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Cervical cancer screening in Switzerland: time to rethink the guidelines

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In a previous letter published in *Swiss Medical Weekly*, we emphasised the need for Switzerland to change from cytology-based to human papillomavirus (HPV) screening for cervical cancer in women aged 30 years and older [1]. According to a recent study published in *The Lancet* [2], which included individual level data from four randomised controlled trials (RCTs) conducted in Sweden (Swedescreen [3]), the Netherlands (POBASCAM [4, 5]), England (ARTISTIC [6]) and Italy (NTCC [7]), Ronco and colleagues demonstrated that HPV screening is more effective than cytology in preventing cervical cancer. This study had a median follow-up time of 6.5 years and involved more than 175,000 women. As such, it provides a significant milestone for cervical cancer detection based on HPV testing. The authors demonstrated that HPV screening offers 60–70% greater protection against cervical cancer compared with cytology and showed that HPV testing performed at 5-year intervals is safer than a 3-year interval for cytology.

The implications of these findings for cervical cancer prevention are immediate and global, and suggest that international and national experts should now consider how to implement the change from cytology-based to HPV-based screening, as well as an extension of the screening interval. In response to overwhelming evidence from several good-quality RCTs, which demonstrated that HPV testing might be a more clinically effective option [8, 9], some Western countries have already adopted it as a stand-alone cervical cancer screening method. Countries with organised population-based screening programmes where decisions can be executed in a relatively short time period, such as England, the Scandinavian countries and the Netherlands, tend to embrace the change more easily than countries not having a well-controlled screening system. Indeed, the Netherlands have already entered the annals of public health history as a pioneer in the implementation of an HPV-based cervical cancer screening protocol [10].

Reluctance to accept the change may come from physicians who consider Pap smears to be part of every woman's annual visit; if intervals for screening are lengthened, they fear that women will not come for an annual check-up and may be less inclined to undergo screening. Price is another important concern, and efforts should be made to ensure that HPV testing is fully refunded by health insurance, as is the case for Pap smears. Concerns about the introduction of HPV testing have to be balanced by societal and epidemiological perspectives, because the best strategy for preventing cervical cancer is to use the most accurate test (maximising the benefits of screening) at the longest possible interval (minimising the potential harm of screening). However, Western countries, with liberal health systems and opportunistic screening depending on the initiative of individual women and physicians, have demonstrated in the history of cervical cancer prevention that, despite the presence of a general agreement in favour of new recommendations, the speed and scope of clinical adoption might greatly vary. This is particularly true because each interest group has its own directives and limitations.

The United States of America was the first country with opportunistic screening to recommend HPV testing. Since 2012, the American College of Obstetricians and Gynecologists and the American Cancer Society have recommended that women aged 30–65 years should undergo "co-testing" with both cytology screening and HPV testing every 5 years if both tests are negative [11]. In fact, HPV testing alone is not recommended. However, this recommendation might be about to change, because the US Food and Drug Administration has approved (on April 24 2014) HPV testing as a first-line screening method for cervical cancer screening [12].

In the case of Switzerland, it is now time to incorporate HPV testing in the national cervical cancer screening recommendation and to update the current guidelines. Evidence suggests that longer screening intervals would be appropriate for HPV testing owing to its high negative predictive value. Furthermore, the extension of the screening interval controls overscreening and reduces the detection of transient HPV infections and insignificant lesions, thus minimising the risk of undergoing unnecessary procedures. Besides the evidence provided by Ronco et al. [2], Elfstrom et al. [13] analysed data from a RCT on HPV testing in Sweden (13 years of follow-up) and found the longitudinal

sensitivity of cytology in the control arm at 3 years (85.9%, 95% confidence interval [CI] 76.9–91.8) to be similar to the sensitivity of HPV testing in the intervention arm at 5 years (86.4%, 95% CI 79.2–91.4). Their results support an HPV screening interval of 5 years. Other previous cohort studies equally suggest that screening intervals of 5 years may be appropriate [14–16]. Subsequently, European [10] and recently Australian authorities [17] suggest that HPV screening can be safely implemented with at least a 5-year interval.

Nevertheless, it should be stressed that 5-year cervical screening using HPV testing should be implemented preferably within a population-based screening programme with a call and recall system, which Switzerland has yet to establish.

HPV testing has mediocre specificity and positive predictive value for cervical cancer screening. A triage involving cytology and genotyping would alleviate this issue by identifying high-risk HPV-positive women at highest risk for cancer [18]. Therefore, HPV testing is generally recommended for women aged 30 to 65 years. For women under 30 years, a screening recommendation providing the best balance of benefits and harms should be introduced.

Finally, the choice of the HPV test to be used should be based on cost-effectiveness and clinical validation as recommended by Meijer et al. [19].

In conclusion, since the introduction of the Pap smear 60 years ago, the incidence of cervical cancer has declined by almost 60%, becoming a major public health success in Switzerland and other Western countries, and being adopted as standard practice. Nevertheless, we now have strong evidence that HPV testing is more effective than cytology for cervical cancer screening, providing increased reassurance and allowing longer screening intervals to be adopted. These data support the transition from a good test (a frequent Pap smear) to a better one (less frequent HPV testing) that is both cost-effective and safer for women. These changes should be accompanied with accurate and unbiased information about benefits and associated risks of an HPV-based screening, which should be given to all women, so they can make an informed choice about cervical cancer screening.

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