Preventing cervical cancer: beyond following guidelines

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See related guideline by the Canadian Task Force on Preventive Health Care on page 35 and at www.cmaj.ca/lookup/doi/10.1503/cmaj.121505

Practising medicine in a time of rapidly changing knowledge can be difficult. An example of such change is our evolving understanding of the role of oncogenic viruses. When Dr. Georgios Papanicolaou developed his famous test in the 1940s, we did not know that cervical cancer is a preventable sexually transmitted infection. As our knowledge continues to evolve, clinicians need to make practical decisions based on best evidence. The publication of the most recent guidelines on screening for cervical cancer[1] is an opportunity for reviewing current practices with this new understanding in mind. It is also an opportunity to educate patients about primary prevention and perhaps debunk the myth that Papanicolaou (Pap) tests are somehow more than secondary prevention for cervical cancer.

What we now know about the relationship between human papilloma virus (HPV) and cervical cancer is that infection with specific strains of HPV is a necessary precursor to this disease.[2] There are many strains of HPV, some of which carry greater risk than others. Some strains cause genital warts, whereas most others do nothing and are eliminated with time by a healthy immune system. Currently, 12 oncogenic strains have been identified that can persist and cause specific cervical changes now known to be precursors to cancer;[2,3] of these strains, HPV16 and HPV18 are the most commonly found in North America.

Cancer screening must be valid, reliable, sensitive and specific, it should have good predictive value, and it should be able to detect the condition at an early enough stage to lead to available, acceptable and safe interventions that work. Each of these parameters hinges upon the baseline prevalence of the disease within a given community. In Canada, we have variable disease prevalences by community, variable uptake of Pap testing, variable access to colposcopy, and people who are at variable levels of risk of cervical cancer. To complicate matters further, there is variable uptake of HPV vaccination. As we better understand the role of HPV in cervical cancer and seek ways to prevent its acquisition and transmission, we can take this opportunity to rethink the role and importance of Pap testing in the prevention of cervical cancer. Indeed, improving uptake and access to HPV vaccination and cervical screening would do more to lower the rates of cervical cancer than deciding at what age to start Pap testing and how frequently it should be done.[3,4]

Screening with Pap testing is secondary prevention, leading to treatment to remove already abnormal cells. In the past 7 decades, we have had time to hone the technique and collect evidence that, overall, Pap testing saves lives. It has been considered one of the most successful screening tools in history, despite its poor single-test sensitivity (about 55%).[5] But what about primary prevention? The National Advisory Committee on Immunization (NACI) recommends the vaccination of boys and girls to prevent the burden of HPV disease.[3] With increasing uptake of vaccination, we expect the landscape of cervical cancer to change. Lower pretest probability of HPV disease will decrease the already low sensitivity of Pap testing in future, requiring changes to screening once again.

In the recent guideline, the Canadian Task Force on Preventive Health Care has chosen to look strictly at evidence concerning deaths from cervical cancer. As a consequence, the guideline focuses on Pap testing and saves the mounting evidence on the natural history of HPV disease for another day's discussion. HPV testing is a more sensitive (about 98%) and specific (about 92%) tool than Pap testing,[3] and it can be more

Key points

- Cervical cancer is the result of persistent sexually transmitted infection with certain strains of the human papilloma virus (HPV) and can be primarily prevented through vaccination against HPV.
- Papanicolaou (Pap) testing is less sensitive and specific than HPV testing, but both are secondary prevention screens leading to treatment to remove already abnormal cells.
- Canada has variable access to prevention through vaccination and has not yet developed the best practice of using organized recall databases.
- Differences in guideline recommendations may be partially due to variability in choices of outcomes, interpretation of evidence and comprehension of harms associated with inappropriate treatment.

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effective and used less frequently.[5] For these reasons, clinicians should understand its role.

While we wait for the task force's advice on the role of HPV testing, we look to provincial and international guidelines for direction. Variability in guidance can lead to confusion. Differences in recommendations may be partly due to variable interpretations of the quality of available evidence and the potential harms of inappropriate intervention in the natural history of HPV infection. The inclusion or exclusion of evidence for the prevention of softer outcomes (e.g., known cancer precursors caused by high-risk strains of HPV) can also affect recommendations.

To be most effective, a screening program for cervical cancer must be organized to maximize recall.[4] Canada has not shown such an organized approach to vaccination or screening. Each province has its own strategy, with variable ages at which screening should start and choices of screening method, in addition to partial components of organized programs. To add to the confusion, there is often no link between HPV vaccination status and the result of cervical screening. Each province may or may not fund vaccination, despite the NACI's universal vaccination recommendation. Currently, only Alberta and Saskatchewan have fully organized recall databases (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121781/-/DC1). Ontario has made the clearest statement to date regarding the role of HPV testing, deferred to once the provincial database is complete and HPV testing is funded by the province. Although the current Ontario guideline looks familiar (i.e., recommending Pap tests), the 2013 protocol will recommend HPV testing as the primary screening tool for women aged 30 years and older, to be repeated every 5 years to age 65 if results remain negative. Pap testing would be done only if the results of an HPV test were positive.[3]

Screening protocols are also changing internationally. The US Preventive Services Task Force recommends screening for women aged 21–65 years with a Pap every 3 years or, for women aged 30–65 years who want to lengthen the screening interval, a combination of Pap and HPV testing every 5 years.[6] In contrast, in some European countries, HPV testing alone is recommended for screening, beginning at age 30 or 35 years (Appendix 1). In general, the age at which testing starts is higher, and its frequency lower, in countries that recommend HPV testing as screening. Furthermore, countries with highly organized screening programs that recommend HPV testing, such as Finland and the Netherlands, have lower rates of cervical cancer.[3,4]

Given this variability, what does the future hold for cervical screening in Canada? The Canadian Partnership Against Cancer maintains the Pan-Canadian Cervical Screening Initiative, comprising representatives from provinces, territories and professional bodies. Its aim is to ensure that the evidence needed to integrate cervical cancer screening programs with HPV testing and vaccine initiatives is gathered, and to develop and harmonize policy and guidelines for screening.[7] With the gradual development of screening programs that are better organized and incorporate information from electronic health records, we can expect to advise our patients to delay starting screening and to screen less often in the future — and that the screening method will most likely not be Pap testing alone.

Pap testing is a single tool in an evolving toolkit to prevent cervical cancer. Although the evidence needed to make evidence-based change is slow to come, we can envision a future where this cancer can either be prevented as a sexually transmitted viral infection or screened for less frequently with better tools.

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