Recommendations for Implementing Human Papillomavirus-Based Cervical Cancer Screening: Lessons Learned from the HPV FOCAL Trial

Laurie Smith, RN, BN, MPH,[1] Dirk van Niekerk, FRCPC,[2] Andrew Coldman, PhD,[1,3] Mel Krajden, MD, FRCPC,[3,4] Eduardo L. Franco, DrPH, FRSC, FCAHS,[5] Gina Ogilvie, MD, MSc, FCFP, DrPH[3,6]

[1]Cancer Control Research, BC Cancer Agency, Vancouver BC

[2]Cervical Cancer Screening Program, BC Cancer Agency, Vancouver BC

[3]Faculty of Medicine, University of British Columbia, Vancouver BC

[4]Hepatitis Division, BC Centre for Disease Control, Vancouver BC

[5]Division of Cancer Epidemiology, McGill University, Montreal QC

[6]Women's Health Research Institute, Vancouver BC

J Obstet Gynaecol Can 2016;38(8):723-726

Cervical cancer screening using the Pap test is one of the most successful public health interventions in the last 60 years, resulting in significant decreases in cervical cancer incidence and mortality in Canada.[1] It is well-established that persistent infection with an oncogenic genotype of the HPV is a necessary, but not sufficient, cause of cervical cancer.[2,3] Research has shown the improved efficacy of HPV testing for the detection of cervical cancer precursors,[4,5] and as a result, provincial programs are planning for the implementation of HPV testing as the primary technology in cervical cancer screening. However, little has been presented regarding the impact of HPV testing on screening participants and the clinicians who provide the service. As HPV testing is adopted, there will be significant changes in practice, such as extending the interval between screening episodes and shifting the focus from testing for abnormal cells on the cervix to testing for a communicable disease. Clarifying the relationship between HPV and cervical cancer will significantly affect the current landscape of cervical cancer screening. If not anticipated and prepared for, concerns from women and health care providers could create barriers to implementation and could result in unintended consequences, such as reduced participation in screening and increased health system costs.

The HPV FOCAL trial is a publicly funded clinical trial, conducted in British Columbia, that is comparing primary HPV testing with liquid-based cytology for cervical cancer screening.[6] From 2008-2012, over 25 000 women consented to participate through the offices of more than 200 collaborating HCPs. To date, over 20 000 women have completed trial procedures. During their participation, women underwent screening for cervical cancer and their cases were managed according to the FOCAL trial protocol.

Because Pap screening is a long-established practice, women have become accustomed to undergoing screening annually or biannually for most of their adult lives. The shift to HPV-based testing implies lengthening the interval between screening events and changing the ages for which screening is recommended, resulting in paradigm shifts in long-established protocols with which women and clinicians are familiar and comfortable. In consequence, the

Key Words: HPV testing, cervical cancer, screening program

Competing interests: None declared.

Received on December 4, 2015

Accepted on January 22, 2016

http://dx.doi.org/10.1016/j.jogc.2016.04.009

FOCAL trial has, over several years, received numerous questions regarding HPV testing from women and HCPs and has addressed a variety of concerns. Therefore, the experiences of FOCAL trial participants and providers may provide valuable insights for program planning and implementation for jurisdictions that are moving towards HPV-based cervical cancer screening.

Some of the most frequently asked questions received from women during the trial are shown in the Table. Participants had different kinds of questions before undergoing their first HPV test and after receipt of HPV-positive results. Prior to their first HPV screen, women wanted to know what HPV was, its relationship with cervical cancer, and why changes to screening were necessary. The safety of the extended interval between screening episodes was regularly and frequently queried. When women received HPV-positive results, their questions centred on the implications of being HPV-positive. The exchange between a woman and her HCP regarding positive screen results had shifted from "you have an abnormal Pap result" to "you are positive for HPV." The connection between an abnormal result and a sexually transmitted infection has not been consistently explained to women, and disclosing an HPV-positive result requires a different approach. It also raises a new set of questions that focus on alleviating women's concerns and anxiety about having an STI. Although these questions were received in the context of research, they likely indicate the questions that will arise with a change in screening practice.

The study team and collaborating HCPs conveyed several key messages about HPV testing that proved useful for women. Providing basic information regarding the natural history of HPV and its association with cervical cancer was important to contextualize why HPV testing is relevant for screening. In addition, destigmatizing HPV infection and emphasizing its high prevalence in the population was one of the most important and essential messages conveyed. Specifically, it was useful to put into context for women that most sexually active people will be exposed to HPV infection during their lifetime.[7] It was important to inform them that HPV is the most common STI and must not be considered in the same light as other STIs (such as syphilis or herpes). In addition, women wanted to understand how the two tests (Pap testing and HPV screening) differed; they found it helpful to know that Pap testing identifies changes in the cells of the cervix that have already occurred and that these changes can lead to cancer and that HPV testing identifies the virus causing these changes to the cells of the cervix. HPV testing therefore has the potential to identify women at risk not only when cell changes are present but also before they occur. Conveying information on the long time interval between infection with HPV and the development of cervical cancer was also useful because many women believed that cervical cancer develops quickly (because it is recommended that Pap tests be done every 2

Table. FOCAL Trial Participants' Frequently Asked Questions

Frequently asked questions	Frequency
Is it safe to go more than two years between tests?	VC*
What is HPV and how do you catch it?	VC
Why change from the Pap?	VC
What's the difference between the Pap and HPV testing?	VC
What's the treatment for HPV?	VC
Do I have/am I going to get cervical cancer?	VC
How do I know when I caught HPV?	VC
What do I tell my partner? Do I need to tell my partner?	VC
After I've received treatment for HPV, can I catch it again?	VC
Is HPV the only cause of cervical cancer?	C
Can I still get a Pap test every year or two in between HPV testing?	C
How can I tell who gave me HPV?	C
I've had the same partner for many years and never had an abnormal Pap. How could this happen? Is my partner unfaithful?	C
Do I need the HPV vaccine now that I've tested positive?	C
I have had genital warts does this mean I will get cervical cancer?	FC
Should my partner get tested? Should my partner get treated?	FC
I thought only young people had HPV, how do I have HPV?	FC
Will having HPV affect my chances of getting pregnant?	FC
My daughter is in her early 20s, why can't she get HPV testing?	R
I've only been intimate with females, why do I need HPV testing?	R
Should I get HPV testing every time I have a new partner?	R
I've had the HPV vaccine, do I still need screening?	R
If I test negative, but get HPV before my next screen, should I get tested sooner?	R

VC: very common (80% to100%); C: common (51% to 79%); FC: fairly common (21% to 50%); R: rare (<20%).

*This was the most frequently asked question throughout the trial.

ABBREVIATIONS

HCP health care provider

STI sexually transmitted infection

to 3 years). When women understood that it takes decades for cervical cancer to develop after infection, they were reassured enough to feel comfortable with the extended interval between screening episodes with HPV-based screening. In a previous survey it was found that 84% of participating women would accept HPV testing instead of Pap tests for cervical cancer screening, but acceptance dropped significantly (to 54%) when the concept of an extended interval between screening episodes was introduced,[8] emphasizing the importance of communicating the safety of the longer interval associated with HPV testing.

In response to the questions asked by HPV-positive women about the implications of this new diagnosis, the primary message conveyed was that having HPV did not indicate that a woman had or would develop cervical cancer. Women were informed that their HPV-positive status allowed their HCP to determine the appropriate follow-up and management that would prevent changes to the cells on her cervix from progressing into cancer. In addition, having an HPV-positive status often resulted in concerns about having an STI. A woman who learns that she is HPV-positive may subsequently feel anxiety, shame, or anger.[9,10] Therefore, re-emphasizing the prevalence of HPV in the population and stressing that having HPV was no reason for shame alleviated such feelings. HPV-positive participants frequently had questions regarding how to tell (or whether to tell) their partners about their HPV status because a positive result often led to concerns about fidelity. Women were advised that deciding to tell a partner about their HPV status was their own decision to make, and they received advice on what to tell partners if they decided to do so. Women were also interested in knowing how HPV is treated and how re-infection could be avoided. These questions are only a sample of those received by trial participants; the complete list of questions, including responses, is available in the FAQ section of the BC Cancer Agency website's section on the HPV FOCAL trial, available at: www.bccancer.bc.ca/hpvfocal.

When HPV testing is implemented, women will seek advice and counsel regarding screening changes primarily from their HCPs. A predictor of a woman's intention to be screened using HPV testing is endorsement by and a recommendation from her HCP.[8,11] As a result, clinicians play a vital role in informing women about changes to screening practices and also in countering the negative effects of receiving a positive HPV result.[12] Clinicians must be prepared for the questions and concerns patients will have and must be equipped to respond adequately. Throughout the FOCAL trial, collaborating clinicians provided valuable feedback that was applicable for planning a future HPV-based cervical cancer screening program. They expressed concerns that the extended interval between screening episodes will negatively affect patient engagement and that women will forgo HCP visits for other health care issues (such as STI screening). In addition, some had concerns that it would take significantly more of their time to educate and counsel women about HPV testing and to inform women about positive HPV results. Clinicians also reported to the study team that when women were equipped with information before a clinic visit, they were more comfortable with HPV testing and required less of a clinician's time to advise and educate. This HCP-specific feedback is valuable as programs initiate communication and educational strategies.

In this era of HPV vaccination and the demonstrated superiority of HPV-based testing over screening cytology, it is inevitable that screening will change from Pap tests to HPV-based screening. Given the decades-long presence of cytology testing in Canadian health care, cervical cancer screening programs will need to be prepared for the concerns and questions stakeholders will inevitably have as HPV testing is implemented. Allocating resources and time to educate and engage before significant changes are made could prove critically important to the success of major initiatives and mitigate challenges in their implementation. The questions and feedback received from participants and clinicians in the FOCAL trial are likely reflective of what will be received by Canadian programs that are considering implementing HPV screening. As a result, the FOCAL experience can be considered a valuable learning opportunity, assisting programs to tailor and plan communication and educational strategies appropriately. More than most countries, Canada has had a very positive experience with cervical cytology for mass screening since its early adoption of this technology 60 years ago. Canadian jurisdictions will need to face the challenges of educating health care consumers and HCPs while the programmatic issues of technical implementation are being discussed.

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