

Japan's HPV vaccine crisis: act now to avert cervical cancer cases and deaths



In May, 2013, a cluster of adverse events suspected to be linked to HPV vaccination were reported in the Japanese media, prompting the Japanese Government to suspend proactive recommendations for the vaccine in June, 2013. Despite no evidence of a link with HPV vaccination being found in the local investigation, and calls by WHO and the global scientific community to resume active recommendation of the cancer-preventing vaccine, the proactive recommendation of HPV vaccination remains suspended in Japan.

In 2017, the Japan Expert Council on Promotion of Vaccination—a body of 17 academic societies from a broad range of fields, including infectious disease, paediatrics, obstetrics and gynaecology, respiratory illness, travel health, and vaccinology—published a statement recommending renewed proactive support for the widespread use of the HPV vaccine.¹ This important public statement was barely mentioned in the local media and had little impact on political processes.

Now, the ground is shifting in the face of increasing numbers of cervical cancer cases and deaths² and growing frustration among health professionals. On Nov 26, 2019, the Liberal Democratic Party (LDP) in Japan took up the HPV vaccine challenge and launched a Parliamentary League to actively promote recommendation of the vaccine.³ House of Representatives member, Junko Mihara, will chair the League, bringing her own experience and personal voice as a cervical cancer survivor to drive the effort.

The November LDP meeting also brought attention to a study by the Ministry of Health, Labour and Welfare,⁴ confirming the safety of the vaccine and showing that the same rate of symptoms reported following HPV vaccination are also occurring among girls of the same age who have not been vaccinated. These findings echoed the conclusion of a European Medicines Agency review of HPV vaccine safety in 2016.^{5,6}

Cervical cancer numbers have been increasing in Japan, particularly among young women in their 20s.² This age group also has a far lower rate of cervical cancer screening, at 22.2%, than other high-income countries. A perfect storm of changing sexual behaviours, low rates of cervical cancer screening, and negligible uptake of HPV vaccination have all contributed to a 9.6%

increase in cervical cancer deaths over the past decade, even while other cancers have been on the decline in Japan.²

In *The Lancet Public Health*, Kate T Simms and colleagues⁷ present estimates of the number of cases and lives lost due to HPV vaccine hesitancy in Japan, which provide crucial and compelling evidence for political action. The so-called vaccine crisis, which led to a rapid drop in HPV vaccination from over 70% uptake in 2013 to current rates of less than 1%,⁸ is estimated to be responsible for 5000–5700 cervical cancer deaths among girls born between 1994 and 2007 who missed vaccination (the lower estimate represents a scenario of 71.9% cross-protection against HPV types 31, 45, and 52 lasting 20 years, and the upper estimate represents a worst-case scenario of no cross-protection). In addition, 24 600–27 300 preventable cervical cancer cases are estimated to occur in the same age group due to missed vaccination. Looking ahead, the study forecasts that for each year that the crisis continues, an additional 700–800 cervical cancer deaths could occur.⁷

This study calls attention to an opportunity to avert the numbers of cervical cancer cases and deaths if positive action is taken immediately. If HPV vaccination coverage is restored in 2020, including catch-up vaccination for those who missed their vaccination, 60% (14 800–16 300) of the projected cases of cervical cancer and 60% (3000–3400) of the related deaths could be prevented.

The stakes are higher than ever in the urgency to reinstate the proactive recommendation of HPV vaccination in Japan. A major challenge will be to reignite positive public awareness about the value of HPV vaccination, so that when the proactive recommendation is finally reinstated, the demand follows. As one local media source reported, “girls are unaware of the existence of this vaccine”.³ The time to act is now.

HJL reports grants from GlaxoSmithKline and serves on the Vaccine Confidence Advisory Board for Merck.

Copyright © 2020 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND 4.0 license.

Heidi J Larson
heidi.larson@lshtm.ac.uk

Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London WC1E 7HT, UK; Department of Health Metrics Sciences, University of Washington, Seattle, WA, USA

- 1 Iwata S, Okada K, Kawana K. Expert Council on Promotion of Vaccination. Consensus statement from 17 relevant Japanese academic societies on the promotion of the human papillomavirus vaccine. *Vaccine* 2017; **35**: 2291–92.
- 2 Ikeda S, Ueda Y, Yagi A, et al. HPV vaccination in Japan: what is happening in Japan? *Expert Rev Vaccines* 2019; **18**: 323–25.
- 3 Iwanaga N. Launch of Parliamentarians' League for active resumption of HPV vaccine promotion (in Japanese). Nov 26, 2019. <https://www.buzzfeed.com/jp/naokoiwanaga/hpvv-giren> (accessed Feb 6, 2020).
- 4 Sawada M, Ueda Y, Yagi A, et al. HPV vaccination in Japan: results of a 3-year follow-up survey of obstetricians and gynecologists regarding their opinions toward the vaccine. *Int J Clin Oncol* 2018; **23**: 121–25.
- 5 European Medicines Agency. HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS. Jan 12, 2016. https://www.ema.europa.eu/en/documents/referral/hpv-vaccines-article-20-procedure-ema-confirms-evidence-does-not-support-they-cause-crps-pots_en.pdf (accessed Feb 5, 2020).
- 6 Larson H. The world must accept that the HPV vaccine is safe. *Nature* 2015; **528**: 9.
- 7 Simms KT, Hanley SJB, Smith MA, Keane A, Canfell K. Impact of HPV vaccine hesitancy on cervical cancer in Japan: a modelling study. *Lancet Public Health* 2020; published online Feb 10. [https://doi.org/10.1016/S2468-2667\(20\)30010-4](https://doi.org/10.1016/S2468-2667(20)30010-4).
- 8 Hanley SJ, Yoshioka E, Ito Y, Kishi R. HPV vaccination crisis in Japan. *Lancet* 2015; **385**: 2571.