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Health Policy Center*

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The HPV Vaccination in Japan

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Rose Wilson, Pauline Paterson, and Heidi J. Larson¹

Introduction

The human papillomavirus (HPV) is the cause of most cervical cancers, which is why the 2006 licensing of an effective HPV vaccine was widely welcomed as an important advance for global public health. In Japan, the HPV vaccine (Cervarix®) was licensed in October 2009; the following year, the Japanese government began subsidizing its delivery, and in April 2013, the HPV vaccine was added to the government of Japan's list of routine vaccinations. Yet, in June 2013, the Japanese Ministry of Health, Labor, and Welfare (MHLW) suspended its recommendation for HPV vaccination after a series of highly publicized alleged adverse events following immunization stoked public doubts about the vaccine's safety. The HPV vaccine has been in a confusing state of limbo in Japan ever since: it is still available for free, yet lacking the ministry's active recommendation for its use.

This paper explores how Japan's response to HPV vaccine concerns has been perceived across the globe and illustrates examples in other countries that have faced similar challenges, such as Australia, France, India, and the United Kingdom. Given HPV's recognized importance in causing multiple cancers, and the vaccine's proven efficacy against it, we believe it is essential to maintain the public's trust in the vaccine. The paper concludes with recommendations to the Japanese government toward that end.

HPV and Cervical Cancer: A Global Overview

According to the World Health Organization (WHO), "cervical cancer is the second most common cancer in women in the world and the third greatest cause of death from cancer in women."² Every year, about 270,000 women die of cervical cancer, over 85 percent of whom are in developing countries³ (see Appendix 1⁴).

Seventy percent of cervical cancers are caused by two strains of human papillomavirus: HPV 16 and 18. HPV is mainly spread through skin-to-skin sexual

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² World Health Organization (WHO), "Human papillomavirus (HPV) and cervical cancer," 2013, <http://www.who.int/mediacentre/factsheets/fs380/en/#>.

³ International Agency for Research on Cancer, "GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012," 2012, <http://globocan.iarc.fr/Pages/Map.aspx#>.

⁴ WHO, "Human papillomavirus (HPV) and cervical cancer."

contact; both women and men can be infected. Currently, there are two vaccines that protect against these strains of HPV: Cervarix® and Gardasil®. The vaccines are delivered in a series of three shots over six months, and work best when received before the vaccine recipient is sexually active.

Initial indications are that the HPV vaccine is exceptionally effective. A study released by the U.S. Centers for Disease Control and Prevention in June 2013 found that the prevalence of these cancer-causing HPV strains had dropped by 56 percent among teen girls since the vaccine's introduction in 2006. Moreover, although the HPV vaccine was initially licensed to address the global burden of cervical cancer, studies have found that HPV is also related to vulvar, vaginal, penile, anal, and oropharyngeal cancers and cancer-related deaths; and significant morbidity from external genital lesions.⁵ The vaccine can thus play a meaningful role in preventing these cancers and mitigating these health threats as well.

HPV vaccines are currently licensed for use in 128 countries—nearly triple the 45 countries in which it had been licensed at the end of 2012.⁶ Recommendations for HPV vaccination exist for females in 57 countries and for males in 6 countries and national funding for vaccination of girls and boys is provided in 54 and 2 countries, respectively.

Since this is a relatively new vaccine, there are no global vaccination coverage estimates yet; however, over 40 million doses of the HPV vaccine have been given worldwide.⁷ In Australia, Scotland, and Rwanda, HPV vaccination coverage (licensed in 2007) is more than 80 percent for the first dose of the HPV vaccine and 70 percent for all three doses.⁸

Over 26,000 subjects from five continents have been enrolled in clinical studies regarding the HPV vaccine. This includes two major randomized, double-blind, placebo-controlled trials (FUTURE I and FUTURE II for the Gardasil vaccine and PATRICIA (PAPilloma TRIal against Cancer In young Adults), which measured vaccine efficacy against CIN3+ (grade three or greater cervical intraepithelial neoplasia) and adenocarcinoma, for the Cervarix vaccine).⁹ These trials have allowed investigation of the effects of race and region on the efficacy and safety of the vaccine. Importantly,

⁵ M. A. Kane, B. Serrano, S. de Sanjosé, and S. Wittet, "Implementation of Human Papillomavirus Immunization in the Developing World," *Vaccine* 30 (2012): F192–F200.

⁶ WHO, "Global Immunization Data," February 2014,

http://www.who.int/immunization/monitoring_surveillance/Global_Immunization_Data.pdf?ua=1.

⁷ Ontario Ministry of Health and Long-Term Care, "Ontario's HPV Vaccination Program," 2014, http://www.health.gov.on.ca/en/ms/hpv/hpv_vaccine.aspx#skipnav.

⁸ E. Crowe et al., "Effectiveness of Quadrivalent Human Papillomavirus Vaccine for the Prevention of Cervical Abnormalities: Case-control Study Nested within a Population Based Screening Programme in Australia," *BMJ* 348 (March 2014): g1458, <http://dx.doi.org/10.1136/bmj.g1458>; U.S. Centers for Disease Control and Prevention, "New Study Shows HPV Vaccine Helping Lower HPV Infection Rates in Teen Girls," 2013, <http://www.cdc.gov/media/releases/2013/p0619-hpv-vaccinations.html>; ISD Scotland, "HPV Immunisation Uptake Statistics," 2013, <https://isdscotland.scot.nhs.uk/Health-Topics/Child-Health/Publications/2013-09-24/HPV-Report-September-2013.pdf?58488100768>.

⁹ M. Lehtinen et al., "Overall Efficacy of HPV-16/18 AS04-Adjuvanted Vaccine against Grade 3 or Greater Cervical Intraepithelial Neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial," *Lancet Oncology* 13 (2012): 89–99.

subgroup analysis has demonstrated that the efficacy, immunogenicity, and safety of the HPV vaccine do not differ between race and region.¹⁰

Still, despite its proven benefits, the HPV vaccine brings challenges. First, the HPV vaccine is relatively complex to introduce. Because it is given in adolescence, it needs a different location to optimize delivery as most childhood vaccines happen during visits to the doctors, whereas by the time a child is in adolescence, s/he no longer has regular check-ups (this could be addressed through school-based programs). Timing also matters. Because effectiveness depends on three shots in six months, completing the HPV vaccine series demands a real commitment from parents. In addition, as the vaccine prevents a sexually transmitted infection (STI), it evokes the moral judgments and religious and cultural taboos that come with discussing and addressing sexual behavior. Therefore, some health professionals¹¹ have been reluctant about vaccination, questioning whether it may “send the wrong message” to teens by seeming to condone premarital sex. Research, however, has confirmed that teens who have received the HPV vaccine are not more sexually active than their peers.¹²

Summary of the HPV Vaccine Experience in Japan

In Japan, cervix uteri cancer is the cancer of the fifth-highest incidence for women (see Figure 1), while the rate of Pap tests, which screen for this cancer, are low at around 25.4 percent¹³ compared to 78.3 percent in the United Kingdom.¹⁴

In addition, oropharyngeal cancers rose dramatically in Japan between 1990 and 2000 (see Appendix 2)¹⁵; while, over the past 10 years, an average of 5,955 cases of genital warts have been reported annually, with men having a consistently higher number of reported cases than women. Genital warts cases are reported in men of all ages, although the majority occur between the ages of 20 and 40 years.¹⁶

Approximately 67.1 percent of cervical cancers in Japan are considered related to HPV types 16 and 18. The prevalence of HPV 16 and 18 infections are as high in Japan as in the United States and Europe. However, it has been suggested that the number of

¹⁰ H. Yoshikawa et al., “Efficacy of Quadrivalent Human Papillomavirus (types 6, 11, 16 and 18) Vaccine (GARDASIL) in Japanese Women Aged 18–26 Years,” *Cancer Science* 104 (2013).

¹¹ H. J. Larson, “The uptake of Human Papillomavirus Vaccination: The Power of Beliefs,” *International Journal of Epidemiology* 42 (2013): 908–10.

¹² N. C. Liddon, J. S. Leichliter, and L. E. Markowitz, “Human Papillomavirus Vaccine and Sexual Behavior among Adolescent and Young Women,” *American Journal of Preventive Medicine* 42 (2012): 44–52.

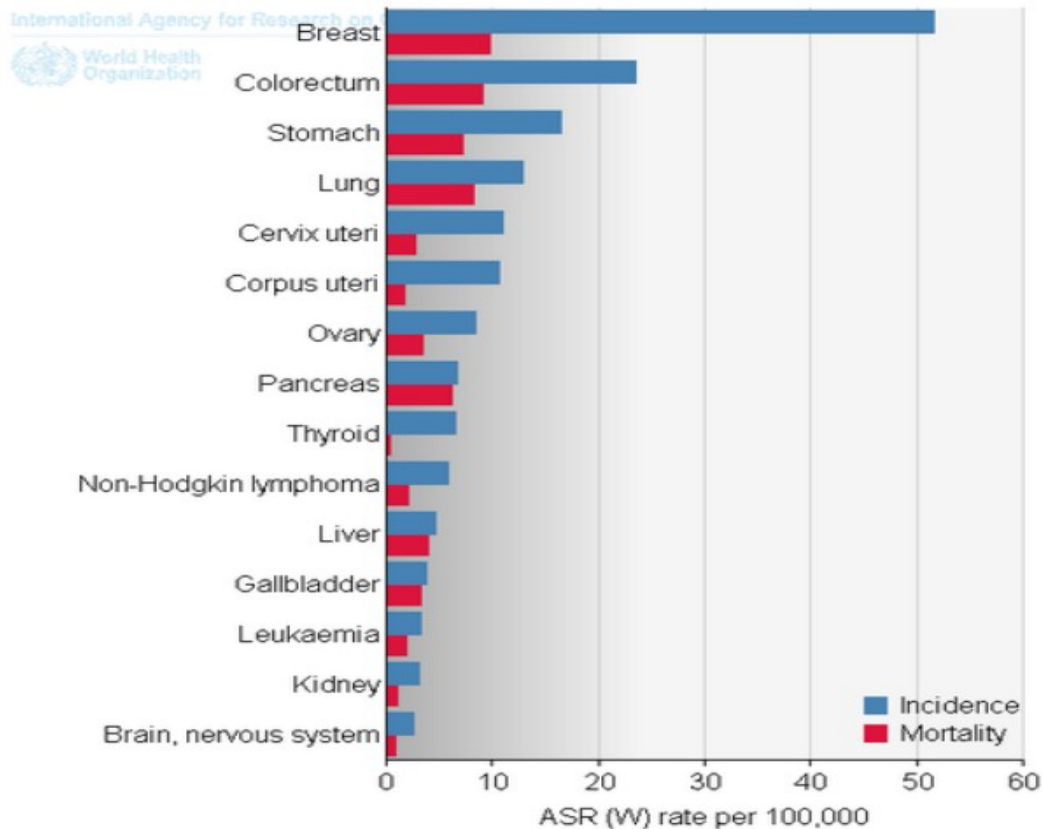
¹³ T. Hoshino et al., “Does Removal of Out-of-pocket Costs for Cervical and Breast Cancer Screening Work? A Quasi-experimental Study to Evaluate the Impact on Attendance, Attendance Inequality and Average Cost per Uptake of a Japanese Government Intervention,” *International Journal of Cancer* 133 (2013): 972–83.

¹⁴ HSCIC, “Cervical Screening Programme England 2012–2013,” 2013, <http://www.hscic.gov.uk/searchcatalogue?productid=12601&q=title%3a+cervical+screening+programme&sort=Relevance&size=10&page=1#top>.

¹⁵ D. Forman et al., “Global Burden of Human Papillomavirus and Related Diseases” *Vaccine* 30 (2012): F12–23.

¹⁶ Yoshikawa et al., “Efficacy of Quadrivalent Human Papillomavirus (types 6, 11, 16 and 18) Vaccine (GARDASIL) in Japanese Women Aged 18–26 Years,” 465–72.

Figure 1. Estimated Age-standardized Incidence and Mortality Rates for Women in Japan¹⁷



cervical cancer cases could be reduced by 73 percent if all 12-year-old girls in Japan were vaccinated.¹⁸

Cervarix® and Gardasil® vaccines, which both protect against HPV types 16 and 18, were licensed in Japan in 2009 and 2011, respectively. From 2009, Cervarix® was partly funded by the Sugunami local government. By April 2010, 32 of 1,747 local governments had decided to provide funding for the HPV vaccine.¹⁹ In October 2010, the central and local governments launched a temporary funding program and in April 2013, the HPV vaccine was included in the National Immunization Program (but was optional) and given for free. According to Asahi

Given the recognized importance of the human papillomavirus in causing multiple cancers, it is critical not to lose public trust in this proven vaccine.

¹⁷ International Agency for Research on Cancer, “GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012,” <http://globocan.iarc.fr/Pages/Map.aspx#>.

¹⁸ R. Konno et al., “Cervical Cancer Working Group Report,” *Japanese Journal of Clinical Oncology* 40 (2010): i44–i50.

¹⁹ T. Uehara and K. Asami, “Vaccine financing in local governments,” *Asahi Shimbun* (Kansai regional edition), March 25, 2010.

Shimbun, by June 2013, an estimated 8.29 million people in Japan had received the HPV vaccine.²⁰

On June 14, 2013—one day after the WHO declared the HPV vaccine safe²¹—the Japanese Ministry of Health, Labor, and Welfare (MHLW) issued a nationwide notice that while the HPV vaccine could still be given for free to girls aged 12 to 16, it should neither be proactively recommended nor promoted. Mariko Momoi, who chairs the panel at the MHLW, stated, “It is necessary to gather information immediately to accurately grasp how often (the side effects) are occurring.”²² A large press conference was held by the Vaccine Adverse Reactions Review Committee (VARRC) the same day, lasting over an hour, and featured girls who alleged to have been affected adversely by the vaccine with claims of convulsions, seizures, severe headaches, and partial paralysis.²³

In suspending its recommendation, the MHLW declared that it would investigate the reported cases, but as of April 2014, no conclusion has been reached. Because of the government’s nearly complete silence on its investigative process, other actors have filled the public information void.

Anti-vaccination groups, as well as associations for parents of cervical cancer vaccination “victims,” have gained strength and public attention both locally and globally. One of the groups is headed by a parent who claims that her daughter, after vaccination with Cervarix®, lost the ability to walk and is now in a wheelchair.²⁴ Parents of another girl tried to claim compensation for suspected complex regional pain syndrome (CRPS). The national government refused because the vaccination was not yet in the National Immunization schedule. The local government of Suginami also initially refused to provide compensation for the family, but after the case was reported at a local assembly meeting in April 2013 and the victims’ group criticized the local government, intense media scrutiny prompted Suginami to agree to provide compensation (although this has not been paid yet).²⁵ The public perceived this as an admission of guilt, and the issue became a tipping point for current anti-HPV vaccine sentiment.

Concerns about the HPV vaccine have also spread through Japanese social networks. Toshie Ikeda, a female politician, is secretary-general of the Nationwide Cervical Cancer Vaccine Victim Liaison Committee, which is a victim support group. She uses her Twitter account and Facebook page to promote the group’s concerns.²⁶ The

²⁰ Editorial, “HPV Vaccine Raises Questions,” *Japan Times*, June 14, 2013, <http://www.japantimes.co.jp/opinion/2013/06/14/editorials/hpv-vaccine-raises-questions/>.

²¹ WHO, “Update on human papillomavirus vaccines,” June 2013, http://www.who.int/vaccine_safety/committee/topics/hpv/Jun_2013/en/index.html.

²² “Cervix Vaccine Issues Trigger Health Notice,” *Japan Times*, June 15, 2013, <http://www.japantimes.co.jp/news/2013/06/15/national/cervix-vaccine-issues-trigger-health-notice/#.Uue5qdLFIdU>.

²³ “Victims Hit Cervical Cancer Vaccines,” *Japan Times*, August 24, 2013, <http://www.japantimes.co.jp/news/2013/08/24/national/victims-hit-cervical-cancer-vaccines/#.Uue9kNLFIdU>.

²⁴ Editorial, “HPV Vaccine Raises Questions.”

²⁵ 子宮頸がんワクチン重い副反応 中学生、長期通学不能, *Apital Asahi*, March 8, 2013, <http://apital.asahi.com/article/news/2013030800002.html>.

²⁶ Hino Councillor Rie Ikeda Official Website, 日野市議会議員 池田利恵 公式ホームページ, 2014, <http://ikedatoshie.com/>. Additional stakeholders involved in the issues surrounding the withdrawal of the HPV vaccination recommendation include the MHLW Adverse Reaction Review Committee (副反応検討部

Table 1. Major Events in Japan Related to the HPV Vaccine (2009–2013)

<p>October 2009 Cervarix® licensed in Japan. (Gardasil® was licensed in July 2011.)</p>	<p>March 2010 After HPV vaccination, 3 girls complain of CRPS and 9 from chronic pain.</p>	<p>April 2010 32 of 1,747 local governments were providing funding for the HPV vaccine.</p>
<p>October 2010 Central and all local governments launch a temporary funding program.</p>	<p>March 8, 2013 Asahi newspaper press report of 50 girls suffering from CRPS and 100 absent from school after receiving the HPV vaccine.</p>	<p>March 10, 2013 Adverse events reported on TV news.</p>
<p>March 25, 2013 Press conference by “victim” group showing videos of girls suffering from walking disturbances and seizures, which was also posted on YouTube.</p>	<p>April 1, 2013 HPV vaccine included in the National Immunization Program (NIP). Optional and given for free.</p>	<p>April 13, 2013 Suginami local government announces its budget for the next fiscal year. This included compensation claimed by the parents of a girl with suspected CRPS following HPV vaccination. Case reported at local assembly meeting.</p>
<p>May 19, 2013 Another press conference by victim group.</p>	<p>June 13, 2013 WHO Global Advisory Committee on Vaccine Safety report released stating HPV vaccine is safe. Not reported in Japanese media.</p>	<p>June 14, 2013 Second joint meeting of the Vaccine Adverse Reactions Review Committee (VARRC). MHLW decided to temporarily suspend recommendation of HPV vaccine.</p>

absence of any media watchdog in Japan and relatively lax libel laws mean that newspapers, news programs, social networks, and victim support groups are able to publish unverified stories and videos of girls who claim to suffer from adverse events following HPV vaccination.²⁷

MHLW has added a page on its website (last updated on June 21, 2013) with a Q&A about the HPV vaccine, including a section on the safety of the vaccine²⁸ and issued

会) and the Japanese Expert Board for the Eradication of Cervical Cancer, the leading organization in Japan promoting social activities for cervical cancer prevention through screening and vaccination. The organization makes proposals and provides information to the Ministry of Health, Labor, and Welfare, local governments, and media. They contributed to the approval of the HPV vaccine in Japan in 2009, but they are not trusted by some members of the public as they are said to have links with the pharmaceutical industry. Other stakeholders are Japan’s Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the National Institute of Infectious Diseases (NIID).

²⁷ A. Gamble and T. Watanabe, *A Public Betrayed: An Inside Look at Japanese Media Atrocities and Their Warnings to the West* (Washington, DC: Regnery, 2004).

²⁸ Ministry of Health, Labor, and Welfare, 般の方向けの情報, 2013, http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou28/qa_hpv.html.

guidance to health care professionals.²⁹ However, despite these laudable efforts to create more positive awareness of the vaccine's safety, the absence of a government decision has enabled the spread of uncertainty and distrust.

Contributing to Distrust: Japan's Prior Experience with Vaccine Programs

Japan's prior experience has contributed to distrust of the pharmaceutical industry, including falsified Novartis data in an Alzheimer's disease study.³⁰ There is also a history of vaccine confidence issues in Japan related to adverse events following immunization.³¹ The Japanese government handled two past vaccine controversies—the measles, mumps, and rubella (MMR) vaccine and Prevenar and Act-HIB—in very different ways:

- The Japanese-manufactured MMR vaccine was introduced in 1989 and suspended in 1993 following high rates of aseptic meningitis associated with a component of the vaccine.³² Subsequently, measles, mumps, and rubella vaccines were given separately. In 1994, major changes were made to Japan's immunization law: all childhood immunizations were no longer mandatory. Individuals were given “strong recommendations” to get the vaccine, but it would be their choice.³³ By 2005, compared to measles (90–100 percent) and rubella (50–60 percent), the uptake of mumps vaccine was low in Japan at 30 percent.³⁴ In 2006, the MR (measles and rubella) combined vaccine was introduced to the National Immunization Program (NIP) with national government funding but adult males were not targeted for rubella vaccination. In 2011, MR vaccine coverage was high at 95.3 percent at age 1 year and 81.4 percent at age 17–18 years. However, the reintroduction of the mumps vaccine into the NIP remains unresolved decades later and an outbreak of rubella in Japan involved 5,442 cases reported between January 1 and May 1, 2013, mostly in men aged over 20.³⁵
- In contrast, in March 2011 the MHLW suspended Pfizer's Prevenar against meningitis and pneumonia and Sanofi's Act-HIB against *Haemophilus influenzae* type b, following fears that the vaccines caused the deaths of four

²⁹ Ministry of Health, Labor, and Welfare, 子宮頸がん予防ワクチンの接種を受ける皆さまへ, 2013, http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou28/pdf/leaflet_h25_6_01.pdf.

³⁰ Agence France-Presse, “Novartis under fire over false Japanese drug data,” *The Local* (Stockholm), July 12, 2013, <http://www.thelocal.ch/20130712/novartis-under-fire-over-false-drug-data>; Agence France-Presse, “Pharmaceutical Firms Accused of Falsifying Data in Major Alzheimer's Study,” *Business Insider*, January 10, 2014, <http://www.businessinsider.com/pharmaceutical-firms-accused-of-falsifying-data-in-major-alzheimers-study-2014-1>.

³¹ H. J. Larson and D. L. Heymann, “Public Health Response to Influenza A (H1N1) as an Opportunity to Build Public Trust,” *Journal of the American Medical Association* 303 (2010): 271–72.

³² M. Kimura et al., “Adverse Events Associated with MMR Vaccines in Japan,” *Acta paediatrica japonica* 38 (1996): 201–11.

³³ G. Harumi and T. Hiroshi, “Why Is Measles Still Endemic in Japan?” *The Lancet* 364 (2004): 328–29.

³⁴ H. Honda, Y. Shimizu, and M. Rutter, “No effect of MMR withdrawal on the incidence of autism: a total population study,” *Journal of Child Psychology and Psychiatry* 46 (2005): 572–79.

³⁵ Centers for Disease Control and Prevention, “National and State Vaccination Coverage among Adolescents Aged 13–17 Years—United States, 2012,” *Morbidity and Mortality Weekly Report* 62, no. 34 (August 30, 2013): 685–93, <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6234a1.htm#Fig1>.

infants. The vaccines were reintroduced a few weeks later after it was proven that the vaccines did not cause the deaths.³⁶

International Perception of the HPV Controversy in Japan

WHO responded to the Japanese government's decision to suspend recommendation of the HPV vaccine with an update on human papillomavirus vaccines in their Global Advisory Committee on Vaccine Safety (GACVS) report (June 2013), which states that

There is little reason to suspect the HPV vaccine [of side effects], given its growing use worldwide in the absence of a similar signal from elsewhere. Recognizing the public concerns voiced, the Committee urges careful documentation of each case and a thorough search for a definitive diagnosis by medical specialists in order to best guide treatment.³⁷

The global coverage of Japan's suspension of its HPV vaccine recommendation has been largely applauded by the anti-vaccination groups but has baffled the global scientific community.

Thanks to the Internet and social media, news of the Japanese government's withdrawal of its active recommendation for the HPV vaccine has reached a global audience—oftentimes with the facts misrepresented or obscured. To give just one example, a story posted on the U.S.-based *Examiner.com* alleging that the Japanese government has “withdrawn administration” of vaccines against HPV was reposted on a Kenyan news site, *Lifestyle*,³⁸ the *Catholic Philippines* Facebook page,³⁹ and the *New Illuminati* Facebook page.⁴⁰ The ambiguity in the decision to suspend “active recommendation” of the vaccine—but not the “administration” of the vaccine—has allowed for multiple interpretations and misinterpretations.

In the United States, several anti-vaccine websites, such as *Age of Autism*, quote a report written by Dr. Sataro Sato, a Japanese internist and cardiologist, which details numbers and types of adverse events following the vaccine, including brain damage.⁴¹ Articles also provide petitions urging abolition of the vaccine for readers to sign, to be

³⁶ K. Matsuyama, “Japan Drug Panel Finds No Link between Child Deaths, Pfizer, Sanofi Shots,” *Bloomberg*, March 8, 2011, <http://www.bloomberg.com/news/2011-03-08/japan-drug-panel-finds-no-link-between-child-deaths-vaccination.html>.

³⁷ WHO, “Global Advisory Committee on Vaccine Safety, Report of meeting held 12–13 June 2013,” http://www.who.int/vaccine_safety/committee/reports/Jun_2013/en/.

³⁸ K. Kaniaru, “Japan stops cancer vaccines as World Health Organization put in sharp focus,” *The Standard* (Nairobi), July 14, 2013, <http://www.standardmedia.co.ke/lifestyle/article/2000088338/japan-stops-cancer-vaccines-as-who-put-in-sharp-focus>.

³⁹ Catholic Philippines, “World Health Organization Accused of Promoting Vaccines to Benefit Manufacturers,” Facebook, July 17, 2013, <https://www.facebook.com/catholicph/posts/177436002428819>.

⁴⁰ New Illuminati, “Japan stops cancer vaccines as World Health Organization put in Sharp Focus: Gardasil & Cevax Too Dangerous and Ineffective,” Facebook, July 16, 2013, <https://www.facebook.com/the.new.illuminati/posts/10151799297344560>; J. Stokowski-Bisanti, “World Health Organization Accused of Promoting Vaccines to Benefit Manufacturers,” *Examiner.com*, July 14, 2013, <http://www.examiner.com/article/world-health-organization-accused-of-promoting-vaccines-to-benefit-manufacturers#sthash.WXd8O43w.gbpl>.

⁴¹ “SaneVax Reports on Japan's Struggle with HPV Vaccination Injuries,” *Age of Autism*, August 26, 2013, <http://www.ageofautism.com/2013/08/sanevax-reports-on-japans-struggle-with-hpv-vaccination-injuries.html>.

handed to the Japanese minister of health, Norisha Tamura. Authors inaccurately describe “the virtually non-existent risk posed by being ‘infected’ with so-called carcinogenic HPV”⁴² and provide links to the 2013 Japanese press conference that shows videos of girls suffering from walking disturbances and seizures.⁴³ An article on PR Web stated, “We wonder why the CDC and FDA are pushing Gardasil so strongly when health ministries in other countries are expressing concern.”⁴⁴

Most of the anti-vaccine sites analyzed by the authors of this paper contain long lists of anti-HPV vaccine comments by readers who state that manufacturers and the government are corrupt and that the Japanese health ministry does not trust the HPV vaccines.⁴⁵

In short, Japan’s suspension of the HPV vaccine recommendation has been largely applauded by the anti-vaccination groups, while it has baffled the global scientific community.⁴⁶ Although anti-HPV vaccine sentiment is not widely spread on mainstream media, it has spread and been reinforced through social networks such as those mentioned above.

HPV Vaccine Country Case Studies

Japan is not alone in confronting reported adverse events following HPV vaccination. Concerns have been raised around the HPV vaccine in many countries, including India, the United Kingdom, France, and Australia (see Table 2). Like all vaccines and medicines, the HPV vaccine carries risks of adverse events, but they are generally minor; and most reported adverse events following immunization (AEFIs) are ultimately found to lack a causal connection. Nonetheless, whether the reported AEFIs are minor or serious, real or perceived, prompt and appropriate responses are critical to sustaining and rebuilding the public’s trust in the vaccine.

In India, initial concerns were about the target population for the HPV vaccination demonstration project; the relevance, safety, and cost-effectiveness of the HPV vaccine; and distrust of the pharmaceutical industry.⁴⁷ When advocacy groups were ignored, they intensified their efforts, culminating on World Health Day—April 7, 2010—when 68 public health organizations and professionals organized a press conference to highlight their concerns regarding the HPV vaccines and issued another “Memorandum to the Health Minister on World Health Day Opposing HPV

⁴² “HPV Vaccines Exposed: Subterfuge in a Syringe?,” Dprogram.net, November 9, 2013, <http://dprogram.net/2013/11/09/hpv-vaccines-exposed-subterfuge-in-a-syringe/>.

⁴³ Mahorobajapan, 子宮頸がんワクチン接種被害者映像 副反応のリスク, YouTube, April 9, 2013, <http://www.youtube.com/watch?v=GRy6SYtCY1M&list=PLVamxbwCqPUI5TqaxPKbV15hciWNMBiYj>.

⁴⁴ “HPV Vaccine: Israel Health Ministry Considers Cancelling Vaccination Due to Side Effects,” Prweb.com, September 4, 2013, <http://www.prweb.com/releases/2013/9/prweb11084444.htm>.

⁴⁵ “SaneVax Reports on Japan’s Struggle with HPV Vaccination Injuries”; N. Erickson, “HPV Vaccines: Japan Leads the Way,” *Robert Scott Bell Show*, June 24, 2013, <http://www.robertscottbell.com/government/hpv-vaccines-japan-leads-the-way-by-norma-erickson/>.

⁴⁶ S. Gilmour et al., “HPV Vaccination Programme in Japan,” *The Lancet* 382 (2013): 768; N. Erikson, “Japan and the HPV Vaccine Controversy,” *Stranger in a Strange Land* (blog), April 10, 2014, <http://mnhopkins.blogspot.co.uk/2014/04/japan-and-hpv-vaccine-controversy-by.html?m=1>.

⁴⁷ H. J. Larson, P. Brocard, and G. Garnett, “The India HPV-Vaccine Suspension,” *The Lancet* 376 (2010): 572–73.

Vaccinations,”⁴⁸ which was available to the general public through the Internet. The April memo called for the immediate halt of the HPV vaccine demonstration projects and an inquiry into, and compensation for, the reported side effects and alleged vaccine-related deaths of four girls who participated in the study.⁴⁹ The government immediately suspended the HPV vaccination demonstration project, despite none of the deaths being attributed to the vaccination. This demonstrates that providing information for the public to make choices regarding vaccination is essential in preventing the spread of rumors generated by insufficient information.

In the United Kingdom, following reports of a young girl’s death after receiving an HPV vaccination, the government investigated and responded within 24 hours, clarifying that the vaccine did not cause the girl’s death. The rapid engagement with the media and the public was crucial to containing the spread of further negative media and loss of public confidence.⁵⁰

In France, contradictory reports were released in response to a young woman’s complaint about an AEFI, although the vaccine continues to be administered under the National Immunization Program and recommendations for vaccination continue.⁵¹

In Australia, positive and transparent information about the HPV vaccine was strengthened following the adverse events experienced by several dozen Melbourne school girls. The state government funded a new service, SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community) in April 2007.⁵² The HPV vaccine was not suspended.

⁴⁸ S. Azad, “Memorandum to the Health Minister on World Health Day Opposing HPV Vaccinations,” April 7, 2010, <http://samawomenshealth.wordpress.com/2010/04/08/memorandum-to-the-health-minister-on-world-health-day-opposing-hpv-vaccinations/>; L. C. Botha, “Breaking News: Organizations in India successfully halt HPV vaccination program,” *Holy Hormones Journal*, April 7, 2010, http://holyhormones.com/sister_song/breaking-news-organizations-in-india-successfully-halt-hpv-vaccination-program/.

⁴⁹ R. Sankaranarayanan, “HPV Vaccination: The Promise & Problems,” *Indian Journal of Medical Research* 130 (2009): 322.

⁵⁰ WHO, “Case Study C: How a Potential HPV Vaccination Crisis Was Averted,” <http://www.vaccine-safety-training.org/c-serious-aeft-day-1.html>.

⁵¹ L. Clavreul and E. Cazi, “Des Experts font le lien entre Gardasil et Sclérose en Plaques,” *Le Monde* (Paris), November 24, 2013, http://www.lemonde.fr/sante/article/2013/11/24/premiere-plainte-contre-le-vaccin-anticancer-gardasil_3519409_1651302.html; “Santé: Le Vaccine Gardasil Bientôt Visé par Trios Nouvelle Plaintes,” *La Parisienne* (Paris), November 24, 2013, <http://www.leparisien.fr/laparisienne/sante/sante-le-gardasil-au-coeur-d-une-plainte-24-11-2013-3344849.php>; Sanofi Pasteur MSD, “Sanofi Pasteur MSD Rejects Opinion of Regional French Compensation Group in Gardasil Vaccination Claim,” media statement, November 25, 2013, https://www.spmsd.co.uk/upload/public/Files/10/Final%20SPMSD%20Media%20Statement_Gardasil%20FR.pdf.

⁵² J. P. Buttery et al., “Mass Psychogenic Response to Human Papillomavirus Vaccination,” *Medical Journal of Australia* 189 (2008): 261–62.

Table 2. HPV Vaccine Concerns in Japan, India, United Kingdom, France, and Australia

Country	Date of licensing	Date of NIP inclusion	Date and prompters of vaccine concerns	When and what was the government response?
Japan	October 2009	April 2013	April 2013: Family of alleged affected girl to be given compensation by Sugunami local government over reported “side effects” of HPV vaccine	June 14, 2013: Government suspends HPV vaccination recommendation.
India	July 2008	Not yet included	October 2009: Public criticism of HPV vaccine demonstration project, vaccine safety concerns, costs, and ethical concerns. April 2010: Press conference and memorandum to health minister highlighting previous concerns and four deaths associated temporally with HPV vaccination. Public interest litigation initiated.	April 2010: Government suspends HPV vaccination demonstration project.
United Kingdom	June 2006	September 2008	September 28, 2009: Young girl in Coventry collapses and dies soon after the first dose of HPV vaccine	Evening of September 28, 2009: UK Department of Health acts quickly to inform the media and the public that the death was not due to the HPV vaccine. No vaccine suspension.
France	July 2007	October 2007	2010: Teenage girl develops vertigo, vomiting, temporary loss of sight and use of legs, and facial paralysis two months following HPV vaccination. In 2013 she files a criminal complaint against Sanofi Pasteur MSD and France’s medicines safety agency (ANSM) and holds a press conference explaining her AEFI	November 2013: The chair of the national committee states there is no evidence to link Gardasil with serious autoimmune conditions, but the <i>Commission régionale de conciliation et d’indemnisation des accidents médicaux</i> (CRCI) acknowledges a link between pathology and vaccination. Sanofi Pasteur issues a press release supporting the safety profile of the HPV vaccine and challenges the CRCI statement. No vaccine suspension.
Australia	April 2007	April 2007	May 2007: 720 girls receive HPV vaccination at a Melbourne girl’s school. 26 girls develop symptoms including dizziness, syncope, and neurological complaints. Four taken to hospital.	Radio interviews with the then-federal health minister and the Victorian state premier. The state government funded a new service, SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community) in April 2007. No vaccine suspension.

The Rumor Mill's Corrosive Impact

In analyzing this issue, it is important to acknowledge the corrosive effects of rumors and their impact on public trust. According to experts in rumor psychology, rumors help people make sense of the world and offer an initial explanation for anxiety-provoking information and events.⁵³ The longer situations of uncertainty and anxiety persist, the easier it becomes for rumors to spread and the more difficult they become to counteract.

Dr. Barbara Reynolds, an expert in governmental risk communication at the U.S. Centers for Disease Control and Prevention (CDC), highlighted five potentially disastrous mistakes in public health communication: mixed messages from multiple experts; information released late; paternalistic attitudes; not countering rumors and myths in real time; and public power struggles and confusion. To avoid these mistakes, the CDC recommends that governments should:

- 1. Be the first to provide information.* Don't withhold factual information. If this is done, it leaves a vacuum that may be filled by people who don't have the public's best interest at heart.
- 2. Be accurate with information.* Accuracy is important, and so is responding quickly. These aspects can sometimes be in tension. The government should release factual information quickly and state what is being done to get additional information. The public is better served by receiving reliable information sequentially than a fully complete report months after an event.
- 3. Be credible.* Governments should not withhold information to avoid embarrassment or a possible public "panic" that rarely if ever happens. Uncertainty is worse than not knowing; rumors are more damaging than hard truths.
- 4. Express empathy.* When government officials acknowledge in words what people are feeling, it builds trust. Officials can say, "We understand why this might be concerning." This should be followed by information that addresses public concerns.
- 5. Promote action.* Giving people positive steps they can take, such as, "Talk to your doctor," or "You can find out more on this website," encourages them to feel more in control and empowered.
- 6. Show respect.* In particular, governments should never be paternalistic, either withholding information from the public to "protect" them or dismissing concerns.

⁵³ N. DiFonzo and P. Bordia, *Rumor Psychology: Social and Organizational Approaches* (Washington, DC: American Psychological Association, 2006).

Conclusion and Recommendations

In Japan, the withdrawal of the recommendation of the HPV vaccine, the agreed compensation to several girls from local governments, and rumors spread by social media have caused members of the public to distrust the vaccine. Even if the government renews its active recommendation, the climate of fear and uncertainty could hinder the success of the HPV vaccination program, which is especially worrying due to low rates of Pap tests and high rates of cervical and oropharyngeal cancer in Japan. The Japanese government must act quickly to reassert control of the message, or risk losing a historic opportunity to save the lives of girls and women in the years ahead.

First, the government of Japan must engage in an open and ongoing way with the media, key stakeholders, and the public to provide clear information regarding the process currently underway (i.e., research regarding safety profiles of the vaccine, especially for Japanese people).

Moving forward, steps to restore public confidence and trust should include:

- Providing the public with a clear and concise decision, restoring an active recommendation for HPV vaccination, supported by evidence including statistics on the vaccine's safety and highlighting the successful implementation and high uptake rates of the vaccine in other countries. Organizations such as the Brighton Collaboration based in Switzerland and the Strategic Advisory Group of Experts (SAGE) based in the United States, United Kingdom, and Indonesia, can aid public health authorities in making decisions surrounding vaccination, based on large databases and safety research standards. (See recommended links to regional websites containing information about the HPV Vaccine in Appendix 3.)
- Providing physicians, nurses, and other health care providers with accurate materials they can use with their patients to address concerns and questions. Among other things, this information should reinforce that:
 - While Pap tests are invaluable for detecting early signs of cervical cancer and other issues, they do not prevent the development of precancerous lesions from occurring;
 - HPV vaccination can also protect against oropharyngeal cancer and other life-threatening illnesses;
 - HPV vaccination does not cause sexual promiscuity;
 - HPV vaccination is important for reproductive health. This information can be disseminated at schools, in doctors' surgeries and clinics and online through websites similar to Australia's cancer council and social media (see Appendix 3).
- Actively promoting HPV vaccination to parents (mothers in particular). Mothers are typically the family health care decisionmakers. They need to have

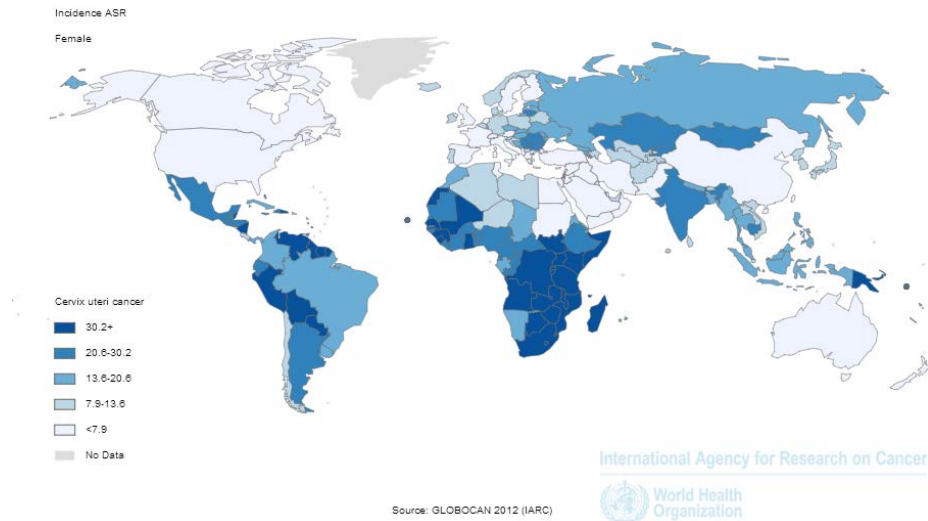
their questions and concerns addressed in order to feel comfortable taking their daughters to be vaccinated.

- Advising that the HPV vaccine, like any other vaccine, may cause side effects but that these do not occur at a rate higher than other vaccines and that preventing cancer is far better than treating it.
- Developing school-based vaccination programs, so that students do not have to miss class or find their own way to a medical clinic. School-based programs also allow for the engagement of parent-teacher associations, which can offer an important venue for dialogue and for cultivating parental buy-in. According to Fujiwara et al.,⁵⁴ school-based vaccinations and public subsidies are the most effective method to improve HPV vaccination coverage.
- Establishing a system that allows the public to express concerns and receive swift, evidence-based answers.

As evident in Japan, if government support is lost, even if vaccination is provided for free, coverage rates can fall substantially. Therefore, once a decision has been made, the government should have a strong, evidence-based communications plan, enabling it to respond to public concerns or questions surrounding the HPV vaccine.

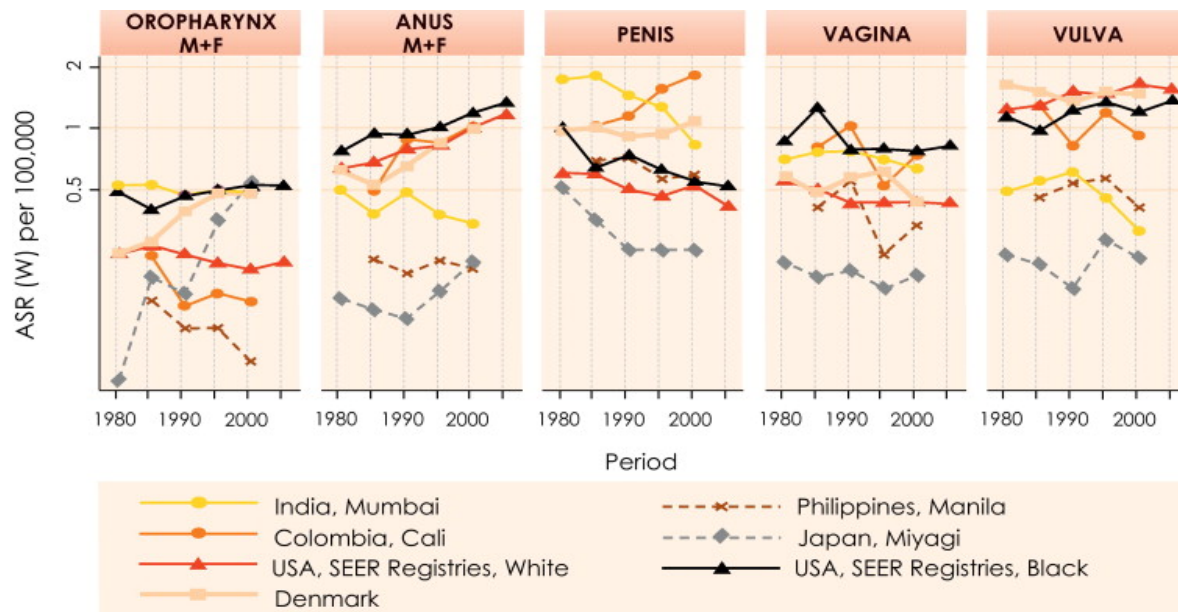
⁵⁴ H. Fujiwara et al., “Community-Based Interventions to Improve HPV Vaccination Coverage among 13- to 15-Year-Old Females: Measures Implemented by Local Governments in Japan,” *PLoS One* 8 (2013): e84126.

Appendix 1. Incidence of Cervix Uteri Cancer Globally (weighted mean of age-specific rates) (IARC 2012)



N.B. Data for Japan estimated from national mortality by modeling, using incidence mortality ratios derived from recorded data in country-specific cancer registries. International Agency for Research on Cancer (IARC).

Appendix 2. Cancers, Other than Cervix Uteri, Associated with HPV Infection, Age-standardized (world standard) Incidence Rates per 100,000, 1978–2007, per 5-year Period, in Selected Cancer Registry Populations (all ages)



Based on International Agency for Research on Cancer (IARC), *Cancer Incidence in Five Continents*, Volumes V to IX (Lyon, France: IARC, various years); Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute; and David Forman et al., “Global Burden of Human Papillomavirus and Related Diseases,” *Vaccine* 30, supp. 5 (November 2012), <http://www.sciencedirect.com/science/article/pii/S0264410X12010808> - bib0125. Data are for males (M) and females (F) combined for oropharynx and anus; oropharynx does not include base of tongue nor tonsils. ASR (W): Age-standardized (world standard) rate.

Appendix 3. Recommended Links to Regional Websites Containing Information about the HPV Vaccine

Europe

European Cervical Cancer Association

http://www.ecca.info/fileadmin/user_upload/HPV_Vaccination/ECCA_HP_Vaccination_April_2009.pdf

United Kingdom

National Health Service (NHS)

<http://www.nhs.uk/Conditions/vaccinations/Pages/hpv-human-papillomavirus-vaccine.aspx>

<http://www.nhs.uk/Conditions/vaccinations/Pages/hpv-vaccine-cervarix-gardasil-side-effects.aspx>

Australia

Cancer Council Australia

<http://www.hpvvaccine.org.au/the-hpv-vaccine/has-the-program-been-successful.aspx>

New Zealand

Ministry of Health

<http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/hpv-immunisation-programme/hpv-vaccine>

United States

Centers for Disease Control and Prevention (CDC)

<http://www.cdc.gov/vaccinesafety/vaccines/HPV/Index.html>

Canada

Public Health Agency of Canada

<http://www.phac-aspc.gc.ca/std-mts/hpv-vph/hpv-vph-vaccine-eng.php>

Immunize BC

<http://www.immunizebc.ca/diseases-vaccinations/hpv>

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