Abstract

This study examined Papanicolaou (Pap) test utilization, Pap test results, and cervical cancer incidence among First Nations (FN) women living in Manitoba, Canada taking into account age group, time period, and area of residence. Six population-based data sources were linked at an individual level. Negative binomial regression was used to compare Pap test utilization and results between FN and all other Manitoba (AOM) women. Poisson regression was used to compare cervical cancer incidence. Among women younger than 25 years, FN were more likely than AOM women to have had a Pap test [rate ratio (RR) = 1.37, 95% confidence intervals (CI), 1.22–1.53, 18–19 year olds; RR = 1.17, 95% CI, 1.05–1.31, 20–24 year olds]. There was no difference in Pap test use for women 25 to 29 or 30 to 39 years. FN 40 years and older were less likely to have a Pap test than AOM women (RR = 0.84, 95% CI, 0.75–0.93, 40–49 years old; RR = 0.71, 95% CI, 0.63–0.79, 50–59 years old; RR = 0.59, 95% CI, 0.52–0.66, 60–69 years old). FN were more likely than AOM women to have a high (RR = 1.88, 95% CI, 1.65–2.13) or low-grade Pap test result (RR = 1.60, 95% CI, 1.48–1.73). The invasive cervical cancer incidence rate was double for FN women 25 to 39 years of age (21.9 per 100,000, FN; 10.2 per 100,000, AOM, P = 0.006) and 40 to 69 years of age (24.3 per 100,000, FN; 12.3 per 100,000, AOM, P = 0.007). In conclusion, cervical cancer screening among FN women over 40 years of age must be increased to address the higher cervical cancer incidence. Cancer Prev Res; 8(1): 49–55. ©2014 AACR.

Introduction

Since the introduction of the Papanicolaou (Pap) test for cervical cancer screening, there have been significant decreases in cervical cancer incidence and mortality in Canada (1). However, despite the availability of the Pap test and the development of organized cervical cancer screening programs, some women are less likely to be screened. Reasons for lower Pap test use are often related to socioeconomic status (SES), age, health status, access to the health care system, and ethnicity (2). Several Canadian studies have found that visible minority women are significantly less likely to be screened for cervical cancer (3–8). Historically, cervical cancer screening rates among Aboriginal women (Métis, Inuit, and First Nations; FN) have also been lower than the rest of the population (9, 10). However, recent surveys indicate that the gap in Pap test use between FN and all other women may be lessening: 3-year screening rates reported for Aboriginal women in Canada range from 69% to 85% depending on the source of data and the populations that were included (11). In comparison, data from a national report on cervical cancer screening found that 69.4% of Canadian women had had a Pap test from 2009 to 2011 (12).

To ensure that all Manitoba women receive organized, high-quality, cervical cancer screening services, a provincial cervical cancer screening program (CervixCheck) was implemented in 2001. The program includes a registry that collects Pap test, colposcopy, and histology information, a fail-safe strategy to ensure that the appropriate follow-up tests are performed after an abnormal Pap test, and on-going quality assurance and evaluation. The objectives of this study were to describe the frequency of Pap test utilization for cervical cancer screening, the distribution of Pap test results, and the incidence of invasive cervical cancer among FN women living in Manitoba compared with all other Manitoba (AOM) women.

Materials and Methods

Setting and population

The province of Manitoba, located in central Canada, has a population of approximately 1.2 million. Half of the population lives in the capital city of Winnipeg. In 2011, there were 105,815 registered FN individuals living in Manitoba, which represented 8.8% of the provincial population (13). Registered refers to those FN individuals who, under the Federal Indian Act, are entitled to Treaty rights (14). FN groups in Manitoba include Ojibway, Cree, Ojibway-Cree, Dakota, and Dene. FN constitutes 1.9% of the Canadian population or 45.5% of the total Indigenous population living in Canada (which includes FN, Inuit, and Métis individuals; ref. 15). FN individuals reside in urban and rural areas including 63 FN communities in Manitoba, some of which are isolated and/or northern communities (13).
Data sources

Six data sources were used for this study: the Federal Indian Register, the Manitoba Health Population Registry (MHPR), the CervixCheck registry, the Medical Claims database, the Manitoba Cancer Registry (MCR), and the Hospital Abstracts database. The Federal Indian Registry is a national registry that contains a complete list of status "Indians" as defined by the Federal Indian Act (16). Permission was received from Aboriginal and Northern Affairs Canada (the federal data steward) to link the Federal Indian Register to the MHPR (17). The MHPR includes all Manitoba residents covered by the Manitoba Health insurance program (~99% of the population). Through a multistep data linkage process, registered FN individuals were identified in the MHPR creating a FN file (17). This deidentified FN file included a scrambled identifier unique to CancerCare Manitoba (CCMB; Winnipeg, Manitoba). The FN file was then linked to the CervixCheck registry at CCMB using the scrambled identifier to identify women who had had a Pap test.

The CervixCheck registry is a repository of all Pap tests and colposcopies performed by health care providers in Manitoba. The registry includes the date of the Pap test as well as cervical cytologic and histologic results. The Medical Claims and the Hospital Abstracts databases were used to identify women who previously had had a hysterectomy. The provincial Medical Claims database is generated by claims filed by physicians for payment of services and includes a billing tariff code, service date, an International Classification of Diseases (ICD) 9th version diagnosis code, and provider identification. The Hospital Abstracts database includes demographic and clinical information (gender, postal code, up to 25 ICD 10th version diagnoses codes, and procedure codes) for all separations from acute and chronic care facilities in Manitoba. The Hospital Abstracts database also includes information for all Manitobans admitted to out-of-province facilities. The MCR was used to identify women diagnosed with invasive cervical cancer. The MCR is a population-based database that has recorded all cancers diagnosed in residents of Manitoba since 1956. Reporting cancer cases to the MCR is mandated by law. The quality of the MCR is high with consistently high levels of reporting completeness and histologic verification (18).
Statistical analyses

Descriptive statistics were used to illustrate the characteristics of the individuals (females ages 18–69 years) in the study. Pap test rates were calculated beginning in 2003 for 3-year time periods to reflect current cervical cancer screening guidelines in Manitoba (19). If a woman had more than one Pap test over the 3-year time period, the most recent Pap test was used. Pap test rates were adjusted for hysterectomy by excluding women from the numerator and denominator whose first Pap test during the time period occurred after a hysterectomy. When calculating rates, a woman’s age was calculated at the midpoint of each time period (June 30, 2004 for 2003–05 and June 30, 2007 for 2006–08) for the numerator and as the year of the first Pap test minus her birth year for the denominator. High-grade Pap test results included cytologic results of atypical squamous cells-high-grade (ASC-H), atypical glandular cells, high-grade intraepithelial lesions, cervical carcinoma in situ, and invasive cervical carcinoma. Low-grade Pap test results included cytologic results of atypical squamous cells of undetermined significance and low-grade intraepithelial lesions.

Since count data were used, negative binomial regression was used to compare the rates of Pap test use and the rates of high- and low-grade Pap test results among women who had a Pap test in the time period between FN and AOM women. The negative binomial regression was also used to correct for overdispersion in the data (which can result in an underestimation of the standard errors and an overestimation of the test statistics; ref. 20). The following covariables were included in the analysis: age (18–19, 20–24, 25–29, 30–39, 40–49, 50–59, 60–69 years for Pap test use and 18–24, 25–39 years, and 40–69 years for Pap test results), time period (2003–05, 2006–08), and area of residence (north, rural, south, urban). For Pap test utilization rates, women 20 to 24 years of age were chosen as the reference group because cervical cancer screening is not recommended for women 18 to 19 years of age (19). When examining high-grade and low-grade Pap test result rates, three age groups were used (18–24, 25–39 years and 40–69 years) because of the small number of women who had an abnormal Pap test result. Area of residence was determined using each woman’s six digit postal codes and the Regional Health Authority in which she lived. The type III P value was used to determine whether there was a significant effect of each variable on the likelihood of having a Pap test.

Because of the small number of cases, invasive cervical cancer incidence was calculated for 2003 to 2008 for three age groups: 18 to 24, 25 to 39, and 40 to 69 years. Poisson regression was used to compare invasive cervical cancer incidence rates for FN and AOM women. All analyses were conducted in SAS version 9.2 (SAS Institute Inc.).

Ethical approvals were received from the University of Manitoba (Winnipeg, Manitoba) Health Research Ethics Board, the Manitoba Health’s Health Information Privacy Committee, CCMB’s Research Impact Committee, and the Assembly of Manitoba Chief’s Health Information and Research Governance Committee.

Results

Table 1 shows the characteristics of FN and AOM women 18 to 69 years of age in 2003–05 and 2006–08. In both time periods, a higher percentage of FN women lived in the north (35.7% in 2003–05 and 35.6% in 2006–08) than AOM women (2.9% in 2003–05 and 2.7% in 2006), whereas a higher percentage of AOM women lived in an urban area (66.7% in 2003–05 and 66.9% in 2006–08) compared with FN women (33.4% in 2003–05 and 33.9 in 2006–08). A higher percentage FN women were younger (18–39 years of age) compared with AOM women (64.0% in 2003–05 and 62.1% in 2006–08 for FN women; 45.7% in 2003–05 and 45.0% in 2006–08 for AOM women).

Figure 1 shows the percentage of FN and AOM women who had at least one Pap test by time period and area of residence. In Figure 2, the percentage of FN and AOM who had at least one Pap test by time period and age group.
2003–05, 60.8% [95% confidence intervals (CI), 55.8–68.9] of FN and 64.8% [95% CI, 57.3–73.3] of AOM women had at least one Pap test. In 2006–08, 60.7% [95% CI, 53.9–68.3] of FN and 65.7% [95% CI, 58.4–73.9] of AOM women had at least one Pap test. The ratio of Pap test utilization amongst FN women compared with AOM women was 0.94 (95% CI, 0.79–1.12) in 2003–05 and 0.92 (95% CI, 0.78–1.09) in 2006–08. Pap test rates were slightly lower in the north compared with the rural south or urban areas but the differences between FN and AOM women were not significant (data not shown). Figure 2 shows the rate of Pap test utilization by age group for each time period. Compared with AOM women, Pap test rates were significantly higher for FN women less than 25 years of age but significantly lower for FN women 40 years of age and older.

Table 2 shows the relative rate (FN/AOM) of Pap test utilization by area of residence, age group, and time period. In the unadjusted model, there was no difference in the likelihood of having a Pap test for FN compared with AOM women [rate ratio (RR) = 0.93, 95% CI, 0.83–1.05]. After adjusting for area of residence, age group, and time period, FN women were less likely to have had a Pap test compared with AOM women (RR = 0.89, 95% CI, 0.83–0.96). There was a significant main effect for area of residence (P = 0.0003) and age group (P < 0.0001). Interactions between ethnicity and area of residence and ethnicity and age group were tested; only the interaction between ethnicity and age group remained significant (P < 0.0001).

Among women less than 25 years of age, FN women were more likely than AOM women to have had a Pap test (RR = 1.37, 95% CI, 1.22–1.53 for 18–19 year olds; RR = 1.17, 95% CI, 1.05–1.31 for 20–24 year olds). There was no difference in the likelihood of having a Pap test for FN and AOM women 25 to 29 or 30 to 39 years of age. For FN women 40 years of age and older, a decreasing trend in the likelihood of having had a Pap test was observed (RR = 0.84, 95% CI, 0.75–0.93 for women 40–49 years of age; RR = 0.71, 95% CI, 0.63–0.79 for women 50–59 years of age; and RR = 0.59, 95% CI, 0.52–0.66 for women 60–69 years of age).

Table 3 shows the relative rates (FN/AOM) of a high-grade Pap test result among all women who had a Pap test. After adjusting for area of residence, age group, and time period, FN women were significantly more likely to have a high-grade Pap test compared with AOM women (RR = 1.80, 95% CI, 1.63–1.99). The interaction between ethnicity and age group was not significant, but the interaction between ethnicity and area of residence was significant (P = 0.0002). Therefore, regardless of whether a woman lived in the north, rural south, or an urban area, FN women who had a Pap test were significantly more likely to have had a high-grade Pap test than AOM women. However, the RR was...
lower for women who lived in the north (RR = 1.32, 95% CI, 1.09–1.60) and higher for those who lived in the rural south (RR = 2.16, 95% CI, 1.86–2.51) or in an urban area (RR = 2.10, 95% CI, 1.82–2.43).

Table 4 shows the relative rates (FN/AOM) of a low-grade Pap test result among all women who had a Pap test and after adjusting for area of residence, age group, and time period. FN women were significantly more likely to have a low-grade Pap test result compared with AOM women (RR = 1.57, 95% CI, 1.46–1.69) but, as with high-grade Pap test results, the interaction between ethnicity and area of residence was significant (P = 0.008). Therefore, the RR of having a low-grade Pap test result was lower for women who lived in the north (RR = 1.32, 95% CI, 1.14–1.52) and higher for women who lived in the rural south (RR = 1.78, 95% CI, 1.58–2.00) or in an urban area (RR = 1.65, 95% CI, 1.47–1.84).

The invasive cervical cancer incidence rate for women 18 to 24 years of age was 2.4 per 100,000 for both FN and AOM women (P = 0.97). For women 25 to 39 years of age, the invasive cervical cancer incidence rate was 21.9 per 100,000 for FN women and 10.2 per 100,000 for AOM women (P = 0.006). For women 40 to 69 years of age, the invasive cervical cancer incidence rate was 24.3 per 100,000 for FN women and 12.3 per 100,000 for AOM women (P = 0.007).

Discussion

Our study found that 61% of FN women and 65% of AOM women had had a Pap test in the previous 3 years. Both participation rates fall below the cervical cancer screening participation target of ≥80% recommended by the Pan-Canadian Cervical Cancer Screening Network (21). The rate of Pap test utilization among FN women in Manitoba is also less than that found from previous studies, such as the 2008–10 First Nations Regional Health Survey, which reported that 74% of FN women had had a Pap test in the previous 3 years (22). The higher rates from survey data are likely due to the self-reported nature of the data and not correcting for pervasive hysterectomy.

FN women less than 25 years of age were more likely to have a Pap test than AOM women. This may be related to the younger maternal age observed in FN women compared with the general population and the subsequent increased number of interactions with a health care provider and opportunities to have a Pap test (23). If screened, they were more likely to have a low-grade or high-grade Pap test result that necessitates further follow-up tests (i.e., additional Pap tests or colposcopy). However, there was no difference in the rate of invasive cervical cancer between FN and AOM women in this age group. Therefore, although it is likely that the detection and treatment of high-grade cervical dysplasia in young FN women prevent future cases of invasive cervical cancer, the high rate of low-grade cervical dysplasia may represent overscreening and overtreatment.

There was no difference in the likelihood of having a Pap test for FN women 25 to 40 years of age yet FN women in this age group were also more likely to have had a high- or low-grade Pap test result compared with AOM women. Most importantly, the rate of invasive cervical cancer was twice as high among FN women 25 to 39 years of age. The increased rate of high-grade Pap tests and cases of invasive cervical cancer may be due to a higher prevalence of persistent human papillomavirus (HPV) among FN women. A study of the prevalence of HPV in Northern Canada found a 50% increase among Aboriginal women compared with all other women (24). The study also found that the age-specific HPV prevalence among Aboriginal women showed a "U" shape which contrasted to a consistent decrease among non-Aboriginal women. This pattern of HPV prevalence may explain the increase in cervical cancer incidence with age observed in this study and might indicate the importance of screening for cervical cancer using HPV testing instead of cervical cytology for FN women.
The lower percentage of FN women over 40 years of age who had a Pap test is a concern. Overall, Pap test use tends to decrease with age even after adjusting for previous hysterectomy but the incidence of invasive cervical cancer increases (21). The rate of high-grade Pap test results was lowest for women over 40 years of age regardless of ethnicity although FN women in this age group had higher high-grade Pap test result rates than AOM women. In addition, FN women over 40 years of age had the highest incidence rate of invasive cervical cancer in Manitoba. This is consistent with the incidence of invasive cervical cancer found in other groups of Aboriginal women such as American Indian and Alaska Native women (25). Clearly, improving the screening participation of FN women over 40 years of age should be a priority.

Previous research found that invitation letters significantly increased the cervical cancer screening participation rate in Manitoba among older, never-screened women (26). However, the increase was small and any further improvements in cervical cancer screening participation will require a multifaceted approach that combines invitation and recall letters with local, culturally appropriate initiatives. HPV self-sample may also represent a new approach to cervical cancer screening particularly among hard-to-reach women. Recent studies that have examined HPV self-sampling among unscreened women have found a wide range of uptake rates from 10% in the United Kingdom to 39% in the Netherlands (27). In Canada, a pilot study that included 49 FN women from Northern Ontario who previously had a Pap test found that self-sampling was an acceptable and feasible screening strategy (28). Eventually, HPV self-sampling may be used in Manitoba to screen FN and AOM women for cervical cancer who have low participation rates or no previous cervical cancer screening history.

Our findings should be considered in the context of several study limitations. We did not include any measures of SES in the analysis. Previous studies have found that education and income are often independent predictors of screening and that differences in screening uptake due to ethnicity are reduced after the adjustment for SES (29). Finally, this study included registered FN who represented 93% of all FN living in Manitoba but did not distinguish between several distinct FN cultural groups. This information, however, is an important part of collaborating and planning local strategies designed to improve cancer screening in the population.

In conclusion, the lower Pap test utilization rate among FN women over 40 years of age must be addressed in an effort to help reduce the significantly higher incidence of cervical cancer. Further research is also needed to determine whether the higher rate of screening in younger FN women leads to the diagnosis and treatment of cervical dysplasia preventing cervical cancer or if younger FN women are overscreened leading to overtreatment and harm. It will also be important to determine whether or not follow-up tests after an abnormal Pap test differ for FN and AOM women.

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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