



ICO Monograph Series on HPV and Cervical Cancer: General Overview

Early Experience with Human Papillomavirus Vaccine Introduction in the United States, Canada and Australia

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ABSTRACT

Successful incorporation of a new vaccine into a nation's vaccination program requires addressing a number of issues, including: 1) establishing national recommendations; 2) assuring education of and acceptance by the public and medical community; 3) establishing and maintaining an appropriate infrastructure for vaccine delivery; 4) financing the vaccine and the program, in addition to political will. This article reviews the early experience with implementation of human papillomavirus (HPV) vaccination programs. It focuses on the United States of America and Canada and provides a brief report on Australia, where introduction is underway.

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1. Introduction

Formulating and carrying out a comprehensive plan for introducing new vaccines into a nation's vaccination program are crucial to overall acceptance and use of new vaccines. The first milestone for new vaccines in every country is licensure of the vaccine and, in many countries, development of national recommendations. The comprehensive plan for success must include identifying funding to support the program, ensuring adequate vaccine supply and distribution capacity, educating the public and health care sector, monitoring the safety and effectiveness of vaccine, and establishing venues for delivering the vaccine. The challenges and lessons learned in the United States, Canada, and Australia may be helpful as other countries begin introducing human papillomavirus (HPV) vaccine.

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¹ The views expressed are those of the author(s) and do not necessarily represent the views of the organization(s) they represent.

2. United States of America

2.1. Process and framework for vaccine decision-making

The Food and Drug Administration (FDA) has regulatory authority to license vaccines based on information regarding safety, immune response and efficacy submitted by the manufacturer (Table 1) [1]. Following licensure, national recommendations for vaccine use are primarily formulated by the Centers for Disease Control and Prevention (CDC) through its Advisory Committee on Immunization Practices (ACIP). The ACIP is a federal advisory committee providing recommendations to the CDC and its parent organization, the USA Department of Health and Human Services, which issue the final written recommendations and supporting evidence-base through the Morbidity and Mortality Weekly Report's Recommendations and Reports series. The ACIP issues a vaccination schedule for children, adolescents and adults annually, and these schedules are harmonized whenever possible with recommendations of the major USA health care professional organizations (Table 2).

Table 1
Major components of vaccination programs in the United States and Canada and participating groups

Component	United States of America – Major participating groups	Canada – Major participating groups
Vaccine production and distribution	Vaccine industry, commercial distributors, state and local governments	Vaccine industry (production); Provincial, territorial and local government (public distribution)
Regulation	Federal government (FDA)	Federal government (Health Canada)
Vaccine policy	Federal government (ACIP), professional medical organizations	Vaccine schedule and recommendations: NACI; Recommendations on program options - CIC (federal, provincial and territorial governments)
Vaccine financing	Federal government (VFC, Section 317 of Public Health Service Act), state and local governments, insurance companies, individuals	Provincial and territorial governments; Federal Trust Fund
Vaccine administration	Private health care providers, state and local public health providers	Local public health or health care provider-delivered (publicly funded programs), health care providers (non-publicly funded)
Settings for vaccine delivery	Private and public health care provider settings, school-based settings (rarely)	Provincial, territorial and local governments (public health clinics, school-based settings, health care providers)
Monitoring vaccine use	Federal government (biologics surveillance, national coverage surveys, IIS), vaccine industry, state and local governments	School-based programs through local public health (primary setting), immunization coverage surveys
Monitoring vaccine effectiveness	Federal government, state and local governments, vaccine industry	Provincial, territorial and local governments; federal government for national level monitoring; vaccine industry
Monitoring vaccine safety	Federal government (VAERS, VSD, CISA), vaccine industry	Federal government coordinates the national vaccine safety monitoring system (CAEFISS, IMPACT), with reporting through provincial, territorial and local governments; vaccine industry
Vaccine injury compensation and liability	Federal government (VICP)	Province of Quebec has the only vaccine injury compensation program in Canada

ACIP: Advisory Committee on Immunization Practices; CAEFISS: Canadian Adverse Events Following Immunization Surveillance System; CIC: Canadian Immunization Committee; CISA: Clinical Immunization Safety assessment Network; FDA: Food and Drug Administration; IIS: Immunization Information Systems; IMPACT: Immunization Monitoring Program ACTIVE; NACI: National Advisory Committee on Immunization; VAERS: Vaccine Adverse Event Reporting System; VFC: Vaccines for Children Program; VICP: National Vaccine Injury Compensation Program; VSD: Vaccine Safety Datalink.
Adapted from [1].

2.2. Immunization programs funding and implementation

The United States does not have a single or universal national health system. Vaccines in the USA are financed by both public and private sources [2]. For children, almost 60% of vaccine doses are purchased through federal contracts - a federal entitlement called the Vaccines for Children (VFC) program. In contrast, vaccines for adults are largely purchased in the private sector and only a small proportion (<5%) of adult vaccines are purchased through a federal contract (in preparation, Wallace G., Centers for Disease Control and Prevention). Since 1994, the VFC program has supplied private and public providers with federally purchased vaccines for use among eligible children (uninsured, Medicaid eligible or American Indian or Alaska Native) between the ages 0–18 years [3]. The ACIP has the authority to add vaccines to this entitlement program. Individual states decide when to purchase vaccines through the VFC federal contract so that timing of vaccine introduction may vary across states.

As part of the Public Health Service Act (Section 317), public sector funding also supports a program that provides federal funds to state and local health departments. This funding can support a wide range of immunization-related activities and services for both children and adults (e.g., surveillance, public education, vaccines and administration, personnel and program management); however, funding levels have markedly varied. State and local government funding is also used to support immunization program activities although this funding is requested from state legislatures resulting in tremendous variation by state and local areas.

2.3. Settings for delivery of vaccines

In the USA, vaccines are delivered in both the public and private sectors. Adolescent vaccines are delivered in wide range of traditional primary care medical care settings (e.g., pediatrician, family physician, internist, or gynecologist practices; community health centers, sexually transmitted disease (STD) clinics, pharmacies, hospital emergency departments and family planning clinics). Less often, vaccines have been delivered in the school setting, either through school-based health clinics or through one-time immunization campaigns located in schools.

2.4. Status of HPV vaccination programs

2.4.1. National HPV vaccine recommendations

In 2004, the ACIP HPV Vaccine Workgroup was formed in anticipation of licensure for future HPV vaccines. This group collected and reviewed data on the epidemiology, HPV vaccine immunogenicity, efficacy and safety, vaccine acceptability, sexual behavior, feasibility of delivery and economic analyses. The quadrivalent HPV vaccine was licensed in June 2006, and national recommendations were approved by the ACIP the same month (Fig. 1).

The ACIP recommended that the quadrivalent HPV vaccine be administered to 11- to 12-year-old females as a 3-dose series, with catch-up for females aged 13 through 26 years. Consistent with the FDA-approved licensure indications, ACIP recommended vaccination for girls as young as 9 years [4–6] ACIP also voted for the vaccine to be covered by the VFC program.

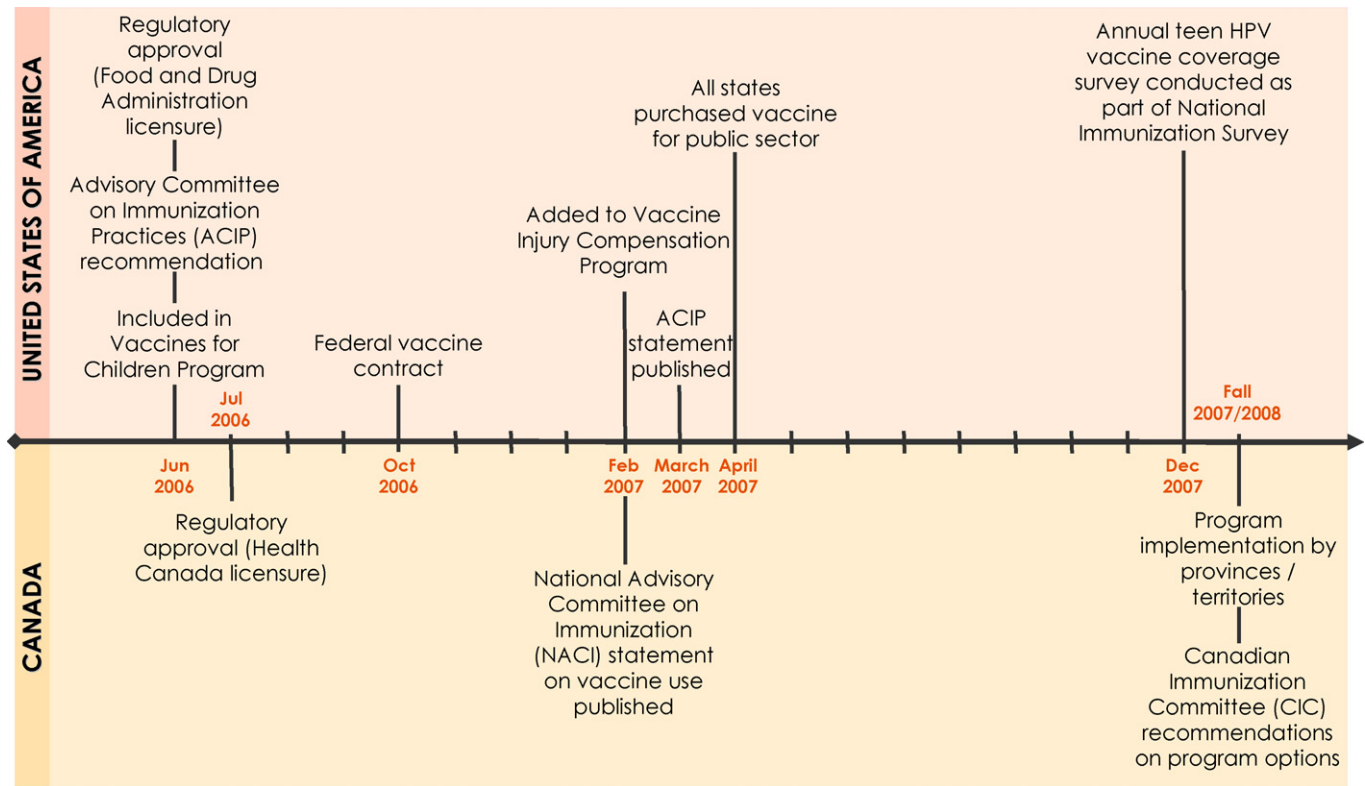


Figure 1. Quadrivalent HPV vaccine introduction timeline in the United States of America and Canada.

Four months following the ACIP recommendation, a federal contract for vaccine purchase was negotiated. The contract allowed states to purchase vaccine with public funds (either federal or state) at a reduced rate of \$96/dose compared to the published catalogue price of \$120/dose.

2.4.2. Adolescent schedule

With the ACIP recommendation, the quadrivalent HPV vaccine became the third vaccine to be recommended for routine use in adolescents. The two other vaccines, meningococcal polysaccharide-protein conjugate vaccine (MCV4) and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) had been licensed and recommended in 2005. These three new vaccines are recommended at the 11- to 12-year-old routine adolescent preventive visit [6,7]. Because only a minority of this population receive primary or well-care visits where vaccines might be routinely delivered, increased access to these preventive health care visits will be required [8,9]. For several years, three other vaccines (hepatitis B virus (HBV), measles, mumps and rubella (MMR), and varicella) have been recommended for “catch-up” administration for adolescents who had not already received these vaccines (or in the case of varicella, had not had the disease).

Compared to infants and children, adolescent coverage is low: 81.3%, 86.9% and 65.5% of 13-17-year-olds were fully immunized for HBV, MMR and varicella in 2006, respectively, and only 60.1% received ≥ 1 dose of Td or Tdap booster (MCV4 had been in use < 1 year, and coverage was 11.7%) [10]. There are several reasons contributing to the low coverage of primary vaccinations (single or multi-dose) or boosters in teens: infrequent annual preventive visits unlike infants and young children, vaccination is considered an intervention for young children and missed opportunities for vaccination occur even when adolescents receive health care [8,9,11,12].

Ensuring vaccines are administered to the adolescent population will require adopting a broader view by both health care providers and parents.

2.4.3. Settings for HPV vaccine delivery

HPV vaccine is being introduced through a variety of primary care and specialized provider sites. The choice of health care provider varies according to the patient's age, younger adolescents are more likely to visit primary care providers and older adolescents are more likely to visit specialized venues [8,13]. Primary care providers have been integral to delivery of immunizations [14], although the optimal settings for delivery of HPV vaccines are currently under evaluation. For example, the state of Iowa is evaluating delivery of the quadrivalent HPV vaccine to girls in several middle schools, through a partnership among the schools, private medical clinics and a community partnership organization.

2.4.4. Strategies to raise immunization coverage

State-based school entry vaccination laws have been used to rapidly increase vaccination rates among adolescents for the HBV vaccine [15,16]. In addition, school-based programs may also improve coverage but this has only been shown for HBV vaccine [15]. A recent study also found that reminder/recall for adolescents in an urban setting was only minimally successful in improving coverage for HBV and Td vaccine, as well as preventive care visits [17].

2.4.5. Program activities

Determining when to introduce a vaccine varies state-by-state, and increased financing beyond VFC entitlement results in differences in the timing of vaccine purchases under federal contracts. As of April 2007, all states had purchased HPV vaccine through VFC federal contracts.

VFC funding alleviates providers' requirement for upfront purchases to establish a vaccine inventory for VFC-eligible children. As of 2006, approximately 44,000 provider sites (both private and public) were participating in VFC. In 2007 and 2008, state immunization programs received federal funds to hire adolescent immunization coordinators and increase the number of providers and/or clinical sites that were enrolled and participating in VFC. To provide more opportunities for HPV vaccine delivery, many states are expanding access to VFC covered vaccines at specialized health-care settings such as STD clinics, teen clinics, hospital emergency rooms, family planning clinics and pharmacies that serve older children and adolescents.

2.4.6. Public education, awareness, and acceptability

HPV vaccine introduction has required efforts by federal and local public health departments, and various professional organizations to increase education and awareness about HPV and HPV vaccine. CDC, in partnership with the American Academy of Pediatrics, launched a preteen campaign in August 2007 that promoted use of three ACIP recommended vaccines for 11- to 12-year-olds (Tdap, MCV4, and for girls, HPV) together with promotion of a preteen checkup to facilitate anticipatory guidance for adolescent health issues (Table 2).

In contrast to many vaccines recommended for young children, HPV vaccine was actively marketed in the USA through direct consumer advertising and several public awareness campaigns by the manufacturer. Legislators and policy makers were also educated through similar efforts.

Public acceptance of HPV vaccine is estimated to be high and will be assessed in various populations and settings [18]. One study conducted at the time of vaccine licensure suggests that approximately 80% of parents surveyed were likely to vaccinate their daughter [19].

2.4.7. Legislative issues

In the USA, HPV vaccine has raised complex philosophical, legal, policy and political concerns [20]. Proposals to use state laws to mandate HPV vaccine as a requirement before school enrollment have been controversial. Historically, school entry requirements or mandates have been effective in raising immunization rates among children and adolescents in the USA [15,16]. As of June 2007, almost half of all states had proposed legislation requiring HPV vaccination before school enrollment with various "opt-in" and "opt-out" requirements (i.e., to actively give permission or to actively decline participation, respectively) [20]. However, to date, only one state has passed a law mandating HPV vaccination for school entry and will require it for girls entering the sixth grade (typical age range 11 to 12-year-olds). This proposal only passed into law after expanding parents' rights to decline vaccination for their daughters. Many experts believe that before laws are enacted requiring HPV vaccination, provisions for financing vaccines for youth who are unwilling or unable to pay are needed. Since school entry mandates are the responsibility of individual states, it is possible that as states gain more experience with HPV vaccine programs and address financing issues, there may be more interest in requiring HPV vaccination of girls as a condition of school entry for 11- to 12-year-olds.

2.4.8. Early implementation by state immunization programs

Shortly after the ACIP recommendation for the HPV vaccine, a majority of states (34 of 51) focused HPV vaccine efforts on all 9- to 18-year-olds VFC-eligible children; less than half the states were able to provide publicly funded vaccine to adolescents whose insurance did not cover HPV vaccine in private (16 states) or public health care settings (22 states) [21]. Using a combination of federal and state funds to purchase and distribute HPV vaccine, at least two

states are able to make vaccine available at no cost to all girls 9-18 years of age, regardless of their insurance status. These funds cover only the cost of the vaccine and do not cover costs to administer the vaccine.

2.4.9. Coverage, safety and disease impact

2.4.9.1. Coverage. Through June 2007, approximately 7.5 million doses of HPV vaccine were distributed in the USA; however, there are no national data yet on the number of doses administered, persons vaccinated or completed the vaccine series. The female birth cohort in the USA is estimated to be 2 million. Coverage data will be obtained from the National Immunization Survey, a random digit dialing survey validated with medical records, that is conducted by the CDC annually to assess HPV vaccine coverage among girls 13-17-year-olds [10]. This survey provides both national and state-specific estimates of vaccine coverage. HPV coverage data among persons >18 years of age are being collected through other national and state surveys, including the National Health Interview Survey and the Behavioral Risk Factor Surveillance Survey. Outcomes of these surveys will provide data on vaccination status, socio-demographics and economic characteristics of the vaccinee.

2.4.9.2. Safety. The National Vaccine Injury Compensation Program (VICP) is a federal program that provides compensation to persons who may have been injured by certain vaccines regardless of who is at fault. HPV vaccine was added to VICP in February 2007, but claims are covered 8 years retrospectively (Table 2).

Post-licensure monitoring of vaccine safety is being conducted by CDC, FDA and the vaccine manufacturer. Monitoring of vaccine safety occurs through passive reporting through the Vaccine Adverse Event Reporting System (VAERS), a national reporting system jointly operated by CDC and FDA. Although VAERS has well-recognized limitations, including underreporting and the inability to determine causal relationships between adverse events and vaccination, it can be monitored for signals of possible trends that merit investigation and generate hypotheses about potential safety issues. Syncope has been one of the most common reported adverse event after vaccination, the ACIP has reinforced its general recommendations to observe all vaccine recipients for 15 minutes after vaccination [22].

HPV vaccine safety is also monitored through special studies and evaluations conducted through the Vaccine Safety Datalink (VSD) project (Table 2). VSD is a collaborative project between CDC and a group of managed health care organizations (MCOs) that investigate possible vaccine-related events through systematic studies and evaluations of data collected in the MCOs. In addition, a registry has been established by the manufacturer to monitor women who receive vaccine during pregnancy (Table 2).

2.4.9.3. Monitoring impact. The USA has an excellent system of cancer registries to monitor the incidence of cervical cancer and other HPV-related cancers after HPV vaccine introduction. Two systems of registries, the National Program of Cancer Registries (NPCR) and Surveillance Epidemiology and End Results (SEER) cover approximately 99% of the USA population (Table 2).

Because expected reductions in invasive cervical cancer incidence related to HPV vaccination may not be observed for 20 or 30 years, other proximal measures, such as cervical intraepithelial neoplasia (CIN), prevalence of vaccine HPV types, incidence of cervical cancer precursors, and ano-genital warts are important to monitor. Since 2002, the National Health and Nutrition Examination Survey has monitored type-specific HPV DNA prevalence using self-collected vaginal swabs [23]. New pilot projects have been initiated to collect data on HPV types associated with lesions and

population-based CIN2/3 data in some states and in sentinel sites. To evaluate clinical and public health impact of HPV vaccination, systems to collect immunization data and linkages to various outcome data need to be established. Finally, to evaluate outcomes due to HPV types -6 and 11, data on anogenital warts are being evaluated in a network of STD clinics as well as through administrative databases.

3. Canada

3.1. Process and framework for vaccine decision-making

Health Canada's Biologics and Genetic Therapies Directorate is the federal regulatory authority that authorizes vaccines for sale in Canada after reviewing the scientific evidence of a product's safety, immunogenicity, efficacy and quality (Table 1). Canada has a universal health care system that is responsible for purchase and delivery of vaccines, although a minority of citizens purchase vaccines through private health insurance plans or pay out of pocket. Canada's National Advisory Committee on Immunization (NACI) is the expert body that provides medical and scientific advice on vaccines and develops recommendations for vaccine use in Canada, taking into account available evidence on disease characteristics (epidemiology and burden) and vaccine characteristics (safety, immunogenicity, efficacy). The Canadian Immunization Committee (CIC) is a committee made up of vaccine program representatives from the federal, provincial and territorial ministries of health that provides advice and recommendations on vaccine program planning and implementation and promotes harmonization of immunization programs in Canada. The CIC develops national goals and targets for immunization programs and recommended options on publicly funded programs, including an assessment of cost-benefit analyses, feasibility and acceptability of recommended delivery strategies or target age groups.

3.2. Overview of immunization program funding and implementation

Although vaccine recommendations are made at the national level, publicly funded immunization programs are primarily a provincial/territorial responsibility. This requires that each province/territory must plan, fund and deliver programs independently. Since 2003, the federal government has had a role in supporting provinces and territories in immunization program planning, funding and implementation of new vaccine programs through three key initiatives: the National Immunization Strategy and the Budget 2004 and 2007 Immunization Trust Funds.

Most vaccines used for public immunization programs are purchased through a bulk procurement program (BPP) that is administered by the federal government and overseen by the CIC's Vaccine Supply Working Group. The program enables participants to take advantage of larger combined purchase volumes, which reduces the cost of vaccines and ensures that all jurisdictions are treated equally regardless of the size of their purchase. Since its introduction, this program has lowered the purchase price for all vaccines. Participation in the BPP is voluntary and the provinces and territories are responsible for the payment of vaccines purchased under the program, as well as for paying a small administrative fee to participate.

3.3. Settings for delivery of vaccines

Vaccine delivery in Canada is primarily administered by the provinces and territories. After reviewing NACI recommendations,

each province or territory conducts decision analysis to determine whether a specific vaccine will be included in the publicly funded program. The settings for vaccine delivery vary throughout the country. In some jurisdictions, public health clinics, public health offices and school-based clinics deliver most publicly funded vaccines. In other jurisdictions, vaccines are delivered primarily through physician-based practices. Most jurisdictions utilize both modes of delivery.

3.3.1. Status of HPV vaccination program

The quadrivalent HPV vaccine (Gardasil[®], Merck & Co., Inc., Whitehouse Station, NJ, USA) was authorized for marketing by Health Canada on July 10, 2006, for females 9 through 26 years of age (Fig. 1). The quadrivalent HPV vaccine was recommended by NACI for females between ages 9–13 years, before the onset of sexual intercourse and for females aged of 14–26 years, even if they are already sexually active, have had previous Pap abnormalities or have had a previous HPV infection. The vaccine was not recommended by NACI for females under 9 years of age, males or pregnant women. In addition, NACI did not recommend the use of the vaccine in woman over the age of 26 years, but indicated that its use could be considered in individual circumstances [24].

NACI's recommendations are used by provinces and territories as one component of their vaccine program decision-making and may guide individual providers administering the vaccine in the private sector. To assist provinces and territories in their decision making for publicly funded programs, a multi-disciplinary joint CIC-NACI HPV Vaccine Workgroup is developing comprehensive scientific and programmatic recommendations for HPV vaccine programs in Canada. Their analytic framework includes HPV disease characteristics and burden, vaccine characteristics, alternate immunization strategies, social and economic costs and benefits of vaccination, feasibility and acceptability of vaccination, ability to evaluate vaccine programs and research questions and consideration for the Canadian health care system [25].

Based on the work of the joint CIC-NACI HPV Vaccine Workgroup, the CIC is developing a Statement on HPV Vaccine Programs that will describe national goals for HPV immunization programs, recommendations on disease reduction, vaccine coverage targets and recommended options for routine immunization programs. While national recommendations are made by NACI and CIC, provinces and territories will consider their own set of circumstances for decisions on the funding and implementation of HPV immunization programs.

3.3.2. Settings for HPV vaccine delivery

Within Canada, school-based programs for adolescents have been very successful in delivering HBV vaccine, a multi-dose primary vaccination series, in every province and territory of the country between grades 4 to 7 (ages 9 to 12 years) [26]. Owing to this programmatic success, it is anticipated that most routine HPV vaccination programs will be delivered through a school-based system. The most recent national coverage data showed that in 2004, 60% of 17-year-olds were fully immunized for HBV.

3.3.3. Program activities

As of August 2007, four provinces had announced publicly funded HPV vaccination programs, utilizing existing school-based immunization program infrastructure for delivery. Other provinces and territories may wait until completion of the CIC statement on recommended program options. Prior to implementation of publicly funded programs, individuals can obtain the vaccine through their health care providers although the cost incurred would be paid individually or through private health insurance plans. Traditionally, only a minority of the population have accessed vaccines

through this route prior to their inclusion in publicly funded programs.

In 2007 the federal budget provided CAN\$300 million to provinces and territories through a third-party trust fund to launch HPV vaccination programs. The HPV Vaccine Trust is intended to support the purchase of HPV vaccine by the provinces and territories for use in a publicly funded HPV immunization program for all residents, including First Nations and Inuit residents living on and off reserves, over the next 3 years. Provinces and territories can use this allocation in a flexible manner as appropriate within their jurisdictions (e.g., to target vaccination to populations at highest risk of cervical cancer).

3.3.4. Public education, awareness, and acceptability

Development of resources for public, professionals and the intended group is an integral part of program planning functions. The resources are varied and their contents are designed to meet the needs of the intended target groups. At the federal level, funding was provided to the Society of Obstetricians and Gynecologists of Canada (SOGC) to develop resources for teachers and health providers. In addition, Public Health Agency of Canada also provided information about HPV on its web site (Table 2).

HPV vaccine was actively marketed in Canada by the manufacturer through direct consumer advertising and public awareness campaigns related to HPV and the link between HPV, cervical cancer and genital warts and the importance of the Pap test.

Public acceptance of HPV vaccine is estimated to be high. Several studies conducted in 2006–2007 suggest that 74–89% of parents were likely to vaccinate their daughter [27,28]. Studies are underway, including an assessment of acceptability by providers and feasibility of HPV vaccination programs from the perspective of family physicians, obstetrician/gynecologists and public health nurses and physicians.

3.3.5. Legislative issues

There are no mandatory immunization programs in Canada with the exception of some jurisdictions that require certain vaccinations before school enrollment, but none of these currently include HPV vaccines. When they do exist, mandates generally have fairly broad provisions for exemptions. HPV vaccines are not expected to be included as part of school entry requirements in any jurisdiction in Canada.

3.3.6. Coverage, safety and disease impact

3.3.6.1. Coverage. The National Immunization Coverage Surveys, conducted every 2 years, provide national-level estimates for vaccine coverage among 17-year-olds as part of the childhood survey, and in the general adult population, and can be adapted to include HPV vaccine coverage [29]. However, these surveys are not able to assess subpopulations, and non-participation bias cannot be excluded. A national network of immunization registries is currently under development that could be used to estimate HPV vaccine coverage. To date, five provinces have fully functional registries, and the remaining jurisdictions are either planning or evaluating new systems.

3.3.6.2. Safety. The Public Health Agency of Canada coordinates and supports the Canadian Adverse Events Following Immunization Surveillance System, a passive surveillance system which collects reports from health care providers on adverse events following immunization. Canada also has an active surveillance system for adverse events following immunization through 12 pediatric hospitals across Canada, called Immunization Monitoring Program ACTIVE (IMPACT). Causal association between vaccination and severe or unexpected adverse events reported to the Public

Health Agency of Canada is judged by a national expert scientific committee, the Advisory Committee on Causality Assessment, after an assessment of each report [29].

3.3.6.3. Disease impact. Canada supports comprehensive cancer registries within several provinces and territories that track invasive cervical cancer. HPV-related cancer incidence and prevalence will be able to be monitored through these systems, but not CIS or CIN2/3. To monitor HPV vaccine impact on more proximal outcomes of vaccine-related HPV type infection or precancerous cervical lesions, some provinces are considering special pilot studies that will for the first time link established immunization and cancer screening registries, a challenging issue. Monitoring of cervical disease outcomes will require development of population-based reporting systems for HPV-associated infections. Planning for a sentinel surveillance system in monitoring type-specific HPV prevalence is under way. Evaluation plans to monitor HPV vaccination impact on cervical cancer screening practices and on adherence to screening practices among vaccinated women need to be developed.

4. Australia

The processes involved in introduction of a new vaccine in Australia are similar to those in the USA and Canada and are described by Garland *et al.* 2008 [30]. The Therapeutic Goods Administration (TGA) is the federal regulatory authority that initially reviewed the new HPV vaccines for registration. The quadrivalent HPV vaccine was registered in Australia in June 2006. This vaccine was registered for use in females aged 9–26 and males aged 10–15 years, based on Phase III clinical trials and immuno-bridging data [31]. In November 2006, following review of cost-benefit analyses submitted by the vaccine sponsor and advice from the Australian Technical Advisory Group on Immunization (ATAGI) [32], the Pharmaceutical Benefits Advisory Committee (PBAC), a group that makes recommendations about government funding of new vaccines recommended government funding of the quadrivalent vaccine for 12-year-old females, with a catch up campaign to age 26 years.

A government-funded school-based program targeting females aged 12–18 years was implemented in April 2007. Under the auspices of the local or State government, schools provided general information about HPV and vaccine safety and efficacy data to parents of eligible girls for vaccination and written consent was required for vaccination.

After the first year of this school-based program, compliance through dose 3 was estimated at 75 to 80% among targeted girls and initial cohorts covered by programs varied slightly by State and Territory. The ongoing target group is school year seven (girls aged 11 to 12 years) with a staggered catch-up of school years 8 to 12 (girls aged 13 to 18 years). Starting in July 2007, the government funded a two-year catch-up program of the quadrivalent vaccine for all females not enrolled in school up to age 26.

The Australian government and State and Territory Departments of Health have promoted the HPV vaccine program through education and awareness via print media, radio and television. Post-licensure monitoring of vaccine safety is being conducted through the TGA's Adverse Drug Reactions Advisory Committee. State-based specialist programs have been implemented in some states for adverse events surveillance and clinical advice, such as the Surveillance of Adverse Events Following Vaccination in the Community (SAEFVIC) in Victoria. The National HPV Vaccination Program Register, which will begin in 2008, will monitor vaccination coverage, as well as population-based studies of vaccine effectiveness.

Table 2
Resources referenced in this article for vaccine related information and HPV vaccines

Agency	Report/Program name	Website ^a
Centers for Disease Control and Prevention, USA	Morbidity and Mortality Weekly Report's Recommendations and Reports series	www.cdc.gov/mmwr
Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices	Immunization recommendations	http://www.cdc.gov/vaccines/recs/schedules/default.htm
Centers for Disease Control and Prevention	Vaccines for Children Program	http://www.cdc.gov/nip/vfc/st_immz_proj/data/data.htm
Centers for Disease Control and Prevention	Vaccines and Preventable Diseases, Sexually Transmitted Diseases	http://www.cdc.gov/vaccines/vpd-vac/hpv/default.htm ; http://www.cdc.gov/std/HPV
Centers for Disease Control and Prevention	Pre-Teens Vaccine Campaign	http://www.cdc.gov/vaccines/spec-grps/preteens-adol/07gallery/default.htm
US Dept of Health and Human Services, Health Resource and Services Administration	National Vaccine Injury Compensation Program	http://www.hrsa.gov/vaccinecompensation
Centers for Disease Control and Prevention	Vaccine Safety Datalink	http://www.cdc.gov/od/science/jiso/research.htm
Merck and Co., Inc.	Pregnancy registry for Gardasil®	http://www.merckpregnancyregistries.com/gardasil.html
Centers for Disease Control and Prevention	National Program of Cancer Registries	http://www.cdc.gov/cancer/npcr
National Cancer Institute	Surveillance, Epidemiology, and End Results Program	http://seer.cancer.gov/about
Public Health Agency of Canada	Fact Sheet National Immunization Strategy (NIS) for Canada	http://www.phac-aspc.gc.ca/media/nr-rp/2005/2005.14bk1_e.html
Society of Obstetricians and Gynecologists of Canada	Information for Teachers	http://www.hpvinfos.ca/hpvinfo/teachers/index.aspx
Society of Obstetricians and Gynecologists of Canada	Information for Professionals	http://www.hpvinfos.ca/hpvinfo/professionals/index.aspx
Public Health Agency of Canada	What Everyone Should Know About Human Papillomavirus (HPV): Questions and Answers	http://www.phac-aspc.gc.ca/std-mts/hpv-vph/hpv-vph-qaqr_e.html

^a Last accessed on April 2008.

The bivalent vaccine (Cervarix™, GlaxoSmithKline Biologicals, Rixensart, Belgium) was registered in May 2007 for use in females aged 10 to 45 years of age, and was recently recommended in November 2007 by the PBAC for government funding up to 26 years of age.

5. Conclusions

The United States of America, Canada and Australia are all in the early stages of introducing HPV vaccine and have used different methods to set clinical recommendations, secure funding, identify delivery options and monitor safety and impact. Both USA and Canada are starting to establish the most appropriate settings to deliver vaccine to the target population, minimize financial barriers to parents and providers and assure adequate infrastructure support. Canada is planning for a school-based delivery similar to the Australian model. There are many other challenges and questions related to HPV vaccination of adolescents in these countries that are not covered in this report, including informed consent to vaccination by minors, predictors of vaccine uptake and refusal, the need to reinforce continued cervical cancer screening despite vaccination, what coverage levels can be achieved over what time frames and ensuring that vaccines are utilized by populations at highest risk for cervical cancer such as those less likely to be screened for cervical cancer later in life. More data on the long-term duration of vaccine protection, the impact of immunization on cervical cancer screening and surveillance to measure the effectiveness of vaccination on disease burden is needed. Monitoring various vaccine delivery strategies in Australia, the USA and Canada may be informative for high-income countries with well established primary care health systems as they implement HPV vaccination programs.

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