb 4;110(3):584-92. doi: 10.1038/bjc.2013.791. Epub 2013 Dec 24. PMID: 24366304; PMCID: PMC3915139.

29. Fernando SM, Qureshi D, Sood MM, et al. Suicide and self-harm in adult survivors of critical illness: population based cohort study. *BMJ*. 2021 May 5;373:n973. doi: 10.1136/bmj.n973. PMID: 33952509; PMCID: PMC8097311.

30. Mason SA, Nathens AB, Byrne JP, et al. association between burn injury and mental illness among burn survivors: A population-based, self-matched, longitudinal cohort study. *J Am Coll Surg.* 2017 Oct;225(4):516-524. doi: 10.1016/j.jamcollsurg.2017.06.004. Epub 2017 Jul 31. PMID: 28774550; PMCID: PMC7865206.

31. Fox KR, Franklin JC, Ribeiro JD, Kleiman EM, Bentley KH, Nock MK. Meta-analysis of risk factors for nonsuicidal self-injury. *Clin Psychol Rev*. 2015 Dec;42:156-67. doi: 10.1016/j.cpr.2015.09.002. Epub 2015 Sep 12. PMID: 26416295; PMCID: PMC4772426.

32. Ahn MH, Park S, Lee HB, et al. Suicide in cancer patients within the first year of diagnosis. *Psychooncology*. 2015 May;24(5):601-7. doi: 10.1002/pon.3705. Epub 2014 Oct 21. PMID: 25336020.

33. Saad AM, Gad MM, Al-Husseini MJ, et al. Suicidal death within a year of a cancer diagnosis: A population-based study. *Cancer*. 2019 Mar 15;125(6):972-979. doi: 10.1002/cncr.31876. Epub 2019 Jan 7. PMID: 30613943.

34. Montgomery M, McCrone SH. Psychological distress associated with the diagnostic phase for suspected breast cancer: systematic review. *J Adv Nurs*. 2010 Nov;66(11):2372-90. doi: 10.1111/j.1365-2648.2010.05439.x. PMID: 21039773.

35. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med*. 2000 Jul 24;160(14):2101-7. doi: 10.1001/archinte.160.14.2101. PMID: 10904452.

36. Carlson LE, Bultz BD. Benefits of psychosocial oncology care: improved quality of life and medical cost offset. *Health Qual Life Outcomes*. 2003;1:8. Published 2003 Apr 17. doi:10.1186/1477-7525-1-8

37. Bethell J, Rhodes AE. Identifying deliberate self-harm in emergency department data. *Health Rep*. 2009;20(2):35.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, explain how loss to follow-up was addressed	5
		(*e*) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	Report numbers of outcome events or summary measures over time	7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7 NA NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Figure 1. Cohort Creation

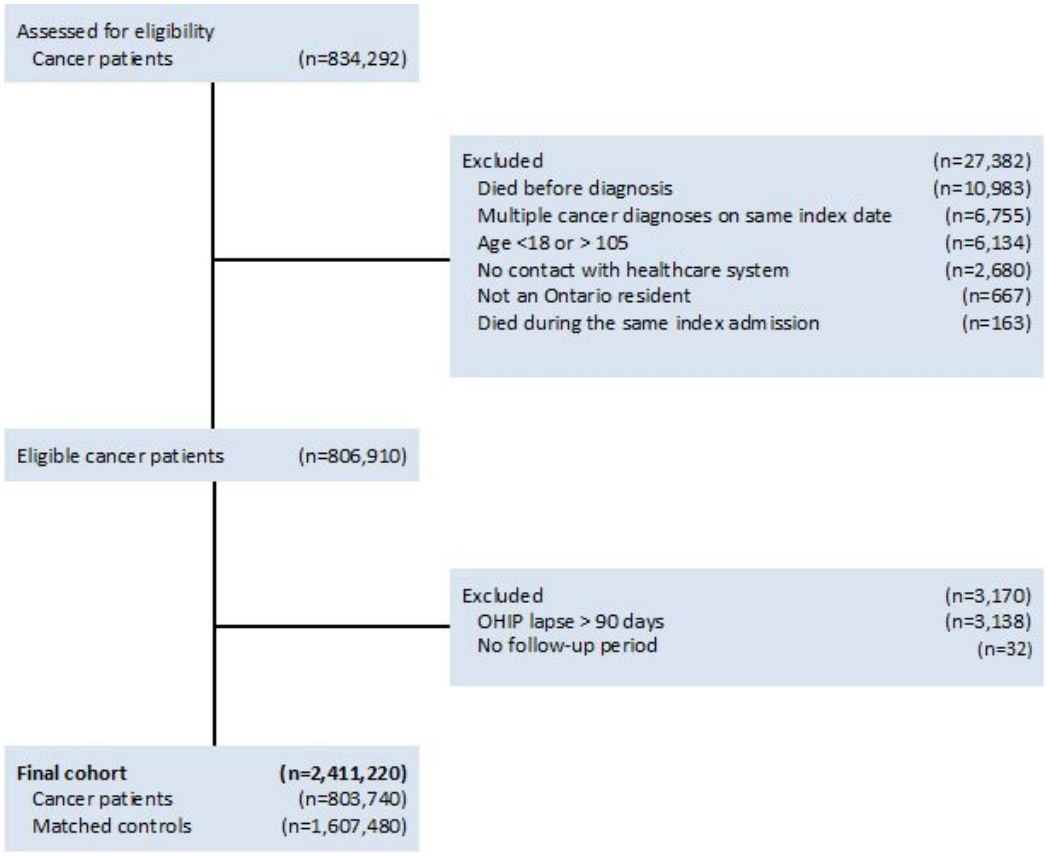

Figure 2. Forest Plot of Multivariable Models (Adjusted for Elixhauser Index) in Years 0-1

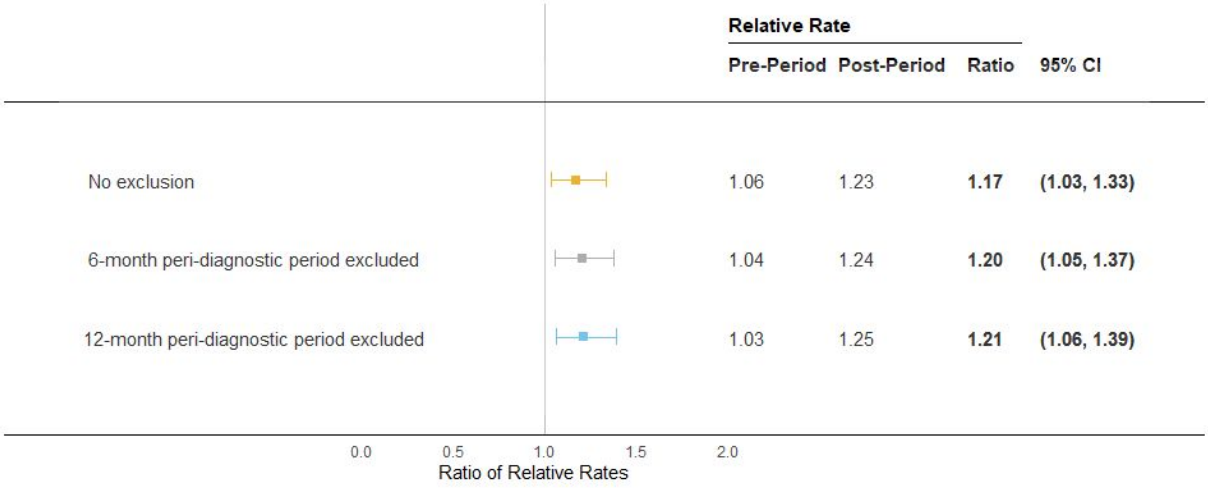

Figure 3. Forest Plot of Multivariable Models (Adjusted for Elixhauser Index) in Years 0-5

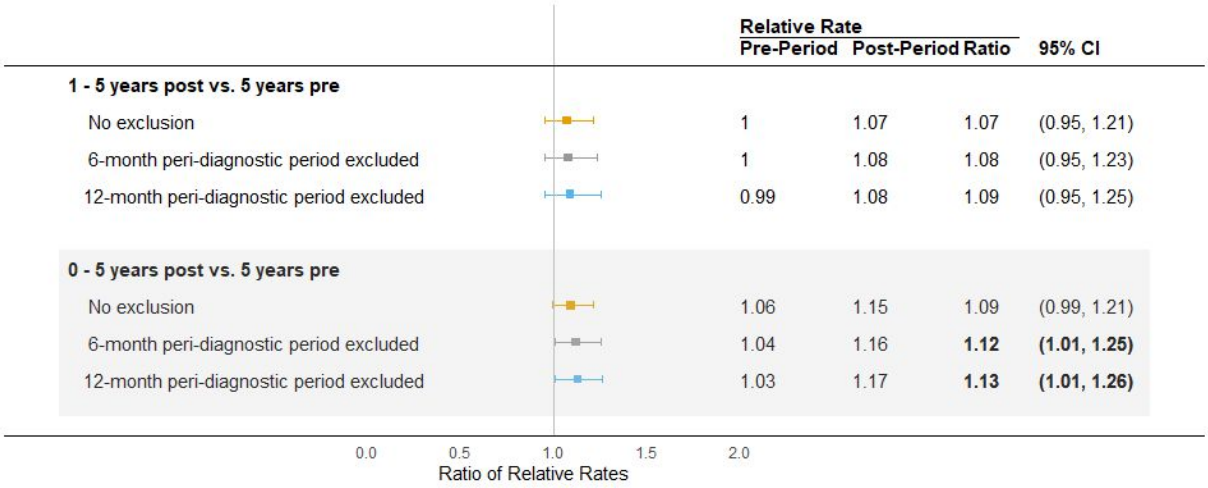

Table 1. Distributions of Baseline Characteristics among Cancer Patients and Cancer-free Controls

Characteristic	No. of Individuals (%)		Standardized Difference
	Cancer-free Controls	Cancer	
Sample Size	1,607,480	803,740	NA
Age at Diagnosis			
18-39	75,689 (4.7%)	37,827 (4.7%)	0.00
40-49	129,643 (8.1%)	64,616 (8.0%)	
50-59	292,016 (18.2%)	146,033 (18.2%)	
60-69	431,711 (26.9%)	215,979 (26.9%)	
≥70	678,421 (42.2%)	339,285 (42.2%)	
Sex			
Female	800,122 (49.77%)	400,061 (49.77%)	0.00
Male	807,358 (50.23%)	403,679 (50.23%)	
Rurality			
Urban	1,449,450 (90.26%)	721,830 (89.87%)	0.01
Rural	156,331 (9.74%)	81,369 (10.13%)	
Deprivation Quintile			
Q1 (least)	320,027 (20.08%)	160,154 (20.07%)	0.00
Q2	319,160 (20.02%)	160,118 (20.06%)	
Q3	315,001 (19.76%)	158,534 (19.86%)	
Q4	319,604 (20.05%)	159,311 (19.96%)	
Q5 (most)	320,046 (20.08%)	160,005 (20.05%)	
Elixhauser Comorbidity Score			
0-3 (low)	1,500,636 (93.35%)	727,865 (90.56%)	**0.10**
4+ (high)	106,844 (6.65%)	75,875 (9.44%)	
Prior Mental Health Services Usage			
No Mental Health Use	991,004 (61.65%)	486,962 (60.59%)	0.02
Inpatient	13,503 (0.84%)	6,583 (0.82%)	
Outpatient	29,524 (1.84%)	14,246 (1.77%)	
Mental Health Use	573,449 (35.67%)	295,949 (36.82%)	
Year of Diagnosis			
2007-2008	-	120,304 (14.97%)	NA
2009-2010	-	127,051 (15.81%)	
2011-2012	-	132,911 (16.54%)	
2013-2014	-	132,133 (16.44%)	
2015-2016	-	136,091 (16.93%)	
2017-2018	-	139,179 (17.32%)	
2019	-	16,071 (2.00%)	
Cancer Site			
Bone, Sarcoma, and PNS	-	1,647 (0.20%)	NA
Breast	-	112,300 (13.97%)	
Broncho-pulmonary	-	103,831 (12.92%)	
CNS	-	10,597 (1.32%)	
Endocrine	-	32,234 (4.01%)	
Gastro-intestinal	-	151,560 (18.86%)	
Genito-urinary	-	169,990 (21.15%)	
Gynecologic	-	49,417 (6.15%)	
Haematopoietic and lymphoma	-	92,175 (11.47%)	
Head and Neck	-	19,116 (2.38%)	

Skin	-	36,748 (4.57%)	
Other	-	24,125 (3.00%)	
Cancer Stage			
0	-	1,732 (0.22%)	NA
I	-	149,293 (18.57%)	
II	-	144,163 (17.94%)	
III	-	93,937 (11.69%)	
IV	-	107,763 (13.41%)	
Missing/Unknown	-	306,852 (38.18%)	

Imbalance of Elixhauser score is indicated by a standardized difference of ≥ 0.10. This covariate was adjusted for in the multivariable model.
PNS = peripheral nervous system
CNS = central nervous system

Table 2. Difference-in-Differences Calculation of Non-Fatal Self-Injury in the First Year After Diagnosis

Period	Exposure	N	NFSI Frequency	Follow-up Time (Person-years)	Rate (per 10,000)	Difference in Rates	Relative Rate	Estimates	
								DID	Ratio of Relative Rates
Pre-Diagnosis	Cancer	792,724	3,704	3,952,538	9.37	0.73	1.08	1.43	1.16
	Controls	1,585,448	6,803	7,870,255	8.64				
Post-Diagnosis	Cancer	792,724	716	688,600	10.40	2.16	1.26		
	Controls	1,585,448	1,264	1,534,334	8.24				

Pre-diagnosis period is 5 years before diagnosis
Post-diagnosis period is years 0-1 after diagnosis
DID: Difference in Differences (Difference in the post-index period – Difference in the pre-index period)
Ratio of Relative Rates: Relative Rate in the post-index period/ Relative Rate in the pre-index period