Title: Comparing cancer incidence, stage at diagnosis and outcomes of Manitoba First Nations living on-reserve and off-reserve: A Retrospective Analysis

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None.

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Abstract

Background: Significant cancer-related disparities exist between First Nations (FN) and non-Indigenous Canadians, however, no study has investigated differences between status FN living on-reserve and off-reserve. The objectives of this study were to compare cancer incidence, stage at diagnosis and mortality outcomes in status FN people living on-reserve and off-reserve.

Methods: A retrospective analysis of population-level administrative health databases in Manitoba was conducted. Cancers diagnosed between April 1, 2004 and March 31, 2011 were linked with the Indian Registry System and five provincial databases. Differences in baseline characteristics, cancer incidence, site and stage at diagnosis were compared between status FN living on and off reserve. Linear regression models examined trends in annual cancer incidence. Cox proportional hazard regression models examined mortality.

Results: FN living on-reserve were significantly older, with higher Charlson comorbidity scores. A lower proportion of on-reserve patients were diagnosed with Stage I cancers than off-reserve patients (21.7% vs. 26.9%, $p = 0.196$). There were no differences in annual cancer incidence between groups. Adjusted incidence of cancer over the combined study years was higher in the off-reserve group (287.9 vs. 247.9 per 100,000, $p = 0.0243$). No significant differences in mortality were found.

Interpretation: The lower proportion of on-reserve patients diagnosed with cancer at Stage I is concerning, suggesting less access to screening services or potential delays in diagnosis. Further research is needed to understand patterns in diagnosis, differences in cancer site, and overall cancer incidence between status FN living on and off-reserve.

Key Words:
Indigenous
Aboriginal health
First Nation
oncology
cancer
epidemiology
diagnosis
incidence
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survival analysis

Introduction

Cancer and other chronic diseases are now leading causes of morbidity and mortality among First Nations (FN) people in Canada, and addressing cancer is a growing health priority among FN people (1–4). Compared to non-FN Canadians, FN peoples experience higher incidence of cancers of the kidney (2,5–9), liver (2,7,10), gallbladder (6,9,10), cervix (2,5,7–12), and colon and rectum (2,7,8,10,13). Emerging evidence also indicates that FN peoples are more likely to be diagnosed with cancers at later stages than non-FN Canadians (13–16), and experience significantly lower survival (8,10,17–19). Multiple factors contribute to these disparities, including individual patient factors, environmental exposures, socioeconomic factors (particularly income), and access to healthcare services (2,8,20,21).

Approximately 11% of Manitoba residents self-identify as FN people; of these, nearly 10% are "registered" or "status" FN (22). Status FN people are those individuals registered under the *Indian Act*, which entitles them to live on designated tracts of land known as reserves (23). In 2016, 52% of all registered FN people lived in one of the 63 FN communities ('reserves') in Manitoba (22). The provision of healthcare services is not entirely similar between status FN people living on-reserve and those living off-reserve. In general, healthcare services in Canada are publically funded, providing universal coverage for medically necessary hospital, physician and specialist services to all residents. In addition, Status FN people are eligible for the federal non-insured health benefits (NIHB) program, which provides a range of services not covered by other insurance programs. The federal government also funds and/or delivers public health services and limited primary health care to those living on-reserve. Despite these additional services, many FN communities are located in remote areas of Manitoba with severely limited access to medically necessary services provided in hospitals and by physicians and specialists.

The health outcome effects of limited access to some healthcare services for FN peoples living on-reserve are not clear.

Health and social policies, including the differences in funding and delivery healthcare services to FN on and off-reserve can have important impacts on individual and population health. While there is evidence of significant differences in cancer stage at diagnosis and survival outcomes between FN and non-FN Canadians, both in Manitoba and elsewhere, to our knowledge, differences between status FN living on-reserve compared to those living off-reserve have not yet been investigated. This article reports on the findings from a larger study of provincial health administrative data (16) to address three objectives: a) to describe the demographics, comorbidities, site and stage of cancer at diagnosis in status FN people living on-reserve and status FN people living off-reserve who received a cancer diagnosis between April 1, 2004 and March 31, 2011; b) to compare annual cancer incidence rates for each cohort; and c) to investigate mortality outcomes for each cohort.

Methods

Study Design and Data Sources

We conducted a retrospective study of cancer incidence and five-year mortality among status FN people living on and off-reserve using administrative health data housed in the Manitoba Centre for Health Policy (MCHP) Population Research Data Repository. Data files in the repository do not contain names or other identifying information; an encrypted identifier allows linkage across files at the individual level, while protecting privacy. We identified and included all status FN people with any newly diagnosed cancer (excluding "non-melanoma skin & in situ skin" cancers) between April 1, 2004 and March 31, 2011 in Manitoba. Seven data sets within the MCHP repository were used (Table 1). The linkage of the Manitoba Health Insurance

Registry and the Indian Registry System (IRS) was used to create a file of FN patients, and was approved through the research protocols of the Assembly of Manitoba Chiefs prior to 2014 and Nanaandawewigamig First Nations Health and Social Secretariat of Manitoba thereafter. The FN file was linked to the Manitoba Cancer Registry (MCR) to identify all newly diagnosed cancers among status FN. This file was then linked to hospital abstracts, medical claims, 2006 Canada Census, and Vital Statistics Mortality Registry files. Approval for this study was obtained from the University of Manitoba Education & Nursing Research Ethics Board, the Manitoba Health Information Privacy Committee, CancerCare Manitoba, and the Health Information Research Governance Committee at Nanaandawewigamig.

Table 1

Outcomes

The primary outcome examined was all-cause mortality. Patients were followed for five years from the date of cancer diagnosis. Five year cancer-specific mortality was explored as a secondary outcome.

Variable Definitions

Variables measured at the time of diagnosis included: age, sex, region of residence, area-level income, Charlson Comorbidity Index score, and cancer stage and site. Two measures of region of residence were used: 1) Regional Health Authority (RHA), and 2) on/off reserve. Manitoba is divided geographically into five RHA regions; each RHA is responsible for the delivery of health services within their area. Patient residential postal code within the IRS data file identified residence as on or off-reserve. Patients were categorized into area-level income quintiles based on average household incomes calculated for each Census dissemination areas. Separate income quintiles were calculated for urban and rural residents from the 2006 Census.

For income quintiles, urban residents referred to those living in one of Manitoba's two largest cities (Winnipeg and Brandon), while rural residents referred to those living in all other areas. Both the Urban/Rural, and the RHA methods are based on patient residential postal codes and municipal codes. Charlson Comorbidity Index determined each patient's health status at time of diagnosis (24). Each comorbidity category has specific ICD-9-CM and ICD-10-CA codes (25), which were found in the hospital discharge abstract and medical claims databases during the one year period prior to cancer diagnosis. Cancer stage was categorized using the American Joint Committee on Cancer Staging system (26), ranging from stage I (least severe) to IV (most severe) based on characteristics of the tumor. A fifth category was also used to categorize patients with cancers that could not be assessed. Cancer site was determined from the MCR, based on the International Classification of Diseases for Oncology Third Edition.

Statistical Analyses

Descriptive analysis and comparisons of characteristics at time of cancer diagnosis between on and off-reserve status FN groups were conducted. Chi-squared tests were used to test for significant differences in sex, urban/rural residency, RHA residency, income quintile, cancer site and cancer stage at diagnosis, while t-tests compared group averages for age and Charlson comorbidity score.

Cancer Incidence

Annual cancer incidence was calculated for each year from 2004/2005 to 2010/2011. Separate rates for on and off-reserve populations were determined by identifying the number of individuals with a cancer diagnosed each year divided by the annual population counts of on and off-reserve FN people. Differences in annual crude incidence rates and the cumulative incidence rate over the 7-year period between on- and off-reserve status FN populations were tested for

significance using chi-squared tests. To account for demographic differences between on- and off-reserve populations, adjusted rates using a generalized linear model with a negative binomial log link function was estimated. This model controlled for age, sex, income quintile and RHA area of residence. Trends over time were analyzed with linear regression models fit to the annual rates.

Mortality

Cox proportional hazard regression models compared the risk of mortality between FN patients living on-reserve and those living off-reserve. Time to death was measured in days from the date of cancer diagnosis to the date of death. Patient data was censored at five years if they were still alive, or at the time of discontinuation of health insurance coverage, usually indicating the person moved out of Manitoba. In the analysis of cancer-specific mortality, patient data was censored at the time of death for all non-cancer-related causes of death. Potential confounding variables accounted for in the analyses included age, sex, Charlson comorbidity index, stage of cancer, income quintile and RHA area of residence. All effect estimates are reported as hazard ratios with 95% confidence intervals and the significance level was $p<0.05$. Analysis was completed on the secure server at MCHP using SAS statistical software, V9.4 (SAS Institute).

Results

Characteristics of Patients with a First Diagnosis of Cancer

There were 1,524 newly diagnosed cancers among status FN people in Manitoba between April 1, 2004 and March 31, 2011. On average, those living on-reserve were older (60.6 years vs. 57.5 years, p <0.0001), with a higher Charlson Comorbidity Index score (1.4 vs. 1.3; p= 0.013). In both the on-reserve and off-reserve groups, a higher proportion of women were newly diagnosed with cancer than men.

Table 2

Cancer Diagnoses by Stage & Site

A significant difference was found in cancer stage at diagnosis, with a lower proportion of on-reserve patients diagnosed at Stage I than off-reserve patients (21.7% vs. 26.9%; p=0.019). No other significant differences in stage at diagnosis were found. Regarding cancer sites, we found significantly lower proportions of breast and cervical cancers, and significantly higher proportions of kidney, ovarian and prostate cancers in the on-reserve group than in the off-reserve group.

Table 3

Table 4

Cancer Incidence & Trends

There were no significant differences in yearly crude or adjusted annual incidence rates, except for 2007/08, in which the off-reserve group had a higher adjusted annual incidence of cancer (291 vs. 380/100,000; p=0.0423). The overall adjusted incidence of cancer over the study years was higher in the off-reserve group than in the on-reserve group (287/100,000 vs. 247/100,000; p=0.0243) There were no significant trends in cancer incidence over time in either group.

Table 5

Table 6

Cancer Mortality

The on-reserve group had a significantly higher risk of all-cause mortality than the off-reserve group (HR 1.28, 95% CI 1.11-1.26, p=0.005), however there was no significant

difference after adjusting for covariates. We found no significant difference in the risk of cancer-specific mortality before or after adjustment.

Table 7

Interpretation

This retrospective analysis of health administrative data examined cancer incidence, site, stage at diagnosis, and mortality among Manitoba FN people diagnosed with cancer between 2004/2005 and 2010/2011 living on-reserve and off-reserve. While differences in cancer-related events exist between FN and non-FN people, this is the first study to specifically compare status FN people living on-reserve with those living off-reserve. We found that the on-reserve group was on average older, with higher Charlson Comorbidity Index scores than the off-reserve group. A lower proportion of on-reserve patients were diagnosed at Stage I than off-reserve patients. While there were no significant differences in yearly cancer incidence between groups, the adjusted incidence of cancer over all seven years was higher in the off-reserve group than in the on-reserve group. No significant differences in mortality were found.

Our study found a lower proportion of FN people living on-reserve were diagnosed with cancers in Stage I than those living off-reserve, which may be related to differential access to healthcare services (18). FN people living on-reserve are more likely to live in rural and remote areas, and to experience difficulties in accessing cancer-related diagnostic and specialty care (27,28). For many FN patients, gaining entry "into the system at the front end or diagnostic stage" is a significant problem (26, p. 15). Moreover, FN patients living on-reserve encounter additional bureaucratic 'red tape' and challenges with securing transportation required to access diagnostic and specialty care (28–30), which may result in later stage cancer diagnoses. In addition, for many FN people, access to healthcare and cancer services is determined not only by

where those services are delivered, but *how* they are delivered at the point of care (31,32). In particular, lack of culturally safe services, and frequent experiences of racism substantially impact how and when cancer services are accessed by FN people (31).

Notably, no differences in mortality between FN peoples living on-reserve and those living off-reserve were found through this study. These findings were counterintuitive for our team, as we anticipated FN patients living on-reserve would have worse outcomes due to proximity and accessibility of healthcare services. We assumed those living off-reserve lived in more urban areas and in closer proximity to healthcare services, and therefore have better access to healthcare services and other support services and programs. These findings seem to suggest that proximity to healthcare services does not necessarily decrease mortality. An alternate consideration, raised by our community partners, was that FN people tend to be transient, moving back and forth on and off reserve communities, or between FN communities and other communities. While no definitive conclusions can be draw based on this consideration, it is important to remember that despite the listed place of residence (i.e., on vs. off-reserve), many FN people have similar experiences in accessing healthcare services and our measure for on versus off-reserve may not translate well into lived realities.

Strengths & Limitations

Study findings are strengthened through our use of multiple population-based and well-validated administrative data sets, minimizing bias related to recall or small samples. We also benefitted from strong relationships with FN partners, which enriched our interpretation of findings. Our findings should be considered in relation to several study limitations. First, we included only FN individuals registered under the *Indian Act* ('status' FN). At present, there is no mechanism to identify non-registered FN people in these datasets. Including non-status FN

people may have resulted in additional differences between groups. However, in Manitoba, status FN people represent approximately 97% of all FN (34). Second, we were not able to analyze differences in mortality between the FN people living on and off-reserve by cancer site because of small sample sizes, and there may be significant differences in mortality depending on cancer site. Third, income was measured at the area level only, which does not account for individual and family differences. Fourth, location of residence was calculated at the RHA level, which may obscure important differences between those living in urban vs. rural versus remote areas within an RHA. Fifth, categorization into on or off-reserve residence was based on postal code of residence on a fixed date. As our community partners suggested, FN people tend to be highly mobile, moving between reserve and non-reserve communities, which could result in accessing healthcare services in multiple locations. Finally, this study only included status FN people living in Manitoba, and results may not be generalizable to FN residents living in other Canadian provinces. Although status FN people across Canada experience similar health status, socioeconomic status and healthcare services, there may be differences in the location of reserve communities or other important differences that preclude generalizability of our results.

Conclusion

Our retrospective analysis of provincial health administrative data found differences between FN patients living on-reserve and those living off-reserve. A lower proportion of on-reserve patients were diagnosed with cancers at Stage I compared to those living off-reserve; however, overall cancer incidence over the study years was higher in the off-reserve group. We found no significant differences in 5-year mortality between groups. Further research is needed to better understand the reasons for differences in stage at diagnosis, particularly in relation to access to healthcare.

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Table 1: Data sets used

Data Set	Description of Data Set & Data Used	Variable
Manitoba Health Insurance Registry	Demographic information for all residents of Manitoba Eligible to receive healthcare services	Demographic information
Indian Registry System (IRS)	List of all status FN people, including residence on or off-reserve	FN status Residence on or off-reserve
Manitoba Cancer Registry (MCR)	Information on all incident cases of diagnosed cancer, cancer treatment, tumor characteristics, cancer site and stage at diagnosis.	Cancer incidence Cancer stage at diagnosis Cancer site
Hospital Abstracts	International Classification of Diseases (ICD-9-CM and ICD-10-CA) diagnostic codes and Canadian Classification for Health Interventions (CCI) procedure codes for all hospital admissions in Manitoba.	Patient co-morbidities Patient socio-demographic characteristics
Medical Services	Claims submitted for physician and nurse practitioner services provided in Manitoba (and the associated ICD-9-CM)	Patient co-morbidities Patient socio-demographic characteristics
Census of Canada	Aggregate data file used to create quintiles of area-level income	Socioeconomic characteristics
Vital Statistics Mortality Registry	Records all deaths in Manitoba and the primary cause of death	Mortality

Table 2: Patient Characteristics

Characteristic	On-Reserve n=930 (61%)	Off-Reserve n=594 (39%)	*p* value
Age (yrs) mean ±SD	60.6 +/- 14.5	57.5 +/- 14	<.0001
Male	456 (49.0%)	223 (37.5%)	<.0001
Female	474 (51.0%)	371 (62.5%)	
Rural Residency	846 (91.0%)	266 (44.8%)	
Regional Health Authority			<.0001
IE	257 (27.6%)	81 (13.6%)	
NO	428 (46.0%)	107 (18.0%)	
SO	6 (0.6%)	7 (1.2%)	
WE	68 (7.3%)	20 (3.4%)	
WP	102 (11.0%)	66 (11.1%)	
PT	69 (7.4%)	313 (52.7%)	
Income Quintile			<.0001
NF	12 (1.3%)	9 (1.5%)	
R1 (lowest rural)	508 (54.6%)	79 (13.3%)	
R2	209 (22.5%)	43 (7.2%)	
R3	43 (4.6%)	43 (7.2%)	
R4	75 (8.1%)	51 (8.6%)	
R5 (highest rural)	11 (1.2%)	50 (8.4%)	
U1 (lowest urban)	49 (5.3%)	170 (28.6%)	
U2	12 (1.3%)	67 (11.3%)	
U3	s	38 (6.4%)	
U4	s	32 (5.4%)	
U5 (highest urban)	s	12 (2.0%)	
Charlson Comorbidity Index Score (Mean +/- SD)	1.4 +/- 1.4	1.3 +/- 1.3	0.0132

Table 3: Cancer Stage at Diagnosis by Location

Cancer Stage	On-Reserve	Off-Reserve	*p* value
I	202 (21.7%)	160 (26.9%)	0.0196
II	207 (22.3%)	133 (22.4%)	0.9517
III	176 (18.9%)	109 (18.4%)	0.7791
IV	216 (23.2%)	126 (21.2%)	0.3581
Unknown	129 (13.9%)	66 (11.1%)	0.1157

Table 4: Cancer Site by Location

Cancer Site	On-Reserve n=930	Off-Reserve n=594	*p* value
Bladder	s	8 (1.3%)	0.0939
Breast	99 (10.6%)	111 (18.7%)	<.0001
Cervix	19 (2.0%)	26 (4.4%)	0.0087
Chronic lymphocytic leukemia	s	s	0.0776
Colorectal	153 (16.5%)	87 (14.6%)	0.3454
Corpus uteri	19 (2.0%)	19 (3.2%)	0.1582
Kidney	96 (10.3%)	40 (6.7%)	0.0166
Lung and Bronchus	131 (14.1%)	74 (12.5%)	0.3636
Melanoma of the Skin	s	s	s
Non-Hodgkin Lymphoma	33 (3.5%)	32 (5.4%)	0.0832
Other Cancers	197 (21.2%)	113 (19.0%)	0.3071
Ovary	25 (2.7%)	7 (1.2%)	0.0450
Pancreas	19 (2.0%)	13 (2.2%)	0.8468
Prostate	100 (10.8%)	34 (5.7%)	0.0007
Stomach	18 (1.9%)	11 (1.9%)	0.9072
Thyroid	10 (1.1%)	10 (1.7%)	0.3089

Table 5: Annual Crude Cancer Incidence by Location

	On-Reserve		Off-Reserve		
Fiscal Year	**Count**	**IR per 100,000**	**Count**	**IR per 100,000**	***p* value**
2004/2005	116	308.9	75	301.8	0.8758
2005/2006	123	318.6	71	279.7	0.3817
2006/2007	131	330.7	71	273.1	0.1941
2007/2008	121	297.4	88	331.6	0.4377
2008/2009	154	367.2	119	440.0	0.1387
2009/2010	164	378.4	92	329.9	0.2927
2010/2011	159	355.0	100	347.9	0.8742
Overall	**968**	**337.8**	**616**	**330.4**	**0.6647**

Table 6: Annual Adjusted Cancer Incidence by Location

	On-Reserve		Off-Reserve		
Fiscal Year	**Count**	**IR per 100,000**	**Count**	**IR per 100,000**	***p* value**
2004/2005	116	245.1	75	280.1	0.3934
2005/2006	123	256.3	71	255.4	0.9827
2006/2007	131	260.8	71	247.3	0.7318
2007/2008	121	233.6	88	292.4	0.1316
2008/2009	154	291.0	119	380.3	0.0423
2009/2010	164	307.2	92	280.3	0.5078
2010/2011	159	283.3	100	294.8	0.7692
Overall	**968**	**247.9**	**616**	**287.9**	**0.0243**

Table 7: Mortality Hazard Rations

	HR	95% CI	*p* value
All-cause mortality – Crude	1.28	1.11 – 1.26	0.0005
All-cause mortality 5 years post diagnosis - Adjusted	1.18	0.98 – 1.41	0.0652
Cancer-specific mortality – Crude	1.09	0.98 – 1.22	0.1172
Cancer-specific mortality 5 years post diagnosis - Adjusted	1.03	0.90 – 1.19	0.6008