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Original Article

Access to radiotherapy and its association with cancer outcomes in a high-income country: Addressing the inequity in Canada

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A B S T R A C T

Background and purpose: Canada is a high-income country with universal healthcare. In international comparisons, its overall level of access to radiotherapy appears sufficient. However, challenges exist due to Canada's large geographic area and small population density. The association between access and cancer outcomes nationally has not yet been described.

Materials and methods: We quantified geographic accessibility for 2012 using the linear distance from each Canadian health region centroid to the nearest radiotherapy center. We used geospatial analytic techniques to detect clusters of age-standardized all-cancer mortality-to-incidence ratios (MIRs) across health regions, from 2010–2012. Global ordinary least squares (OLS) and geographically-weighted regression (GWR) were conducted to examine relationships between distance and MIR, adjusting for sociodemographic factors.

Results: Median distance from health region centroid to nearest radiotherapy center was 101.73 km (range 1.14–2095.12). One cluster of worse outcomes (MIR range 0.45–0.88) involved most of northern Canada, with a second cluster of better outcomes (MIR range 0.40–0.41) in southern British Columbia. In both regression models, regions with longer distance to radiotherapy center ($ß$ = 0.0001), increased smoking ($ß$ = 0.002), and poorer food security ($ß$ = –0.003) were significantly associated with worse outcomes (OLS R^2 = 0.70, GWR R^2 = 0.74). Distance remained independently associated with MIR for lung and colorectal cancer subgroups, but not breast and prostate.

Conclusions: A clear north–south discordance in cancer outcomes exists in Canada, with poorer outcomes in the north, while radiotherapy centers are concentrated along the south. Increased distance to radiotherapy, along with other sociodemographic and health-system factors, are associated with poorer cancer outcomes. Our study could be replicated, particularly in other high-income countries, to help identify national patterns and regional disparities in access and outcomes.

Cancer is the leading cause of death and premature mortality in Canada [1]. Despite being a high-income country with a universal healthcare system, regional disparities in cancer outcomes persist. This may be related to poorer accessibility to cancer services, particularly for low-income populations, those residing in rural and/or remote areas, the elderly, and new immigrants [2]. Indeed, disparities in access to healthcare were recently highlighted by the Lancet Commission as one of Canada's major challenges [3].

Radiotherapy is part of the Universal Health Coverage Package in many high-income countries, and is needed in more than half of all cases of cancer to cure localized disease, palliate symptoms, and control disease in incurable cancers [4,5]. Radiotherapy also has a population benefit on overall survival when optimally used [6]. An analysis of global radiotherapy capacity by the International Atomic Energy Agency (IAEA) in 2012 demonstrated that Canada was among the most well-resourced, with less than 500,000 people being served by one radiotherapy unit [7]. However, despite having enough radiotherapy capacity in the country as a whole, Canada's large geographic area and small population density create unique challenges in providing equal geographic accessibility to this specialized cancer treatment. Indeed, longer distance, or travel time,

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to radiotherapy center is a significant barrier to accessing radiation therapy, and has been associated with decreased utilization of radiotherapy across multiple disease sites and in the palliative setting [8,9].

As most radiotherapy centers are located in larger, more populated tertiary centers of southern Canada, this suggests that residents of the northern regions, which are furthest away from radiotherapy centers, might experience sub-optimal access and poorer cancer outcomes. While previous studies have examined the impact of geographic accessibility to radiotherapy on its utilization at the regional level,[8,9] none to date have examined its association with cancer outcomes at a national level.

Our aim was to first characterize regional variations in: (1) geographic accessibility to radiotherapy, and (2) cancer outcomes across Canada. We then sought to investigate the association of geographic accessibility with cancer outcomes, after controlling for sociodemographic factors. Addressing this knowledge gap is a critical first step towards future planning of radiotherapy service delivery in Canada. Our study may also serve as a blueprint for examining access to radiotherapy in other countries worldwide, highlighting regional disparities that can help inform national radiotherapy planning, particularly in high-income countries where overall levels of access may appear sufficient.

Methods and materials

Study design

We conducted a cross-sectional study using cancer incidence and mortality data per health region, which are administrative areas within each Canadian province defined by provincial ministries of health. They provide the most granular level for which cancer data are consistently available across the country.

Data sources and statistical analyses

Distance to nearest radiotherapy center

We obtained a list of Canadian radiotherapy centers from The Directory of Radiotherapy Centers, an electronic and centralized database of international radiotherapy centers created and maintained by the IAEA [10]. This list was supplemented with data from local Canadian experts and from the Canadian Association of Radiation Oncology. We filtered the database to include only radiotherapy centers that were operational in 2012, to most closely match the time-period for our incidence and mortality data. We then applied Geographic Information Systems (GIS) software (QGIS v.2.18) to map all Canadian health regions using 2015 boundary files from Statistics Canada [11]. The geographic center (centroid) of each health region was auto-calculated. We measured the linear distance from each health region centroid to the nearest radiotherapy center, irrespective of provincial boundaries.

Mortality-to-incidence ratios

We obtained all-cancer incidence and mortality rates for each health region from Statistics Canada, which were age-standardized to the 2011 Canadian Census population and available in three-year aggregates [12,13]. To account for differences in case-mix of cancer incidence across health regions, we also obtained tumour-specific incidence and mortality rates for lung, breast, prostate and colorectal cancers, which are the four cancer sites with the highest incidence in Canada. We used the most recently available data from 2010 to 2012 for all provinces and territories, apart from Québec, for which the most recently available incidence data were from 2008 to 2010. Age-standardized mortality-to-incidence ratios (MIRs) for each health region were calculated as the age-standardized mortality rate divided by the age-standardized incidence rate.

Sociodemographic variables

We calculated population density per health region using the geographic area and population count from the 2011 Canadian Census. We obtained sociodemographic and lifestyle variables by health region from the 2011 National Household Survey (NHS), and the 2011–2012 Canadian Community Health Survey (CCHS) administered by Statistics Canada (Table 1) [14,15]. Both were voluntary surveys with the 2011 NHS sampling 30% of all private dwellings in Canada, and the 2011–2012 CCHS representing more than 97% of Canadians aged 12 and over. The CCHS did not include persons living in Région du Nunavik and Région des Terres-Cries-de-la-Baie-James in Québec. All variables available in both surveys that could have a potential association with cancer incidence and mortality were considered (Table 1). Aboriginal identity, as defined in the survey, included persons who reported being an Aboriginal person, including First Nations, Métis, or Inuit, and/or those who reported Registered or Treaty Indian status, and/or those who reported membership in a First Nation or Indian band [14]. Definitions for food-secure households were based on the CCHS Food Security module, which included questions reflecting food security status, such as not being able to afford eating balanced meals, being hungry but not eating, and not eating for the whole day [16].

Geospatial and regression analyses

To examine whether and where clustering of high or low all-cancer MIRs occurred by health regions across Canada, we calculated the Moran's I statistic, which is commonly used as a measurement to describe spatial relationships between variables (spatial autocorrelation) in numerous fields, including health [17]. A positive Moran's I would indicate clustering of regions based on MIR, a negative value dispersion, and a value of zero randomness [18]. The Local Indicators of Spatial Association (LISA) test was then applied to identify where clustering of high or low MIRs occurred among the health regions [19]. For this test, we chose a more stringent significance level of $p \leq 0.01$ (rather than 0.05), to reduce the risk of Type I errors due to multiple comparisons [18].

To explore the variables that predicted all-cancer MIR, we first conducted univariate analyses with distance to radiotherapy center and each sociodemographic variable as the independent variables. All significant ($p \leq 0.05$) independent variables in the univariate analyses were included in a step-wise backwards elimination method of multiple regression analysis (ordinary least squares, OLS). Variables were dropped if found to have high multi-collinearity within the model (based on a Variance Inflation Score (VIF) >10), and then in order of least significance, until all remaining variables were significantly associated at $p \leq 0.05$.

The analysis was re-run using geographically-weighted regression (GWR). GWR is a regression modeling method that accounts for spatial structure and can therefore produce a more robust model than OLS when spatial dependency is suspected [20]. The global R^2 of the OLS and GWR models were compared to assess the model of fit, with a higher R^2 indicating that a greater proportion of the variance in MIR was explained by the model. We also used the Akaike Information Criterion (AIC) to compare the two models, with a lower value indicating higher accuracy [21].

We controlled for differences in cancer incidence case-mix by including lung cancer incidence as an independent variable in the regression analysis for all-cancer MIR. We also repeated the OLS regression analysis separately with lung, breast, prostate and colorectal MIRs, excluding lung cancer incidence as an independent variable.

Table 1
Descriptive statistics and univariate association of each independent variable with all-cancer age-standardized mortality-to-incidence-ratio.

Variable	Description	Median	Minimum	Maximum	P-value
Distance	Linear distance from health region centroid to nearest radiotherapy center (kilometers)	101.73	1.14	2095.12	<0.001
Food security	% Households that were food secure*	92.50	60	97	<0.001
Education	% High school graduates aged 25–29 as a proportion of population aged 25–29◇	86.35	27.70	95.80	<0.001
Income	% Employment rate among 25–54 years, as a proportion of population aged 15 years and over◇	79.85	47	87.50	<0.001
Housing	% Households that were suitable, referring to whether a private household is living in suitable accommodations according to the National Occupancy Standard◇	96.24	62.86	98.20	<0.001
Immigrant population	% Immigrant population as a proportion of the total population◇	7.09	0	59.63	0.001
Aboriginal population	% Self-identified Aboriginals as a proportion of the total population◇	4.29	0.45	96.03	<0.001
Body mass index	% Self-reported overweight or obese of those ≥18 years of age	57.85	33.40	71.10	0.045
Diet	% Reporting consuming fruit and vegetables ≥ 5 times per day*	37.70	13	54	0.014
Physical activity	% Reporting moderately active or active physical activity during leisure-time*	53.25	37.30	72.10	0.982
Alcohol consumption	% Heavy drinking (males reporting having ≥5 drinks, or women ≥4 drinks, on one occasion, at least a month in the past year)*	19.90	11.60	31.20	<0.001
Smoking	% Current smoker, daily or occasional*	22.25	10	59.70	<0.001
Population density	Population count divided by geographic area'	11.39	0.02	4705.18	0.062
Lung cancer incidence	Lung cancer incidence per 100,000 persons	74.60	45.40	238	<0.001

* Data obtained from the 2011–2012 Canadian Community Health Survey (Statistics Canada) and excludes two Quebec health regions (Région du Nunavik and Région des Terres-Cries-de-la-Baie-James).
◇ Data obtained from the 2011 National Household Survey (Statistics Canada).
' Data obtained from the 2011 Canadian Census (Statistics Canada).

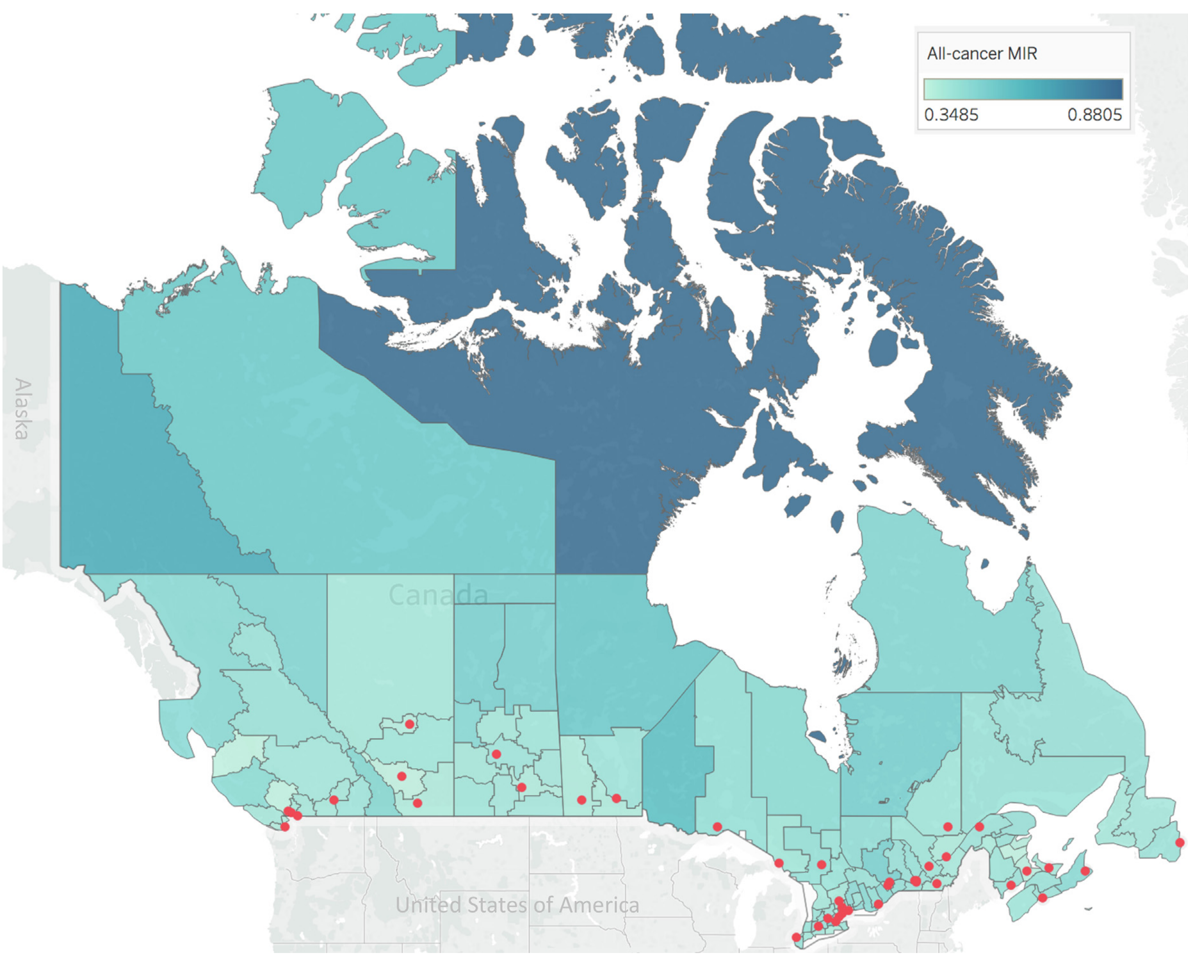

Fig. 1. All-cancer mortality-to-incidence ratios (MIR) by Canadian health region between 2010–2012, with radiotherapy centers in 2012. Dots represent radiotherapy centers.

We used GeoDa v1.12.1.59 to calculate the Moran's I statistic and GWR analyses, and JMP v.12 for all other statistical analyses. Choropleth maps were generated using Tableau v.10.4.

Results

The median geographic area of the 112 health regions in Canada was 16,428 km^2 (IQR 4,072–44,686), and the median population size was 162,515 (IQR 75,586–391,976) in 2011. Thirty-seven percent (41/112) of all health regions had one radiotherapy department in 2012, including two health regions with more than one. Mapping of the radiotherapy centers revealed that nearly all were located along the country's southern border (Fig. 1). Median linear distance from health region centroid to nearest radiotherapy center was 101.73 km (interquartile range: 36.97–230.88). The closest distance was from British Columbia's Vancouver Health Service Delivery Area (1.14 km), and the furthest distance from Nunavut (2095.12 km).

For the 112 health regions in Canada from 2010–2012, the median all-cancer MIR was 0.43. The lowest all-cancer MIR was in Ontario's York Regional Health Unit (0.35), and the highest all-cancer MIR was in Nunavut (0.88).

The global Moran's I for all-cancer MIR was 0.35 (p = .001), indicating statistically significant spatial autocorrelation with clustering of health regions. Mapping of the clusters and further analysis using the LISA test revealed two significant clusters. One cluster of significantly higher all-cancer MIRs (worse outcomes) was observed in northern Canada, including two of the three territories (Northwest Territories = 0.55, Nunavut = 0.88), the most northern region in Manitoba (Northern Regional Health Authority = 0.56), and several of the most northern regions in Québec (Région des Terres-Cries-de-la-Baie-James = 0.61, Région du Nunavik = 0.49) and Ontario (Porcupine Health Unit = 0.47, Thunder Bay District Health Unit = 0.45) (Fig. 2). A second cluster of significantly lower all-cancer MIRs was observed in the southern regions of British Columbia (Fraser North and East Health Service Delivery Areas, at 0.40 and 0.41, respectively).

Descriptive statistics for each independent variable considered in the regression analysis for all-cancer MIR are presented in Table 1. In univariate analyses, distance to radiotherapy and each sociodemographic variable were significantly associated with all-cancer MIR ($p \leq 0.05$), except for physical activity and population density, which were excluded from regression analyses.

In the OLS regression model for all-cancer MIR, the proportion of Aboriginal peoples and housing variables were excluded due to high multi-collinearity (VIF = 12 and 11, respectively). Longer distance to radiotherapy, poorer food security and higher smoking rates were found to be statistically significant predictors of increased all-cancer MIR (worse outcomes) (R^2 = 0.70, F = 81.85, p < .01, AIC = −415.70) (Table 2). These same variables remained significant in the GWR model and resulted in an improved fit when accounting for spatial dependency (R^2 = 0.74, AIC = −426.99).

Fig. 2. Clustering of all-cancer mortality-to-incidence ratios (MIR) by Canadian health region between 2010–2012.

Table 2
Significant predictors of all-cancer age-standardized mortality-to-incidence-ratio based on multiple regression using ordinary least squares (OLS) and geographically-weighted regression (GWR).

Unstandardized beta coefficient	OLS	Standard Error	p-Value	GWR	Standard Error	p-Value
Distance	0.00011	0.00002	<0.001	0.00013	0.00002	<0.001
Food security	−0.00319	0.00114	0.006	−0.00297	0.00104	0.004
Smoking	0.00196	0.00064	0.003	0.00170	0.00067	0.011
R-squared	0.70			0.74		
Akaike Information Criterion	−415.70			−426.99		

When repeating the OLS regression analysis by tumour site, distance to radiotherapy remained significantly associated to MIR in the final regression model for lung ($ß = 0.0002$, SE = 0.00003, $p < .001$) and colorectal cancers ($ß = 0.00005$, SE = 0.00002, $p = .011$), but not for breast and prostate cancers (supplementary Table 1).

Discussion

Canada is a high-income country with a universal healthcare system. Despite this, regional disparities in cancer outcomes exist across the country, which may be due to inequitable access to cancer services, including radiotherapy. Our novel study has described the variations in geographic accessibility to radiotherapy and cancer outcomes across Canada, and identified an association between geographic accessibility to radiotherapy and cancer outcomes after controlling for sociodemographic factors.

A clear north–south geographic pattern of cancer MIRs emerged, with poorer MIRs in the northern regions of Canada. Moreover, there was a wide variation in geographic accessibility to radiotherapy across Canada, as measured by distance to radiotherapy center. All radiotherapy centers were in southern Canada, despite the observed need in the north. Notably, no radiotherapy centers existed in any of the Canadian territories (the northernmost regions of Canada), requiring a travel distance of over 2000 kilometers in the most extreme case for Nunavut.

The current placement of radiotherapy centers in southern Canada is understandable given its higher population density. Despite the lower population density in northern Canada, opening new radiotherapy centers in the north is one possible solution to increase accessibility. Indeed, following our study time-period (2010–2012), two new radiotherapy centers opened closer to the northern regions in British Columbia and Alberta. Other studies have shown increased radiotherapy utilization and reduced rates of mastectomy after the opening of new radiotherapy centers in underserved regions; however, these benefits are not necessarily uniform across the region [8,22]. In addition, most northern regions tend to be rural, and opening new rural centers may not necessarily increase utilization for several patient and provider-related reasons, including awareness of radiotherapy as a treatment option [23]. While work is ongoing to explore the optimal strategy of choosing locations for any new radiotherapy center, [24] it will be important to integrate both quantitative and qualitative data in determining how best to deliver radiotherapy to underserved populations.

Global assessments of radiotherapy access have typically displayed high-income countries, including Canada, as having adequate access to radiotherapy based on country-wide averages. However, our findings demonstrate that disparities exist at a regional level due to geographic accessibility, and that increased distance to radiotherapy centers, particularly for Canada's northern regions, contributes to these regions' worse cancer MIRs, independent of sociodemographic and lifestyle factors. To this end, while studies on disparities in access to cancer services have traditionally focused on low-and-middle-income countries, we propose to include within-country disparities on global maps of radiotherapy access (Fig. 3), to highlight the currently easily overlooked disparities that exist particularly in high-income countries.

Despite previous studies demonstrating the critical role that geographic accessibility can play in radiotherapy utilization [8,9], our study is the first to demonstrate its association with cancer outcomes on a national level within Canada. Other high-income countries face similar issues, particularly those with a large geographic area and low population density. Indeed, an Australian study linking geographic accessibility and cancer outcomes showed a 6% increase in mortality risk for every 100-kilometer increase in distance to radiotherapy center among rectal cancer patients in the state of Queensland [25]. Few other studies have examined the impact of geographic access to radiotherapy on cancer outcomes, particularly in high-income countries. While our findings are also concordant with a recent global analysis of radiotherapy access showing that countries with a greater density of radiotherapy units demonstrated decreased cancer MIRs [26], this highlights again that the benefits of such access are not necessarily reflected uniformly across the country, due to geographic accessibility. Our methodological approach consolidating regional data across the whole country allowed us to identify regional disparities and national patterns in access that could otherwise have been missed using traditional methods siloed to one region, or that were diluted through country-wide averaging.

Distance to radiotherapy center was not the only significant factor associated with cancer MIRs. Higher rates of food insecurity and smoking were also related to worse cancer outcomes across Canada. Food insecurity was similarly one of the strongest factors mediating the association between income and cancer deaths in a recent county-level study in the United States [27]. It plays a significant role among cancer patients given the often-intense treatment protocols required, and the disease process itself, such as cachexia, impacting both survival and quality of life [28]. Cigarette smoking has also been a long-established significant risk factor for cancer, and its link to cancer mortality is clear, with an estimated 80% of lung cancer deaths being attributable to cigarette smoking in Canada [29].

Longer distance to radiotherapy center, and higher rates of food insecurity and smoking all remained significantly associated with increased MIRs in the GWR model. This not only suggests that the combination of these variables is significantly associated with cancer outcomes, but also the presence of a geographic association between them. Rural residents in Canada, who typically live further away from radiotherapy centers, have reported higher all-cause mortality rates, higher rates of smoking, and higher rates of food insecurity [30]. In addition, many are regions with a higher proportion of Indigenous peoples. Notably, Nunavut, comprising of about 85% Inuit, has the highest rates of smoking and food insecurity across Canada [30]. While we had initially included the proportion of self-identified Aboriginal peoples per health region in the regression analyses, it was excluded due to a high correlation with the remaining sociodemographic and lifestyle variables. Given the dearth of literature on access to radiotherapy among Indigenous populations, further work is required to explore the impact of distance to radiotherapy center among this population.

Our study also showed a small cluster of regions in southern British Columbia with significantly lower MIRs compared to the rest of Canada. As these regions were not located closest to a radiotherapy center, their improved cancer outcomes are likely, in part, due to other factors, such as the province's lower rates of smoking, which is even lower among the southern regions [31]. Southern British Columbia also has a different case-mix of cancer incidence, exhibiting lower rates of lung cancer and higher rates of other histologies such as skin cancer [31], which could skew the observed regional MIRs given their contrasting mortality rates. Although distance to radiotherapy center may not entirely explain these regions' improved outcomes, it did remain associated with MIRs in our regression model independent of lung cancer incidence and other sociodemographic factors, including smoking. Furthermore, distance continued to be independently associated with MIR when analyzed by tumour site, for lung and colorectal cancers. This non-uniform association across disease sites is consistent with a previous study examining the relationship between travel time to a radiotherapy center and its utilization in British Columbia [8]. Here, the odds of utilization significantly decreased after 20

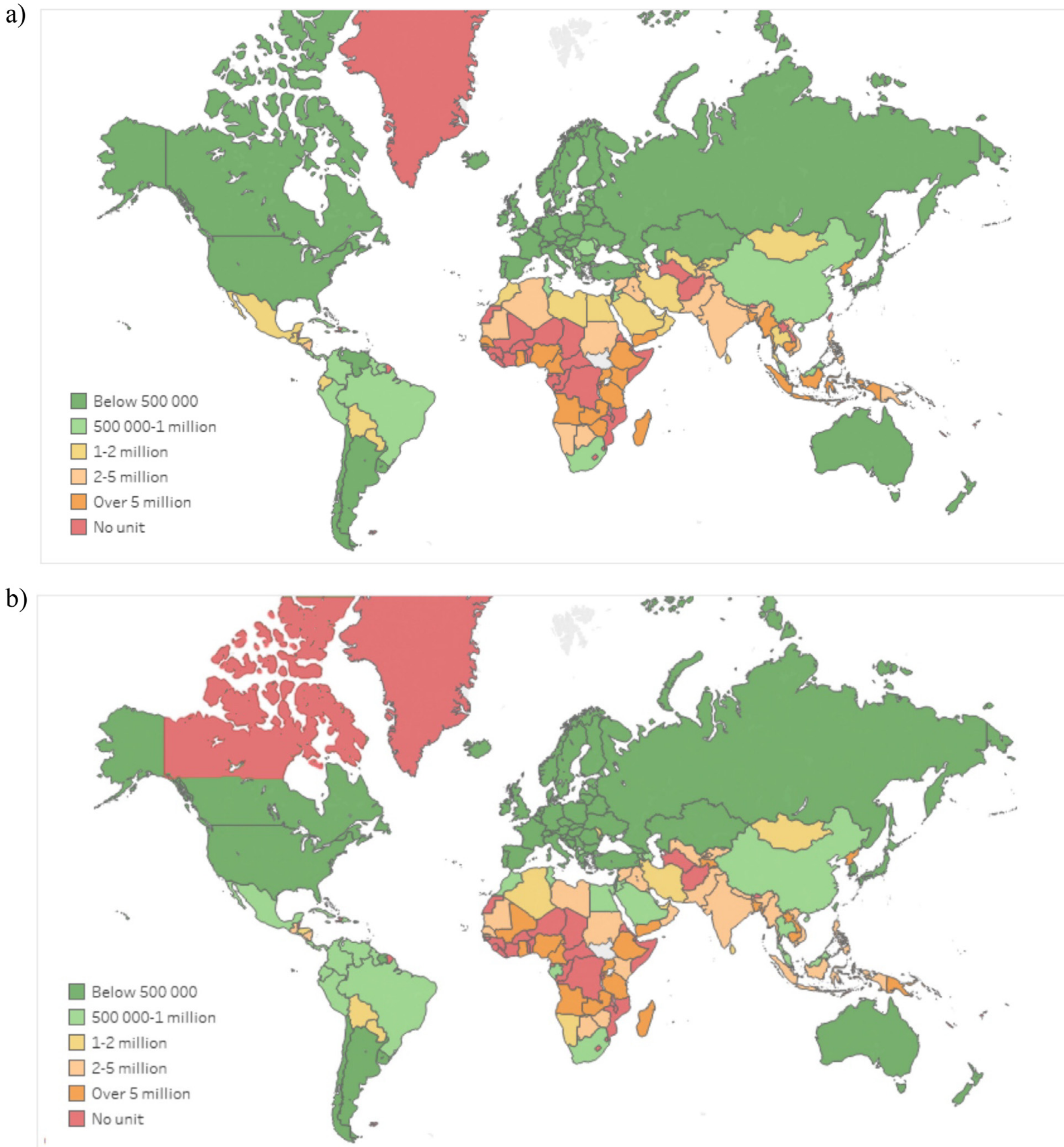

Fig. 3. Global radiotherapy coverage map (number of people served by one radiotherapy unit) based on data from The Directory of Radiotherapy Centers [10]. a) Original figure produced by the International Atomic Energy Agency (IAEA), displaying access using normal conventions of country-wide averaging (2012) [7]. Uniform adequate access is seen across Canada. b) Modified figure with updated data from 2018, incorporating results from the current study which displays within-country inequities in Canada. This now demonstrates a lack of radiotherapy units in the country's territories and was previously not apparent. Reproduced and adapted with permission from the IAEA.

minutes (driving time) for lung cancer patients, 2 hours for breast cancer patients and for all-cancers, and was relatively independent of driving time for genitourinary cancer patients. While this study did not examine colorectal cancer patients separately, the positive association between distance to radiotherapy and rectal cancer mortality has been previously shown [25]. Reasons behind these differences by disease site require further exploration, but could include stage, access to cancer surgery and patient preferences.

Our study has several limitations. As our data were drawn at the health region level, our ecological study provides only a high-level account of the current state of cancer outcomes, radiotherapy access, and the associated variables, but cannot be interpreted at the level of the individual patient. In addition, distance to radiotherapy center was the only direct health service accessibility variable in our model. Other potential confounding variables were not accessible at the health region level for this analysis, such as wait times for treatment or distance to a cancer surgery center. We also could not examine MIRs for disease sites where radiotherapy is often the primary modality of oncologic treatment, such as with cervix or head and neck cancers, and could not adjust for differences in cancer stage between regions.

In addition, the MIR is a relatively crude measure of cancer outcomes. A more robust measure could include survival; however, survival data are only available from Statistics Canada at a provincial level, and exclude the territories where the most significant issues in access to radiotherapy were identified. As such, we felt that with only ten provinces, this loss of granularity would result in a dataset with insufficient power to support regression analyses. In many settings, MIRs have been increasingly used to assess the efficacy of cancer control programs within [32], and between countries [26]. It can highlight disparities in access and uptake of treatment, as in our study examining distance to radiotherapy. However, other factors influencing MIRs include screening and prevention practices, which must also be considered. In our study, two examples of such practices were reducing smoking and improving food security. In addition, radiotherapy is just one of several components of cancer treatment required to improve patient outcomes, including surgery and chemotherapy. Our findings regarding distance to radiotherapy can therefore be viewed as a proxy reflecting access to tertiary care centers where these other cancer services are often provided. However, geography may have more of an impact on access to radiotherapy because it often can only be offered in larger tertiary care centers with greater infrastructure. Despite these limitations, the use of GIS to conduct cluster analyses of all-cancer MIRs provides a unique aspect that helps to highlight important insights on disparities within Canada as a first step. These data can then be used to inform further studies describing radiotherapy accessibility in Canada and other high-income countries on a more granular level.

In conclusion, our findings demonstrated a clear geographic pattern of cancer outcomes and radiotherapy centers in Canada, with worse outcomes in the north, and radiotherapy centers in the south. We also found an independent association between increased distance to radiotherapy and poorer cancer outcomes, which persisted for lung and colorectal cancer subgroups. The implications of our findings may extend well beyond our country's borders. Our study highlights the wide range of factors that can contribute to poorer cancer outcomes, which can impact any country, including those that may be prominent but less well-documented in high-income countries such as geography and how vulnerable populations are impacted. Our approach of analyzing regional data nationally, combined with the use of real-world observations rather than the commonly employed modeling methods to measure the impact of access, are strengths in study design which could be replicated in many countries. Ultimately, we hope this can help to inform national radiotherapy programs as part of a wider cancer plan, including awareness, prevention, early detection and treatment.

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Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2019.09.009.

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