



Paving pathways: Brazil's implementation of a national human papillomavirus immunization campaign

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SYNOPSIS

In 2014, Brazil introduced an HPV immunization program for girls 9–13 years of age as part of the Unified Health System's (SUS) National Immunization Program. The first doses were administered in March 2014; the second ones, in September 2014. In less than 3 months more than 3 million girls received the first dose of quadrivalent HPV vaccine, surpassing the target rate of 80%. This paper examines three elements that may influence the program's long-term success in Brazil: sustaining effective outreach, managing a large technology-transfer collaboration, and developing an electronic immunization registry, with a focus on the State of São Paulo. If these three factors are managed, the Government of Brazil is primed to serve as a model of success for other countries interested in implementing a national HPV vaccination program to decrease HPV-related morbidity and mortality.

Key words: immunization programs; vaccination; papillomavirus vaccines; papillomavirus infections; registries; technology transfer; health promotion; Brazil.

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Since their respective approvals in 2006 and 2008, human papillomavirus (HPV) prophylactic vaccines have been introduced in several areas around the world, including Latin America, where rates of cervical cancer and other HPV-related diseases are high (1). In March 2014, Brazil introduced an HPV immunization program for girls 9–13 years of age as part of the Unified Health System's (SUS) *Programa Nacional de Imunização* (National Immunization Program; PNI). Brazil adopted an extended dosing schedule for the quadrivalent HPV vaccine, Gardasil,[®] (Merck Sharp & Dohme Corporation, a subsidiary of Merck & Company, Incorporated, Kenilworth, New Jersey, United States) where the second and third doses are administered at 6 months and 5 years. This extended schedule corresponds with clinical trials demonstrating non-inferior immune responses with two doses compared to three doses for the quadrivalent vaccine (2). The vaccine has recorded long-term protective benefits against genital warts, cellular dysplasia, early low-grade cancers, pre-cancerous lesions, and HPV-related cancers (3).

The HPV vaccination campaign in Brazil has been extremely successful in its initial phase. It surpassed its target rate of 80% vaccination for the first dose by reaching 3 million girls in less than 3 months. As of August 2014, 87% of eligible adolescent girls had been vaccinated nationwide. These rates vary by geographic area, state, and municipality; nonetheless, overall coverage is very high with state coverage ranging from 80.5%–98.7%.⁵ Prior to inclusion on the PNI immunization schedule, HPV vaccination rates for girls 10–14 years of age in Brazil were 1.54%, 1.31%, and 0.07% for first, second, and third doses, respectively (4).

To implement an effective long-term HPV immunization program, the Government of Brazil is considering strengthening its technological capacity and infrastructure. The aim of the authors in this paper is to consider three elements that may influence the HPV immunization program's long-term success: sustaining effective program outreach, managing a large technology-transfer collaboration, and developing an electronic immunization registry. While these topics are addressed for the country as a whole, the information is primarily focused on experiences in the State of São Paulo in southeastern Brazil.

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⁵ This range does not include data from Amazonas and Brasília (Distrito Federal), two states that launched individual HPV vaccine campaigns prior to 2014.

Program outreach and promotion

Brazil implemented a school-based immunization strategy for the HPV vaccine to ensure greater access to the target population. This has likely been a reason for the program's success to date. This was the first major, school-based vaccine initiative in Brazil, and was rolled out by the Ministry of Health (MOH) following a successful pilot study in São Paulo (5) and similar promising findings from other school-based HPV vaccination programs (6). The education, outreach, and promotional materials for the HPV vaccination campaign in Brazil were developed by the MOH and managed at the state and municipal levels. These included television advertisements, radio scripts, billboards and signs, and educational pamphlets. There were three important components of the promotional effort: emphasis on education of health professionals, appropriate information framing the vaccine, and successful marketing of the vaccination campaign (7).

The MOH has strongly emphasized the role of health professionals in supporting the HPV vaccination campaign. Along with state partners, the MOH created a HPV vaccine Technical Guide and an Information Guide specifically for health professionals (8). The MOH also developed an online, 15-hour training module on the Universidade Aberta SUS (UNA-SUS) website targeting doctors, nurses, nurse technicians, and nursing supporting staff (9). Training materials and other educational materials were offered free of charge and users were not required to register for access. However, the percentage of health professionals that accessed and utilized these training materials is unknown since usage data was not captured.

When planning its public marketing strategy, the MOH faced the difficult task of deciding how to frame and promote the HPV vaccine. In many countries, addressing HPV in relation to sexual contact has proven problematic. Hesitancy among parents and providers to discuss adolescent sexuality is often an obstacle to successful vaccine promotion. One of the questions in Brazil was whether to market the HPV vaccine as prevention for cervical cancer or genital warts, or both. The MOH decided to focus on cervical cancer prevention. If the campaign eventually includes adolescent boys, it is unclear how the message might change.

Overlaid with framing of the vaccine information was the actual dissemination to the target population on a mass scale. One key component of this campaign was television advertising. A vaccine for the adolescent population presents the unique opportunity and challenge of presenting its benefits to both the parent, and directly, to the target population. The television campaign capitalized on the role of adolescents in decision-making by encouraging girls to participate in and promote vaccination. However, there were concerns about the effectiveness of direct-to-consumer (DTC) advertising among adolescents since it is unclear how much DTC information they comprehend and internalize (10). Future research should focus on evaluating the impact of the Brazilian HPV media campaign on

the knowledge and attitudes of the vaccine recipients and their parents.

By contrast, parents received HPV information through presentations at school, informative pamphlets, and programs at the *unidade básica da saúde* (primary health posts; UBS). Studies in other countries have shown that parents tend to be more receptive to educational messaging provided through mass media, community events, interpersonal recommendations, and doctors' recommendations (11), so the campaign in Brazil incorporated these.

By using a wide range of information venues, the MOH of Brazil endeavored to positively influence the whole spectrum of decision-makers: adolescents, parents, and health professionals. Follow-up research will determine if these methods effectively educated parents and children on HPV, cervical cancer, and the HPV vaccine, and whether or not parents were prompted to have their children vaccinated. The roll-out of the second dose of HPV vaccine began in September 2014 and is currently ongoing.

HPV vaccine technology-transfer

During the past two decades, the Government of Brazil has established a legal infrastructure to support technology-transfer programs with a particular focus on increasing access to vaccines for the whole population (12, 13). These legal measures have paved the way for what will likely be a successful transfer of HPV vaccine technology. Legislation, such as the Innovation Law of 2005, encourages scientific collaboration and provides the infrastructure to support continuous domestic production of vaccines at affordable rates (14). These vaccine technology initiatives are led by two of Brazil's major biomedical research institutes: Butantan Institute (BI) in São Paulo and Bio-Manguinhos in Rio de Janeiro.

In 2013, Merck, Sharp & Dohme Corporation, the United States-based producer of the HPV vaccine used in Brazil, partnered with the BI for a US\$ 480 million technology-transfer agreement. Under the agreement, by 2018 the BI will become responsible for all domestic HPV vaccine production. In the first year, the BI was primarily focused on delivery and distribution of the vaccine produced in the United States. In following years, the BI assumes increasing responsibility for manufacturing the vaccine. This partnership is expected to ensure low-cost HPV vaccine production for subsequent cohorts of Brazilian girls 9–13 years of age and may also facilitate broadening the target range to include boys and older girls.

While Brazil is primed to experience successful HPV vaccine technology-transfer, there are a few challenges ahead. For one, the process may be delayed due to immunobiological or regulatory issues. Success is also dependent on the construction of a new manufacturing site at the BI, specifically for the HPV vaccine. It will likely be funded in part by the *Banco Nacional de Desenvolvimento Econômico e Social* (BNDES), among other investors, and require additional, iterative legal

agreements between Merck & Co., the BI, and the BNDES. Despite these challenges, the Government of Brazil is poised to continue a successful HPV vaccination program.

Electronic immunization registries

Electronic immunization registries (EIRs) serve as valuable tools for monitoring immunization coverage, providing both individual- and community-level benefits (15). Improvements in measuring coverage run parallel to improved coverage (16). Thus, an EIR plays a critical role in the success of a national immunization initiative by providing a database for monitoring program implementation, creating and adjusting vaccination strategies, and identifying areas of low coverage (17).

As of March 2014, in Latin America and the Caribbean (LAC), only Mexico and Uruguay had nationwide EIR systems (17). Brazil is working to achieve national implementation of an EIR called *Sistema de Informações do Programa Nacional de Imunizações* (SI-PNI), developed by PNI in collaboration with the Informatics Department of SUS (DATASUS) to utilize nominal data on immunizations for informed, public health decision-making (18). Evaluations of small-scale EIR systems in Brazil, such as the local EIR implemented in Curitiba, have been conducted (19); however, large-scale, nationwide evaluations could provide valuable evidence for the utility of such software in assisting policymakers and health systems staff implement vaccination programs.

SI-PNI is important for Brazil's current HPV vaccination campaign, especially for monitoring the uptake of all three HPV doses in the extended schedule. The MOH issued a proposed course of action called "Execution of HPV Vaccine Implementation" that designates the management of the SI-PNI database to state- and municipal-level organizations (7). In-school immunizations are recorded on a paper immunization registry form, *Registro Nominal das Adolescentes*, by the school. This form is then submitted to the corresponding health post where the information is transferred into the SI-PNI database. To address technical gaps, a UBS without access to SI-PNI may send the data to the State Secretary of Health for input into the system (8). Countries looking to establish a nationwide EIR system, such as the United States, are often limited by insufficient funding, training, and time to implement the necessary technological equipment and support (20). All of these are challenges that Brazil will need to navigate to establish and maintain a

successful system for evaluating the impact of its immunization services.

Independent of the EIS, Brazil has a passive surveillance system to cover nationally-reported adverse events. In the HPV immunization campaign's first phase, the vaccine was briefly recalled in Southeastern Brazil and vaccine safety messaging was released after adverse events were reported in São Paulo (21). These events did not heavily impact coverage rates.

CONCLUSION

While the Government of Brazil faces complicated challenges with promoting, implementing, and sustaining the national HPV vaccination program, it is uniquely primed to serve as a model of success for other countries. If these three factors—sustained program outreach, large-scale technology-transfer, and a nationwide electronic immunization registry—are managed effectively, the Government of Brazil will decrease HPV-related morbidity and mortality in its population.

Future research should focus on evaluating each component of the HPV program in Brazil to ensure continued programmatic success and improved health outcomes. The authors recently finished collecting formative qualitative and quantitative data on the knowledge, attitudes, and practices of health professionals and parents at five UBSs in the municipality of São Paulo. The forthcoming results may prove integral to informing future, generalizable projects. Given that health care professionals and parents are primary influencers of vaccination, evidence of their HPV-related perceptions and practices will serve as an important tool for program monitoring and evaluation.

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SINOPSIS

Allanando el camino: implementación de una campaña nacional de vacunación contra el virus del papiloma humano en Brasil

En el 2014, se introdujo en Brasil un programa de vacunación contra los VPH dirigido a niñas de 9 a 13 años de edad como parte del Programa Nacional de Vacunación del Sistema Unificado de Salud (SUS). Las primeras dosis se administraron en marzo del 2014; las segundas, en septiembre del 2014. En menos de tres meses, más de tres millones de niñas recibieron la primera dosis de vacuna tetravalente contra los VPH, superando la tasa prevista de 80%. En este artículo se analizan tres elementos que pueden influir en el

éxito a largo plazo del programa en Brasil: el mantenimiento de actividades de extensión eficaces, la administración de una amplia colaboración en materia de transferencia de tecnología, y la creación de un registro electrónico de vacunaciones, con hincapié en el Estado de São Paulo. Si se gestionan estos tres factores, el Gobierno de Brasil está dispuesto a servir como modelo exitoso a otros países interesados en introducir un programa nacional de vacunación contra los VPH con objeto de disminuir la morbilidad y la mortalidad relacionadas con los VPH.

Palabras clave: programas de inmunización; vacunación; vacunas contra papillomavirus; infecciones por papillomavirus; sistema de registros; transferencia de tecnología; promoción de la salud; Brasil.

REFERENCES

- Pan American Health Organization. Cervical Cancer in the Americas. Washington, DC: PAHO; 2014.
- Dobson SR, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. *JAMA*. 2013; 309(17):1793–802.
- McCormack PL, Joura EA. Spotlight on quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine (Gardasil(R)) in the prevention of premalignant genital lesions, genital cancer, and genital warts in women. *BioDrugs*. 2011;25(5):339–43.
- Ministry of Health of Brazil. Sistema de Informações do Programa Nacional de Imunizações. Estratégia de Vacinação contra HPV 2014. Available from: http://pni.datasus.gov.br/consulta_hpv_14_selecao.php Accessed on 12 August 2014.
- Fregnani JH, Carvalho AL, Eluf-Neto J, Ribeiro Kde C, Kuil Lde M, da Silva TA, et al. A school-based human papillomavirus vaccination program in barretos, Brazil: final results of a demonstrative study. *PloS one*. 2013; 8(4):e62647.
- Paul P, Fabio A. Literature review of HPV vaccine delivery strategies: considerations for school- and non-school based immunization program. *Vaccine*. 2014;32(3):320–6.
- Ministry of Health of Brazil. Operacionalização da implantação da vacina HPV: Proposta de Ações. Brasília: Ministerio da Saúde; 2014.
- Secretaria de Estado da Saúde do Estado de Santa Catarina. Informe técnico sobre a vacina papilomavírus humano (HPV) na atenção básica. Santa Catarina: Diretoria de Vigilância Epidemiológica; 2014.
- Universidade Aberta SUS. Vacinação contra o Papilomavírus Humano (HPV). Available from: www.unasus.gov.br/cursos/hpv Accessed on 27 August 2015.
- Leader AE, Cashman R, Voytek CD, Baker JL, Brawner BM, Frank I. An exploratory study of adolescent female reactions to direct-to-consumer advertising: the case of the Human Papillomavirus (HPV) Vaccine. *Health Mark Q*. 2011;28(4):372–85.
- Hull PC, Williams EA, Khabele D, Dean C, Bond B, Sanderson M. HPV vaccine use among African American girls: qualitative formative research using a participatory social marketing approach. *Gynecol Oncol*. 2014; 132(suppl 1):S13–20.
- Homma A, Tanuri A, Duarte AJ, Marques E, de Almeida A, Martins R, et al. Vaccine research, development, and innovation in Brazil: a translational science perspective. *Vaccine*. 2013;31(suppl 2):B54–60.
- Miyaki C, Meros M, Precioso AR, Raw I. Influenza vaccine production for Brazil: a classic example of successful North-South bilateral technology transfer. *Vaccine*. 2011;29(suppl 1): A12–5.
- Homma A. The Brazilian vaccine manufacturers' perspective and its current status. *Biologicals* 2009;37(3): 173–6.
- Centers for Disease Control and Prevention. Development of community- and state-based immunization registries. CDC response to a report from the National Vaccine Advisory Committee. *MMWR*. 2001; 50(RR-17):1–17.
- Papania M, Rodewald L. For better immunisation coverage, measure coverage better. *Lancet*. 2006;367(9515): 965–6.
- Danovaro MC. Immunization registries in Latin America and the Caribbean. Geneva: World Health Organization; 2014.
- Ministry of Health of Brazil. Sistema de Informações do Programa Nacional de Imunizações. Available from: <http://pni.datasus.gov.br/> Accessed on 27 August 2015.
- Luhm KR, Cardoso MR, Waldman EA. Vaccination coverage among children under two years of age based on electronic immunization registry in Southern Brazil. *Rev Saude Publica*. 2011;45(1):90–8.
- Ford EW, Menachemi N, Phillips MT. Predicting the adoption of electronic health records by physicians: when will health care be paperless? *J Am Med Inform Assoc*. 2006;13(1): 106–12.
- Globo Comunicação e Participações S.A. Fantástico. Efeitos colaterais à vacina do HPV são reação emocional, dizem médicos. Available from: <http://globo.com/redesocial/fantastico/v/efeitos-colaterais-a-vacina-do-hpv-sao-reacao-emocional-dizem-medicos/3629541/> Accessed on 27 August 2015.

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