Preventing Cervical Cancer Globally: Are We Making Progress?

Emma R. Allanson and Kathleen M. Schmeler

ABSTRACT

An unacceptable number of women continue to die from cervical cancer around the world each year. Despite established primary and secondary prevention measures, and a natural history of disease which provides a long latent phase in which to intervene, there are still more than 500,000 women diagnosed with cervical cancer globally each year, and 300,000 related deaths. Approximately 90% of these cervical cancer cases and deaths occur in low- and middle-income countries (LMIC). The World Health Organization (WHO) recently launched a *Global Strategy to Accelerate the Elimination of Cervical Cancer* that outlines 3 key steps: (i) vaccination against human papillomavirus (HPV); (ii) cervical screening; and (iii) treatment of precancerous lesions and management of invasive cancer. Successful implementation of all 3 steps could reduce more than 40% of new cervical cancer cases and 5 million related deaths by 2050. However, this initiative requires high level commitment to HPV immunization programs, innovative approaches to screening, and strengthening of health systems to provide treatment for both precancerous lesions as well as invasive cervical cancer.

Introduction

Cervical cancer remains one of the most common cancers worldwide, particularly in low- and middle-income countries (LMIC; ref. 1). It has been established that virtually all cases of cervical cancer are caused by persistent infection with the Human Papillomavirus (HPV; ref. 2). This knowledge has led to the development of preventative vaccines. In 2006, the Gardasil quadrivalent HPV vaccine (covering HPV types 16, 18, 6, and 11) became commercially available, followed shortly thereafter by the bivalent (HPV 16 and 18) Cervarix vaccine. The Gardasil9 nonavalent vaccine (with additional coverage of the HPV genotypes 31, 33, 45, 52, and 58) entered the market in 2018. These vaccines have been shown to be safe and effective, and are projected to prevent 70% to 90% of cervical cancer (3). However, current HPV vaccines do not treat preexisting HPV infections and associated precancerous lesions. Thus, there are several generations of at-risk women, those that have already been exposed to HPV, who will not benefit from HPV vaccination. Primary prevention with HPV vaccination is therefore augmented by secondary prevention with cervical screening in order to identify preinvasive disease such that intervention can prevent progression to cancer. Secondary prevention may take the form of screening with the Papanicolou (Pap) smear, HPV testing, or visual inspection with acetic acid (VIA), followed by excisional or ablative treatments of precancerous lesions.

Despite established primary and secondary prevention options, and a natural history of disease which provides a long latent phase in which to intervene between acquiring HPV infection and developing cancer, there are still more than 500,000 women diagnosed with cervical cancer globally each year and over 300,000 related deaths. Approximately 90% of these cervical cancer cases and deaths occur in LMICs (4). In May 2018, the Director General of the World Health Organization (WHO) put out a call to action at the World Health Assembly to achieve the global elimination of cervical cancer. The following targets, to be met by 2030, were established to achieve this goal: (i) fully vaccinate 90% of girls against HPV by age 15; (ii) screen 70% of women with a high-performance test by age 35 and again by age 45; and (iii) treat 90% of women identified with cervical disease (precancerous lesions and invasive cancer). The resolution was adopted at the 2020 World Health Assembly with 194 countries committing to the elimination of cervical cancer (5).

HPV Vaccination

To date, HPV vaccination, including gender-neutral vaccination (whereby both males and females are immunized), has been implemented to varying degrees, primarily in high-income countries. Australia has been a leader in this area by introducing a national, government-funded, school-based HPV vaccination program in 2007. It initially provided HPV immunization to 12- and 13-year-old girls, and in 2013 added boys in the same age group. This model has resulted in more than 75% of the targeted populations completing the scheduled vaccinations (6). Recent modeling shows that the incidence of cervical cancer in Australia will be less than 1 per 100,000

Department of Gynecologic Oncology & Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas.

Corresponding Author: Kathleen M. Schmeler, Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030. Phone: 713-745-3518; Fax: 713-745-7586; E-mail: kschmele@mdanderson.org

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women in the first half of the 21st century if vaccination and screening continue at the current rates (7).

Several other high-income countries, including the United Kingdom and Denmark have had similarly successful HPV-immunization coverage to Australia (8). However, countries such as Greece (9) and Germany (10), have immunization rates below 50% despite access to the HPV vaccine. Another example of low coverage of HPV immunization in a high-income country is Japan, where despite government support and infrastructure for the vaccine, a vocal social media campaign against the vaccine has led to immunization rates of less than 1 in 20 girls (11). There remain several challenges to overcoming vaccine hesitancy and increasing to HPV vaccine access in high-income countries, including addressing provider and participant misconceptions about the vaccine as well as a lack of school-based immunization programs in some high income settings.

However, the most critical need for HPV vaccination scale up is in LMICs. One example is sub-Saharan Africa (SSA), where the burden of cervical cancer is the highest in the world, and the need for adequate HPV immunization most critical. Approaches in SSA countries provide insight into the various challenges that may be faced in making progress to end cervical cancer in LMICs in general. Brisson and colleagues have modeled the impact of scaling up both HPV vaccination and cervical-cancer screening in LMICs. Introducing the HPV vaccination to girls (without screening) will result in the prevention of more than 60 million cases and, in settings with a lower incidence of disease, result in elimination of cervical cancer, without the addition of a screening program (12). Currently, few LMICs report a national HPV-immunization program (13). In SSA, national immunization programs are reported in Angola, Botswana, Lesotho, Rwanda, South Africa, Uganda, and United Republic of Tanzania (8, 13), however the structure and level of immunization coverage as a result of these programs are variable. The capacity to deliver adequate national immunization programs in LMICs, and particularly in SSA, is significantly impacted by the complexities of ensuring a functioning broader health system (14).

A successful example is Rwanda, which is reported to be the first low-income country to provide universal access to HPV immunization. Rwanda implemented a school-based HPV immunization program in 2011 and has achieved a vaccine coverage rate of more than 93% (15). On the back of several years of health-system strengthening, a comprehensive plan was formed and actioned over several months to enable stakeholder engagement, enhancement of human and physical resources, and, possibly most critically, a national population-sensitization program. Extraordinarily, following these steps, nearly 94,000 Rwandan school girls were immunized in just 2 days in 2011 (16).

Like many other preventative immunization programs, wide-scale HPV prevention is achievable in LMICs. Botswana's initial trials of HPV vaccination achieved greater than 95% 3-dose coverage of the more than 2,000 school-aged girls who commenced the vaccination schedule during the program. The success of this program is attributed to the multiple arms involved in achieving vaccination, including involvement of the Ministry of Health and additional private–public partnerships, widespread stakeholder consultation, parental education, training of public health-care teams, and opportunities to receive the vaccine in the health care setting if the school visit was missed (17). The Botswana program was then replicated in Zambia with the assistance of Pink Ribbon Red Ribbon, a public–private partnership involved in the Botswana initiative. Following widespread parent education and engagement with younger people through social media, 48,000 Zambian girls were immunized against HPV (18).

School-based programs for HPV immunization are used in both LMICs and high-income countries. Success of this approach in several African countries has been attributed to integration with existing programs (such as school-based vision screening), particularly in settings with high enrolment rates. Specific contextual and system features have to be taken in to account in considering the right model of delivery for a vaccine program. An interesting challenge in the school-based programs is the lack of birthdate data in the school records in some SSA settings, thus having an age-targeted program in school is less successful than a specific school-grade based program (19). South Africa's school-based program for 9-year-old girls was commenced in 2015 and achieved initial vaccine coverage of 87%. However, some districts with immunization rates as low as 40% faced challenges with obtaining parental consent, according to an assessment of the national school-based program by Delany-Moretlwe and colleagues. The authors point out that vaccine hesitancy and concerns about vaccine safety (apparently driven by small antivaccination social media campaigns) may have contributed to this. Furthermore, they report that moving to an opt-out approach (where the immunization is given unless the parents specifically withdraw consent for it) may be difficult to implement in South Africa due to a historical legacy of unconsented medical interventions (20). The small landlocked nation of Lesotho began HPV immunization in 2009 using a mixed-methods model of delivery including both school and clinic-based immunizations. The school-based aspect limited loss to follow-up whereas the clinic-based component improved reporting of adverse events and integrated immunization with existing health resources. However, education of young girls and their guardians regarding cervical cancer and the need for immunization was hampered by the absence of an equivalent word for cervix in the local languages (21).

While there have been successes in LMICs, often in smaller trials, national immunization programs are far more complex to implement. Following initial smaller pilot programs, national rollout of the HPV vaccine occurred in Uganda in 2015, yet less than 1 in 4 Ugandan girls aged 10 to 14 years have been vaccinated. Isabirye and colleagues identify that significant socioeconomic disparities in access to vaccination exist (despite the vaccine being free for all), and this is likely a marker of

broader health-system deficiencies and inequalities across the country (22). Furthermore, in many settings, sociocultural challenges continue to be a factor in implementing HPV immunization programs, including misconceptions that vaccinations are being used as a means to sterilize young girls, or "authorize" the initiation of sexual behaviour (23).

Another barrier has been the HPV vaccination schedule. The initial guidelines were for 3 doses (at 0, 1–2, and 6 months). However, the WHO has since recommended a 2-dose schedule (24). Even in countries (both high- and low-income) with a national HPV vaccination program, the number of young girls completing a full vaccination schedule (2 or 3 doses) frequently falls short of any acceptable targets (25). Fortunately, there is emerging evidence showing at least some benefit to a single-dose regimen. Several cohort and retrospective analyses appear to confer similar vaccine efficacy against HPV in women having had 1, 2, or 3 doses (26, 27). In addition, there is an ongoing randomized-controlled trial comparing 1- to 2-dose schedules for the prevention of persistent high-risk HPV infection in 25,000 women, with the results anticipated to be available in 2024 (28). Concerns about the variations in immune responses to HPV vaccination in different populations (e.g., in regions of Africa with high rates of malaria and HIV infection) are also being taken in to account in considering the introduction of single-dose vaccination. Initial results from a Tanzanian-based trial specifically addressing this issue are also expected in 2024 (29).

Cervical Cancer Screening

Cervical cancer screening has traditionally been performed with a Pap smear (cytology). Women with abnormal results are then referred for diagnostic work-up with colposcopy and cervical biopsies. If high-grade precancerous lesions are diagnosed (cervical dysplasia), treatment is performed using ablation (cryotherapy or thermal ablation) or excision [loop electrosurgical excision procedure (LEEP) or cold-knife-cone biopsy (CKC)]. While this is a very effective approach, the cost, infrastructure, number of trained health-care providers needed, and number of separate visits required by a patient to achieve adequate screening and treatment make this approach almost universally unachievable in most LMICs (30). Many LMICs have therefore introduced VIA to overcome some of these issues. VIA consists of applying acetic acid to the cervix with direct inspection without a colposcope. If acetowhite changes are noted (VIA-positive), immediate treatment with ablation can be performed for a "Screen & Treat" approach. Although this approach is low-cost and can be performed by nurses and other nonspecialists, it is hampered by poor sensitivity and specificity and often results in overtreatment (31).

In more recent years, screening has transitioned to include HPV testing from self-collected or provider-obtained cervicovaginal samples. However, most currently available HPV tests are expensive, require significant laboratory infrastructure and must be run in batches, resulting in delays from sample collection to results. While the use of HPV testing is sensitive and allows for potentially less frequent screening than is done with Pap smears, the potential expense confers on HPV testing the same challenges as cytology-based screening for LMICs. Fortunately, inexpensive point-of-care HPV tests are becoming available. Examples include the Xpert HPV assay (GeneXpert; Cepheid), careHPV (QIAGEN), and HPV AmpFire (Fujirebio). In addition, the Covid-19 pandemic in 2020 saw significant changes to the way people interact with the health care system, including an increasing reliance on remote-care options such as telemedicine. This provides a prime opportunity to examine options for cervical screening that do not require a visit to a health care provider. Self-sampling (woman collected) of cervico-vaginal secretions or urine to allow testing for high-risk HPV provides similar sensitivity compared with samples collected by a health care provider and allows for further judicious use of resources, particularly in LMICs (32). Self-sampling has several clear benefits in LMIC, including being able to reduce the need for clinic visits, allow for judicious use of provider resources, and extend access to cervical screening to women who are geographically remote or otherwise not engaged with screening services.

While affordable, point-of-care rapid HPV testing is a game-changing approach to screening, a clear ongoing challenge in the global elimination of cervical cancer will be the capacity in LMICs to triage and treat women with HPV-positive results. The usual pathway in well-resourced settings would involve colposcopy with cervical biopsies by a trained doctor or advanced-practice provider with histologic diagnosis provided by a pathology lab to determine if treatment is needed. However, this process is unlikely to be an achievable in LMICs due to a lack of laboratory and clinical infrastructure, few trained providers and patients unable to return for the multiple required visits. A study by Holme and colleagues in Nicaragua reported that even when HPV-positive women could proceed to assessment (VIA or colposcopy) and treatment without confirmative biopsy, treatment rates were only 27.8% (33). Alternate options include treating all HPV-positive women with ablation, an approach that has been shown to be feasible in LMICs when point-of-care HPV testing is used and treatment is performed at the same visit (34). However, this approach results in significant overtreatment as the majority of women with HPV will have a transient infection and never develop high-grade cervical dysplasia. A promising approach is to triage women who test positive for HPV with technology assisted VIA or colposcopy that can provide a diagnosis without requiring a biopsy. This includes capturing an image of the cervix and using artificial intelligence (AI) and deep-learning algorithms to identify high-grade precancerous lesions (35). This would also allow for point-of-care screening and diagnosis followed by immediate treatment for appropriate women.

Treatment of Precancerous Lesions

The final goal of the WHO initiative is to treat 90% of those with a precancerous lesion (5). While excisional treatment (e.g., LEEP or CKC) may be the standard of care in well-resourced

settings, the equipment, supplies and trained personnel to achieve this in LMICs are often nonexistent and make the treatment option frequently inaccessible to women (36). While excisional treatment is required for some precancerous lesions, most cases can be managed with cryotherapy or thermoablation. While cryotherapy (freezing a cervical lesion using carbon dioxide or nitrous oxygen to a temperature of −58°F/−50°C for 3–5 minutes) is effective in the treatment of high-grade precancerous lesions (37) and has traditionally been used in LMICs, it requires a constant reliable supply of gas, and meeting this is challenged by both resource constraints and transportation issues. In 2019, the WHO released guidelines on the use of thermal ablation, which uses electricity rather than gas, can be executed in a shorter time (20–30 seconds) than traditional cryotherapy, and can be supplied with portable, battery-powered equipment (38).

The benefit of both cryotherapy and thermal ablation includes that they can be delivered by advanced-practice providers and primary-care physicians, which can help alleviate the constraints on a limited workforce of specialists (gynecologists and oncologists), who are already stretched in their capacity to deliver adequate services to treat women with confirmed cervical cancer. It is important to note that if women are diagnosed with precancerous cervical lesions but do not undergo treatment, no impact will be made towards the elimination of cervical cancer.

In addition to improving access to screening, it is critical that we continue to find ways to strengthen the workforce in LMICs. Project Extension for Community Healthcare Outcomes (ECHO) is a telementoring program that has been instituted in several LMICs to provide training and ongoing support for clinicians performing cervical cancer screening, diagnosis, and treatment (39). For the management of women with invasive cervical cancer, the International Gynecologic Cancer Society (IGCS) developed the *Global Curriculum & Mentorship Program* in 2017, whereby clinicians from low resource regions without formal gynecologic oncology training are partnered with institutions and mentors from high-resource settings in order to complete a 2-year fellowship (40).

Conclusions

An unacceptable number of women continue to die from cervical cancer around the world each year. It is abundantly clear that the steps needed to achieve the WHO goal to eliminate this disease require high-level commitment to HPV immunization programs, innovative approaches to screening, and strengthening of health systems to provide treatment options. As discussed, there are enormous disparities in national capacities to provide HPV immunization and cervical screening, often driven by huge divides in available resources. Partnerships between high-resource and low-resource regions is critical, and includes governments, professional societies, academic institutions, nongovernmental organizations (NGO) and others. These partnerships can help with cancer-control policy development, education, and training of clinicians and resource allocation to advance the prevention of cervical cancer.

Cervical cancer disproportionately affects women in LMICs. The approaches to cervical-cancer prevention that have been employed in high-income settings have not been feasible or successful in LMICs. We must therefore mobilize as a global health community to build contextually appropriate, multifaceted approaches to the prevention of cervical cancer in LMICs that incorporates innovative technologies, supported education and training, and the bolstering of infrastructure such that the long-term prevention of cervical cancer is a sustainable goal.

Authors' Disclosures

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References

1. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Global Health 2020;8:e191–203.
2. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol 1999;189:12–9.
3. Toh ZQ, Kosasih J, Russell FM, Garland SM, Mulholland EK, Licciardi PV. Recombinant human papillomavirus nonavalent vaccine in the prevention of cancers caused by human papillomavirus. Infect Drug Resist 2019;12:1951–67.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424.
5. World Health Organization. Global strategy towards the elimination of cervical cancer as a public health problem 2020. Available from: https://www.who.int/initiatives/cervical-cancer-elimination-initiative.
6. Hall MT, Simms KT, Lew J-B, Smith MA, Saville M, Canfell K. Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017–2035: example from Australia. PLoS One 2018;13:e0185332.
7. Hall MT, Simms KT, Lew J-B, Smith MA, Brotherton JM, Saville M, et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. Lancet Public Health 2019;4:e19–27.
8. Bruni L, Diaz M, Barrionuevo-Rosas L, Herrero R, Bray F, Bosch FX, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. Lancet Global Health 2016;4:e453–e63.
9. Karamanidou C, Dimopoulos K. Greek health professionals' perceptions of the HPV vaccine, state policy recommendations and their own role with regards to communication of relevant health information. BMC Public Health 2016;16:467.
10. Poethko-Müller C, Buttmann-Schweiger N. [HPV vaccination coverage in German girls: results of the KiGGS study: first follow-up (KiGGS

Wave 1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2014;57:869–77.
11. Ueda Y, Enomoto T, Sekine M, Egawa-Takata T, Morimoto A, Kimura T. Japan's failure to vaccinate girls against human papillomavirus. Am J Obstet Gynecol 2015;212:405–6.
12. Brisson M, Kim JJ, Canfell K, Drolet M, Gingras G, Burger EA, et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet 2020;395:575–90.
13. Bruni L, Albergo G, Serrano B, Mena M, Gómez D, Muñoz J, Bosch FX, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World [cited 22 January 2019]. Available from: https://hpvcentre.net/datastatistics.php.
14. Amponsah-Dacosta E, Kagina BM, Olivier J. Health systems constraints and facilitators of human papillomavirus immunization programmes in sub-Saharan Africa: a systematic review. Health Policy Plan 2020;35:701–17.
15. Baussano I, Sayinzoga F, Tshomo U, Tenet V, Vorsters A, Heideman DAM, et al. Impact of human papillomavirus vaccination, Rwanda and Bhutan. Emerg Infect Dis 2021;27:1–9.
16. Binagwaho A, Wagner CM, Gatera M, Karema C, Nutt CT, Ngabo F. Achieving high coverage in Rwanda's national human papillomavirus vaccination programme. Bull World Health Organ 2012;90:623–8.
17. Raesima MM, Forhan SE, Voetsch AC, Hewitt S, Hariri S, Wang SA, et al. Human papillomavirus vaccination coverage among school girls in a demonstration project—Botswana, 2013. MMWR Morb Mortal Wkly Rep 2015;64:1147–9.
18. Wieland J. HPV Vaccination: Helping girls become healthy women; A Partnership in Prevention. Pink Ribbon Red Ribbon; 2017.
19. Abdullahi LH, Hussey GD, Wiysonge CS, Kagina BM. Lessons learnt during the national introduction of human papillomavirus (HPV) vaccination programmes in 6 African countries: Stakeholders' perspectives. S Afr Med J 2020;110:525–31.
20. Delany-Moretlwe S, Kelley KF, James S, Scorgie F, Subedar H, Dlamini NR, et al. Human papillomavirus vaccine introduction in South Africa: implementation lessons from an evaluation of the national school-based vaccination campaign. Glob Health Sci Pract 2018;6:425–38.
21. Ladner J, Besson M-H, Hampshire R, Tapert L, Chirenje M, Saba J. Assessment of eight HPV vaccination programs implemented in lowest income countries. BMC Public Health 2012;12:370.
22. Isabirye A, Mbonye M, Asiimwe JB, Kwagala B. Factors associated with HPV vaccination uptake in Uganda: a multi-level analysis. BMC Womens Health 2020;20:145.
23. Ladner J, Besson MH, Audureau E, Rodrigues M, Saba J. Experiences and lessons learned from 29 HPV vaccination programs implemented in 19 low and middle-income countries, 2009–2014. BMC Health Serv Res 2016;16:575.
24. Whitworth HS, Gallagher KE, Howard N, Mounier-Jack S, Mbwanji G, Kreimer AR, et al. Efficacy and immunogenicity of a single dose of human papillomavirus vaccine compared to no vaccination or standard three and two-dose vaccination regimens: a systematic review of evidence from clinical trials. Vaccine 2020;38:1302–14.
25. Oberlin AM, Rahangdale L, Chinula L, Fuseini NM, Chibwesha CJ. Making HPV vaccination available to girls everywhere. Int J Gynaecol Obstet 2018;143:267–76.
26. Safaeian M, Sampson JN, Pan Y, Porras C, Kemp TJ, Herrero R, et al. Durability of protection afforded by fewer doses of the HPV16/18 vaccine: the CVT trial. J Natl Cancer Inst 2018;110:205–12.
27. Kreimer AR, Struyf F, Del Rosario-Raymundo MR, Hildesheim A, Skinner SR, Wacholder S, et al. Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA Trials. Lancet Oncol 2015;16:775–86.
28. ClinicalTrials.gov [Internet]. Identifier: NCT03180034 Comparing One or Two Doses of the Human Papillomavirus Vaccine for the Prevention of Human Papillomavirus Infection, ESCUDDO Study (ESCUDDO): Bethesda (MD): National Library of Medicine (US); 2020. Available from: https://clinicaltrials.gov/ct2/show/study/NCT03180034.
29. Baisley KJ, Whitworth HS, Changalucha J, Pinto L, Dillner J, Kapiga S, et al. A dose-reduction HPV vaccine immunobridging trial of two HPV vaccines among adolescent girls in Tanzania (the DoRIS trial) – Study protocol for a randomised controlled trial. Contemp Clin Trials 2021;101:106266.
30. Mezei AK, Armstrong HL, Pedersen HN, Campos NG, Mitchell SM, Sekikubo M, et al. Cost-effectiveness of cervical cancer screening methods in low- and middle-income countries: a systematic review. Int J Cancer 2017;141:437–46.
31. Jeronimo J, Bansil P, Lim J, Peck R, Paul P, Amador JJ, et al. A multicountry evaluation of careHPV testing, visual inspection with acetic acid, and papanicolaou testing for the detection of cervical cancer. Int J Gynecol Cancer 2014;24:576–85.
32. Arbyn M, Smith SB, Temin S, Sultana F, Castle P. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ 2018;363:k4823.
33. Holme F, Maldonado F, Martinez-Granera OB, Rodriguez JM, Almendarez J, Slavkovsky R, et al. HPV-based cervical cancer screening in Nicaragua: from testing to treatment. BMC Public Health 2020;20:495.
34. Salcedo MP, Oliveira C, Andrade V, Mariano AAN, Changule D, Rangeiro R, et al. The Capulana study: a prospective evaluation of cervical cancer screening using human papillomavirus testing in Mozambique. Int J Gynecol Cancer 2020;30:1292–7.
35. Hu L, Bell D, Antani S, Xue Z, Yu K, Horning MP, et al. An observational study of deep learning and automated evaluation of cervical images for cancer screening. J Natl Cancer Inst 2019;111:923–32.
36. Besanąa G, Giattasą MR, Plotkiną M, Mohammed M, Makeneą C, Curran K, editors. Access to Loop Electrosurgical Excision Procedure (LEEP) in Cervical Cancer Prevention Is Critical for HIV-Endemic Settings: Experiences from Tanzania. In Proceedings of the International Conference on AIDS and STI's in Africa (ICASA); 2013; Cape Town, South Africa.
37. Martin-Hirsch PPL, Paraskevaidis E, Bryant A, Dickinson HO. Surgery for cervical intraepithelial neoplasia. Cochrane Database of Systematic Reviews 2013.
38. World Health Organization. WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions; 2019.
39. Lopez MS, Baker ES, Milbourne AM, Gowen RM, Rodriguez AM, Lorenzoni C, et al. Project ECHO: a telementoring program for cervical cancer prevention and treatment in low-resource settings. J Glob Oncol 2016;3:658–65.
40. International Gynecologic Cancer Society. IGCS Gynecologic Oncology Global Curriculum and Mentorship Program; 2019.