



## Towards the global elimination of cervical cancer

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### ABSTRACT

Two very effective prevention strategies for cervical cancer exist – vaccination against the human papillomavirus (HPV) and cervical screening with primary HPV testing followed by treatment of precancerous lesions. In 2018, the World Health Organisation called for action towards achieving the global elimination of cervical cancer, and a strategic plan encompassing elimination goals and targets for the scale-up of HPV vaccination, cervical screening and precancer and cancer treatment, particularly in low and middle income countries, will be presented to the 2020 World Health Assembly. The first published estimates suggest that achieving rapid scale-up of both vaccination and twice lifetime cervical screening in all countries would avert up to 13.4 million cervical cancer cases over the next half century, with the majority (but not all) countries achieving incidence of < 4 per 100,000 women by 2100. However, there are significant challenges - (i) including vaccine manufacturing pipeline, supply, delivery and hesitancy, (ii) cervical screening HPV self-collection and point-of-care evaluation, acceptability, and scaling up effective precancer treatment processes, (iii) configuration of appropriate referral pathways, cancer treatment services and palliative care for those women who do develop cervical cancer, as well as (iv) the effective financing of both HPV vaccination and cervical screening on a large scale. It is hoped and anticipated that the WHO elimination initiative will galvanise concerted action to address these issues.

### 1. Introduction

In May 2018, the Director-General of the World Health Organisation (WHO), called for action towards achieving the global elimination of cervical cancer. In January 2019, the Executive Board of WHO, consisting of several member states, “request[ed] the Director-General to develop, in consultation with Member States and other relevant stakeholders, a draft global strategy to accelerate cervical cancer elimination, with clear goals and targets for the period 2020–2030.” [1] This strategy will be considered at the World Health Assembly in May 2020. In 2018, the International Papillomavirus Society also released a statement encouraging governments to “adhere to international standards developed by WHO to develop national, regional and local plans to ultimately achieve the goal of cervical cancer elimination as a public health problem.” [2] Considering this background, the potential for cervical cancer elimination has become a major organising framework for implementation research in HPV-related cancer prevention and treatment, and this was a major focus of discussion at the 32nd International Papillomavirus Society Meeting in Sydney, Australia, in October 2018.

#### 1.1. The road towards elimination

Currently, cervical cancer is estimated to be the fourth most common cancer in women worldwide and the leading cause of cancer death in some of the world's poorest countries, for example those in sub-Saharan Africa [3]. Cervical cancer is preventable via HPV vaccination (primary prevention for pre-adolescent and young adolescent girls) and cervical screening (secondary prevention for women). Organised and comprehensive approaches to cervical screening have thus far been implemented mainly in high income countries, and as a direct consequence, 85% of cervical cancers occur in less-developed regions [4]. Furthermore, in 2014, estimated rates of HPV vaccine uptake in young adolescent females were over 30% in developed countries but less than 3% in less-developed regions [5]. Thus, discussions around achieving cervical cancer elimination centre mainly on the opportunities and challenges in scaling up vaccination, screening and precancer and cancer treatment in low and middle income countries (LMIC). An active global discussion coordinated by the World Health Organisation seeks to establish an appropriate definition of cervical cancer elimination as a public health problem [6]. It is important to understand that the concept of *elimination of cervical cancer* is distinct from that of *eradication of*

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the HPV virus. The aim is to establish a target (or perhaps, alternate targets for different country categories) where, if achieved, cervical cancer would be considered to be controlled as public health issue. Achieving elimination does not, by itself, suggest that active intervention is no longer required via the ongoing delivery of cervical screening and HPV vaccination. Thus, the concept of cervical cancer elimination must be considered with two important associated concepts – firstly, that elimination means that the disease is controlled (not necessarily eradicated), and secondly, that this has been achieved via active intervention and appropriate cancer registry-based surveillance of cervical cancer outcomes over time.

Analyses of the possible timeline towards cervical cancer elimination which have been published thus far consider two potential elimination thresholds for cervical cancer incidence [4,7]. The first is a rate of 6 per 100,000 women, which is used in some jurisdictions to denote a rare cancer. This rate is lower than currently estimated rates of cervical cancer for most, but not all, countries [3] – in a few settings the reported lower rates may be related to historically lower rates of HPV exposure and/or limitations of cancer registry systems. A second threshold that has been considered is a lower rate of 4 per 100,000 women. In some high income countries with long established cervical cancer screening and widespread and early adoption of HPV vaccination, elimination of cervical cancer as a public health problem is likely to be achieved relatively rapidly. In Australia for example, due to the success of the HPV vaccination program, the implementation of both-sex vaccination, the recent switch to a 2-dose nonvalent vaccination schedule, and the 2017 changes to the National Cervical Screening Program to move to primary HPV screening, estimates suggest that rates of less than 4 per 100,000 women are likely to be achieved by 2035 if current rates of screening and vaccination coverage can be maintained [7]. Australia is thus on track to be the first country in the world to eliminate cervical cancer as a public health problem, but other high income countries are expected to follow over the decade or two following. It has been estimated that the current vaccination coverage achieved, mostly in high income countries, will avert approximately one million cases of cervical cancer in the half century from 2020 to 2069; however, without further action 44.4 million cervical cancer cases are still predicted to occur over this period [4]. If high coverage vaccination can be implemented quickly, a substantial impact on the burden of disease will be seen after 3-4 decades, but earlier impact will require delivery of cervical screening to older cohorts who will not benefit from HPV vaccination. Widespread coverage of both HPV vaccination and (at least) twice lifetime cervical screening from 2020 onwards has potential to avert up to 12.5–13.4 M cases by 2069 and could achieve average cervical cancer incidence rates of < 4 per 100,000 globally, and on the average for all human development index (HDI) categories, by the end of the century, although even under these circumstances, some individual countries are still predicted to have rates higher than 4 per 100,000 women per annum by the end of the century. Ongoing comparative modelled analyses, sponsored by the WHO and involving several leading groups, is supporting the ongoing elimination workplan [6].

### 1.2. Challenges in achieving elimination

The challenges to effective scale-up include vaccine manufacturing pipeline, supply, and delivery challenges. A further major issue currently confronting policy makers is vaccine hesitancy, and experiences in Japan, Denmark and Ireland have shown the potentially devastating consequences of vaccine hesitancy on HPV vaccine coverage. However, coverage has been partially restored in Ireland after a well-coordinated campaign to address the issues. Longer term, countries should consider investments into ongoing information campaigns to provide parents with the evidence on vaccine safety; ongoing work is considering the cost-effectiveness of such proactive investment [8].

Scaling up cervical screening in low and lower-middle income

countries, even to achieve coverage of the majority of women once or twice a lifetime, has historically been very challenging. WHO recommendations released in 2013 recommend either Visual Inspection with Acetic Acid or HPV testing [9]; but based on emergent evidence showing that VIA has a cancer downstaging effect but a limited effect on reduction of cervical cancer incidence [10], the 2016 ASCO resource-stratified cervical screening guidelines generally recommend HPV-based screening [11]. Technology development and low cost production methodologies for HPV self-collection and point-of-care testing, and potentially new screening approaches such as Automated Visual Evaluation will potentially provide increasingly practical and cost-effective methods of screening [12]. Cervical screening throughput, self-collection of HPV, point-of-care testing, acceptability, and scaling up effective precancer treatment processes will all be key to effective scale-up in different settings. A further challenge will be the configuration of appropriate referral pathways and cancer treatment services and palliative care for those women who do develop cervical cancer. Finally, the effective financing and coordination of primary and secondary prevention, and referral and treatment services will require the configuration of central financing and purchasing mechanisms, the establishment of public/private partnerships, and the prioritisation of cervical cancer control in national cancer control plans.

## 2. Conclusion

Two very effective prevention strategies for cervical cancer exist – vaccination against the human papillomavirus (HPV) and cervical screening with primary HPV testing followed by treatment of detected precancerous lesions. Achieving rapid scale-up of both vaccination and twice lifetime cervical screening in all countries would avert up to 13.4 million cervical cancer cases over the next half century, with the majority (but not all) countries achieving incidence rates of < 4 per 100,000 women per annum by the end of the century. However there are significant challenges in effective scale-up, including vaccine supply issues, delivery of cervical screening in low and lower-middle income countries, effective financing of both HPV vaccination and cervical screening in all countries, and configuration of cancer treatment services and palliative care for those women who do develop cervical cancer. It is anticipated that the WHO elimination initiative will galvanise concerted action to address these issues. A variety of key stakeholder groups are and will continue to be involved, including the HPV research community and research funders, civil society, aid agencies and governments.

### Disclaimer

The views expressed here are my own, and do not represent that of Cancer Council, WHO or any other agency.

### COI statement

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pvr.2019.100170>.

#### References

- [1] World Health Organization, Accelerating the Elimination of Cervical Cancers as a Global Public Health Problem. Draft Decision Proposed by Australia, Brazil, Canada, Colombia, Ecuador, India, Kenya, Monaco, Mozambique, New Zealand, Peru, Republic of Korea, South Africa, Sri Lanka, Ukraine, United States of America, Uruguay and the European Union and its Member States, [Internet] World Health Organization, Geneva, 2019 [cited 2019 18 March]. Available from: [http://apps.who.int/gb/ebwha/pdf\\_files/EB144/B144\\_CONF1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB144/B144_CONF1-en.pdf).
- [2] International Papillomavirus Society (IPVS), IPVS Statement: Moving towards Elimination of Cervical Cancer as a Public Health Problem, [Internet] International Papillomavirus Society (IPVS), Geneva, 2018 [cited 2019 18 March]. Available from: <https://ipvsoc.org/wp-content/uploads/2018/02/IPVs-statement-on-elimination.pdf>.
- [3] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *Cancer J. Clin.* 68 (6) (2018) 394–424.
- [4] K.T. Simms, J. Steinberg, M. Caruana, M.A. Smith, J.B. Lew, I. Soerjomataram, et al., Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study, *Lancet Oncol.* 20 (3) (2019 Mar) 394–407.
- [5] L. Bruni, M. Diaz, L. Barrionuevo-Rosas, R. Herrero, F. Bray, F.X. Bosch, et al., Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis, *Lancet Glob. Health* 4 (7) (2016) e453–e463.
- [6] M. Brisson, M. Drolet, Global elimination of cervical cancer as a public health problem, *Lancet Oncol.* 20 (3) (2019) 319–321.
- [7] M.T. Hall, K.T. Simms, J.B. Lew, M.A. Smith, J.M. Brotherton, M. Saville, et al., The projected timeframe until cervical cancer elimination in Australia: a modelling study, *Lancet Public Health* 4 (1) (2019 Jan) e19–e27.
- [8] L.S. Velentzis, M.A. Smith, K.T. Simms, J.B. Lew, M. Hall, S. Hughes, et al., Pathways to a cancer-free future: a protocol for modelled evaluations to maximize the future impact of interventions on cervical cancer in Australia, *Gynecol. Oncol.* 152 (3) (2019) 465–471.
- [9] World Health Organization, *Comprehensive Cervical Cancer Control: A Guide to Essential Practice*, second ed., World Health Organization, Geneva, 2014, p. 364.
- [10] S.S. Shastri, I. Mitra, G.A. Mishra, S. Gupta, R. Dikshit, S. Singh, et al., Effect of VIA screening by primary health workers: randomized controlled study in Mumbai, India, *J. Natl. Cancer Inst.* 106 (3) (2014) dju009.
- [11] J. Jeronimo, P. Castle, S. Temin, L. Denny, V. Gupta, J. Kim, et al., Secondary prevention of cervical cancer: ASCO resource-stratified clinical practice guideline, *J. Glob. Oncol.* (2016) 1–23.
- [12] L. Hu, D. Bell, S. Antani, Z. Xue, K. Yu, M.P. Horning, et al., An observational study of deep learning and automated evaluation of cervical images for cancer screening, *J. Natl. Cancer Inst.* (2019 Jan 10).