## OPEN

# Cervical Screening Practices and Outcomes for Young Women in Response to Changed Guidelines in Calgary, Canada, 2007–2016

Sayeeda Amber Sayed, MBBS, MPH,<sup>1</sup> Christopher Naugler, MD, FRCPC,<sup>2</sup> Guanmin Chen, MD, PhD,<sup>1</sup> and James A. Dickinson, MBBS, PhD<sup>3</sup>

**Objective:** The aim of the study was to describe temporal trends in screening and outcomes for women, after changes in guidelines in Alberta, Canada, that raised starting age to 21 years, then to 25 years of age, and reduced frequency to 3 yearly.

Materials and Methods: Calgary Laboratory Information System data were used to examine screening rates, follow-up procedures, and cancer among women 10–29 years from 2007 to 2016 in the whole population of Calgary. Interrupted time-series analyses were used to assess changes in screening and subsequent diagnostic procedures over the 10-year period. **Results:** Annual screening rates dropped by approximately 10% at all ages older than 15 years after the 2009 Alberta cervical cancer screening guidelines, followed by a steady decrease. Further change continued subsequent to minimal apparent effect of the 2013 Canadian Task Force on Preventive Health Care guidelines. The rates of abnormal test results decreased in concert with decreased screening. No increases in cervical intraepithelial neoplasia 1, cervical intraepithelial neoplasia 2/3, or invasive cervical cancer rates were observed after reduced testing.

**Conclusions:** The largest decrease in screening and follow-up procedures occurred in the period immediately after implementation of 2009 Alberta screening guidelines. The number of consequent procedures also decreased in proportion to decreased screening, but there was no increase in cancer rates. Starting screening at the age of 25 years and reducing intervals seem to be safe.

Key Words: cervical cancer screening,

cervical cancer screening guidelines, screening recommendations, young women, screening age, Canada

(J Low Genit Tract Dis 2021;25: 1-8)

**R** ecommendations for cervical cancer screening have evolved over time as new evidence has become available.<sup>1,2</sup> Canadian health care is publicly funded and free to all residents, organized

- S.A., C.N., and J.D. contributed in the study conception and design. S.A. drafted the initial manuscript and performed the data analysis. G.C. assisted in the interrupted time series data analysis. All authors contributed to revisions, read, and approved the final manuscript.
- Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jlgtd.com).
- Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the ASCCP. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/LGT.000000000000574

and administered by each province. In Calgary, Alberta, cervical screening is largely performed by family physicians<sup>3</sup> and followup colposcopy by focused-practice gynecologists. Since 2003, an organized screening program coordinates invitation and reminder letters, colposcopy, and laboratory quality assurance.<sup>4</sup> Before 2009, most women older than 18 years were screened annually.5 In October 2009, the Alberta provincial guidelines were changed to recommend screening initiation for sexually active women at the age of 21 years and, after 3 tests within 5 years, to repeat every 3 years.<sup>6</sup> Subsequently in February 2013, the Canadian Task Force on Preventive Health Care (CTFPHC) recommended against screening younger than 25 years and endorsed the 3-year interval.<sup>2</sup> The later initiation of screening and extended interval was intended to minimize the harms caused by treating abnormalities that are unlikely to progress to cancer in young women.<sup>7,8</sup> Some opinion leaders consider these modifications in guidelines controversial and raise concerns that without early onset and frequent screening, more advanced disease will present, either before screening commencement, or at later screening.<sup>7-9</sup> These guideline changes also created confusion between providers and women.<sup>10,11</sup> Both physicians and women had to understand these new guidelines and change their behaviors accordingly, a process that takes time.<sup>12</sup>

Using a citywide pathology service database, we sought to describe how physicians and women in Calgary responded to these changes in recommendations<sup>2,6</sup> and their effects on outcomes. We measured the rates of cervical cancer screening for each age group from 10- to 29-year-old women in Calgary from 2007 to 2016. We assessed subsequent diagnostic testing including rates of abnormal tests and biopsies to measure changes in downstream testing as screening was reduced. To assess whether later screening initiation leads to increased harms to young women, we also measured reporting of cervical intraepithelial neoplasia (CIN) 2/3 and invasive cervical cancer through this period.

## **METHODS**

We performed a population-wide audit of cervical screening, subsequent follow-up testing, and outcomes over 10 years, in a city of approximately 1.3 million people, 50% female. The population increased by 15% from 2007 to 2016.<sup>13</sup>

#### DATA SOURCE

Calgary Laboratory Services provides all cytopathology services and cervical pathology specimen analysis to Calgary and surrounding regions in Southern Alberta since 2006. Cervical cancer screening data and pathology results without personal identifying information were extracted from the Laboratory Information System (LIS) from January 01, 2007, to December 31, 2016. The extracted variables were as follows: LIS-generated patients' proxy ID numbers, date of birth, physician's name and clinic address, laboratory site, dates of screening and laboratory reading, result, and follow-up recommendations. Ethics approval for the study was

<sup>&</sup>lt;sup>1</sup>Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; <sup>2</sup>Departments of Pathology and Laboratory Medicine, Family Medicine, and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; and <sup>3</sup>Departments of Family Medicine and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada Correspondence to: James A. Dickinson, MBBS, PhD, Department of Family

Correspondence to: James A. Dickinson, MBBS, PhD, Department of Family Medicine Research Office, FMC G012 3330 Hospital Dr NW, Calgary, AB, Canada T2N 4N1. E-mail: dickinsj@ucalgary.ca

The authors have declared they have no conflicts of interest.

Funding was provided by a Canadian Institute of Health Research Foundation Grant (No. RN254781-333204) to C.N.

Ethics approval for the study was obtained from the University of Calgary Conjoint Health Review Board (REB13-0376).

obtained from the University of Calgary Conjoint Health Review Board (REB13-0376).

**Inclusion Criteria.** We included all cervical cytology test requisitions ordered by a family physician for 10- to 29-year-old women with a valid Alberta health care number and a residential address in Calgary. If a woman had multiple tests in a year, the first test and its result were chosen. Individuals without Alberta health care insurance were excluded. However, they represented less than 1% of the population.

Abnormal test rates are determined from the diagnosis given by the Calgary laboratory services and the population estimate for that year and age group. To investigate the consequences of subsequent diagnostic testing after abnormal screening tests, we counted all biopsies including cervical, loop electrosurgical excision procedure (LEEP), and cone biopsies for 2007–2016. Although these data did not include referrals to colposcopy, as an indicator we counted the number of women who had cervical biopsies because guidelines now recommend a biopsy be taken at every colposcopy. We then measured the precancers and invasive cervical cancer reported from these specimens.

#### **DATA ANALYSIS**

Population-adjusted cervical cancer screening rates were calculated using Statistics Canada census data and annual estimates to provide the denominators.13 We do not provide confidence intervals for these rates, because the data come from a total population. To assess the effect of guideline changes, we used interrupted time series analysis (ITSA) to evaluate changes in cervical screening test rates.<sup>14</sup> The ITSA uses segmented linear regression, which divides a time series into preintervention and postintervention segments. The Alberta guidelines were introduced in October 2009, so we chose 2010 as the beginning of the first intervention. The CTFPHC guidelines were introduced in January 2013; to evaluate postguideline changes, we considered that it was the start of the second intervention. Thus, 3 periods were constructed for comparison of rates: the preintervention period 2007-2009 and the 2 postintervention time periods, 2010-2012 and 2013-2016. A linear regression model in ITSA has 2 parameters: the level and slope. A change in level between the preintervention and postintervention segments indicates an immediate change and a change in slope repre-sents postintervention change per year.<sup>14</sup> The changes were estimated and compared in ITSA using the Newey-West estimator, and the p value of less than .05 was used as the threshold for statistical significance between preintervention and postintervention segments

(further details of the ITSA methodology are attached as Appendix 1, http://links.lww.com/LGT/A190). All analyses were conducted using Stata/SE Version 14 (College Station, TX).

The funding source had no input to design, analysis, writing, and reporting of this study.

#### RESULTS

We analyzed 435,772 tests on approximately 130,000 women over the 10-year period. Between the ages of 10 and 14 years, there were an average of 52 tests per year between 2007 and 2009, which reduced to an average of 5 per year in 2014-2016. Subsequent abnormal results were too few to analyze. Figure 1 depicts cervical cancer screening rates for individual ages from 15 to 29 years. Slight declines occurred in the first 3 years, and then after the Alberta 2009 recommendations, immediate reductions by approximately 10% were observed, less at lower ages. Subsequently, rates continued to decrease, relatively more for the youngest ages and less for those older than 22 years. The gradual decline continued with little apparent change after the 2013 CTFPHC cervical cancer screening recommendations, except for women aged 21-25 years, where a small further change is apparent. To determine whether there is seasonality in screening rates, we also analyzed the quarterly data and observed no differences (results not shown).

Table 1 aggregates data in three 5-year age groups 15–19, 20-24, and 25-29 years. Among women aged 15-19 years, annual screening rates decreased from 16.9% in 2009 to 1.8% in 2016. For the ages of 20-24 years, the test rate declined from 53.2% to 27.1%, and for the ages of 25-29 years, the test rate declined from 59.6% to 38.7%. Table 2 aggregates data in the three 5-year age groups for abnormal screening results and subsequent diagnostic testing. Figure 2 shows the trend of ITSA analysis based on the rates of three 5-year age groups presented in Tables 1 and 2. Observed screening rates are presented as yearly data points, and the predicted line shows the trend of changes in ITSA. As cervical screening rates declined, the rate of diagnosed abnormalities declined in parallel. The cervical biopsy rate changed in a more complex manner. Table 3 provides the statistics of changes between pre- and post-guideline recommendations. It confirms that the changes include an immediate drop in screening rates after the late 2009 guidelines (p < .001 for all 3 age groups) and then a decline continued. After the CTFPHC guideline recommendations in 2013, there was no significant immediate change, but a slight flattening of the rate of decline for each age group.

Table 3 and Figure 2 demonstrate that there already were nonsignificant declines in abnormal readings, and then after the



FIGURE 1. Cervical screening tests by age in Calgary from 2007 to 2016.

| No. women w       | who had a cervi | cal screening te | st      | Fe      | male populat | ion     | Cervical screening rat |         |         |
|-------------------|-----------------|------------------|---------|---------|--------------|---------|------------------------|---------|---------|
| Year/age          | 15–19 y         | 20–24 y          | 25–29 y | 15–19 y | 20–24 y      | 25–29 y | 15–19 y                | 20–24 y | 25–29 y |
| 2007              | 6863            | 21,391           | 27,704  | 39,540  | 38,970       | 45,120  | 17.4                   | 54.9    | 61.4    |
| 2008              | 6707            | 20,871           | 28,109  | 38,610  | 39,300       | 47,610  | 17.4                   | 53.1    | 59.0    |
| 2009              | 6317            | 20,450           | 28,703  | 37,330  | 38,460       | 48,170  | 16.9                   | 53.2    | 59.6    |
| 2010              | 3616            | 16,812           | 24,448  | 37,050  | 38,370       | 48,760  | 9.8                    | 43.8    | 50.1    |
| 2011 <sup>b</sup> | 2614            | 15,222           | 23,094  | 37,430  | 39,170       | 50,470  | 7.0                    | 38.9    | 45.8    |
| 2012              | 1879            | 14,611           | 22,318  | 37,660  | 40,200       | 51,960  | 5.0                    | 36.3    | 42.9    |
| 2013              | 1434            | 13,710           | 22,166  | 38,120  | 40,820       | 54,030  | 3.8                    | 33.6    | 41.0    |
| 2014              | 1196            | 13,680           | 22,607  | 38,400  | 40,750       | 55,750  | 3.1                    | 33.6    | 40.5    |
| 2015              | 1047            | 13,327           | 22,757  | 39,070  | 39,970       | 55,250  | 2.7                    | 33.3    | 41.2    |
| 2016 <sup>b</sup> | 694             | 10,649           | 20,776  | 39,030  | 39,240       | 53,630  | 1.8                    | 27.1    | 38.7    |

<sup>a</sup>Rates are calculated using the total female population of Calgary for that age group and year as the denominator.

<sup>b</sup>Indicates census years: other year populations are estimates.

2009 Alberta guidelines, there was an immediate decrease in abnormal test rates for those aged 15–19 years, but not for those older, followed by decreases for all 3 age groups. After the 2013 guidelines, there was minimal difference for the youngest group, the decline continued at nonsignificantly lower rates for those younger than 24 years, and the 25- to 29-year age group showed a slight increase in abnormal test results.

Table 3 and Figure 2 also show that initially cervical biopsy rates were rising for all age groups. After the 2009 guidelines, there were immediate drops, followed by a consistent decline. After the 2013 guidelines, the decline persisted with no significant changes among those aged 15–19 and 20–24 years. However, cervical biopsy rates for the 25- to 29-year-old group increased by 0.4% (95% CI = 0.1–0.7,  $p \le .001$ ) and rose thereafter. Loop electrosurgical excision procedure and cone biopsies also dropped to zero for the younger group, to one third among 20- to 24-year-old women, and to two thirds among 25- to 29-year-old women.

## **Cervical Biopsy Results and Invasive Cervical Cancer**

Table 4 presents declining numbers of biopsies and rates expressed as percentage of the population in that age group, in proportion to the reduction in number of tests. It also shows the reductions in numbers of pathological diagnoses for the women. For 15- to 19-year-old women, biopsies and diagnoses dropped to zero. Among 20- to 24-year-old women, the CIN I and atypical squamous cells of undetermined significance rate decreased from 2% in 2007 to 1% in 2016, whereas CIN 2 and 3 declined from 2% in 2007 to 0.5% in 2016. Despite this reduced screening and biopsy activity, no invasive cancer was diagnosed among teenagers and only 3 adenocarcinomas among 20- to 24-year-old women during 2007-2016. By contrast, among 25- to 29-year-old women, the total biopsy rates were similar in 2007 and 2016 with fluctuation between. Similarly, the diagnosis of CIN I increased from 1% in 2007 to 2% in 2016, but the CIN 2 and 3 rates dropped from approximately 1.5% to approximately 1% over the 10-year study period. All the invasive cancer cases (n = 8) diagnosed from 2007 to 2016 among 25- to 29-year-old women were adenocarcinomas.

## DISCUSSION

Initially, there was considerable screening among teenagers, progressively more frequent with age, increasing to approximately 60% of women older than 22 years being screened each year.

|      |                                 | 15–19 y                               |                                   |                                 | 20–24 y                               |                                   |                                 | 25–29 y                               |                                   |
|------|---------------------------------|---------------------------------------|-----------------------------------|---------------------------------|---------------------------------------|-----------------------------------|---------------------------------|---------------------------------------|-----------------------------------|
|      | Abnormal<br>screening<br>result | Women who<br>had cervical<br>biopsies | Cervical<br>LEEP/cone<br>biopsies | Abnormal<br>screening<br>result | Women who<br>had cervical<br>biopsies | Cervical<br>LEEP/cone<br>biopsies | Abnormal<br>screening<br>result | Women who<br>had cervical<br>biopsies | Cervical<br>LEEP/cone<br>biopsies |
| Year |                                 |                                       |                                   |                                 | n (%)                                 |                                   |                                 |                                       |                                   |
| 2007 | 1182 (2.99)                     | 295 (0.75)                            | 33 (0.08)                         | 3785 (9.71)                     | 2353 (6.04)                           | 282 (0.72)                        | 3003 (6.66)                     | 2499 (5.54)                           | 305 (0.68)                        |
| 2008 | 1054 (2.73)                     | 307 (0.80)                            | 34 (0.09)                         | 3391 (8.63)                     | 2824 (7.19)                           | 313 (0.80)                        | 2767 (5.81)                     | 3102 (6.52)                           | 408 (0.86)                        |
| 2009 | 1062 (2.84)                     | 334 (0.89)                            | 20 (0.05)                         | 3303 (8.59)                     | 2958 (7.69)                           | 270 (0.70)                        | 2865 (5.95)                     | 3512 (7.29)                           | 330 (0.69)                        |
| 2010 | 709 (1.91)                      | 156 (0.42)                            | 6 (0.02)                          | 3100 (8.08)                     | 1746 (4.55)                           | 163 (0.42)                        | 2749 (5.64)                     | 2100 (4.31)                           | 322 (0.66)                        |
| 2011 | 480 (1.28)                      | 83 (0.22)                             | 2 (0.01)                          | 2590 (6.61)                     | 1635 (4.17)                           | 156 (0.40)                        | 2377 (4.71)                     | 2098 (4.16)                           | 268 (0.53)                        |
| 2012 | 339 (0.90)                      | 45 (0.12)                             | 2 (0.01)                          | 2457 (6.11)                     | 1364 (3.39)                           | 115 (0.29)                        | 2311 (4.45)                     | 1911 (3.68)                           | 232 (0.45)                        |
| 2013 | 252 (0.66)                      | 31 (0.08)                             | 0 (0.00)                          | 2302 (5.64)                     | 1346 (3.30)                           | 109 (0.27)                        | 2368 (4.38)                     | 2314 (4.28)                           | 249 (0.46)                        |
| 2014 | 170 (0.44)                      | 14 (0.04)                             | 3 (0.01)                          | 2383 (5.85)                     | 1536 (3.77)                           | 125 (0.31)                        | 2432 (4.36)                     | 2891 (5.19)                           | 244 (0.44)                        |
| 2015 | 140 (0.36)                      | 11 (0.03)                             | 0 (0.00)                          | 2237 (5.60)                     | 1289 (3.22)                           | 108 (0.27)                        | 2544 (4.60)                     | 3016 (5.46)                           | 261 (0.47)                        |
| 2016 | 109 (0.28)                      | 4 (0.01)                              | 0 (0.00)                          | 1782 (4.54)                     | 1167 (2.97)                           | 86 (0.22)                         | 2477 (4.62)                     | 2995 (5.58)                           | 214 (0.40)                        |

© 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the ASCCP.



FIGURE 2. Trends in annual rates of cervical screening, abnormal results, and cervical biopsy among women aged 15–29 years in Calgary from 2007 to 2016.

After the 2009 guidelines, there was an immediate drop of approximately 10% and thereafter a steady decline, minimally affected by the 2013 recommendations of the Canadian Task Force on Preventive Health Care. Given the reduced number of screening tests, there was a corresponding decline in colposcopy rates, cervical biopsies, and diagnoses among women aged 15–24 years. For women aged 25–29 years, after declines in screening and abnormal results as for the younger groups, there was a slight rise of abnormal results and biopsy. The rates of CIN 2 and 3 among the biopsies declined for those younger than 24 years and remained stable among those aged 25–29 years. There has been a general move away from treating women younger than 25 years aggressively with LEEPs and biopsies, with changed colposcopy guidelines in Canada and United States.<sup>15,16</sup> No invasive squamous carcinoma was found during this period among women younger than 30 years, and there was no measurable trend in adenocarcinoma detection.

Physicians were informed about the change of guidelines in 2009 by one mail-out. Women were informed through media coverage, the "Screening for Life" Web site, and education pamphlets. If physicians and patients had followed the guidelines, there should have been an immediate stop to teenage screening, and the rates for women older than 21 years should have reduced dramatically and then resumed at a lower rate after 2 years, because the interval had lengthened from annual to every 3 years. After 2009, when Calgary Laboratory Services received samples from girls younger than 15 years, pathologists made comments on the reports and sometimes phoned the ordering physicians to ask why the test was performed and encourage them to follow the guidelines (Waghray R, personal communication, February 18, 2020). This likely affected testing among older adolescents as well. The Canadian Task Force Guidelines<sup>2</sup> were publicized through national media, with distribution to members of the Canadian Medical Association with their journal. However, the provincial screening program did not update their guidelines following the 2013 CTFPHC recommendations, until 2016, when the start age of 25 years was adopted, so no extra local publicity occurred until then.<sup>6</sup> Our data demonstrate that health care providers mostly follow the provincially based screening program guidelines.

We had hypothesized that adherence to the guidelines might result in more selective screening, so that women being screened would have a higher rate of abnormal results. However, at each age, the fraction of screening tests diagnosed as abnormal was stable, so the overall rate of abnormal test results among the total female population decreased in proportion to the reduced number of tests.

|                                  |  |   | )  | ,  | ,  |
|----------------------------------|--|---|--|--|--|
|                                  |  | Postinterventi  | ion trend 2010   | Postinterventio  | n trend 2013   |
|                                  | Baseline trend                             | Immediate change after late 2009<br>guideline recommendations | Change per year after late<br>2009 guideline recommendations | Immediate change after 2013<br>guideline recommendations | Change per year after 2013 guideline recommendations |
| Age group/category               |  |   | Parameter coefficient (95% CI, p)                            |  |  |
| Cervical cancer scree            | ning rates                                 |   |  |  |  |
| 15-19                            | -0.2 (-0.5  to  0.0, p = .07)              | -7.2 (-8.0  to  -6.3, p < .001)                               | -2.4 (-2.8  to  -2.0, p < .001)                              | 1.3 $(0.4 \text{ to } 2.2, p = < 0.05)$                  | -0.6 (-0.8  to  -0.5, p < .001)                      |
| 20–24                            | -0.9 (-1.8  to  0.1, p = .07)              | -8.6 (-10.5  to  -6.7, p < .001)                              | -3.7 (-5.0  to  -2.5, p < .001)                              | 2.6 (-3.3  to  8.5, p = .28)                             | -2.0 (-4.5  to  0.6, p = .10)                        |
| 25–29                            | -0.9 (-2.4  to  0.6, p = .17)              | -8.3 (-11.2  to  -5.4, p < .001)                              | -3.6 (-4.4  to  -2.8, p < .001)                              | 2.2 ( $-0.3$ to 4.7, $p = .07$ )                         | -0.6 (-1.5  to  0.3, p = .13)                        |
| Abnormal cervical sc             | reening test rates                         |   |  |  |  |
| 15-19                            | $-0.1 \ (-0.3 \ \text{to} \ 0.1, p = .30)$ | -0.8 (-1.2  to  -0.5, p < .001)                               | -0.5 (-0.6  to  -0.4, p < .001)                              | $0.3 \ (0.0 \ \text{to} \ 0.5, p < .001)$                | -0.1 (-0.2  to  -0.1, p < .001)                      |
| 20–24                            | -0.6 (-1.1  to  0.2, p = .04)              | 0.1 $(-1.0 \text{ to } 1.1, p = .90)$                         | -1.0 (-1.5  to  -0.5, p < .001)                              | 1.0 $(-0.7 \text{ to } 2.7, p = .20)$                    | -0.4 (-0.9  to  0.1, p = .10)                        |
| 25-29                            | -0.4 (-0.9  to  0.2, p = .10)              | 0.1 $(-0.9 \text{ to } 1.1, p = .80)$                         | -0.6 (-0.9  to  -0.2, p < .001)                              | 0.6 (-0.1  to  1.3, p = .10)                             | $0.1 \ (0.0 \text{ to } 0.2, p < .001)$              |
| Cervical biopsy rates            |  |   |  |  |  |
| 15-19                            | $0.1 \ (0.0 \text{ to } 0.1, p < .001)$    | -0.6 (-0.6  to  -0.5, p < .001)                               | -0.2 (-0.2  to  -0.1, p < .001)                              | $0.1 \ (0.0 \ \text{to} \ 0.2, p < .001)$                | $0.0 \ (0.0 \ \text{to} \ 0.0, p < .001)$            |
| 20–24                            | $0.8 \ (0.5 \text{ to } 1.2, p < .001)$    | -4.0 (-4.6  to  -3.4, p < .001)                               | -0.6 (-0.8  to  -0.4, p < .001)                              | 0.7 (0.0  to  1.3, p < .001)                             | -0.2 (-0.5  to  0.2, p = .30)                        |
| 25–29                            | 0.9 (0.8  to  1.0, p < .001)               | -3.8 (-4.1  to  -3.6, p < .001)                               | -0.3 (-0.5  to  -0.1, p < .001)                              | 1.1 (0.5 to 1.7, $p < .001$ )                            | 0.4 (0.1 to 0.7, $p < .001$ )                        |
| <sup>a</sup> Rates are calculate | d using total female population of         | Calgary as the denominator.                                   |  |  |  |

© 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the ASCCP.

After initiation of sexual activity, more than 80% of women are infected with human papillomavirus (HPV). Infections are mostly asymptomatic, and 90% are cleared by the immune system.<sup>17</sup> A few oncogenic HPV types might persist but usually take 10-20 years for progression to cancer.<sup>18</sup> However, many women younger than 25 continue to undergo cervical screening with the discovery of lesions that would spontaneously regress in the vast majority of them.<sup>6,19</sup> Treating precursor lesions that might otherwise resolve spontaneously causes physical and psychological harm<sup>20</sup> and affects a young woman's quality of life.<sup>21</sup> In addition to being uncomfortable, invasive testing and procedures require taking time away from work or studies<sup>22</sup> and often lead to anxiety.<sup>20</sup> After an abnormal screening test, follow-up procedure such as colposcopy may produce pain, bleeding, and discharge. In addition, LEEP procedures may double the rates of premature labor.<sup>23</sup> This risk is more serious in younger women who are less likely to have started or completed their families and most can be classified as "overtreatment" because few of these lesions would progress to cancer.23

The ability of screening to reduce the few cases of invasive cancer among young women is limited. In countries where screening starts at the age of 20 years, rates of cervical cancer in women younger than 25 years are not significantly different than in countries that start screening at the age of 30 years.<sup>21,24,25</sup> A population-based case-control study in United Kingdom with prospectively recorded data also demonstrated that cervical screening in women aged 20–24 years has little or no impact on rates of invasive cervical cancer up to the age of 30 years.<sup>26</sup> These findings corroborate the evidence from UK, US, Canadian, and Australian national statistics where regular and frequent screening among young women made minimal difference to incidence and mortality in such young women.<sup>2,25–28</sup> The American Cancer Society guidelines also recently changed to start screening from the age of 25 years.<sup>29</sup>

False-positive rates are progressively less frequent among older women, so the balance of harms caused by false positives against the benefits gained from finding and treating precancers changes dramatically as cancer incidence rises with age.<sup>30</sup> Understanding this change in the balance should underpin the strength of recommendations for women in different age groups.<sup>2,31</sup>

It is unclear how much the reduction in screening is due to clinician adherence to guidelines and how much is due to change in patient expectations.<sup>2,4</sup> Some physicians continue annual screening from young ages. Physicians in practice for many years often have established patterns of practice and their patients have learned to expect this pattern, so making and explaining change are sometimes difficult.<sup>32</sup>

## **Strengths and Limitations**

In Alberta, health care including screening tests is free to users, so there is high uptake by the population, but as elsewhere, women with lower social status and new immigrants are less likely to be screened.<sup>33</sup> Because all pathology specimens in the region are sent to the Calgary Laboratory Services the study captured all tests from this population. Liquid-based cytology was introduced to Calgary in 2006, and reflex HPV testing was introduced for women older than 30 years, but there were no changes in laboratory protocols for those younger than 29 years, whereas diagnostic criteria were stable during the 10-year study period. The screening program was extended to the whole province but was stable in Calgary for the study period. We have no data on referrals to colposcopy, so as an indicator of colposcopy, we measured the number of women who had biopsies. Colposcopy policies changed over this period from being selective to taking a biopsy on every patient, which likely accounts for the rises in

|              |                                | 1                                     | 15–19 y                  |                                  |                             |                                |                                   | 20–24 y                           |                        |                            |                         |                              | 25–29 y                  |                        |                            |
|--------------|--------------------------------|---------------------------------------|--------------------------|----------------------------------|-----------------------------|--------------------------------|-----------------------------------|-----------------------------------|------------------------|----------------------------|-------------------------|------------------------------|--------------------------|------------------------|----------------------------|
| -            |                                |                                       | (%) <i>u</i>             |                                  |                             |                                |                                   | (%) <i>u</i>                      |                        |                            |                         |                              | (%) <i>u</i>             |                        |                            |
| Voar         | Negative<br>bionsies           | LSIL (CIN I<br>and ASCUS)             | HSIL<br>(CIN 2<br>and 3) | ICC<br>cases<br>and<br>rates per | Total                       | Negative<br>hioneiee           | LSIL<br>(CIN I and<br>ASCUS)      | HSIL (CIN<br>2 and 3)             | ICC cases<br>and rates | Total                      | Negative<br>hionsias    | LSIL<br>(CIN I and<br>ASCUS) | HSIL (CIN<br>2 and 3)    | ICC cases<br>and rates | Total                      |
| 1000         |                                |                                       |                          |                                  |                             |                                |                                   | 0                                 | or nd                  |                            |                         |                              |                          | or nd                  |                            |
| 2007<br>2008 | 89 (0.23)<br>94 (0.24)         | 128 (0.32)<br>160 (0.41)              | 78 (0.2)<br>59 (0.15)    | (0) (0)<br>0                     | 295 (0.75)<br>313 (0.81)    | 728 (1.87)<br>877 (2.23)       | 793 (2.03)<br>973 (2.48)          | 608 (1.56)<br>611 (1.55)          | $(0) \\ 0 \\ 0$        | 2129 (5.46)<br>2461 (6.26) | 768 (1.7)<br>925 (1.94) | 647 (1.43)<br>813 (1.71)     | 634 (1.41)<br>745 (1.56) | 3 (6.65)<br>1 (2.1)    | 2052 (4.55)<br>2484 (5.22) |
| 2009         | 103 (0.28)                     | 130 (0.35)                            | 65 (0.17)                | 0 (0)                            | 298 (0.8)                   | 840 (2.18)                     | 947 (2.46)                        | 591 (1.54)                        | 0 (0)                  | 2378 (6.18)                | 899 (1.87)              | 875 (1.82)                   | 659 (1.37)               | 0 (0)                  | 2433 (5.05)                |
| 2010         | 56 (0.15)                      | 67 (0.18)                             | 33 (0.09)                | 0 (0)                            | 156 (0.42)                  | 627 (1.63)                     | 693 (1.81)                        | 425 (1.11)                        | 1 (2.61)               | 1746 (4.55)                | 698 (1.43)              | 740 (1.52)                   | 661 (1.36)               | 1 (2.05)               | 2100 (4.31)                |
| 2011         | 31 (0.08)                      | 34 (0.09)                             | 18 (0.05)                | (0) (0)                          | 83 (0.22)                   | 596 (1.52)                     | 629 (1.61)                        | 410 (1.05)                        | 0 (0)                  | 1635 (4.17)                | 828 (1.64)              | 683 (1.35)                   | 585 (1.16)               | 2 (3.96)               | 2098 (4.16)                |
| 2012         | 11 (0.03)                      | 24 (0.06)                             | 10 (0.03)                | (0) (0)                          | 45 (0.12)                   | 409 (1.02)                     | 655 (1.63)                        | 298 (0.74)                        | 2 (4.98)               | 1362 (3.39)                | 629 (1.21)              | 777 (1.5)                    | 505 (0.97)               | (0) (0)                | 1911 (3.68)                |
| 2013         | 13 (0.03)                      | 11 (0.03)                             | 7 (0.02)                 | (0) (0)                          | 31 (0.08)                   | 566 (1.39)                     | 504 (1.23)                        | 276 (0.68)                        | (0) 0                  | 1346 (3.3)                 | 994 (1.84)              | 762 (1.41)                   | 558 (1.03)               | (0) (0)                | 2314 (4.28)                |
| 2014         | 4(0.01)                        | 3 (0.01)                              | 7 (0.02)                 | (0) (0)                          | 14(0.04)                    | 699 (1.72)                     | 526 (1.29)                        | 311 (0.76)                        | (0) 0                  | 1536 (3.77)                | 1528 (2.74)             | 823 (1.48)                   | 537 (0.96)               | 1 (1.79)               | 2889 (5.18)                |
| 2015         | 3 (0.01)                       | 5 (0.01)                              | 3 (0.01)                 | (0) (0)                          | 11 (0.03)                   | 592 (1.48)                     | 437 (1.09)                        | 260 (0.65)                        | 0 (0)                  | 1289 (3.22)                | 1648 (2.98)             | 808 (1.46)                   | 560 (1.01)               | (0) (0)                | 3016 (5.46)                |
| 2016         | (0) (0)                        | 1(0)                                  | (0) 0                    | (0) (0)                          | 1 (0)                       | 554 (1.41)                     | 408 (1.04)                        | 205 (0.52)                        | 0 (0)                  | 1157 (2.95)                | 1548 (2.89)             | 921 (1.72)                   | 525 (0.98)               | 1 (1.86)               | 2995 (5.58)                |
| Rati         | es are calcul;<br>JUS indicate | ated using the to<br>s atypical squan | tal female pu            | opulation of<br>undetermir       | Calgary for the significant | that age grou<br>ce; HSIL, hig | p and year as 1<br>gh-grade squai | the denominate<br>mous intraepitl | or.<br>helial lesion;  | LSIL, low-grad             | le squamous in          | traepithelial le             | sion.                    |                        |                            |

biopsy rates. We only measured the number of women who had a test in each year, not the intervals between tests, so to the extent that intervals are longer than 1 year, the proportion of women being screened is higher than these percentages. Because we could not determine whether tests were part of a follow-up for an abnormal result, such women were included in our counts, thus increasing the apparent numbers screened. Future studies should exclude follow-up tests and measure how many women have more than 1 screening test in 3 years, thereby potentially increasing the risk of harm. The new guidelines recommend against screening women who have not been sexually active, but we do not have data on rates of sexual activity so we could not use women eligible for screening as a denominator. Hysterectomy prevalence among these young women is less than 1 per 1,000, so we did not make allowance for hysterectomies. We did not link data, so we cannot discern whether women who developed adenocarcinoma had previously been screened.

Human papillomavirus mass immunization programs initially commenced in Alberta in the 2008/2009 academic year with the cohort of girls born in 1997/1998.<sup>34</sup> For a 3-year catch-up program in 2009/2010, the vaccine was also given to grade 9 girls born in 1995/1996 and the subsequent 3 years. However, only approximately 70% were immunized. Thus, they were 12 years old at the beginning of the study, and by 2016, they were aged 20 years.<sup>34</sup> In addition, fewer than 5% of older women paid for their own immunization. Immunization likely has caused some reduction in abnormalities in the later years of the study.

#### Conclusions

Cervical screening rates among young women in Calgary have declined slowly after guideline changes. Less testing leads to less diagnosis of abnormalities, therefore presumably fewer referrals for colposcopy, and subsequent potential for harms to women. With the changed pattern of practice, large numbers of abnormalities remain undetected among young women and seem likely to have regressed spontaneously, so these women do not experience from overdiagnosis and unnecessary colposcopy, biopsy, or treatment. These results in a total population study should provide reassurance that it is safe to raise the starting age for screening to 25 years, even before HPV immunization of young women is universal. Resources should be focused on women with lower rates of cervical screening, such as women living in rural areas, indigenous, and immigrant women. A first test for these women at higher risk provides more value than testing women at low risk who are younger than 25 years.

#### ACKNOWLEDGMENTS

The authors thank Maggie Guo of the Calgary Laboratory Services who acquired the LIS data and helped in the initial analysis.

#### REFERENCES

- US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, et al. Screening for cervical cancer: US preventive services task force recommendation statement. *JAMA* 2018;320:674–86.
- Dickinson J, Tsakonas E, Conner Gorber S, et al. Recommendations on screening for cervical cancer. *Can Med Assoc J* 2013;185:35–45.
- Symonds CJ, Chen W, Rose MS, et al. Screening with papanicolaou tests in Alberta: are we choosing wisely? *Can Fam Physician* 2018;64:47–53.
- Canadian Partnership Against Cancer. Cervical Cancer Screening in Canada: Environmental Scan. Toronto: Canadian Partnership Against Cancer; 2018.
- Toward Optimized Practice (TOP) Working Group for Cervical Cancer. Guideline for the Screening for Cervical Cancer. Edmonton, AB: Toward Optimized Practice. c2009.; 2009.

- Towards Optimized Practice: Cervical Cancer Screening Clinical Practice Guideline. Alberta: Canada; 2016:1–2. Available at: https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/Cervical-Cancer-Screening-CPG.pdf. Accessed February 17, 2019.
- Blake J. What's needed for Canada's cervical cancer endgame? CMAJ 2019;191:E481.
- Curry SJ, Krist AH, Owens DK. Age of initiation of cervical cancer screening – reply. JAMA 2019;321:612.
- Dollin J. Preventing cervical cancer: beyond following guidelines. CMAJ 2013;185:13–4.
- Boone E, Lewis L, Karp M. Discontent and confusion: primary care providers' opinions and understanding of current cervical cancer screening recommendations. J Womens Health (Larchmt) 2016;25:255–62.
- Haas JS, Sprague BL, Klabunde CN, et al. Provider attitudes and screening practices following changes in breast and cervical cancer screening guidelines. J Gen Intern Med 2016;31:52–9.
- Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines?: a framework for improvement. JAMA 1999;282:1458–65.
- Statistics Canada. 2017. Calgary, CY [Census subdivision], Alberta and Division No. 6, CDR [Census division], Alberta (table). Census Profile. 2016 Census. Statistics Canada Catalogue no. 98-316-X2016001. Ottawa, Canada. Released November 29, 2017. Accessed July 27, 2020.
- Linden A. Conducting interrupted time-series analysis for single- and multiple-group comparisons. *Stata J Promot Commun Stat Stata* 2015;15: 480–500.
- Bentley J, Executive Council of the Society of Canadian Colposcopists; Special Contributors. Colposcopic management of abnormal cervical cytology and histology. *J Obstet Gynaecol Can* 2012;34:1188–202.
- Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2013;17(5 suppl 1):S1–27.
- Winer RL, Hughes JP, Feng Q, et al. Early natural history of incident, type-specific human papillomavirus infections in newly sexually active young women. *Cancer Epidemiol Biomarkers Prev* 2011;20:699–707.
- Bosch FX, Burchell AN, Schiffman M, et al. Epidemiology and natural history of human papillomavirus infections and type-specific implications in cervical neoplasia. *Vaccine* 2008;26(suppl 10):K1–16.
- Landy R, Birke H, Castanon A, et al. Benefits and harms of cervical screening from age 20 years compared with screening from age 25 years. *Br J Cancer* 2014;110:1841–6.
- Frederiksen ME, Njor S, Lynge E, et al. Psychological effects of diagnosis and treatment of cervical intraepithelial neoplasia: a systematic review. *Sex Transm Infect* 2015;91:248–56.
- Habbema D, Weinmann S, Arbyn M, et al. Harms of cervical cancer screening in the United States and the Netherlands. *Int J Cancer* 2017;140: 1215–22.
- Shireman TI, Tsevat J, Goldie SJ. Time costs associated with cervical cancer screening. Int J Technol Assess Health Care 2001;17:146–52.
- Kyrgiou M, Athanasiou A, Paraskevaidi M, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ* 2016;354:i3633.
- Lönnberg S, Anttila A, Luostarinen T, et al. Age-specific effectiveness of the Finnish cervical cancer screening programme. *Cancer Epidemiol Biomarkers Prev* 2012;21:1354–61.
- Smith M, Canfell K. Impact of the Australian National Cervical Screening Program in women of different ages. *Med J Aust* 2016;205:359–64.
- Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. *BMJ* 2009;339:b2968.
- Morris CP, Chowsilpa S, Mustafa S, et al. Impact of the current US Preventive Services Task Force Recommendations for cervical cancer

screening in young women 21 to 29 years old. Am J Clin Pathol 2020; 153:734-42.

- Beachler DC, Tota JE, Silver MI, et al. Trends in cervical cancer incidence in younger US women from 2000 to 2013. *Gynecol Oncol* 2017; 144:391–5.
- Fontham ETH, Wolf AMD, Church TR, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. *CA Cancer J Clin* 2020;70:321–6.
- Kulasingam SL, Havrilesky L, Ghebre R, et al. Screening for Cervical Cancer: A Decision Analysis for the U.S. Preventive Services Task Force.

AHRQ Publication No. 11-05157-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; May 2011.

- Phillips SP, Bates S, Mavriplis C, et al. Cervical cancer screening for young women. Can Fam Physician 2020;66.
- Gupta DM, Boland RJ Jr., Aron DC. The physician's experience of changing clinical practice: a struggle to unlearn. *Implement Sci* 2017;12:28.
- Kerner J, Liu J, Wang K, et al. Canadian cancer screening disparities: a recent historical perspective. *Current Oncology* 2015;22:156–63.
- Liu XC, Bell CA, Simmonds KA, et al. HPV vaccine utilization, Alberta 2008/09-2013/14 School year. *BMC Infect Dis* 2016;16:15.