

## Cervical cancer prevention becomes more efficient

Cervical cancer prevention and control is quickly evolving. Basic scientists, epidemiologists, clinician insight, health communication scientists, women's and gender studies scientists, public health scientists, engineers, implementation scientists, and industrial science all contribute to the understanding of the multiple inputs that are necessary to have a patient-centered efficient program reducing cervical cancer.

Unlike more focused groups, the World Health Organization (WHO) promotes a comprehensive program to realize this potential.<sup>1</sup> The vaccination, screening, and treatment goals remain the same, but the specifics of each continue to evolve. Starting with HPV vaccination, we have now seen that three doses shrink to only one necessary HPV dose<sup>2</sup> to protect girls from persistent HPV infection that lasts through womanhood to the age of onset of screening. One dose provides efficiency in vaccine delivery and less burden on registries for timely follow-up doses. Regardless of number of doses, vaccination remains the first step of this process and requires uptake to be successful.

Screening strategies are the second step. They continue to evolve with primary HPV testing being much more sensitive than cytology for cervical cancer screening. Many European countries have adopted primary HPV testing for cervical cancer screening.<sup>3</sup> In the United States, two of the guideline groups, the USPSTF and the American Cancer Society have challenged US physicians to adopt primary HPV testing.<sup>4,5</sup> Primary HPV testing, such as using isothermal amplification with lateral flow dipstick detection of HPV 16/18, has provided low- and middle-income countries (LMICs) a screening process with minimal in-field technology requirements<sup>6</sup> that is much simpler than a cytology system. Women in all countries benefit from primary HPV testing.

While HPV is the indisputable detectable screening outcome, we are evolving the method of collecting the HPV specimen. Speculum exams are uncomfortable, embarrassing, violate modesty cultures, reopen post-traumatic sexual horrors, and are demeaning for those whose disabilities make the exam intolerable. Moving from a physician-held swab to gather cells for HPV detection to a self-collected device would reduce speculum exams by about 80%, reserving them only for necessary exams. Self-collection devices matter for women. Vaginal swabs have been created in different industrial designs, but all rely on the ability of the woman to reach her vagina and to have enough mucosal moisture to insert it without pain or bleeding. Urine collection requires a “dirty” catch without prior genital cleaning, as has been historically common. Both collection methods are possible.<sup>7,8</sup> Women will have different preferences about which type of device they prefer as they age through menopause. Having

that choice increases her investment, with her healthcare making it more likely she will return for a follow-up exam if necessary.

In this issue of the journal, Pedersen et al have provided the first cost-effectiveness model that accounts for differing strategies of HPV vaccination uptake along with HPV-focused screening strategies in a well-developed, well-resourced country.<sup>9</sup> In their models, cytology acts as secondary triage requiring a speculum exam in only a small fraction of the general population. Importantly, the authors consider scenarios for age and birth cohorts of women who consider direct and indirect protection from HPV vaccination. This work shows that opt-in and opt-out choices for self-sampling lead to the most cost-effective cervical cancer screening adjusted for quality of life in all scenarios of HPV vaccine uptake. The physician-based collection exam was dominated in all modeled scenarios by the self-sampling choices, adjusted for vaccination. The starkest realization from this model is that vaccination and screening are entirely dependent on willful participation by women, which can vary tremendously on the way the screening message is communicated to the women.<sup>10</sup>

This work definitely flips the screening algorithm. Women can now screen themselves for primary HPV infection at home, in their own space, at the clinic, wherever she chooses. This allows physicians the time to focus on enforcing the primary care relationship instead of just “doing a test.” Discussing health behaviors that lead to HPV infection, discussing treatment follow-ups, discussing smoking cessation and barrier methods to reduce HPV transmission are the building blocks of the physician-patient dyad. Many have shown that women inaccurately self-report whether a cervical smear was taken during the pelvic exam<sup>11</sup> because the focus of the experience is not on what the test means for the woman, but rather on the physician getting sufficient material for the test itself. Cervical cancer screening needs to be woman-centered, not test-centered. We now have cost-effectiveness research that supports this change. Some degree of adoption of HPV vaccination, primary HPV testing, and women's self-collection has strong evidence for cost-effective population implementation with no loss in health benefits for women.

### CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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**REFERENCES**

1. Das M. WHO launches strategy to accelerate elimination of cervical cancer. *Lancet Oncol.* 2021;22(1):20-21.
2. Basu P, Malvi SG, Joshi S, et al. Vaccine efficacy against persistent HPV 16/18 infection at 10years after one, two and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study. *Lancet Oncol.* 2021. Online ahead of print.
3. Maver PJ, Poljak M. Primary HPV-based cervical cancer screening in Europe: implementation status, challenges, and future plans. *Clin Microbiol Infect.* 2020;26(5):579-583.
4. US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening for cervical cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2018;320(7):674-686.
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(5):321-346.
6. Kumvongpin R, Jearanaikoon P, Wilailuckana C, et al. Detection assay for HPV16 and HPV18 by loop-mediated isothermal amplification with lateral flow dipstick tests. *Mol Med Rep.* 2017;15(5):3203-3209.
7. Cadman L, Reuter C, Jittal M, et al. A randomized comparison of different vaginal self-sampling devices and urine for human papillomavirus testing-predictors 5.1. *Cancer Epidemiol Biomarkers Prev* 2021; 30(4):661-668.
8. Hawkes D, Keung MHT, Huang Y, et al. Self-collection for cervical screening programs: from research to reality. *Cancers (Basel).* 2020; 12(4):1053.
9. Pedersen K, Portnoy A, Sy S, et al. Switching clinic-based cervical cancer screening programs to HPV self-sampling: a cost effectiveness analysis of vaccinated and unvaccinated Norwegian women. *Int J Cancer.* 2021. Online ahead of print.
10. Yeh PT, Kennedy CE, de Vuyst H, Narasimhan M. Self-sampling for human papillomavirus (HPV) testing: a systematic review and meta-analysis. *BMJ Glob Health.* 2019;4(3):e001351.
11. Anderson J, Bourne D, Peterson K, Mackey K. *Evidence Brief: Accuracy of Self-Report for Cervical and Breast Cancer Screening.* Washington (DC): Department of Veterans Affairs (US); 2019.