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## with high-grade cervical lesions following the Japanese HPV vaccination program

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### Abstract

The Japanese government began a human papillomavirus (HPV) vaccination program for girls aged 12-16 years in 2010 but withdrew its recommendation in 2013 because of potential adverse effects, leading to drastically reduced vaccination uptake. To evaluate population-level effects of HPV vaccination, women younger than 40 years of age newly diagnosed with cervical intraepithelial neoplasia grade 1-3 (CIN1-3), adenocarcinoma in situ (AIS), or invasive cervical cancer (ICC) have been registered at 21 participating institutes each year since 2012. A total of 7709 women were registered

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during 2012-2017, of which 5045 were HPV genotyped. Declining trends in prevalence of vaccine types HPV16 and HPV18 during a 6-year period were observed in CIN1 (50.0% to 0.0%,  $P_{\rm trend} < .0001$ ) and CIN2-3/AIS (83.3% to 45.0%,  $P_{\rm trend} = .07$ ) only among women younger than 25 years of age. Overall, HPV vaccination reduced the proportion of HPV16/18-attributable CIN2-3/AIS from 47.7% to 33.0% (P = .003): from 43.5% to 12.5% as routine vaccination (P = .08) and from 47.8% to 36.7% as catch-up vaccination (P = .04). The HPV16/18 prevalence in CIN2-3/AIS cases was significantly reduced among female individuals who received their first vaccination at age 20 years or younger (P = .02). We could not evaluate vaccination effects on ICC owing to low incidence of ICC among women aged less than 25 years. We found HPV vaccination to be effective in protecting against HPV16/18-positive CIN/AIS in Japan; however, our data did not support catch-up vaccination for women older than 20 years. Older adolescents who skipped routine vaccination due to the government's suspension of its vaccine recommendation could benefit from receiving