

# HPV self-sampling: A promising approach to reduce cervical cancer screening disparities in Canada

M. Vahabi RN PhD\* and A. Lofters MD PhD†

Human papillomavirus (HPV) is the primary cause of cervical, anal, and other genital cancers, which are preventable through screening and early treatment. Cervical cancer is a major public health problem, with profound individual impacts in terms of life expectancy and quality of life, as well as societal impacts in terms of economic burden<sup>1-4</sup>. In Canada, an estimated 1,550 women will be diagnosed with cervical cancer in 2017, and 400 will die from it. In Ontario, Canada's most populous and diverse province, 630 women are diagnosed annually with cervical cancer, and 150 die from it<sup>2</sup>. The mean overall health care cost per patient during the first five years after being diagnosed with cervical cancer is projected to be about \$68,745<sup>4</sup> in Ontario. This does not include the cost associated with loss of economic productivity and family life disruption related to emotional and psychological stress.

Cervical cancer deaths and associated health care and social costs can be avoided through appropriate screening. Currently, screening is performed via the Pap test (cytological examination of the peeled cells from the cervix), which requires a visit to a doctor's office. This approach has shown effectiveness for early identification and removal of precancerous abnormalities<sup>5</sup> and has been considered as the primary reason for the observed reduction in cervical cancer incidence and mortality in high-income countries like Canada<sup>2,3,6-8</sup>. The most current cervical cancer screening guidelines recommend that women be screened by Papanicolaou (Pap) tests at least once every three years starting at 21 years of age if sexually active and discontinuing at age 70<sup>2</sup>. For HIV-positive women, recommendation includes receiving screening at the initial assessment and at six months, with an annual follow-up for women with normal results. Despite these clear screening guidelines and a universal health care system, screening participation has remained lower than desired over the past two decades in Ontario, holding steady at 60% to 65% since 2002<sup>3</sup>.

Under/never utilization of cancer screening has been reported to be more predominant among certain vulnerable women, such as immigrants and women of low income, those belonging to visible minority groups, women living with HIV (WLHIV) and those with disability<sup>9-23</sup>. Low levels of screening among these hard-to-reach women have been related to individual-level barriers such as cultural barriers (e.g., modesty, language), lack of knowledge about cervical

cancer risk factors and preventive measures, not knowing where to go for the test, and transportation difficulties; physician-level barriers, such as lack of a family physician, lack of physician recommendation, or having a male provider; and system-level barriers, such as inconvenient clinic hours and indirect costs associated with screening (e.g., for childcare, taking time off work)<sup>10-15,17-27</sup>. Two Canadian retrospective population-based studies in Ontario showed that cancer screening was low among WLHIV. Close to half of the HIV-positive women had not received cervical screening, even though more than 80% of these women were connected to health care<sup>26</sup>. The lowest testing rates were among women receiving exclusively HIV specialist care (33.7%) and women with low engagement with health care (18.95%)<sup>26,27</sup>.

The persistence of these disparities over decades suggests that innovative methods are urgently needed to overcome these barriers and promote screening uptake among hard-to-reach women.

Since empirical evidence clearly shows HPV is the cause of all cases of cervical cancer and HIV and HPV co-infections promote vulnerability to cervical cancer, HPV DNA testing is viewed as a promising primary screening approach for cervical cancer. Several international and Canadian studies have compared the effectiveness of this method of screening with that of cervical cytology and found greater sensitivity and slightly lower specificity in detecting high-grade precancerous lesions<sup>28-33</sup>. These results are consistent with other randomized controlled studies conducted in Europe<sup>29,31-33</sup>, as well as recent meta-analyses of both randomized and non-randomized trials<sup>34-35</sup>, which showed a much better performance than cytology-based screening for detection of high-grade cervical cancer among women aged 30 years and more. Human papillomavirus infection has been found to be more prevalent and transient among younger women (i.e., under 30 years old) than older women<sup>36</sup>. Human papillomavirus DNA testing has been found to allow for longer screening intervals (i.e., every 5 years). Studies found lower risk of high-grade pre-cancerous lesions following a negative HPV result compared with a negative cytology result and suggested that screening women every five years with HPV DNA testing is as safe as screening with cytology every three years<sup>37-39</sup>. Furthermore, HPV DNA testing is an automated and objective procedure to detect HPV and less







# HVP Self Sampling Symposium

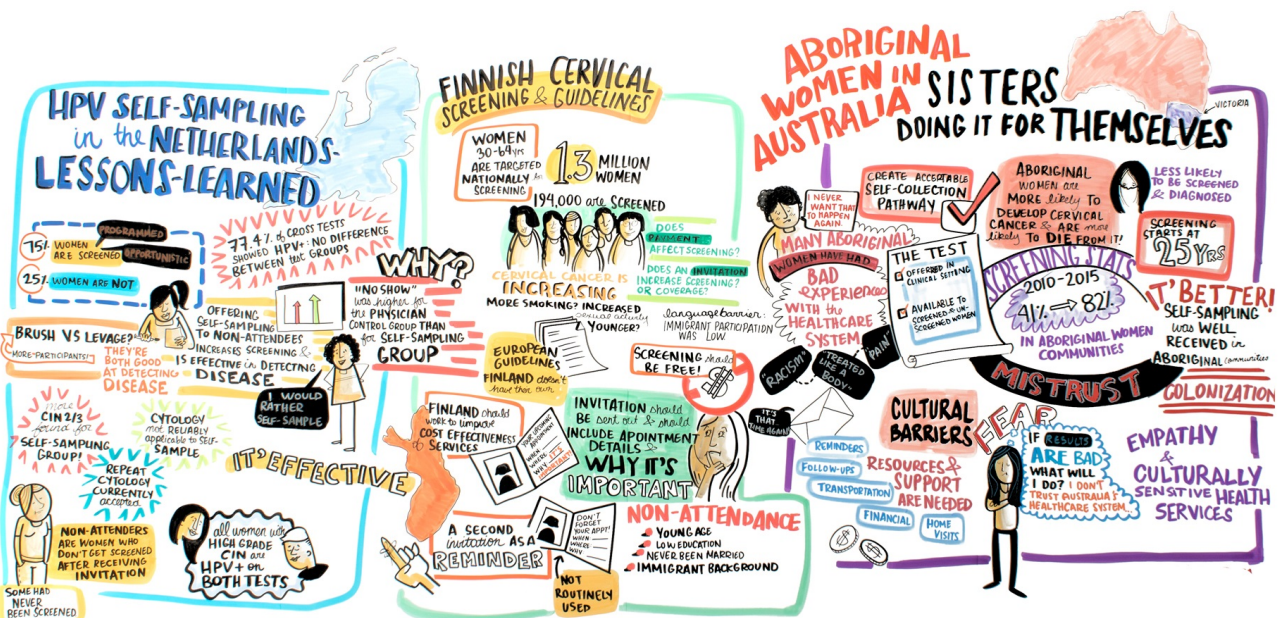
ERICA BOTA



Toronto, Ontario

Friday October 14th, 2016

FIGURE 2 HPV self-sampling Symposium, Toronto, Ontario, 14 October 2016.



# HVP Self Sampling Symposium

ERICA BOTA



Toronto, Ontario

Friday October 14th, 2016

FIGURE 3 HPV self-sampling Symposium, Toronto, Ontario, 14 October 2016.



The study showed that, although there was consensus on important action points such as a need for provincial programs to shift to HPV primary screening, there was disagreement on whether self-sampling evidence was appropriate for implementation. There was little consensus between respondents on whether the state of evidence was satisfactory to integrate a self-sampling option into policy, or whether more Canadian research was needed. The findings from this research suggest that political priorities and system barriers may be important challenges to implementing tailored screening, like self-sampling, to reach marginalized women.

The papers by Saville and colleagues and McLachlan and colleagues use quantitative methods to examine acceptability of HPV self-collection and factors that promote uptake among never-screened/under-screened women who refused conventional cervical screening in the context of alternative pathways of the Australian Renewed National Cervical Screening Program (NCSP). These studies showed high acceptability of HPV self-collection and found similar rates of squamous abnormality and oncogenic HPV positivity for the women who undertook the self-collection pathway compared with those reported in the literature. Furthermore, clear explanations on HPV self-collection procedure and development of a trusting relationship with primary care providers are critical to the successful completion of the self-collection pathway.

The paper by Pedersen and colleagues provides a commentary about the challenges and considerations for implementing HPV self-sampling for under-screened women in high-income settings. The paper provides a general overview of the “paradigm shift towards HPV screening globally” and then gives a comprehensive overview of the implications to the health care system and important issues to be considered for its implementation, such as human resources, record keeping, recall, invitation, follow-up, and education.

Finally, the commentary by Franco clearly demonstrates the need for HPV testing to become the paradigm in cervical cancer screening, and this cannot be done without the move towards self-sampling, which allows screening coverage for the most vulnerable segments of the population.

The body of work contained in this special issue serves to provide a comprehensive picture of available evidence to influence the place that HPV primary screening, particularly HPV self-collection could have in the Canadian health care environment.

#### AUTHOR AFFILIATIONS

\*Daphne Cockwell School of Nursing, Ryerson University, Co-Director, Ryerson Centre for Global Health and Health Equity, Graduate Program in Immigration and Settlement Studies, Ryerson University, Toronto, ON; †Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, and Department of Family and Community Medicine, University of Toronto, Toronto, ON.

#### REFERENCES

1. Canadian Cancer Statistics. Toronto: Canadian Cancer Society; 2017. [Available at: <http://www.cancer.ca/en/cancer-information/cancer-type/cervical/statistics/?region=on>; cited 5 March 2017]
2. Cervical Cancer Screening: Cancer Care Ontario. n.d. [Available at: <http://www.cancercare.on.ca/pcs/screening/cervscreening/>; cited 9 February 2016.]
3. Screening: Cancer Screening Quality Index. n.d. [Available at: [http://www.csqi.on.ca/by\\_patient\\_journey/screening/](http://www.csqi.on.ca/by_patient_journey/screening/); cited 19 September 2017]
4. Pendrith C, Thind A, Zaric GS, Samra S. Cost of cervical cancer treatment: population-based estimates from Ontario. *Curr Oncol* 2016;23(2):e109–15.
5. Wardel J, Robb K, Vernon S, Walter J. Screening for prevention and early diagnosis of cancer. *Am Psychol* 2015;70(2):119–33.
6. Jemal A, Ward E, Thun M. Declining death rates reflect progress against cancer. *PLOS One* 2010;5:e9584.
7. Arbyn M, Raifu AO, Weiderpass E, Bray F, Anttila A. Trends of cervical cancer mortality in the member states of European Union. *Eur J Cancer* 2009;45:2640–8.
8. Tota JE, Bentley J, Blake J, et al. Introduction of molecular HPV testing as the primary technology in cervical cancer screening: acting on evidence to change the current paradigm. *Prev Med* 2017;98:5–14.
9. Tilbrook D, Polsky J, Lofters A. Are women with psychosis receiving adequate cervical cancer screening? *Can Fam Physician* 2010;56(4):358–63.
10. Lofters A, Vahabi M, Kim E, Ellison L, Graves E, Glazier RH. Cervical cancer screening among women from Muslim majority countries in Ontario, Canada. *Cancer Epidemiol Biomarkers Prev* 2017;26(10):1493–9.
11. Redwood-Cambell L, Fowler N, Laryea S, Howard M, Kaczorowski J. “Before you teach me, I cannot know”: immigrant women’s barriers and enablers with regard to cervical cancer screening among different ethnolinguistic groups in Canada. *Can J Pub Health* 2011;102(3):230–4.
12. Waller J, Jackowaska M, Marlow L, Wardle J. Exploring age differences in reasons for nonattendance for cervical cancer screening: a qualitative study. *BJOG* 2012;119(1):26–32.
13. Logan L, McIlpatrick S. Exploring women’s knowledge, experiences and perceptions of cervical cancer screening in an area of social deprivation. *Eur J Cancer Care* 2011;20(6):720–7.
14. Brown DR, Wilson RM, Boothe MAS, Harris CES. Cervical cancer screening among ethnically diverse black women: knowledge, attitudes, beliefs and practices. *J Natl Med Assoc* 2011;103(8):719–28.
15. Salmon KF. Heath beliefs and practices related to cancer screening among Muslim women in an urban community. *Health Care Women Int* 2012;33:45–74.
16. Agenor M, Krieger N, Austin SB, Haneuse S, Gottlieb BR. Sexual orientation disparities in Papanicolaou test use among US women: the role of sexual and reproductive health services. *Am J Public Health* 2014;14(2):e68–73.
17. Vahabi M. Knowledge of breast cancer and screening practices among Iranian immigrant women. *J Community Health* 2011;36(2):265–73.
18. Vahabi M. Iranian women’s perception and beliefs about breast cancer. *Health Care Women Int* 2010;31(9):817–30.
19. Vahabi M, Lofters A, Glazier R. Breast cancer screening disparities in Ontario, Canada. *BMC Public Health* 2015;15:679–91.
20. Lofters AK, Hwang SW, Moineddin R, Glazier RH. Cervical cancer screening among urban immigrants by region of origin: a population-based cohort study. *Prev Med* 2010;51(6):509–16.
21. Lofters A, Guilcher S, Glazier RH, Jaglal S, Voth J, Bayoumi AM. Screening for cervical cancer in women with disability and multimorbidity: a retrospective cohort study in Ontario, Canada. *CMAJ Open* 2014;2(4):E240–7.
22. Amankwah E, Ngwakongnwi E, Quan H. Why many visible minority women in Canada do not participate in cervical cancer screening. *Ethn Health* 2009;14(4):337–49.

23. Tracy JK, Lydecker AD, Ireland L. Barriers to cervical cancer screening among lesbians. *J Women Health* 2010;19(2):229–37.
24. Black AT, McCullon A, Martin RE, Kan I. Young women and cervical cancer screening: what barriers persist? *Can J Nurs Res* 2011;43(1):8–21.
25. McDonald JT, Kennedy S. Cervical cancer screening by immigrant and minority women in Canada. *J Immigrant Minority Health* 2007;9:323–34.
26. Kendall CE, Taljaard M, Younger J, Hogg W, Glazier RH, Manuel DG. A population-based study comparing patterns of care delivery on the quality of care for persons living with HIV in Ontario. *BMJ Open* 2015;5(5):e007428.
27. Leece P, Kendall C, Touchie C, Pottie K, Angel JB, Jaffey J. Cervical cancer screening among HIV-positive women: retrospective cohort study from a tertiary care HIV clinic. *Can Fam Physician* 2010;56(12):e425–31.
28. Isidean SD, Mayrand MH, Ramanakumar AV, et al. Canadian Cervical Cancer Screening Trial Study Group. Human papillomavirus testing versus cytology in primary cervical cancer screening: end-of-study and extended follow-up results from the Canadian cervical cancer screening trial. *Int J Cancer* 2016;139(11):2456–66.
29. Kitchener HC, Almonte M, Thomson C, et al. HPV testing in combination with liquid-based cytology in primary cervical screening (ARTISTIC): a randomised controlled trial. *Lancet Oncol* 2009;10(7):672–82.
30. Mayrand MH, Duarte-Franco E, Rodrigues I, et al. Canadian Cervical Cancer Screening Trial Study Group. Human papillomavirus DNA versus Papanicolaou screening tests for cervical cancer. *NEJM* 2007;357(16):1579–88.
31. Naucier P, Ryd W, Törnberg S, et al. Human papillomavirus and Papanicolaou tests to screen for cervical cancer. *NEJM* 2007;357(16):1589–97.
32. Ronco G, Giorgi-Rossi P, Carozzi F, et al. on behalf of the New Technologies for Cervical Cancer screening (NTCC) Working Group. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. *Lancet Oncol* 2010;11(3):249–57.
33. Anttila A, Kotaniemi-Talonen L, Leinonen M, et al. Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomised study within organized screening programme. *BMJ* 2010;340:c1804–12.
34. Richardson I, Tota J, Franco E. Optimizing technology for cervical cancer screening. *Expert Rev Obstet Gynecol* 2011;6(3):343–53.
35. Murphy J, Kennedy EB, Dunn S, et al. HPV testing in primary cervical screening: a systematic review and meta-analysis. *J Obstet Gynaecol Can* 2012;34(5):443–52.
36. Bartholomew DA. Human papillomavirus infection in adolescents: a rational approach. *Adolescent Med Clin* 2006;15(3):569–95.
37. Katki HA, Kinney WK, Fetterman B, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. *Lancet Oncol* 2011;12:663–72.
38. Schiffman M, Wentzensen N, Wacholder S, Kinney W, Gage JC, Castle PE. Human papillomavirus testing in the prevention of cervical cancer. *J Natl Cancer Inst* 2011;103(5):368–83.
39. Gage JC, Schiffman M, Katki HA, et al. Reassurance against future risk of pre-cancer and cancer conferred by negative human papillomavirus test. *J Natl Cancer Inst* 2014;106(8):dju153.
40. Giorgi-Rossi PG, Fortunato C, Barbarino P, et al. on behalf of the HPV Self-sampling Italian Working Group. Self-sampling to increase participation in cervical cancer screening: an RCT comparing home mailing, distribution in pharmacies, and recall letter. *Br J Cancer* 2015;112(4):667–75.
41. Virtanen A, Nieminen P, Lustarinen T, Anttila A. Self-sample HPV tests as an intervention for non-attendees of cervical cancer screening in Finland: a randomized trial. *Cancer Epidemiol Biomarkers Prev* 2011;20(9):1960–9.
42. Virtanen A, Anttila A, Lustarinen T, Nieminen P. Self-sampling versus reminder letter: effects on cervical cancer screening attendance and coverage in Finland. *Int J Cancer* 2011;128(11):2681–7.
43. Arbyn M, Castle PE. Offering self-sampling kits for HPV testing to reach women who do not attend in the regular cervical cancer screening program. *Cancer Epidemiol Biomarkers Prev* 2015;24(5):769–72.
44. Szarewski A, Cadman L, Ashdown-Barr L, Waller J. Exploring the acceptability of two self-sampling devices for human papillomavirus testing in the cervical screening context: a qualitative study of Muslim women in London. *J Med Screening* 2009;16(4):193–8.
45. Sancho-Garnier H, Tamlet C, Halfon P, et al. HPV self-sampling or the Pap-smear: a randomized study among cervical screening non-attenders from lower socioeconomic groups in France. *Int J Cancer* 2013;133(11):2681–7.
46. Wikström I, Lindell M, Sanner K, Wilande E. Self-sampling and HPV testing or ordinary Pap-smear in women not regularly attending screening: a randomised study. *Br J Cancer* 2011;105(3):337–9.
47. Szarewski A, Cadman L, Mesher D, et al. HPV self-sampling as an alternative strategy in non-attenders for cervical screening—a randomised controlled trial. *Br J Cancer* 2011;104(6):915–20.
48. Cadman L, Ashdown-Barr L, Waller J, Szarewski A. Attitudes towards cytology and human papillomavirus self-sample collection for cervical screening among Hindu women in London, UK: a mixed methods study. *J Fam Plan Reprod Health Care* 2015;41(1):38–47.
49. Cadman L, Wilkes S, Mansour D, et al. A randomized controlled trial in non-responders from Newcastle upon Tyne invited to return a self-sample for human papillomavirus testing versus repeat invitation for cervical screening. *J Med Screen* 2015;22(1):28–37.
50. Bosgraaf RP, Ketelaars PJW, Verhoef VMJ, et al. Reasons for non-attendance to cervical screening and preferences for HPV self-sampling in Dutch women. *Prev Med* 2014;64:108–13.
51. Broberg G, Gyrd-Hansen D, Miao Jonasson J, et al. Increasing participation in cervical cancer screening: offering a HPV self-test to long-term non-attendees as part of RACOMIP, a Swedish randomized controlled trial. *Int J Cancer* 2014;134(9):2223–30.
52. Forrest S, McCaffery K, Waller J, et al. Attitudes to self-sampling for HPV among Indian, Pakistani, African-Caribbean and white British women in Manchester, UK. *J Med Screen* 2004;11(2):85–8.
53. Racey S, Withrow DR, Gesink D. Self-collected HPV testing improves participation in cervical cancer screening: a systematic review and meta-analysis. *Can J Public Health* 2013;104(2):e159–66.
54. Ogilvie G, Krajden M, Maginley J, et al. Feasibility of self-collection of specimens for human papillomavirus testing in hard to reach women. *CMAJ* 2007;177(5):480–3.
55. Ogilvie G, Partrick DM, Schulzer M, et al. Diagnostic accuracy of self-collected vaginal specimens for human papillomavirus testing compared to clinician collected human papillomavirus specimens: a meta-analysis. *Sex Transm Inf* 2005;81(3):207–12.
56. Lofters A, Vahabi M. Self-sampling for HPV to enhance cervical cancer screening uptake: has the time come in Canada? *CMAJ* 2016;188(12):853–4.

57. Mitchell S, Ogilvie G, Steinberg M, Sekikubo M, Biryabarema C, Money D. Assessing women's willingness to collect their own cervical samples for HPV testing as part of ASPIRE cervical cancer screening project in Uganda. *Int J Gynecol Obstet* 2011;114(2):111–5.
58. Vahabi M, Lofters A. Muslim immigrant women's views on cervical cancer screening and HPV self-sampling in Ontario, Canada. *BMC Public Health* 2016;16(1):868–81.
59. Lofters A, Vahabi M, Fardad M, Raza A. Exploring the acceptability of HPV self-sampling among Muslim immigrant women in Greater Toronto Area, Ontario, Canada. *Cancer Manage Res* 2017;9:323–9.
60. Zehbe I, Moeller H, Severini A, *et al.* Feasibility of self-sampling and human papillomavirus testing for cervical cancer screening in First Nations women from Northwest Ontario, Canada: a pilot study. *BMJ Open* 2011;1(1):e000030.
61. Howard M, Lytwyn A, Lohfeld L, Redwood-Campbell L, Fowler N, Karwalajtys T. Barriers to acceptance of self-sampling for human papillomavirus across ethnolinguistic groups of women. *Can J Public Health* 2009;100(5):365–9.
62. Karwalajtys T, Howard M, Sellors JW, Kaczorowski J. Vaginal self-sampling versus physician cervical sampling for HPV among younger and older women. *Sex Transm Infect* 2006;82(4):337–9.