The looming health hazard: A wave of HPV-related cancers in Japan is becoming a reality due to the continued suspension of the governmental recommendation of HPV vaccine

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WHO adopted a global strategy towards eliminating cervical cancer by promoting HPV vaccine, cervical cancer screening and appropriate care and treatments. In Japan, cervical cancer incidence has been significantly increasing in recent years (annual percent change = 3.8, 95% confidence interval, 2.7–4.8; age-adjusted rate: 28.0 in 1976, 9.1 in 2000, 14.1 in 2012).1 Japan started its HPV vaccination program for girls aged 13–16 in 2010. By 2013, Japan’s vaccination rate was about 70%.2 However, due to repeated media reports of diverse symptoms after HPV vaccination, the government announced a suspension of its proactive recommendation for the vaccine, leading to a decline in vaccination rates to less than 1%.3 WHO noted that policy decisions based on weak evidence, leading to lack of use of safe and effective vaccines, can result in real harm.4

Due to continued suspension of the governmental recommendation of HPV vaccine, girls born in 2000 and thereafter, ‘the vaccine-suspension generation’, almost uniformly failed to get vaccinated. We predicted they will have higher HPV-16/18 infection rates1 and higher incidences of and death from cervical cancer5 compared to the ‘vaccination generation’ born in 1994–1999 who benefited from high HPV vaccination rates. The ‘vaccine-suspension generation’ are now reaching the starting age for cervical cancer screening in Japan, age 20.

We obtained data on the cumulative rate of HPV vaccination of girls aged 16 or younger under public subsidies, which did not include self-funded vaccinations. We also obtained the results of cervical cancer screening at age 20 (including those at 21 who skipped screening at age 20) for each birth year from 24 municipalities, corresponding to one-tenth of Japan’s population. Among these 24 municipalities, HPV test was not used for cervical cancer screening at age 20.

We evaluated the changes over time in the cumulative HPV vaccination rate up to age 16 and the abnormal cytology rate at age 20, for each birth year. As for females of ‘vaccine-suspension generation’ born in 2000, the results of screening at age 21 are not yet included because they were not yet all 21. The screening rates at age 20, not including age 21, of ‘vaccine-suspension generation’ was 1.9%, which was not lower than that of ‘pre-introduction generation’ (1.8%) and ‘vaccination generation’ (1.4%), suggesting that change of background characteristics of those receiving cervical cancer screening due to COVID-19 pandemic was negligible.

The curves showed logarithmically approximated trends of the abnormal cytology rate at age 20 for each birth year of the ‘pre-introduction generation’ from 1989 to 1993 and the ‘vaccination generation’ from 1994 to 1999, respectively, during the study period (Fig. 1). Abnormal cytology rate in the ‘vaccination generation’ was clearly lower than that predicted based on trends in the ‘pre-introduction generation’. Similarly, the abnormal cytology incidence in the ‘vaccine-suspension generation’ was close to the expected rate from the trend of ‘pre-introduction generation’, and was higher than predicted based on the ‘vaccination generation’ tendencies. These trends were consistently the same.
even when linear or exponential approximation was used instead of logarithmic approximation (data not shown). The abnormal cytology rate at age 20 of the females born in 2000, 5.04%, significantly higher than that of the ‘vaccination generation’ (3.76%). These findings possibly suggested an increase of abnormal cytology rate among the ‘vaccine-suspension generation’ compared to the ‘vaccination generation’. This increased rate of abnormal cytology in those born in 2000, the ‘vaccine-suspension generation’, compared to the ‘vaccination generation’, will correspond to the increase of nearly 3700 incidences and 900 deaths of future cervical cancer predicted in our previous study.4

We should continue to pressure our government to resume its vaccine recommendation, but at the same time we must recommend that women of the ‘vaccine-suspension generation’ receive ‘catch-up HPV vaccinations’, although its effectiveness was unfortunately shown to be limited for females older than 20 in Japan.7 Those females should be strongly encouraged to undergo regular cervical cancer screening and receive appropriate treatments for cervical lesions.

The statistical data were provided from 24 municipalities for this research project. The bold line graph represents the cumulative HPV vaccination coverage up to age 16 for each birth year. The bar graphs represent the incidences of abnormal cytology (ASC-US+). The thin solid and broken curves are logarithmically approximated trend of the abnormal cytology rate at age 20 for each birth year of the “pre-introduction generation” from 1989 to 1993 and the ‘vaccination generation’ from 1994 to 1999, respectively, during the study period.

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Fig. 1. Changes over time (by birth year) in the cumulative HPV vaccination rate and the incidence of abnormal cytology (ASC-US+) during cervical cancer screening at age 20.
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