Strategies to accelerate the elimination of cervical cancer in British Columbia, Canada: a modelling study

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Abstract

Background: To eliminate cervical cancer in Canada by 2040, defined as an annual age-standardized incidence rate (ASIR) lower than 4.0 per 100 000 women, the Canadian Partnership Against Cancer (CPAC) identified 3 priorities for action: increasing human papillomavirus (HPV) vaccine coverage, implementing HPV-based screening and increasing screening participation, and improving follow-up after abnormal screen results. Our objective was to explore the impact of these priorities on the projected time to elimination of cervical cancer in British Columbia.

Methods: We used OncoSim-Cervical, a microsimulation model led and supported by CPAC and developed by Statistics Canada that simulates HPV transmission and the natural history of cervical cancer for the Canadian population. We updated model parameters to reflect BC's historical participation rates and program design. We simulated the transition to HPV-based screening and developed scenarios to explore the additional impact of achieving 90% vaccination coverage, 95% screening recruitment, 90% on-time screening, and 95% follow-up compliance. We projected cervical cancer incidence, ASIR, and year of elimination for the population of BC for 2023–2050.

Results: HPV-based screening at current vaccination, participation, and follow-up rates can eliminate cervical cancer by 2034. Increasing on-time screening and follow-up compliance could achieve this target by 2031. Increasing vaccination coverage has a small impact over this time horizon.

Interpretation: With the implementation of HPV-based screening, cervical cancer can be eliminated in BC before 2040. Efforts to increase screening participation and follow-up through this transition could potentially accelerate this timeline, but the transition from cytology- to HPV-based screening is fundamental to achieving this goal.

A long-term, persistent infection with an oncogenic genotype of the human papillomavirus (HPV) is a necessary condition for the development of cervical cancer. Nine types of high-risk HPV are responsible for more than 90% of cervical cancer cases globally, with 71% caused by HPV types 16 or 18.[1] Cervical cancer can be prevented through vaccination against HPV and through early detection and treatment of precancerous lesions with screening. For decades, cytology (Pap testing) has been the primary approach to screening. Cytology-based screening has been a public health success, but since the mid-2000s the incidence of cervical cancer in Canada has remained largely unchanged, with an age-standardized incidence rate (ASIR; 2011 Canadian population) at around 7.1 per 100 000 females.[2,3] To further reduce the burden of cervical cancer, interventions to prevent HPV infection and to enhance cervical screening are necessary.

In Canada, publicly funded school-based HPV vaccination programs have been in place for girls starting in 2007, and for boys starting in 2013.[4,5] Vaccination against HPV is highly effective at preventing cervical precancer;[6] however, the current screen-eligible population is largely unvaccinated, as the first vaccinated cohorts have only recently reached screening age. Primary screening with HPV testing has shown higher sensitivity than cytology for detection of cervical precancer.[7,8] Unlike cytology testing, which involves a speculum examination by a clinician for cervical cell collection, HPV testing can be performed on cervical or self-collected vaginal samples. The option for self-collection may also reduce barriers to access and increase screening uptake among those who are never- or under-screened.[9,10] HPV-based screening is now being implemented in many jurisdictions to replace cytology testing.[11–14]

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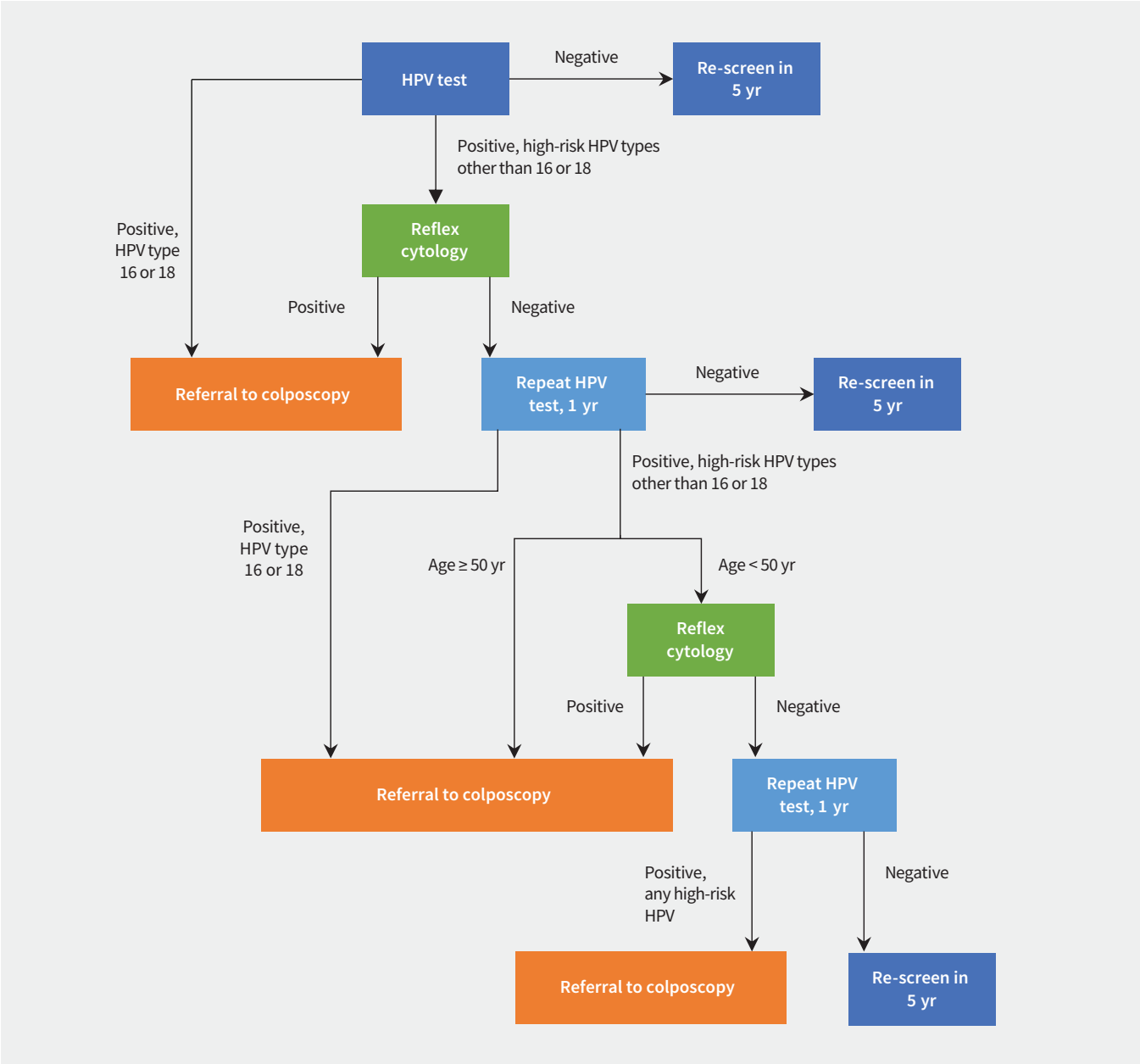

Figure 1: Simulated human papillomavirus (HPV)-based screening and follow-up process: HPV-based screening is offered every 5 years for women and people with a cervix aged 25–69 years. People with a result positive for HPV type 16 or 18 are referred directly to colposcopy; those positive for high-risk HPV types other than 16 or 18 (including types 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 [www.bccancer.bc.ca/screening/Documents/Cervix-Program-Overview.pdf]) receive reflex cytology. If reflex cytology is positive, they are referred to colposcopy; otherwise, they return for repeat HPV testing in 1 year. On repeat testing, those positive for HPV type 16 or 18 or positive for high-risk HPV types other than 16 or 18 and aged 50 years or older are referred to colposcopy. Those positive for high-risk HPV types other than 16 or 18 and younger than 50 years, with normal cytology, return for a second round of repeat testing in 1 year. People with a positive HPV result on second re-testing are referred directly to colposcopy. See Related Content tab for accessible version.

In 2020, the World Health Organization (WHO) committed to eliminating cervical cancer as a global public health problem, defining elimination as an annual ASIR of lower than 4.0 per 100 000 women.[15] Similarly, the Canadian Partnership Against Cancer (CPAC) developed an action plan to eliminate cervical cancer in Canada by 2040.[16] The action plan lays out strategies and targets in 3 priority areas to achieve this goal: improving uptake of HPV vaccination, implementing HPV-based screening and increasing screening participation, and improving follow-up after abnormal screening results.[16]

British Columbia recently launched a 10-year cancer plan, which includes the goal of reducing cervical cancer incidence, and commenced the transition to HPV-based screening in January 2024.[17] The objective of our study was to explore when and how BC can achieve elimination of cervical cancer, defined as an ASIR lower than 4.0 per 100 000, following the

transition to HPV-based screening. We explored the relative impact of the 3 priorities of the CPAC action plan on incidence of cervical cancer and projected year of elimination. With identification of the areas that will have the greatest impact on prevention of cervical cancer, action in critical policy areas can be prioritized.

Methods

We used the OncoSim-Cervical model[18] (version 3.6.2.5) to project outcomes for the population of BC under alternative screening scenarios. OncoSim is led and supported by CPAC, with model development from Statistics Canada. OncoSim-Cervical combines an interacting agent model to simulate HPV infection, with a Monte Carlo microsimulation model to simulate the natural history of cervical cancer (Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.231682/tab-related-content). The model is calibrated using data on prevalence of cervical cancer by disease phase, and has been validated against incidence rates and stage distribution from the Canadian Cancer Registry.[19] The model incorporates strategies to control cervical cancer, including HPV vaccination, cervical screening, precancer treatment, and cancer therapy, and provides projections of both the health and resource impacts of these programs.

We modified OncoSim model parameters to reflect BC vaccination and cervical-screening program structure and participation levels. British Columbia offers publicly funded school-based vaccination of girls and boys in grade 6 with the nonavalent HPV vaccine,[20] and vaccination coverage is approximately 70%.[21] At the time of the analysis, BC offered cytology screening every 3 years for women and people with a cervix from age 25 to 69 years. Approximately 90% of eligible people have ever received a screening test, approximately 70% are up to date on recommended screening,[22] and 88% of people who are recommended for colposcopy following an abnormal screen receive the procedure.[22]

Screening scenarios

We developed 2 reference scenarios for the model: a scenario representing BC's cytology-based screening program at the time of the analysis, and an HPV base case simulating the implementation of primary HPV testing. The HPV base-case scenario was defined as primary HPV testing every 5 years, for people with a cervix aged 25–69 years (Figure 1). Referral to colposcopy or follow-up testing was conditional on HPV genotype and age.[23] To reduce the impact of the transition to HPV-based screening on downstream health resources, including colposcopy and precancer treatment, we implemented HPV-based screening gradually over 5 years in the model.

The study team identified model parameters associated with the priority areas in CPAC's action plan (Box 1). We developed model scenarios (Table 1) to explore the effect of increasing HPV vaccination coverage in the school-based program from 70% to 90% (priority 1), increasing screening recruitment (i.e., the probability of ever receiving a screening test) from 90% to 95% (priority 2a), increasing on-time screening from 70% to 90% (priority 2b), and increasing follow-up compliance from 80% for follow-up HPV testing and 88% for colposcopy to 95% for both (priority 3). We also included scenarios combining screening and follow-up targets (priorities 2 and 3), and all 3 targets simultaneously.

We simulated outcomes for the BC population of females from 2023 to 2050. The population is a dynamic cohort, with approximately 1.62 million people of screening age in 2023. We used the maximum simulation size in OncoSim to reduce random error in the projections. Outcomes of interest were ASIR of

Box 1: Summary of Canadian Partnership Against Cancer priority areas, selected targets, and corresponding model scenarios

Priority 1: to improve rates of HPV vaccination

Target 1: 90% of 17-year-olds are fully vaccinated with the HPV vaccine[16]

- OncoSim model parameter: vaccine coverage percentage, defined as the percentage of the eligible population who are fully vaccinated
- Model scenario for priority 1: 90% vaccine coverage, increased from base-case level of 70%[21]

Priority 2: to implement HPV screening

Target 2a: 90% of eligible individuals have been screened with an HPV test[16]

- OncoSim model parameter: screening recruitment rate, defined as the probability an individual will enroll in the screening program if they are not currently screened
- Model scenario for priority 2a: 95% screening recruitment rate, increased from base-case level of 90%;* re-screen rate held constant at 80%[22]

Target 2b: 90% of eligible individuals are up to date with current screening

- OncoSim model parameters: screening recruitment rate, defined as the probability an individual will enroll in the screening program if they are not currently screened, and re-screen rate, defined as the probability an individual will be re-screened on time if they are currently in the screening program
- Model scenario for priority 2b: recruitment rate of 95%, increased from base-case level of 90%, and 95% re-screen rate, increased from base case of 80%,[22] to give overall on-time participation of 90%

Priority 3: to improve follow-up of abnormal results

Target 3: 90% of individuals with an abnormal screening result have a clear plan of appropriate follow-up[16]

- OncoSim model parameter: follow-up compliance, defined as the probability of attending recommended follow-up, by follow-up modality
- Model scenario for priority 3: colposcopy follow-up compliance of 95%, increased from current level for British Columbia of 88%,*[22] and HPV follow-up compliance of 95%, increased from OncoSim default of 80%

Note: HPV = human papillomavirus.
*Parameters for screening recruitment (priority 2a) and follow-up compliance (priority 3) were set to levels above the action plan targets of the Canadian Partnership Against Cancer, because base-case levels are at or near the target values.

Table 1: Summary of model parameters for alternative priority scenarios

Scenario	OncoSim model parameter				
	Vaccination coverage, %	Recruitment rate (ever screened), %	Re-screen rate among screened, %	Follow-up compliance, HPV, %	Follow-up compliance, colposcopy, %
HPV primary screening base case	70	90	80	80	88
Priority 1: increase vaccination	**90***	90	80	80	88
Priority 2a: increase screening recruitment	70	**95***	80	80	88
Priority 2b: increase on-time screening	70	**95***	**95***	80	88
Priority 3: improve follow-up	70	90	80	**95***	**95***
Priorities 2 and 3	70	**95***	**95***	**95***	**95***
All priorities combined	**90***	**95***	**95***	**95***	**95***

Note: HPV = human papillomavirus.
*Bold values indicate changes relative to base-case scenario.

cervical cancer, age-standardized using the WHO World Standard Population to be consistent with elimination target,[24] projected number of cases of cervical cancer in BC, and year of elimination of cervical cancer, defined as the first year in which the ASIR stayed below 4.0 per 100 000.[15,16] Secondary outcomes were colposcopy and precancer treatment volume by year.

Sensitivity analysis

We conducted sensitivity analyses to explore the effect of baseline parameters for on-time screening participation and vaccination coverage. Lower limits for these parameters were selected based on the variability observed by region and over time.[21,22] Scenarios included on-time screening participation of 65%, vaccine coverage of 65%, and a combination of both (Appendix 1, Table S1), for the cytology screening and HPV base-case scenarios.

Ethics approval

The University of British Columbia–BC Cancer Research Ethics Board gave ethics approval for this study (H21-01184).

Results

Using cytology-based screening, BC would not achieve an ASIR of cervical cancer lower than 4.0 per 100 000 until 2045 (Figure 2). Implementation of HPV-based screening at current participation levels with cytological screening would eliminate cervical cancer by 2034 and prevent 942 cases of cervical cancer compared with cytology screening (Table 2). Increasing the proportion of people ever screened or increasing vaccination coverage would achieve elimination by 2033. Increasing on-time screening or increasing follow-up compliance would achieve elimination by 2032, and prevent 406 or 322 more cervical cancers than the HPV base case, respectively.

Combining priorities 2 and 3, with increased screening and follow-up rates, would potentially reach an ASIR lower than 4.0 per 100 000 by 2031. Achieving 90% vaccination in addition to the screening and follow-up targets had little effect on incidence by 2050.

Projected colposcopy and precancer treatment volumes increased considerably under all HPV-based screening scenarios (Figure 3) in the short term. In the HPV base case, colposcopy and precancer treatment volumes would peak at 82% and 48% above cytology-based screening levels by 2026, respectively, returning to cytology-based screening levels by 2045. Achieving priorities 2 and 3 combined would result in the highest demand for colposcopy and precancer treatment (139% and 88% increase over cytology-based screening).

Incidence projections are moderately sensitive to baseline parameters for screening and vaccination coverage (Appendix 1, Figure S2). Lower on-time screening participation would delay elimination by 3–5 years. Combined with lower vaccination coverage, elimination would be delayed by at least 8 years (Appendix 1, Table S2).

Interpretation

Under the previous cytology-based screening program, with no changes to vaccination or screening participation rates, BC would not reach the WHO and CPAC goal of cervical cancer elimination (4.0 cases/100 000 women) until at least 2045. Implementation of HPV-based screening, with genotyping for HPV types 16 or 18 and reflex cytology to inform triage and follow-up, would allow this threshold to be reached by 2034, preventing more than 900 cases of cervical cancer by 2050. Achieving any of the targets in CPAC's priority areas individually could accelerate the elimination of cervical cancer; however, if it were possible to achieve the target levels in on-time screening participation and follow-up simultaneously, cervical cancer could potentially be eliminated in BC as early as 2031.

Our projections of time to elimination are similar to results from other high-income countries. Modelling from the United States indicates that cervical cancer can be eliminated with cytology-based screening in a 15- to 21-year time horizon.[25] Using HPV-based screening, the elimination threshold should be achieved in 2025 in Australia (8 yr after implementation),[26]

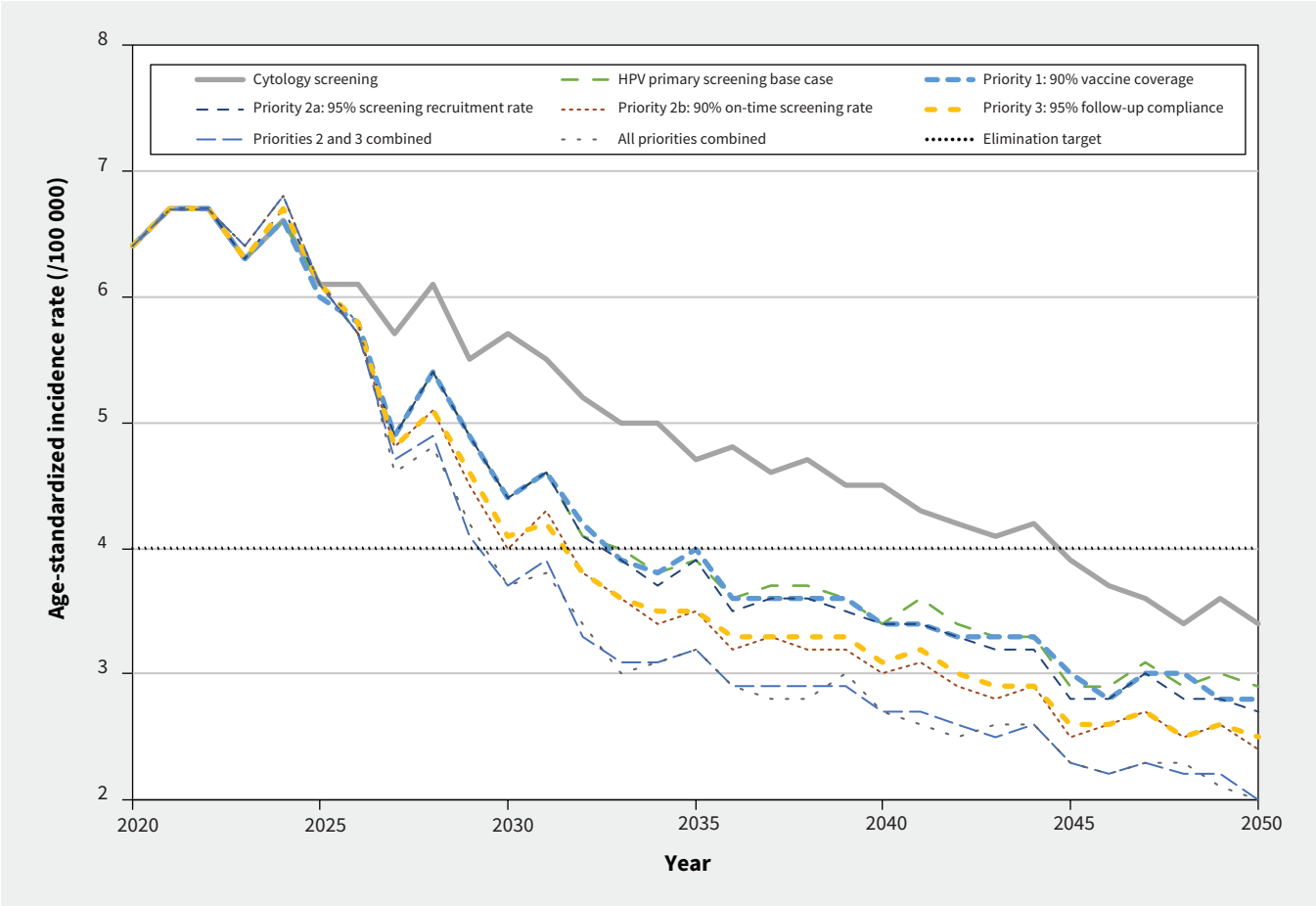

Figure 2: Projected age-standardized cervical cancer incidence rate for British Columbia, to 2050. Age-standardized to World Health Organization World Standard Population; incidence expressed as cases per 100 000 females. Dotted line indicates elimination target of 4.0 per 100 000. Note: HPV = human papillomavirus.

Table 2: Year of elimination* of cervical cancer and number of cervical cancer cases avoided in British Columbia, 2023–2050

Scenario	Elimination year	Cases of cervical cancer avoided v. cytology screening
Cytology screening	2045	–
HPV primary screening base case	2034	942
Priority 1: 90% vaccination	2033	966
Priority 2a: 95% recruitment	2033	1020
Priority 2b: 90% on-time screening	2032	1348
Priority 3: 95% follow-up rate	2032	1274
Priorities 2 and 3	2031	1669
All priorities combined	2031	1675

Note: HPV = human papillomavirus.
*Elimination is defined as an annual age-standardized incidence rate lower than 4.0 per 100 000.

2035 in Norway (15 yr after implementation),[27] and 2042 in the Netherlands, where low-frequency (every 5 yr starting at age 30 yr, then every 10 yr for people with a negative screen at age 40 yr) HPV screening has been offered since 2017.[28] Although screening program design, vaccination coverage, and screening participation vary across jurisdictions, previous studies consistently report that adoption of HPV-based screening and increasing on-time participation have the largest impact on projected incidence.[25,27–29]

Increasing on-time screening participation among never-screened and underscreened individuals, or increasing adherence to recommended follow-up would have the largest impact on eliminating cervical cancer in a shorter time frame. Both scenarios achieved the elimination threshold 2 years earlier than the HPV base case. Of these 2 strategies, increasing on-time screening participation had a slightly larger impact on the number of cervical cancers prevented by 2050. Our base-case scenario assumes that current screening participation rates remain the same after the implementation of HPV-based primary screening. However, HPV testing presents opportunities for innovative approaches to screening, including self-collection, which have the potential to increase participation among never- or underscreened populations. Self-collection of vaginal samples for HPV

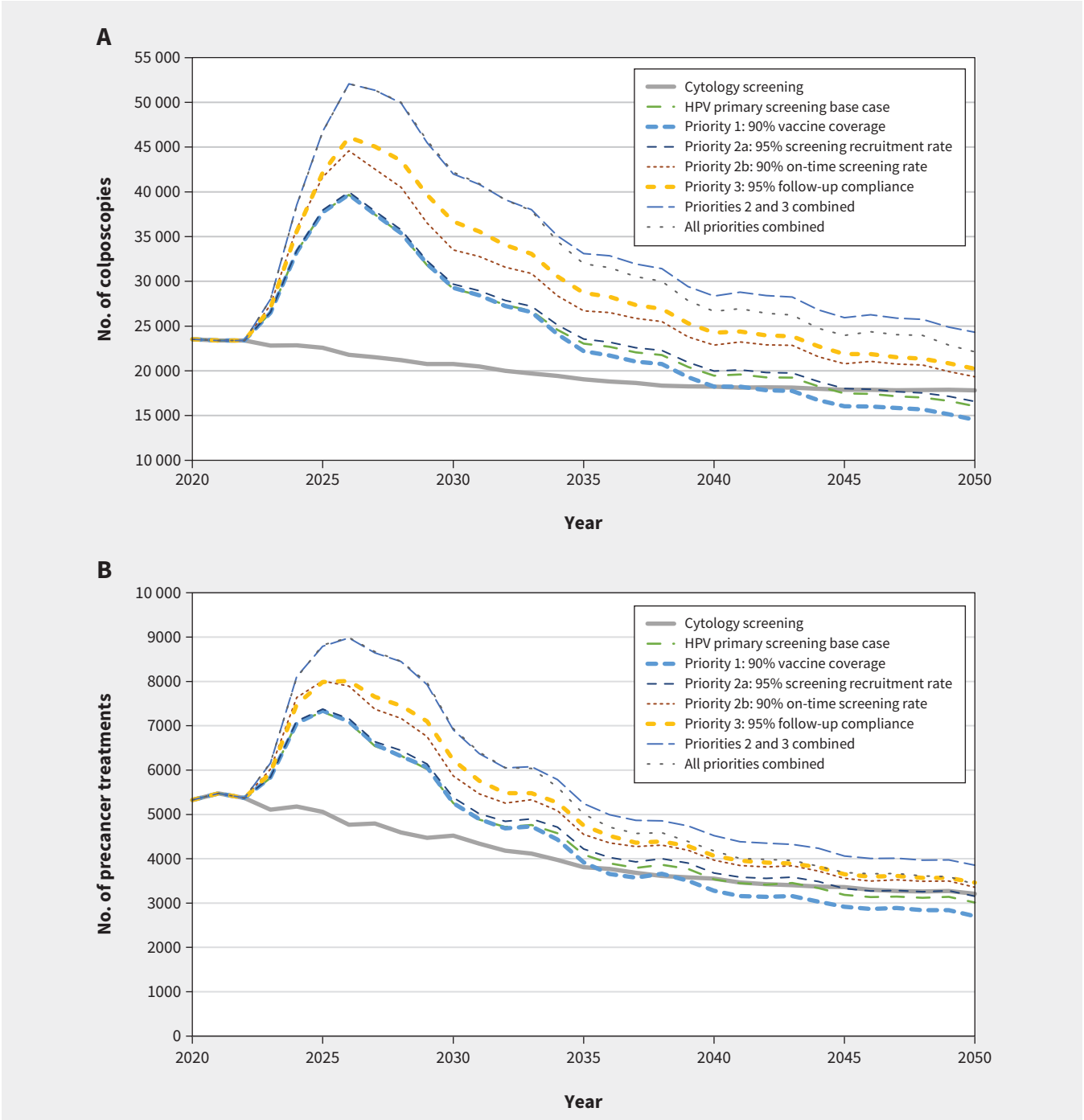

Figure 3: (A) Projected colposcopy volume, by screening scenario and year, 2023–2050. (B) Projected precancer treatment volume, by screening scenario and year, 2023–2050. Note: HPV = human papillomavirus.

testing has been shown to be highly acceptable and can increase access to cervical screening.[30] A pilot self-collection program was successfully undertaken in BC, and the program has now been expanded provincially as part of the transition to HPV primary screening.[31] A randomized controlled trial conducted in the US found that women with low incomes who were overdue for screening were almost twice as likely to complete screening if they received a mailed HPV self-collection kit, compared with an invitation to schedule an in-person screening visit.[9]

A concern regarding the transition to HPV-based screening has been the subsequent increase in demand for colposcopy and precancer treatment over the short term.[32,33] We found that in all HPV-based screening scenarios, volumes peaked shortly after full implementation of HPV testing, and decreased gradually to near or below cytology-based screening levels by 2050. This is consistent with data from the HPV for Cervical Cancer Screening trial, which showed an initial surge in colposcopy rates after participants' first HPV tests, followed by a decrease below the rate observed in the

cytology-screened comparators.[33] Managing the initial surge in demand for colposcopy and precancer treatment caused by detection of prevalent HPV infections could be a challenge for health care systems. However, this surge in demand could be mitigated with alternative implementation strategies, such as phased introduction of HPV testing by age. Future research is needed to explore implementation strategies and queuing models, and to evaluate the system-wide costs and cost-effectiveness of implementation.

Our modelling indicated that increasing vaccination has a relatively small impact on time to elimination. The HPV vaccine is highly effective at preventing cervical cancer, as well as other HPV-attributable anogenital, and head and neck cancers.[1] However, the benefits of increased vaccination will be observed beyond the time horizon of the model, as the vaccinated birth cohorts age. Catch-up vaccination programs targeting older unvaccinated populations have been proposed, but their projected impact is small.[25] Achieving a 90% vaccination rate in the school-based program in BC will require efforts to educate the public, parents, guardians, and schools on the safety and benefits of HPV vaccination. Developing targeted strategies to increase vaccination in underserved populations will also be necessary to achieve this vaccination rate.[5] Shifting from a 2-dose to single-dose vaccine schedule may increase vaccination coverage with little additional investment. Long-term follow-up of HPV vaccine trials has shown that vaccine efficacy against infection with HPV types 16 or 18 is as high after a single dose of vaccine as it is after 2 or 3 doses.[34,35] Removing the requirement for subsequent doses could considerably simplify vaccination programs and support efforts to increase uptake.

We did not explore the effect of different screening recommendations based on vaccination status, but previous studies suggest that prioritizing screening of unvaccinated individuals may be an effective way to eliminate cervical cancer while reducing the potential harms of unnecessary testing and follow-up. A study from the Netherlands found that increasing vaccine coverage to 90% and reducing the number of lifetime screens among vaccinated women could eliminate cervical cancer while maintaining follow-up referral rates at current levels.[28] Similarly, modelling from China found that a strategy in which screening is scaled back as vaccinated cohorts age through the population was most cost effective.[36] Reducing screening frequency or modifying triage and follow-up pathways based on vaccination status may be tools to support the implementation of HPV-based screening and reduce unnecessary follow-up testing.

Limitations

We were unable to model results for population subgroups, including equity-deserving communities. Addressing inequities in access to cervical cancer prevention and care is an important component of the CPAC action plan. Equity targets have been established for 2 of the 3 priority areas: that in any identifiable subgroup, no fewer than 80% of individuals are up to date with cervical screening, and no fewer than 90% of individuals receive recommended follow-up after abnormal results.[16] Furthermore, First Nations, Inuit, and Métis partners identified the additional priorities of culturally appropriate cervical cancer prevention and care closer to home; Peoples-specific, self-determined cancer care; and First Nations-, Inuit-, and Métis-governed research and data systems.[16] Many equity-deserving population groups, including immigrant populations, racialized communities, sexual- and gender-diverse populations, and rural or remote populations are at risk of being underscreened.[37–39] Efforts to accelerate the elimination of cervical cancer must also address historical and ongoing inequities in access to health services.[40]

This analysis assumes that HPV-based screening is implemented gradually over 5 years but that all other changes in the model scenarios are effective immediately. In reality, there will be a longer transition as any new policies and programs to achieve these targets will not be implemented or effective immediately, and the true timelines to the elimination of cervical cancer will be extended. However, these results highlight the priority areas that would most effectively support elimination of cervical cancer and reinforce the need to act quickly to achieve elimination goals.

Conclusion

British Columbia began the transition to HPV-based screening in January 2024, and the province now has the potential to eliminate cervical cancer before 2040. Increasing on-time screening participation and adherence to recommended follow-up could accelerate this timeline, but transitioning from cytology- to HPV-based screening is fundamental to achieving CPAC's elimination goal. Screening programs across Canada need to implement HPV-based cervix screening in strategic and innovative ways that increase access to screening services, enhance timely follow-up and treatment, and reduce health disparities across the population.

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