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Final Report

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Quebec City

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Executive Summary

Background

Human papillomavirus (HPV) has been identified as a causative agent of cervical cancer. The virus also causes anogenital warts in both sexes and is associated with anal cancer and cancer of the vulva, vagina and penis. Two new vaccines against HPV are nearing the end of the clinical trials stage, and at least one is expected to be submitted for approval over the next year. There is an urgent need to plan now for the introduction of the vaccines in Canada, and this will necessitate collaboration among experts in vaccines, immunization programs, sexually transmitted infections and cancer, as well as decision-makers, public health, academia and industry. The Public Health Agency of Canada (PHAC) and the Canadian Association for Immunization Research and Evaluation (CAIRE), in partnership with the Canadian Institutes of Health Research (CIHR) Institute of Infection and Immunity and the Institute of Cancer Research, held an invitational HPV Vaccine Research Priorities Workshop on November 17-18, 2005, in Quebec City. It was attended by 53 Canadian and international HPV experts and researchers from the areas of vaccines, cancer, and sexually transmitted infections. The purpose of the meeting was to examine the current Canadian and international status of HPV vaccine research and develop national research priorities before the vaccines become approved for use in Canada.

Workshop Structure/Process

The Workshop consisted of a plenary session at which various speakers provided background information. This was important context for participants, who came from diverse disciplines, and served as a frame of reference for the brainstorming required in the break-out sessions held later that day. Participants heard about the two frameworks (one for decision-making in cancer control and one for evaluating immunization programs) that would guide the structure of the break-out sessions and their deliberations; the value of infectious disease modelling and economic studies in evaluating potential immunization programs; the burden of disease associated with HPV; rates of HPV infection and cervical cancer, as well as the benefits of screening; the characteristics of the HPV vaccine; and other considerations for vaccine program implementation and delivery. The plenary session ended with an account from experts from the

United States (US) and the United Kingdom (UK) on how those two countries are addressing decision-making on HPV vaccine use.

Participants were allocated to one of three break-out groups representing fundamental research (burden of disease), intervention research (vaccines), and program delivery research (immunization programs). Each of these sessions began with a presentation about current research activities and possible areas that would merit further investigation. A template had been created for each of the groups highlighting the areas of the evaluation framework specific to that group in order to facilitate discussion. Each group was asked to discuss the issues raised by particular criteria from the framework and to consider existing research gaps, as well as to identify pertinent infrastructure gaps. The research questions and infrastructure gaps identified during the break-out sessions were presented in plenary the following day, and participants were asked to vote on both the importance and feasibility of each of the research questions and infrastructure gaps according to a 5-point Likert scale. This allowed for some degree of ranking of the research areas.

Research Priorities

Fundamental research*:* Baseline data are needed on the transmission of HPV in specific groups, the distribution of HPV types, and the prevalence, duration, natural history and costs (in terms of screening, diagnosis and treatment) of HPV-associated disease. It would be useful to know the comparative costs of improving the effectiveness and coverage of cervical screening versus a combined immunization and screening approach to the disease. Associated with this is the impact of migration and ethnicity on the effectiveness of primary and secondary prevention programs, and the psychosocial burden on particular groups of identified precursors of disease and medical interventions.

Intervention research*:* The short- and long-term immunogenicity, efficacy, and effectiveness associated with a two-dose rather than three-dose schedule need to be examined. Research is required on whether the two new vaccines are interchangeable for protection against HPV types 16 and 18, on the consequences for safety and immunogenicity of co-administration with other vaccines, and on the safety and immunogenicity of the vaccine during pregnancy and among immunocompromised individuals, as well as in Aboriginal populations. The herd immunity according to level of coverage and the effect of natural infection on the antibody level in vaccinated individuals should be documented. Other areas of priority are the incidence of adverse events following immunization and the impact of HPV immunization programs on cervical screening, not only in terms of compliance and screening intervals but also with respect to the sensitivity, specificity and predictive value of the Papanicolaou test.

Program delivery research*:* In order to deliver an HPV immunization program efficiently there should be research into the optimal age cohort, schedule, and delivery setting for immunization, and the feasibility/cost-effectiveness of catch-up programs. The potential effect of an immunization program on sexual behaviour, cervical screening programs and health care services needs to be investigated. The costs and savings associated with this immunization program and the knowledge/attitudes/beliefs of providers and parents are other priorities for research.

Analysis/Findings

After the Workshop, the Planning Committee reviewed the voting results and determined the best method of further analyzing and presenting the results. For clarity, there were minor editorial adjustments made to the wording of some research questions. A complete summary of the voting results is provided in this report, and Appendix 4 includes additional analysis of the results. The tables presented in the text depict the 10 highest ranked research questions and infrastructure gaps, by importance and feasibility. Results are also given by research components (fundamental, intervention and program delivery research) and by participant subgroups. The total means of all research questions and infrastructure gaps are provided.

Next Steps

Participants felt that national goals for an HPV immunization program should be clearly articulated as the next step, as should the impact of a vaccine program on cervical screening programs. Many questions need to be answered before administration of the new vaccine can be justified, and some of this information may soon be available from the results of follow-up studies from vaccine clinical trials and other international research activities. The results of the voting showed that program delivery research issues were perceived as some of the most important. Possible sources of funds for such research might be CIHR, perhaps in collaboration with PHAC and the private sector. There was a strong feeling that PHAC should have a stronger role in research funding, but that provinces/territories could also lobby for additional funds for post-marketing research. Another alternative is to conduct pilot projects in one or more provinces/territories with collaboration between cancer and immunization experts for monitoring the interaction between immunization and screening services.

Introduction

As early as 1975, evidence suggested that human papillomavirus (HPV), a common sexually transmitted virus spread through direct contact, might be linked with cervical cancer. More recently, improvements in DNA amplification techniques, such as polymerase chain reaction, have allowed investigators to determine that HPV DNA is present in the majority of cervical cancers examined. Almost half a million women worldwide developed cervical cancer in 2002, and approximately 270,000 died; 83% of these cases occurred in developing countries. Estimates of the prevalence of HPV vary depending on the age of the cohort studied, the study population and the country, from 3% in Spain to 43% in Mozambique. In Canada, according to a limited number of studies, the prevalence of HPV is relatively high and varies dramatically with the type of cohort studied, from 13% to 33%; the latter included Aboriginal women (42% of the group). HPV is also associated with anogenital warts and anal cancer.

Large-scale clinical trials of two new HPV vaccines, manufactured by Merck Frosst and GlaxoSmithKline Inc., have been under way for a number of years, and the manufacturers are preparing for submission to the regulatory authorities within the next year. The vaccines have been developed with the use of DNA-free virus-like particles, synthesized from self-assembling protein subunits of the L1 capsid antigen. One of the vaccines is bivalent and protects against the HPV genotypes 16 and 18, which occur in more than 70% of cervical cancer cases. The other vaccine is quadrivalent and protects against these two genotypes and types 6 and 11, which cause genital warts in both sexes. The trials to date have found both vaccines to successfully prevent persistent infection with HPV (100%) and to provide protection (> 90%) against cervical intraepithelial neoplasia, cervical abnormalities that are predictive of cervical cancer.

A number of issues need to be addressed before the new vaccines become available for use in immunization programs. These include the epidemiology of HPV disease in the population and the dynamics of HPV infection in particular subgroups; the effect of population immunity to vaccine genotypes on other circulating HPV genotypes; the population groups that should be the target of an HPV immunization program; the need for booster doses of vaccine; the optimal dosage schedule; and the value of catch-up campaigns. As well, the new vaccine has unique

implications not applicable to previous vaccines, i.e. the effect on cancer prevention efforts in the form of cervical cancer screening with the Papanicolaou (Pap) test.

Planning for the introduction of the HPV vaccines in Canada requires both scientific information in order to answer the above-mentioned questions and collaboration among diverse groups, such as those who work in the fields of vaccines, sexually transmitted infections and cancer; between scientists and decision-makers; and among public health at the federal/provincial/territorial level, academia and industry. In the past, new immunization programs have been introduced differently by individual provinces and territories, leading to inequitable access. Part of the mandate of the National Immunization Strategy (NIS) is to encourage the adoption of necessary immunization programs across Canada and to develop, in collaboration with the provinces and territories, a consistent and logical means of evaluating what a necessary program might be. To this end, and to foster both the collaborative and the research planning components, the Public Health Agency of Canada (PHAC) and the Canadian Association for Immunization Research and Evaluation (CAIRE), in partnership with the Canadian Institutes of Health Research (CIHR), held an invitational HPV Research Priorities Workshop on November 17 and 18, 2005, in Quebec City. A multidisciplinary expert scientific committee was formed to establish the Workshop agenda and process, and to provide scientific/technical input (see Appendix 1: Participant List).

The goal of the Workshop was to develop research priorities for HPV vaccine use in Canada. Its objectives were as follows:

- to take stock of past and current research on HPV vaccine-related issues;
- to identify the key elements to support decision-making on the use of new HPV vaccines;
- to identify the implications to the cervical cancer screening programs in the era of HPV vaccines and to support evaluation activities;
- to identify the gaps remaining among those key elements and translate them into priorities for future research activities;
- to suggest organizational models of collaboration among Canadian researchers from industry, academia and public health to answer those priorities efficiently, despite the usual constraints of confidentiality, conflict of interest, competition, etc.;
- to foster an increased interpersonal knowledge and communication between the key decision-makers and scientists of the various fields and organizations;
- to identify research priorities and suggest mechanisms by which they could be achieved within Canadian funding structures; and
- to identify the next steps required in the short and long term to realize the above objectives.

Fifty-three participants from a variety of backgrounds attended the Workshop, and all participants signed a mandatory conflict of interest form prior to the event.

The Workshop began with a plenary session during the first morning, providing participants with a broad overview by speakers considered experts in their field of work. Presentations included information on the use of frameworks for evaluating potential immunization programs; a review of the available Canadian data about HPV-related disease; a review of epidemiologic modeling and economic analysis; a review of surveillance/monitoring of vaccines, screening and cancer; a review of decision-making for publicly funded immunization programs; and ways in which other countries are approaching the implementation of HPV vaccine programs.

During the afternoon of the first day, participants were split into three break-out groups representing fundamental research, intervention research, and program delivery. They were asked to develop research questions relevant to optimal decision-making both before and after introduction of the HPV vaccine, as well as to identify infrastructure gaps (i.e. capacity, funding, networks) for the research.

On the morning of the second day, participants assembled again in plenary to rank each of the research questions and infrastructure gaps identified during the break-out sessions according to its importance and feasibility. This was followed by general discussion of the next steps towards conducting the necessary research.

November 17: Plenary Presentations

Welcoming remarks from PHAC: Shelley Deeks

Dr. Deeks welcomed everyone to the Workshop, co-hosted by PHAC, CAIRE and CIHR, explaining that the goal was to develop research priorities for HPV vaccine use. The participants consist of a broad range of multidisciplinary experts, reflecting the collaboration that will be needed to plan for the new HPV vaccines. Consultation with experts before vaccine introduction will allow improved delivery and will enhance our knowledge about where best to focus our efforts. Acknowledgement was given to the Organizing Committee, the Scientific Committee and the Secretariat for their planning efforts and efficient work.

Welcoming remarks on behalf of Workshop Chairs: Simon Dobson

Dr. Dobson described the original approach to hepatitis B immunization programs as an example of how not to plan for a new vaccine. Several years were wasted while high-risk groups were targeted for immunization, when these were the individuals already at risk and probably infected. Only when the programs were applied more universally were the benefits seen. This Workshop will contribute towards one of the goals of the NIS, which is to ensure that there is equitable access to vaccines across the country and to have a consistent and logical process in place to evaluate new vaccines. Dr. Dobson also commented on the changing relation of governments with vaccine manufacturers, and the realization that viewing this as a two-way street will lead to gains for both parties. As a final note, he acknowledged that decisions at the provincial/territorial level are not always taken logically, and political expediency may play a role. This is why it is important to continue advocacy efforts for immunization programs that have been evaluated.

Frameworks used to structure the knowledge base

HPV vaccines: from development to implementation, from research to action

Bernard Duval

Although the new HPV vaccines look very promising there will be challenges to their use in Canada. The cost of the vaccine is likely to be high, and so a convincing case will have to be made to governments that an HPV immunization program is worthy of funding and implementation, particularly in light of the delayed benefits to health and the existence of cervical cancer screening programs.

Dr. Duval outlined the objectives of the Workshop: to decide what information is needed for decision-making, review the knowledge base on HPV vaccines and discuss how to fill the main gaps in that knowledge. With the many different areas of expertise represented at the meeting it is important that discussions use common language and concepts. For this reason it was decided to structure the break-out sessions according to two decision-making frameworks, one from the field of cancer control and one from the perspective of immunization programs. The framework from the National Cancer Institute of Canada (NCIC) demonstrates the interrelation between research, program delivery and surveillance/monitoring, all of which are sources of data that can be synthesized for decision-making purposes, with the overall goal of reducing the burden of cancer. The three break-out groups represent three research components from the NCIC framework: fundamental research (what we know about all aspects of the burden of the disease, including screening), intervention research (what we know about the vaccines) and program delivery (what decision-makers need to know about implementation). Cost-effectiveness and evaluation (surveillance/monitoring) are issues to be discussed by all groups.

The second framework, from Erickson, De Wals and Farand, aims to allow a systematic evaluation of all the factors that should be considered in decision-making regarding immunization programs. It consists of 13 categories: burden of disease, vaccine characteristics, immunization strategies, cost-effectiveness, feasibility, ability to evaluate, acceptability of the program, research questions, equity, ethical considerations, legal considerations, conformity of the program (with others) and political considerations. The relevant categories from this list have been allotted to the appropriate break-out groups.

Models of epidemics: epidemic of models

Babak Pourbohloul

Models of epidemics are created so that the effect of specific parameters on the characteristics of the overall epidemic can be tested. Models vary according to the scale of the investigation and the questions that need to be answered; they are useful only if used appropriately. In a Markov model, each individual is assumed to be in one of a finite number of states, and events are represented as transitions from one state to another. Unlike the toss of a coin, which will ultimately result in “heads” 50% of the time and “tails” 50% of the time, the events occurring in

an outbreak of communicable disease are not independent, since people interact with each other. Models of epidemics must incorporate this interaction.

Two models of epidemics are discussed, the network model and the S-I-R or susceptible-infected-recovered model (a compartmental model). The network model incorporates the interactions between individuals, depicted by nodes (the individuals) and their connections with each other. In a sexual network, some individuals will be more active than others, and some, though not necessarily highly active, will serve as a bridge between clusters of activity. This type of model has proved useful for analyzing small, closed populations and suggesting control strategies at the beginning of an outbreak. The model has to become more complex to take account of interactions with the rest of the population, and a theoretical framework for this has been developed in the last 2 years. The S-I-R model involves a less fine analysis, in that it divides the population into groups, rather than individuals, on the basis of their immunologic status. Its assumption of uniform mixing means that epidemics depend only on the total number of susceptible (never infected), infected (able to transmit to others) and recovered (and immune) individuals. This type of model is most useful for assessing the long-term impact of control strategies, but is difficult to manipulate for complex situations (e.g. involving co-infection).

Compartmental models combining both epidemiologic and demographic categories have been used in British Columbia to understand the rebound effects that have resulted from mass treatment of syphilis and chlamydia. The conclusion is that if there is no change in behaviour and no variation in contact rates, then a rebound effect in the rates of transmission are inevitable. Studies in mice suggest that early treatment may block immunologic memory in the case of chlamydia. On the assumption that the same might be true for humans, the model has been modified accordingly, and it has been found that vaccination against disease is likely to produce more complete and permanent reductions in transmission than early treatment. Such models will help to determine optimum vaccination strategies.

Role of economic studies in decision-making for publicly funded immunization programs

Philippe De Wals

The cost of vaccines has increased enormously since the 1990s, when a measles-mumps-rubella vaccine dose cost $8 in Quebec. Currently, the most expensive vaccine in Quebec is the pneumococcal conjugate vaccine, at $70 per dose. It is estimated that the cost of the new HPV vaccine may be as high as $120 per dose, amounting to an annual amount, if vaccinating females only, of $13 million in Quebec and five times that amount for Canada in its entirety. It is therefore essential to conduct economic analyses that will compare the costs and benefits of implementing an immunization program with the costs and benefits of not doing so or of proceeding with an alternative intervention. Economic studies may be classified as cost-effectiveness studies, which assess the health benefits (number of cases or deaths averted, life-years gained) of the intervention in terms of dollars; cost-utility studies, in which years of life gained are adjusted for years of quality of life (QALY); and cost-benefit studies, which include all the costs and benefits that might be associated with the intervention. Nearly all are based on

models of natural epidemiology; they attempt to quantify how the intervention will modify the epidemic and at what cost. They may be used before the introduction of a program to make funding decisions, during the program to determine whether it could be more efficient, and afterwards to ascertain whether the initial cost-effectiveness analysis was accurate. In Quebec in 1994, the hepatitis B immunization program was the first vaccine program in which an economic evaluation was conducted before implementation, and since this time evaluations have been carried out before any vaccine has been introduced, with the exception of influenza.

Quebec has learned a number of lessons from conducting economic evaluations of potential immunization programs. The first is that the decision to implement a publicly funded program is a political one. For instance, the public concern about outbreaks of meningococcal meningitis fuelled the introduction of the meningococcal conjugate vaccine. Nevertheless, economic analysis should be performed for each program and performed in a timely manner, so that when a decision is made there is information in place (e.g. on immunization strategy and schedule) to guide implementation. Economic analyses should be conducted at arms' length from the vaccine manufacturers and from health ministries or the results will be perceived as biased.

Several US studies (all based on a compartmental model) have evaluated HPV vaccines and provide a range from $15,000 to $45,000 per QALY gained. Including males in the immunization program does not substantially alter the reduction in cervical cancer but does dramatically increase the cost per QALY. Because of differences in disease epidemiology, in vaccine costs and health service costs it is difficult to extrapolate the results of US economic studies to Canada. However, it is relatively easy to extrapolate from studies in other provinces/territories within the country. Since expertise and resources are scarce in Canada there is a pressing need for collaboration in order to avoid duplication of effort.

Knowledge synthesis: available Canadian evidence for decision-making on the use of vaccine

Burden of HPV-related disease

Patricia Goggin

There is a universal risk of acquiring HPV among sexually active males and females, although some variation exists in rates and distribution of HPV types among countries. For women, the lifetime incidence is up to 70%, and the peak prevalence occurs among women in their early 20s; in the 3 to 4 years after sexual initiation the prevalence can be up to 40%. Incidence and prevalence rates among men are not as well known.

Cervical cancer is not the only cancer associated with HPV: recent studies have shown that HPV DNA was present in about 85% of anal cancer specimens. The incidence of anal cancer in the general population is rare, at < 1 per 100,000, although men who have sex with men have a higher incidence (up to 35 cases per 100,000). In addition, about 50% of cancers of the vulva, vagina and penis might be associated with HPV. External genital warts, which have a 90%

association with HPV 6 or 11, are considered benign but nevertheless carry important social consequences. In a US study, the estimated prevalence of genital warts in the general population was 1 to 2 cases per 1,000; men aged 25 to 29 and women aged 20 to 24 had the highest prevalence, at an estimated 5 and 6 per 1,000 person-years respectively. Recurrent respiratory papillomatosis is another complication of HPV, affecting mainly children aged < 15 years (HPV 6 and 11) and with an estimated incidence in the US of 4 cases per 100,000 children, increasing to 6 to 7 per 1,000 children born to women with external genital warts.

In Canada, the incidence of cervical cancer is estimated to be 8 cases per 100,000, with a mortality of 2 per 100,000. In 2005, 1,350 cases, 400 deaths and 10,000 potential years of life lost are predicted. Most jurisdictions have organized cervical cancer screening programs, although the policies and practices vary, and recruitment is generally opportunistic. Since screening became established, the incidence and mortality rates of cervical cancer in Canada have roughly halved between the years 1976 and 2005. However, there is a psychosocial impact of screening and associated diagnostic services in terms of the inconvenience and discomfort to affected individuals, the anxiety and psychological distress that they experience, and the potentially altered relationships with sexual partners, families and caregivers. The economic impact of HPV-associated disease can be broken down into the direct costs of hospital care, drugs, physician services, expenditure in other institutions, and administration, as well as the indirect costs, including those associated with years of life lost, and short-term and long-term disability. Any estimate of the cost of HPV-associated diseases must take into account the cost of screening, which according to US estimates may be the most expensive component.

Do the characteristics of the HPV vaccine permit implementation of an effective and safe immunization program?

Marc Dionne

The characteristics of the HPV vaccine can be considered according to the criteria suggested by the Erickson, De Wals and Farand framework with a view to answering the questions that a public health authority might raise when considering establishment of an HPV immunization program.

The HPV vaccine is composed of DNA-free (i.e. no live virus) virus-like particles synthesized by self-assembly of fusion proteins of the antigen L1. The bivalent HPV 16 and 18 vaccine uses AS04 as an adjuvant, and the quadrivalent vaccine (types 6, 11, 16 and 18) uses aluminum. Animal studies have shown that L1 virus-like particles induce neutralizing antibody, providing protection against a large amount of virus. In humans the neutralizing antibodies appear to be type specific and are expected to prevent 65% to 72% of cervical cancer cases. The titres produced are 50 to 145 times greater than titres resulting from natural infection; it is not known whether such high levels are necessary for protection. Although the vaccine appears to be safe and no significant short- or long-term complications have been reported, the same was true after the introduction of rotavirus vaccine, which later had to be recalled. The follow-up duration of clinical trials of the HPV vaccine has been 2 to 5 years, and during that time the efficacy in preventing transient infection has been 90%, persistent infection 100%, any cytological abnormalities > 90% and pre-invasive lesions 97% to 100%. Since reductions in cervical cancer

can only be assessed with long-term studies, pre-invasive lesions are used as surrogate indicators. It is not known whether the protection provided by the vaccine will be lifelong or whether booster doses will be required. It is also unclear whether the immunogenicity found among the subjects aged 10 to 26 years in clinical trials will be replicated in the general population. In addition, few trials have included men in their cohorts.

With respect to the administration and dosage schedule, 9 to 100 µg doses of HPV vaccine given in three 0.5 mL intramuscular injections over 4 to 6 months were highly immunogenic. The schedules most frequently applied have been 0, 2 and 6 months or 0, 1 and 6 months. More information is needed on the effects of administering this vaccine at the same time as others in the immunization schedule and on whether three doses are necessary. Furthermore, it is not known whether the two vaccines being tested are interchangeable for types 16 and 18. HPV vaccine appears to be effective in reducing not only cervical infection but also infections at other sampling sites. There are not enough data about its effect on other types of HPV or whether serotype replacement will occur.

Other issues of interest to public health authorities will be the potential impact of HPV immunization on cervical cancer screening, follow-up and treatment of HPV-related abnormalities. It is hoped that a reduction in infection would have a beneficial impact. Decision-makers also need to know whether there will be enough vaccine available for a universal program, and whether purchasing vaccine from both manufacturers will increase security of supply.

HPV vaccine – considerations for program implementation and delivery

Greg Hammond

In a publicly funded immunization program, decision-making occurs at several points: from the overall legal authority of the provincial/territorial government, the delegated health authority (usually regional), the health care professionals, and finally the consumer, who is the target of the program and who must consent to participate. It is important to determine how decisions are made and how decision-making at all these points can be influenced by research. The way in which governments make decisions may not be open to investigation for a number of reasons, including confidentiality issues, and observation or past experience may be the best guide. One of the most effective ways of influencing government-level decision-making is through funding. New funds available from the federal government, through the NIS, for the provinces and territories to implement publicly funded immunization programs against meningococcal and pneumococcal disease, varicella and pertussis resulted in swift uptake of these programs by jurisdictions. Experience has shown that implementation and delivery of programs are facilitated if the purpose and benefits of the vaccine and the program are clear; the process for review and decision-making has been rational and inclusive; the resources for delivery in the field are adequate; there are enough supporters at all levels and few detractors; and there are few surprises. Public perception or fear of the disease, if strong, may be the overriding factor.

With regard to the benefits of HPV vaccine, the public may not be aware of the virus or its consequences, in which case expectations about the vaccine may be uninformed. Guidance on how to best frame the issue of vaccination against HPV – as a strategy of cancer control, as a personal choice, as another part of sexual health education – would be valuable. The process of decision-making needs to be clear and there should be champions inside the decision-making process, as well as support and advocacy by external partners. Decision-making will be influenced by perceived feasibility, impact and benefits. Factors that need to be taken into consideration in the delivery of programs are the adequacy of vaccine supplies, storage, inventory management, distribution, tracking/monitoring, cold chain management and record-keeping. Unanticipated factors that may work against successful program implementation and delivery are apathy, controversy, fear of the vaccine, fear of perceived program consequences (e.g. promiscuity) and religious or political beliefs.

HPV/cervical cancer surveillance and monitoring in Canada

Tom Wong

Infection with HPV is not reportable in any province or territory of Canada, and so it is difficult to know the prevalence or incidence of such a common virus. A number of Canadian studies have reported on the cumulative proportion of the population testing positive for HPV on the cervix and/or vulva, which at 36 months' follow-up is estimated to be between 60% and 70%. Sellors et al. visited 30 sites in Ontario and found that the point prevalence of HPV was an average of 20% among women aged < 25 years, declining thereafter to 15% at age 25 to 34 and < 10% among women aged 35 to 44 years. A Newfoundland study showed a similar pattern with increasing age but lower rates overall. Canadian data are limited because there is no sentinel surveillance, no information on risk factors, ethnicity or the distribution of HPV types (for instance, there is some evidence that type 31 is predominant in Nunavut), and sampling is generally from the cervix, whereas anal sampling among men who have sex with men would likely provide differing and valuable data. Moreover, HPV can be a transitory infection, making testing at one point in time misleading.

The introduction of an HPV vaccine will likely have an impact on cervical cancer screening, and so it is important to know baseline rates of screening before implementation. Most cervical cancer screening programs in Canada target their efforts to women aged ≥ 18; some do not target women > 69 years of age. Usually, the frequency of screening after three normal Pap smear results is every 2 years. In 2003, about 26% of women aged 18 to 29 years had never had a Pap test and 28% of women in this age group had not had the test in the previous 3 years. In the age range 30 to 69 years, the proportion had dropped to 8% never having had a Pap test and 18% who had not had the test in the previous 3 years. Of those in the 70+ age range, 60% had not had a Pap test in the previous 3 years.

How other countries are addressing decision-making on HPV vaccine use

Development of HPV vaccine recommendations in the US

Lauri Markowitz

The Advisory Committee on Immunization Practices (ACIP), coordinated by the Centers for Disease Control and Prevention (CDC), is the US committee that provides guidance to the Secretary of the Department of Health and Human Services and the Director of the CDC. It comprises 15 voting members, a voting consumer representative and nonvoting members from government agencies and professional associations. It meets 3 times a year. The two functions of ACIP are to develop recommendations for publication in the Morbidity and Mortality Weekly Report to coincide with vaccine licensure, and to recommend childhood vaccines provided free of charge to eligible children through the Vaccines for Children program.

ACIP forms working groups as necessary, one of which is the HPV Working Group, established 18 months ago. The working group prepares background material on the vaccine, clinical trials, the disease and its epidemiology, related sexual behaviour, acceptability, program issues, impact and cost efficacy. It then drafts recommendations to be taken back to ACIP for approval. The HPV Working Group is proceeding under the assumption that the quadrivalent vaccine will be licensed for use in females aged 9 to 26 in mid 2006; a vaccine for men may be available at a later date. The bivalent vaccine will be licensed later.

There is sensitivity in the US about giving a vaccine to children that protects against a sexually transmitted virus, although education about HPV may increase acceptability. A survey of sentinel pediatricians showed that only 45% were likely to recommend the vaccine for children aged 9 to 12, whereas 89% would recommend it for adolescents 16 to 18 years of age. Another issue to be considered is how well the introduction of HPV vaccine will fit with current immunization schedules. There is concern about the feasibility of delivering three doses of a vaccine in adolescence. A conference was held in June to address this issue, the conclusions of which are being finalized. Several cost-effectiveness studies have been carried out, but the majority are industry sponsored. The CDC plans to review dynamic models and to work with modelers to explore further cost-effectiveness analyses. Although the cost of the vaccine is unknown, it may be approximately $300 for three doses. Potential recommendations will be discussed at the ACIP meeting in February, and final recommendations may be available in June. Recommendations about screening are not part of ACIP's mandate, but the American Cancer Society is already considering the likely impact of the new vaccine.

HPV vaccine – the UK perspective

David Salisbury

Immunization of adolescents in the UK has been carried out through the school nursing service and has included rubella (for girls 11 to 12 years of age), BCG (at 13 to 14 years) and recently, on a trial basis, hepatitis B. The UK cervical cancer screening program has become more tightly audited and managed because of a few highly publicized screening failures. An HPV group has been meeting for 18 months and consists of representatives from immunization monitoring/ surveillance (Department of Health), cervical screening (Department of Health), the National Institute for Biological Standards and Control (vaccine quality and safety), the Immunisation Division of the Health Protection Agency, economic modelling, STD surveillance and academia.

The Department of Health has used its systems of qualitative and quantitative research on immunization attitudes, knowledge and practices among parents to explore HPV vaccine acceptability. This topic has been investigated through the use of small group discussions with parents of girls aged 8 to 10 years. A low level of awareness of HPV has been found, and although parents knew about genital warts and about cervical cancer as a risk for women, they did not associate either condition with the virus. There was awareness among women of the prevalence and implications of cervical cancer and screening for it; this was less evident among men. Parents were shocked and concerned to learn about the HPV link with cancer, and they welcomed a vaccine to prevent cervical cancer. However, there was also the element of fear associated with any new vaccine and a defensive attitude towards vaccinating a child against a sexually transmitted virus with the perceived implication of permissiveness towards sex. Parents could be classified as trusting, i.e. those who needed little reassurance and were happy to have the vaccine provided in the school; compliant, with some areas of concern but able to be reassured; and resistant, who may be few in number but tend to be vocal. The facts around HPV risk need to be presented clearly in any campaign, since they are not straightforward.

Critical issues that still need to be resolved are the need for catch-up programs in older adolescents or women, ways of justifying the cost of immunization against HPV, effective implementation of a three-dose schedule in schools, the impact of the vaccine on cervical cancer screening, and whether immunization can be seen as cost-effective if there is no reduction in the amount of screening carried out. Decisions about cervical cancer screening will require collaboration between cancer and immunization groups.

November 17: Break-out Sessions

Participants were allocated to one of three break-out groups to ensure that an interdisciplinary mix of content experts and researchers was represented in each group. The research areas assigned to the break-out groups were (A) Fundamental Research, (B) Intervention Research and (C) Program Delivery Research. Each group was asked to discuss the issues raised by particular criteria from the framework of Erickson, De Wals and Farand (see Appendix 2: Break-Out Group Agendas). Each group was led by a moderator, and a rapporteur summarized the discussions.

The session began with a presentation about current research activities in progress and possible areas in which it would be useful to focus future research, according to the question "What are the important unanswered questions that Canadian research should address?" For each of the criteria specified in the framework, the groups were asked to brainstorm research gaps and decide which gaps should be formulated into research questions for inclusion in the final list of priorities. The final wording of the research questions was decided and a brief supporting statement added, where appropriate. It was suggested that the questions should be neither too specific nor too broad, i.e. on the scale of a typical CIHR project. A final task was to consider what infrastructure, such as funding or expertise, would be needed to conduct the research. All research questions and infrastructure gaps agreed upon by the break-out group participants were included in the final list for voting by the whole group. At the end of the sessions, the moderator and rapporteur from each group and the Workshop Co-chairs met to collate all the research questions and to amalgamate duplicate questions/gaps.

Break-out session A: Fundamental research

Moderator: Philippe De Wals
Rapporteur: Jennifer Beaulac

Speakers: François Coutlee, Marc Brisson, Hughes Bogaerts

This group was asked to consider the criteria of burden of disease (Does the burden of disease justify a control program?), cost-effectiveness (costs of screening and treatment) and ability to evaluate treatment and screening programs. The session began with presentations from the manufacturers of the two new HPV vaccines and from Dr. François Coutlee. The representative from GlaxoSmithKline, Hughes Bogaerts, and Dr. François Coutlee of McGill University, Montreal, described the many research studies that have been carried out at McGill on cervical cancer, HPV transmission, screening, HPV vaccination and psychosocial issues. The representative from Merck Frosst, Marc Brisson, discussed the main goal of research, scientists' contribution to the different phases of research, and the research studies for HPV vaccine.

Break-out session B: Intervention research

Moderator: Scott Halperin
Rapporteur: Robert Lerch

Speakers: David Scheifele, Donald Elrick, James Mansi

The criteria assigned to this group for discussion were vaccine characteristics, cost-effectiveness (with respect to vaccine-related costs) and ability to evaluate vaccines (e.g. coverage, adverse events, linkage with health outcomes). Dr. David Scheifele began the discussion with a consideration of Canada's capacity to conduct post-licensure evaluation of vaccines. There is no organized, funded network of vaccine centres; rather, there are a number of academic and public health-based units, contract research units and special interest teams. CAIRE promotes networking and cooperation among research centres, and lobbies for increased central organization and support of research. Dr. Scheifele's introduction was followed by a presentation from each of the manufacturers summarizing the clinical research that each has conducted internationally and in Canada. Specific details of the trials were not presented. The characteristics of the quadrivalent vaccine, the core objectives in developing the vaccine and the efficacy trials that have been carried out were the topics covered by the Merck Frosst representative. The representative from GlaxoSmithKline discussed the phase III trials that have been conducted or are planned for evaluation of the efficacy, safety and immunogenicity of the bivalent vaccine in women or adolescent girls.

Break-out session C: Program delivery research

Moderator: David Patrick
Rapporteur: Lisa Paddle
Speaker: Ian Gemmill

The criteria assigned to this group included immunization strategy and program (e.g. program objectives, operational objectives, program delivery strategies); cost-effectiveness of the immunization program; acceptability, feasibility and equity of the program; ethical considerations (informed consent, confidentiality); political and legal considerations; and the ability to evaluate the program.

Dr. Ian Gemmill described the program delivery research that has been carried out in other immunization areas. Quebec has done a lot of work in evaluating immunization programs, and there has also been research conducted in British Columbia, Nova Scotia and Ontario. The issues that must be considered in program delivery research for HPV are the methods (e.g. economic analyses, mathematical modelling, opinion surveys, coverage surveys, descriptive studies), aspects of program delivery (e.g. surveillance, evaluation, testing for infection, target groups, acceptance, delivery methods), and the impact on other programs.

November 18: Plenary Presentations of Research Questions

In plenary the moderators from each of the break-out groups presented the research questions, their rationale and any infrastructure gaps that had been identified by group members. No new research questions or changes to the existing wording were introduced at this point. All eligible participants, and these excluded international and industry representatives, were asked to vote on each research question according to two criteria, importance and feasibility.

Voting was conducted through the use of an electronic keypad. First, participants used the keypad to enter their baseline data, as follows:

Primary field of work:

- Vaccinology
- Cancer
- STI

Primary role:

- Decision-maker (is involved in decisions in which funds are allocated to a program in some way; uses the research/knowledge to influence policy)
- Researcher (does research either as a principal investigator [PI] or a co-PI
- Expert (follows research results and translates them into action or into recommendations for decision-maker)

Primary affiliation:

- University
- Government organization (i.e. public health)
- Other

Primary specialization:

- Clinician
- Epidemiologist
- Other

Participants then used the keypad to vote on each research question and infrastructure gap. For each question, participants voted on importance and feasibility using a 5-point Likert scale. For importance, the question they had to bear in mind was "Is this research question important for decision-making on the use of HPV vaccine in Canada?" and for feasibility it was "Is it feasible (e.g. infrastructure and technology exist, costs are relatively low) to design a study in Canada to answer this research question?"

The scale covered 1 = not important/feasible, 2 = low importance/feasibility, 3 = somewhat important/feasible, 4 = high importance/feasibility and 5 = very high importance/feasibility.

After the voting on each research question and infrastructure gap, the aggregate scores for importance and feasibility were displayed on a large screen together with a graphical representation of the scores.

Recommendations for research questions and infrastructure needs

Break-out Session A: Fundamental Research

Note for participants: The following changes were made to the list of questions distributed on site – Question C24 was moved to research question A13.

Fundamental research questions

A1. What is the transmission/acquisition of HPV in Canada with regard to the following:

- type-specific transmission
- population-specific
- sex-specific – prevalence among men
- other modes besides sexual transmission
- networks of transmission (microstudies)
- genetically susceptible populations (ethnicity: First Nations and Inuit)
- cross-protection

A2. What is the prevalence and duration of infection and disease (pre-cancers) in Canada with regard to the following:

- unscreened/underscreened women
- genotype
- management of abnormalities
- secular trends

A3. What is the incidence of co-infection and the magnitude of cross-protection within HPV and other STIs?

A4. What drives the relative distribution of HPV in the population with regard to molecular pathogenesis?

A5 What is the natural history/clinical course of progression of the following conditions:

- anal disease (risk of progression, men and women, at-risk populations)
- VIN (vulvar intraepithelial neoplasia) disease
- cervical cancer (type-specific HPV)

A6. What is the population-based epidemiology of warts in Canada (prevalence, incidence, duration, recurrence)?

A7. What is the relative cost of improving screening versus primary prevention using vaccines together with screening, with regard to the following:

- effectiveness
- efficiency
- coverage

A8. What is the psychosocial burden to specific regions/groups of precursors of disease and medical interventions?

A9. What is the impact of migration and ethnicity on the effectiveness of primary and secondary prevention programs?

A10. What is the feasibility and cost of identifying vaccinated and non-vaccinated individuals in a screening program (immunization registry linked to provincial screening program)?

A11. What is the estimate of the current and anticipated economic burden of HPV-related disease and conditions (screening, diagnosis, follow-up, treatment)?

A12. What would be the cost and value of national/provincial databases and record linkages?

A13. What is the distribution of HPV types in Aboriginal populations?

Infrastructure gaps

A14. Accessibility of provincial/territorial databases for research and modelling

A15. Develop capacity for epidemiologic and economic modelling

A16. Define acceptable levels of conflict of interest

A17. Create formal structure (network) to pool information from different disciplines

A18. Network of sentinel units for fine molecular viral surveillance

A19. NACI equivalent in cancer screening/screening action group (National Strategy on Cancer Control)

A20. Canadian Task Force on Preventive Health Care

A21. Facilitating legislation to implement and monitor progress/challenges

A22. Peer review or review process at national level in order to evaluate the quality and validity of models and to suggest guidelines for analyses, as done in the US

Break-out Session B: Intervention Research

Note for participants: The following changes were made to the list of questions distributed on site – Question C23 was moved to research question B22.

Intervention research questions

B1. What is the efficacy or effectiveness of a two-dose schedule? (A two-dose schedule has not been evaluated in clinical trials to date.)

B2. What is the short-term and long-term immunogenicity of a two-dose schedule in comparison to a three-dose schedule?

B3. What are the correlates of protection? (Identification would help us to answer the question of alternative schedules without repeating efficacy studies and assist in assessing whether there is vaccine interchangeability.)

B4. Are the vaccines interchangeable for serotypes 16 and 18?

B5. Is there an advantage to using both current vaccines in a sequential schedule?

B6. Is the intradermal or transcutaneous route of administration as immunogenic?

B7. What is the effect on safety and immunogenicity of co-administration with other vaccines for adolescents and adults?

B8. What is the safety and immunogenicity of the vaccine in pregnancy? (There has been a lack of pregnant women included in current clinical trials.)

B9. What is the immunogenicity and safety of the vaccine in an immunocompromised population?

B10. What is the response to vaccination in women persistently infected with HPV 16 and 18? (Clinical trials will provide data on previously exposed women but not on persistently infected women. Unique feature of persistent infection.)

B11. What is the immunogenicity of vaccination in Canadian Aboriginal women?

B12. Do variations in estrogen levels have a significant impact on the immune response to the vaccine?

B13. What is the herd immunity according to the level of coverage?

B14. What is the effect of a natural infection on antibody level of a vaccinated individual? Does it negate the need for a booster?

B15. What is the impact of vaccination on circulating genotypes? (Assumes the knowledge of baseline distribution in the general population and various stages of pre-cancer and carcinoma.)

B16. Is there a change in the risk of disease associated with types other than 16 and 18? (The change in circulating types may or may not have an effect on cervical disease.)

B17. For the target population, what is the background incidence and prevalence of clinically significant events that may be age related in onset and thus likely to be temporally associated with vaccine administration? (Need to anticipate what events may occur at the same time.)

B18. What is the long-term safety of the novel adjuvant and expression systems used in the HPV vaccine?

B19. What is the impact of vaccination programs on cervical screening programs (type of test, screening intervals, sensitivity and specificity and predictive value of Pap test and colposcopy, compliance with screening programs)?

B20. What is the impact of immunization on the current practices in treatment and follow-up of CIN1 lesions?

B21. What is the impact of vaccination on non-cervical cancers?

B22. What is the incidence of adverse events following vaccination (passive and active surveillance)?

Infrastructure gaps

B23. Registries of all HPV-related disease

B24. Improvement and linkage across the country of registries

B25. CIHR requests for proposals that focus on multidisciplinary projects

B26. Vaccine registry and link with cancer registries and Pap smear registries

Break-out Session C: Program Delivery Research

Note for participants: The following changes were made to the list of questions distributed on site: integrated questions C1& C2 (now C1) since they were combined during the vote; deleted questions C20, C21 and C22 since they were discarded during the vote.

Program delivery research questions

C1. What is the most efficient way to deliver an HPV vaccine program (best coverage for the least cost)?

- Are catch-up programs worthwhile?
- Universal versus targeted programs
- Optimal age cohort

C2. How can we achieve the greatest coverage with this vaccine in a variety of settings (school versus physician settings)?

C3. As immunization programs progress, what will be observed with cervical screening programs?

- Will the immunization program modify the uptake of cervical screening in the future?
- Will there be a change of predictive value of a given cytological observation?
- Is the age of onset of Pap screening changing?
- Can we reduce the frequency of cervical screening in the immunized population?

C4. Will other behaviours change in the wake of HPV immunization (health-seeking behaviours, sexual behaviours), resulting in missed detection of STDs?

C5. Will universal female vaccination affect the population who develop cervical cancer, i.e. those at high risk?

C6. What are the costs of delivering this type of program, and how do these balance against anticipated savings related to changes in existing programs?

- What would the current incremental cost of an immunization registry be?
- What would the cost of a cervical screening registry be?
- What is the cost of the recommended program?
- What is the impact of the immunization program on cervical cancer screening programs and on external genital warts treatment/programs (follow-up, treatment, opportunity costs, care) in the long term?

C7. Is a catch-up program cost-effective and feasible?

C8. What are the knowledge/attitudes/beliefs (KAB) and acceptability of programs in recipients, providers, and parents? What research has been done by industry on the Canadian population, and does it need to be supplemented by additional parental surveys

(broad assessment of KAB on HPV programs targeting different groups – parents, providers, recipients, funders, politicians)?

C9. What is the most acceptable and effective way of promoting the vaccine program in Canada (as an STD vaccine, a cancer vaccine or both) (potentially affects the acceptability of vaccine), and how will attitudes change over time?

C10. What is the optimal schedule for HPV vaccination (cost-effectiveness, feasibility)?

C11. What is the most efficient way to transport/store vaccines to preserve the cold chain? Do we need tighter controls with respect to supply, delivery, storage?

C12 Would there be health gains for groups that may not be included in an initial program (e.g. MSM – men who have sex with men)?

C13. What are the ethical/legal issues associated with linking immunization and cancer screening databases?

C14. How do you measure the benefits/downsides to linking sexual health programs/education to a vaccine program (program pilot test?)?

Infrastructure gaps

C15. There needs to be articulation of the actual ***goal of the program*** (control versus elimination versus eradication). CIN 2, 3 reduction might be the proximal goal.

C16. Encourage collaborative work in cancer fields/NACI with goal-setting and setting national guidelines.

C17. HPV testing associated with all or a subset of screening programs

C18. Would emancipated minors trump a lack of parental consent when administering the vaccine?

C19. Environmental scan on US and other literature related to acceptability studies

C20. Research funding/support (social science)

C21. Environmental scan regarding sexual debut and school leaving

C22. Interdisciplinary group on Canadian Immunization Committee working specifically on HPV (follow-up)

November 18: Wrap-up

Next Steps

The full group discussed ways in which the identified research priorities might be moved forward. It was suggested that there first needs to be clear articulation of a national goal for an HPV immunization program and that PHAC would be the group to coordinate that. As well, participants emphasized the need to have answers about duration of protection, safety, minimum number of doses, and impact on existing immunization strategies, among other aspects, before administration of the vaccine to children can be justified. One participant responded that in break-out group A there had been input from the manufacturers indicating that there will be a substantial amount of information to draw on from the large follow-up studies being carried out in many countries where clinical trials have taken place. With respect to the group most at risk of cervical cancer, it was pointed out that women or girls who do not participate in cervical screening (and who may be difficult to track) are likely to be the ones not taking full advantage of the immunizations offered, including potential immunization against HPV.

According to the voting results, the research questions associated with programmatic research were the ones ranked highest. This is an area of research not likely to be funded by industry or through the CIHR. One suggestion was that any funds provided to provinces/territories through the NIS should include an amount that is stipulated for program evaluation. However, the NIS is a federal/provincial/territorial initiative, and so it is partly up to the jurisdictions themselves to ensure that evaluation is a component of a new immunization program.

There may be opportunities for funding from CIHR. Six of the Institutes would possibly be interested in this type of research, and although it would not be a high priority for any of them and their budgets are not large, together they might be able to fund a research project, perhaps in partnership with industry or with PHAC. Dr. Gully responded that there have been precedents in terms of funds being made available to PHAC for a specific research area, and the mechanism is for the Agency to work with CIHR to fund it. However, to establish the research area as a priority is a challenge. Partnerships between PHAC and industry are a possibility, but there must be legal consideration given to perceived or actual conflicts of interest. Furthermore, a pilot project

cannot be carried out in isolation, since there has to be an assessment of its impact on other activities (e.g. cancer control). An alternative is for one or more provinces or territories to conduct pilot projects in order to answer some of the research questions raised, but also involving collaboration between cancer and immunization experts for monitoring the interaction between immunization and cervical screening services.

When new programs are being contemplated by the provinces and territories, there is often some hesitation to be the first to launch a program, and the smaller jurisdictions often cannot afford to conduct their own evaluation. Quebec has set the standard with its program evaluation activities. It was felt that there needs to be some mechanism in place for PHAC to have a research funding role. It might also play a part in coordinating any pilot projects that do take place in order to avoid duplication. Dr. Tam stated that this Workshop has been one of the first steps in facilitating collaborative immunization program planning under the NIS, and there is a desire to strengthen the research focus and capacity in the Immunization and Respiratory Infections Division under the Strategy. Funding mechanisms inside and outside the NIS will be examined.

Concluding Remarks: Dr. Paul Gully

Dr. Gully thanked the Organizing Committee, the Scientific Committee, the Secretariat, international contributors and moderators/rapporteurs on behalf of PHAC, CIHR and CAIRE. He stressed the importance, when planning for the new HPV vaccine, of collaboration between those working in cancer control and those in communicable disease control and immunization. The concern is that there will be variation in provincial/territorial policies when the vaccine becomes available, which may result in inequity; this is why the research needs should be formulated now. Furthermore, introduction of the HPV vaccine must not come at the expense of cervical screening and other preventive programs; there is still a need to improve existing cervical cancer screening programs in some areas, such as for First Nations and Inuit. Dr. Gully pointed out that PHAC works collaboratively with CIHR on research priorities. Another possible avenue for the promotion of research and a consistent evaluation of the vaccine is through working with cancer stakeholders and cancer lobby groups.

Workshop Evaluation

At the conclusion of the Workshop, participants were asked to complete a two-page evaluation form to provide feedback and to rate various aspects of the Workshop, including pre-Workshop materials, plenary presentations, break-out sessions, overall process and objectives, and logistical arrangements. Participants were also asked to comment on gaps in the Workshop and suggest improvements for future research priorities workshops.

A total of 29 of a possible 53 evaluations were completed at the meeting, which represents a 55% response rate. There was a section at the end of the evaluation designated for moderators and rapporteurs to give their perspective on the pre-Workshop preparations and the tools used during the break-out session. This section was completed by six respondents (see Appendix 3: Workshop Evaluation Summary).

Voting Results

The voting procedure allowed participants to consider all proposed research questions and infrastructure gaps on the basis of importance and feasibility. Participant demographic information was collected in addition to the participant voting results, making the analysis of the results fairly complex. Ranking of the research questions and infrastructure gaps (always presented separately) was done on the combined total of both importance and feasibility but is also presented for importance and feasibility alone. Appendix 4 includes 28 tables of voting results. In the tables, the wording of the research questions and infrastructure gaps was paraphrased, but the reference numbers in the table are identical to those listed earlier (Recommendations for Research Questions and Infrastructure Needs) in this report.

The tables included in Appendix 4 are organized into four groups:

- General Combined Results (10 highest ranked research questions and highest ranked infrastructure gaps for importance and feasibility – all research components from break-out sessions A, B, and C are combined)
- Results by Research Component (10 highest ranked research questions and highest ranked infrastructure gaps for importance and feasibility, broken down by research component)
- Results by Participant Demographics (research questions and infrastructure gaps ranked by self-identified demographics of all participants)
- Ranking of all identified research questions and infrastructure gaps.

Only a few key observations are presented here. Readers are encouraged to look at the numerous tables in the appendix for deeper insight into the opinions of the experts attending the Workshop.

In general, importance was rated higher than feasibility, and research questions were rated higher than infrastructure gaps. When the highest ranked research questions (Table 1) are reviewed, it is striking to note that the top 3 highest priority items and 5 of the top 10 items are related to program delivery research. The fourth highest priority is determining the immunogenicity of a 2-dose schedule; the effectiveness of a 2-dose schedule ranked ninth overall. The economic burden of the disease is the only research question from the fundamental research group that ranked among the 10 overall top research priorities.

Despite minor variations, the highest priorities among the research questions were generally consensual, as shown in Table 13. The means within a given subgroup were within 0.5 (5%) of the global means, which reveals very good agreement between experts from vaccinology, cancer and STI, regardless of their primary role (clinicians or epidemiologists).

With respect to the research infrastructure gap priorities, the scores are lower than the research priorities, primarily because of their feasibility. There is often a large discrepancy between their perceived importance and their feasibility. For example, the linkage between the vaccine and cancer registries received the highest ranking for importance but scored extremely low for feasibility. Prominent issues identified relate to databases (e.g. linkages, access), networking (e.g.

advisory groups, multi-discipline) and program issues (e.g. goals, conflict of interest). The worrisome conclusion is that the feasibility is low for most of these items, and major collaboration and resources will be needed to address the gaps.

There was lower consensus on the infrastructure gaps than the research priorities. The mean answers from subgroups were often different from the global mean by 1 (10%) or even 2 (20%). More work remains to be done to achieve a better understanding and a common vision of what infrastructure should be put in place for research and for the control and monitoring of a comprehensive HPV program.

The priorities for each research component are detailed in Tables 7 to 12. They would be particularly useful for research groups with expertise in a given area when future projects are being reviewed and for validating their relevance when looking for financial support. It would also be of great interest for funding agencies and other stakeholders who are in a position to support research efforts or infrastructure development.

In summary, the results of the vote by the experts showed that the knowledge base around the burden of disease (fundamental research) and the vaccines (intervention research) is relatively strong compared with what is known about program delivery issues. Furthermore, key infrastructure gaps were identified. These will be challenging to resolve without serious collaborative efforts and funding.

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Appendix 2: Break-out Session Agendas

Break-Out Session 'A' Agenda
Fundamental research

Moderator: Philippe De Wals
Rapporteur: Jennifer Beaulac
Presenter: François Coutlee, Marc Brisson and Hugues Bogaerts

Agenda		
1:30 – 1:45	Introduce moderator, participants, rapporteur Introduction of topic	(Simon Dobson) (Philippe De Wals)
1:45 – 2:15	Presentation of the current research in Canada	François Coutlee, Marc Brisson and Hugues Bogaerts (Moderator/Group)
2:15 – 5:30	**For each category:** Brainstorm research gaps Formulate the research question(s) Brainstorm infrastructure gaps for each research question	
5:30 – 6:30	Break-out Session ends for participants All break-out moderators, chairs, rapporteurs (and workshop support) meet to review (and consolidate, if necessary) research priority lists and delegate next steps	
Evening	Meet to prepare plenary presentation (including research question, rationale, and infrastructure gaps)	(Philippe De Wals, Jennifer Beaulac, Simon Dobson)

Discussion points for Group A

(Using the relevant categories and criteria from the Erickson/De Wals Framework)

Category #1 – Burden of disease

Does the burden of disease justify a control program?

1.1 Nature and characteristics of the infective agent, including reservoirs, mode of transmission and pathogenic mechanisms

1.2 Clinical manifestations and complications of infection

1.3 Epidemiology of the disease, including incidence, time trends, seasonal and geographic variations, clustering of cases

1.4 Specific populations affected and risk factors

1.5 Current disease treatment and preventability by measures other than immunization

1.6 Health impact of the disease in the population, including frequency of cases and deaths, loss of life years

1.7 Social impact of the disease, including intensity of suffering, frequency of survivors with sequelae, reduction of quality of life of affected individuals, and loss of quality-adjusted life years, long-term disability, impact on families/caregivers, fear of disease, stress on communities

1.8 Economic impact of the disease, including direct and indirect costs to patients and families, productivity losses, health service utilization and costs to health system

Category #4 – Cost-effectiveness of program

Note: This group should discuss only the disease treatment and screening program costs since the vaccine and vaccine program costs will be dealt with by the other groups.

Is it possible to obtain funding for the program and are cost-effectiveness indices comparable to those of other health care interventions?

4.1 n/a for this break-out group

4.2 n/a for this break-out group

4.3 Evidence regarding the short- and long-term program effectiveness, including reduction in disease incidence, complications, sequelae and mortality

4.4 Evidence regarding social and economic benefits, including reduction in health care costs, improvement in life expectancy, in quality of life for individuals, families, caregivers and communities, productivity gains

4.5 Other indirect benefits (i.e. reduced microbial resistance, reduced emergency department overcrowding)

4.6 Economic evaluation: net present costs and cost/benefit ratios (from health care and societal perspectives) of alternative strategies (per life saved, case prevented, life year gained, quality-adjusted life year gained), discussion of underlying assumptions, evaluation of robustness of economic model using sensitivity analyses, comparison with other studies, pertinence for local settings, and comparison with other health care interventions

Category #7 – Ability to evaluate programs

Note: This group should discuss only the disease treatment and screening program evaluation since the vaccine and vaccine program evaluation will be dealt with by the other groups.

Can the various aspects of the program be evaluated?

7.1 Desirability of evaluation to families, professionals (nurses, MDs, public health personnel) and political authorities

7.2 n/a for this break-out group

7.3 Availability of information systems for monitoring reduction of disease incidence, complications, sequelae, and mortality

7.4 n/a for this break-out group

7.5 Availability of systems for linking health outcomes databases, immunization registries and population registries

Break-Out Session 'B' Agenda
Intervention Research

Moderator: Scott Halperin
Rapporteur: Robert Lerch
Presenter: David Scheifele

Agenda		
1:30 – 1:45	Introduce moderator, participants, rapporteur Introduction of topic	(Bermard Duval) (Scott Halperin)
1:45 – 2:00	Presentation of the current research in Canada	David Scheifele (Moderator/Group)
2:00 – 5:30	**For each category:** Brainstorm research gaps Formulate the research question(s) Brainstorm infrastructure gaps for each research question	
5:30 – 6:30	Break-out Session ends for participants All break-out moderators, chairs, rapporteurs (and workshop support) meet to review (and consolidate, if necessary) priority lists and delegate next steps	
Evening	Meet to prepare plenary presentation (including research question, rationale, and infrastructure gaps)	(Scott Halperin, Robert Lerch, Bernard Duval)

Discussion points for Group B

(Using the relevant categories and criteria from the Erickson/De Wals Framework)

Category #2 – Vaccine Characteristics

Do the characteristics of the vaccine permit implementation of an effective and safe immunization program?

2.1 Nature and characteristics of immunizing agent (i.e. live, attenuated, killed, absorbed/non-absorbed, viral or bacterial product)

2.2 Characteristics of the commercial products (i.e. preparation, stabilizing agents and preservatives, dosage, combination, storage, handling, conservation, product format)

2.3 Vaccine manufacturers, production capacity and supply to Canada

2.4 Administration schedule, number of doses, association with other vaccines

2.5 Nature and characteristics of immune response

2.6 Immunogenicity in different population groups

2.7 Short- and long-term vaccine efficacy, including reduction of disease and death risks

2.8 Effect of the vaccine on the transmission of the specific and related organisms (i.e. reduction in carriage rate, replacement)

2.9 Short- and long-term population effectiveness (i.e. impact on reduction of burden of disease, including herd immunity)

2.10 Safety: rates and severity of adverse events, contraindications, precautions.

Category #4 – Cost-effectiveness of program

Note: This group should discuss only the vaccine-related costs since the burden of disease, disease treatment, and vaccine program costs will be dealt with by the other groups.

Is it possible to obtain funding for the program and are cost-effectiveness indices comparable to those of other health care interventions?

4.1 *n/a for this break-out group*

4.2 *n/a for this break-out group*

4.3 Evidence regarding the short- and long-term program effectiveness, including reduction in disease incidence, complications, sequelae and mortality

4.4 Evidence regarding social and economic benefits, including reduction in health care costs, improvement in life expectancy, in quality of life for individuals, families, caregivers and communities, productivity gains

4.5 Other indirect benefits (i.e. reduced microbial resistance, reduced emergency room overcrowding)

4.6 Economic evaluation: net present costs and cost/benefit ratios (from health care and societal perspectives) of alternative strategies (per life saved, case prevented, life year gained, quality-adjusted life year gained), discussion of underlying assumptions, evaluation of robustness of economic model using sensitivity analyses, comparison with other studies, pertinence for local settings, and comparison with other health care interventions

Category #7 – Ability to evaluate programs

Note: This group should discuss only the vaccine evaluation since the burden of disease, disease treatment, and vaccine program evaluation will be dealt with by the other groups.

Can the various aspects of the program be evaluated?

7.1 Desirability of evaluation to families, professionals (nurses, MDs, public health personnel) and political authorities

7.2 Availability of information systems to measure coverage (including immunization registries) and vaccine utilization, quality of vaccination services

7.3 *n/a for this break-out group*

7.4 Availability of information systems for monitoring adverse events associated with vaccine administration

7.5 Availability of systems for linking health outcomes databases, immunization registries and population registries

Break-Out Session 'C' Agenda
Program Delivery Research

Moderator: David Patrick
Rapporteur: Lisa Paddle
Presenter: Ian Gemmill

Agenda		
1:30 – 1:45	Introduce moderator, participants, rapporteur Introduction of topic	(Shelley Deeks) (David Patrick)
1:45 – 2:00	Presentation of the current research in Canada	Ian Gemmill (Moderator/Group)
2:00 – 5:30	**For each category:** Brainstorm research gaps Formulate the research question(s) Brainstorm infrastructure gaps for each research question	
5:30 – 6:30	Break-out Session ends for participants All break-out moderators, chairs, rapporteurs (and workshop support) meet to review (and consolidate, if necessary) priority lists and delegate next steps	
Evening	Meet to prepare plenary presentation (including research question, rationale, and infrastructure gaps)	(Shelley Deeks, Lisa Paddle, David Patrick)

Discussion points for Group C

(Using the relevant categories and criteria from the Erickson/De Wals Framework)

Category #3 – Immunization strategy and program

Is there an immunization strategy that allows the goals of the control program as well as sanitary and operational objectives to be attained?

3.1 Existing recommendations/guidelines for use of the vaccine (i.e. NACI, consensus conferences, ACIP, AAP, product monograph)

3.2 Goal of prevention: disease control, elimination, or eradication

3.3 Alternative immunization strategies and programs for meeting goal (i.e. selective versus universal immunization programs, catch-up programs)

3.4 Program delivery strategy/system: nurses versus physicians, private versus public, different locations (i.e. schools, private clinics, public health clinics)

3.5 Specific program objectives in terms of reduction of incidence, complications, sequelae and mortality

3.6 Specific operational objectives, in terms of vaccination coverage for different target groups, and vaccine wastage

Category #4 – Cost-effectiveness of program

Note: This group should discuss only the immunization program costs since the burden of disease and vaccine costs will be dealt with by the other groups.

Is it possible to obtain funding for the program and are cost-effectiveness indices comparable to those of other health care interventions?

4.1 *n/a for this break-out group*

4.2 Total and opportunity costs of program in a societal perspective, including direct and indirect costs for families and the health system, costs for implementing and running the program

4.3 *n/a for this break-out group*

4.4 *n/a for this break-out group*

4.5 Other indirect benefits (i.e. reduced microbial resistance, reduced emergency department overcrowding)

4.6 Economic evaluation: net present costs and cost/benefit ratios (from health care and societal perspectives) of alternative strategies (per life saved, case prevented, life year gained, quality-adjusted life year gained), discussion of underlying assumptions, evaluation of robustness of economic model using sensitivity analyses, comparison with other studies, pertinence for local settings, and comparison with other vaccines and other health care interventions

Category #5 – Acceptability of vaccine (immunization) program

Does a high level of demand or acceptability exist for the immunization program?

5.1 Public perception of disease risk, severity, fear, demand for disease control

5.2 Demand for/acceptability of immunization program to target groups, population at large, health professionals (nurses, MDs, public health personnel) and political authorities

5.3 Priority for new program with respect to other potential/approved programs

Category #6 — Feasibility of program

Is program implementation feasible given existing resources?

6.1 Availability of vaccine and long-term supply

6.2 Availability of funding for vaccine purchase

6.3 Opportunity for implementing new program (i.e. other immunization program targeting same group)

6.4 Existence of operational planning and implementation committee

6.5 Integration of new program with existing immunization programs and schedules

6.6 Impacts of program (including catch-up) on existing immunization services and other health care sectors (physicians, long-term care facilities, hospitals, occupational settings, etc)

6.7 Accessibility of target population and expected levels of uptake/coverage for target groups

6.8 Availability of human, technical and financial resources for distribution, conservation (cold chain stability) and administration of vaccines, including implementation of the new program and catch-up

6.9 Availability of appropriate documentation/consent forms for the population and health care providers

6.10 Availability of system for recording/registering vaccine administration

6.11 Availability of resources for marketing and communication to the public, information and training of health professionals

Category #9 — Equity of the program

Is the program equitable in terms of accessibility of the vaccine for all target groups?

9.1 Equity of new program, including universality, accessibility and gratuity of services for the most vulnerable population groups

Category #10 — Ethical considerations

Have ethical concerns regarding implementation of the immunization program been adequately addressed?

10.1 Ethical considerations, including informed consent and protection of confidentiality of medical information

Category #13 — Political considerations

Will the proposed program be free of controversy and/or produce some immediate political benefits?

13.1 Possible political benefits and risks associated with implementation of new program

Category #7 — Ability to evaluate programs

Note: This group should discuss only the immunization program evaluation since the burden of disease and vaccine evaluation will be dealt with by the other groups.

Can the various aspects of the program be evaluated?

7.1 Desirability of evaluation to families, professionals (nurses, MDs, public health personnel) and political authorities

7.2 Availability of information systems to measure coverage (including immunization registries) and vaccine utilization, quality of vaccination services

7.3 *n/a for this break-out group*

7.4 Availability of information systems for monitoring adverse events associated with vaccine administration.

7.5 *n/a for this break-out group*

Category #11 — Legal considerations

Have legal concerns regarding implementation of the immunization program been adequately addressed?

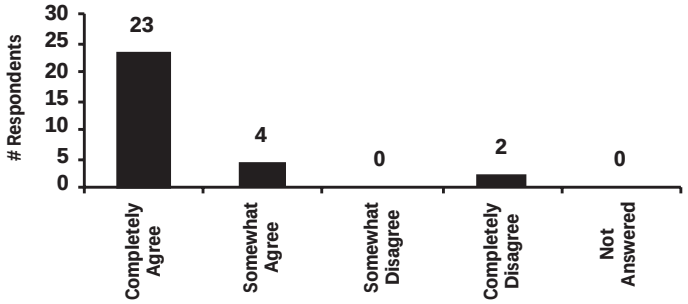
11.1 Legal considerations concerning use of vaccine (i.e. departure from manufacturers' recommendations)

Appendix 3: Workshop Evaluation Summary

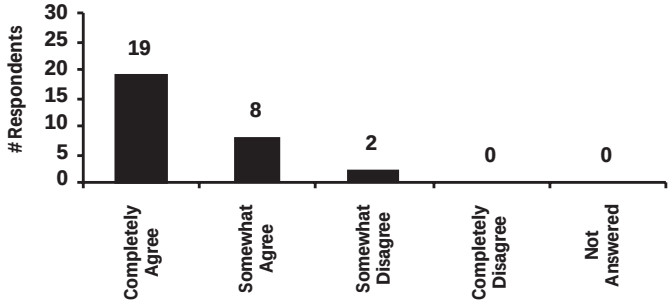
A total of 29 of a possible 53 workshop participants completed the evaluation form, representing a 55% response rate. The results are presented below, and general comments are summarized at the end of this Appendix. A complete evaluation report including all comments and suggestions was also produced for internal planning purposes.

Plenary Sessions

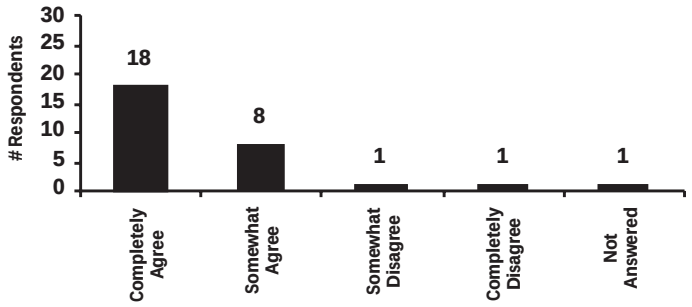
1. "I felt adequately prepared by the pre-workshop material and plenary presentations to provide an informed opinion in the break-out sessions."



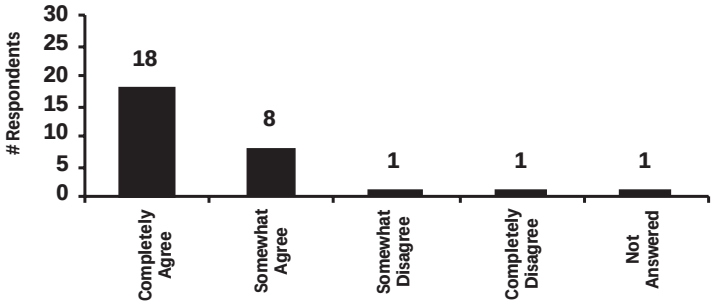
2. "The plenary sessions on the frameworks used to structure the knowledge base were appropriate and useful for a basis of discussion."



3. "The plenary session on knowledge synthesis was appropriate and useful for a basis of discussion."



4. "The plenary sessions on international decision-making on HPV vaccine use were appropriate and useful for a basis of discussion."

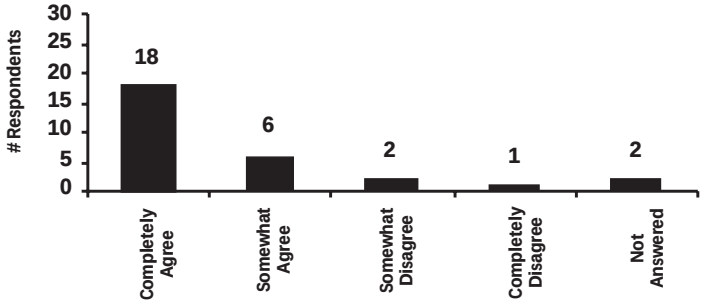


Break-Out Sessions

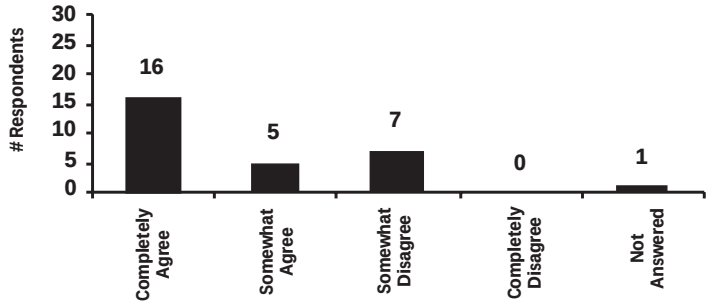
For the questions pertaining to Break-Out Sessions, respondents were asked to specify which of the three break-out groups he/she attended. The number of respondents who submitted an evaluation, by break-out, is as follows:

Break-out session	A	B	C	Group not specified	Total
Responses	8	9	6	6	29

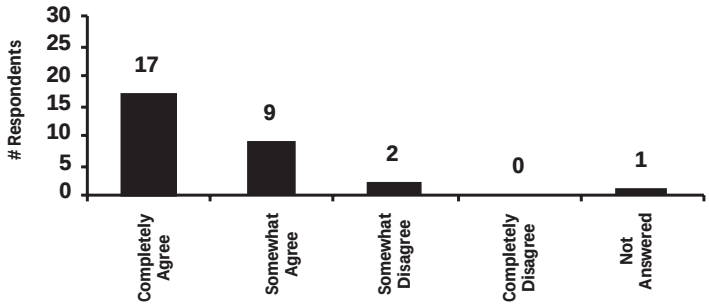
5. "The moderator of the break-out session was well prepared to facilitate the discussions and meet the objectives."



6. "The time in the break-out session was sufficient to make appropriate recommendations."

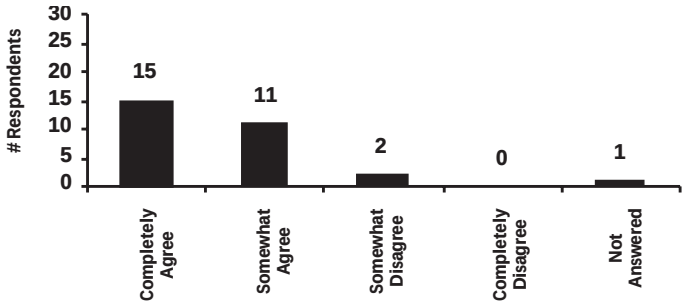


7. "The number of participants and expertise was appropriate for interactive discussion in the break-out session."

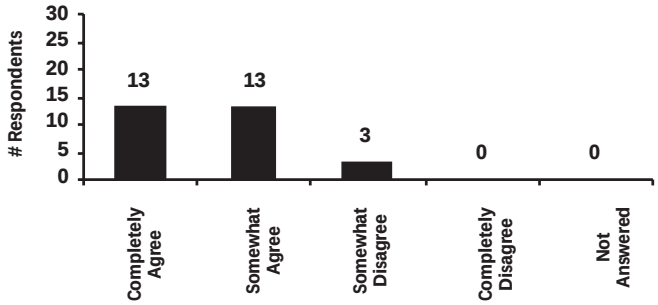


Overall

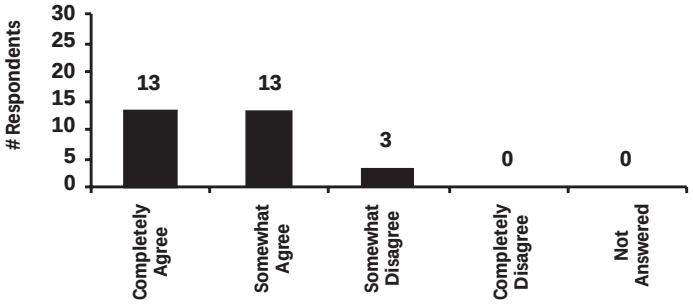
8. "The rapporteur's template was useful in the break-out session."



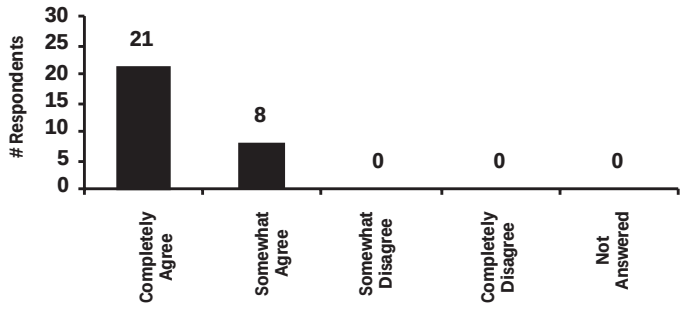
9. "The plenary presentations from the break-out sessions covered appropriate topics to inform the selection of research priorities."



10. "The overall process in developing consensus on research priorities for HPV vaccine use in Canada was appropriate."



11. "The logistical arrangements were adequate i.e. venue/hospitality/presentation material/room set-up etc."



12. "Were there gaps in the workshop that should have been more thoroughly addressed? If so, please specify."

    Responses to this question included suggestions for additional types of pre-workshop reading material; the need to assess the interface with existing cancer screening programs; and a provision for more opportunity for discussion in break-out groups.

13. "What improvements could have been made for future research priorities workshops?"

    Responses to this question included adding a basic vaccinology introduction for the benefit of non-vaccinologists; holding two shorter break-outs rather than one long one; more detailed presenting of rationale from the break-out groups; and providing a debriefing opportunity after the break-outs and before the voting.

14. "Additional comments/suggestions."

    Responses to this question included positive feedback on the voting system for establishing consensus on research priorities; positive comments on the organization of the meeting; incorporating the industry research plans in the plenary presentations; a need to fully evaluate the complex issues of HPV and cervical cancer before adoption of a publicly funded vaccine program; the need for a PHAC/CIHR funding arrangement; better explanation of the voting criteria [feasibility/importance]; and a request for participants to receive the final report.

Appendix 4: Additional Voting Results Tables

1. General Combined Results

All of the tables in this section combine the research questions or infrastructure gaps from each of the three break-out sessions – fundamental (A), intervention (B), program delivery (C).

Table 1. Combined results: 10 highest ranked research questions by importance and feasibility combined

Table 2. Combined results: 10 highest ranked research questions by importance

Table 3. Combined results: 10 highest ranked research questions by feasibility

Table 4. Combined results: 10 highest ranked infrastructure gaps by importance and feasibility

Table 5. Combined results: 10 highest ranked infrastructure gaps by importance

Table 6. Combined results: 10 highest ranked infrastructure gaps by feasibility

Note: The number of respondents may vary from one question to another.

Table 1. Combined results: ten highest ranked research questions by importance and feasibility combined

Question	Label	Importance *n* = 41	Feasibility *n* = 40	Total *n* = 41
C1	Most efficient way to deliver HPV program	4.86	4.14	9.00
C8	KAB in recipients, providers, parents	4.54	4.41	8.95
C6	Vaccine program delivery costs	4.84	4.09	8.92
B2	Immunogenicity of 2-dose schedule	4.64	4.24	8.88
B19	Impact on screening programs	4.85	4.00	8.85
C9	How to promote vaccine	4.64	4.14	8.78
B7	Co-administration with other vaccines	4.66	4.11	8.76
A11	Economic burden of HPV disease	4.51	4.21	8.72
B1	Effectiveness of a 2-dose schedule	4.53	3.97	8.50
C3	Vaccine program's effect on screening	4.58	3.86	8.44

Table 2. Combined results: 10 highest ranked research questions by importance

Question	Label	Mean (*n* = 41)
C1	Most efficient way to deliver HPV program	4.86
B19	Impact on screening programs	4.85
C6	Vaccine program delivery costs	4.84
B7	Co-administration with other vaccines	4.66
B2	Immunogenicity of 2-dose schedule	4.64
C9	How to promote vaccine	4.64
C3	Vaccine program's effect on screening	4.58
C8	KAB in recipients, providers, parents	4.54
B1	Effectiveness of a 2-dose schedule	4.53
A11	Economic burden of HPV disease	4.51

Table 3. Combined results: 10 highest ranked research questions by feasibility

Question	Label	Mean (*n* = 40)
C8	KAB in recipients, providers, parents	4.41
B2	Immunogenicity of 2-dose schedule	4.24
A11	Economic burden of HPV disease	4.21
C1	Most efficient way to deliver HPV program	4.14
C9	How to promote vaccine	4.14
B7	Co-administration with other vaccines	4.11
C6	Vaccine program delivery costs	4.09
A10	Identity of vaccinated in screening	4.00
B19	Impact on screening programs	4.00
B1	Effectiveness of a 2-dose schedule	3.97

Table 4. Combined results: 10 highest ranked infrastructure gaps by importance and feasibility

Question	Label	Importance *n* = 40	Feasibility *n* = 41	Total *n* = 41
A14	Accessibility of P/T databases for modeling	4.63	3.82	8.45
C22	CIC HPV working group	4.23	4.09	8.32
A17	Network of different disciplines	4.21	4.07	8.28
A16	Define acceptable conflict of interest levels	4.21	4.04	8.24
C19	Environmental scan of acceptability studies	3.71	4.39	8.10
C15	Articulation of goal of the program	4.18	3.87	8.05
C16	Collaboration between Cancer/NACI – national guidelines	4.34	3.69	8.04
A15	Capacity of epi/eco modelling	4.29	3.71	8.00
A19	NACI equivalent in cancer screening	3.97	3.94	7.92
B25	CIHR RFPs that focus on multi-disciplines	4.16	3.74	7.89

Table 5. Combined results: 10 highest ranked infrastructure gaps by importance

Gap	Label	Mean (*n* = 40)
B26	Linkages between vaccine & cancer registries	4.68
A14	Accessibility of P/T databases for modeling	4.63
C16	Collaboration betw Cancer/NACI – national guidelines	4.34
A15	Capacity of epi/eco modelling	4.29
B24	Linkage of registries across Canada	4.29
C22	CIC HPV working group	4.23
A16	Define acceptable conflict of interest levels	4.21
A17	Network of different disciplines	4.21
C15	Articulation of goal of the program	4.18
B25	CIHR RFPs that focus on multi-disciplines	4.16

Table 6. Combined results: 10 highest ranked infrastructure gaps by feasibility

Gap	Label	Mean (*n* = 41)
C19	Environmental scan of acceptability studies	4.39
C22	CIC HPV working group	4.09
A17	Network of different disciplines	4.07
A16	Define acceptable conflict of interest levels	4.04
A19	NACI equivalent in cancer screening	3.94
C15	Articulation of goal of the program	3.87
A14	Accessibility of P/T databases for modeling	3.82
A18	Sentinel units for viral surveillance	3.80
C18	Impact of minors' consent	3.78
B25	CIHR RFPs that focus on multi-disciplines	3.74

2. Results by Research Component

A – Fundamental Research

Table 7. Ten highest ranked research questions by importance and feasibility combined
Table 8. Infrastructure gaps ranked by importance and feasibility combined

B – Intervention Research

Table 9. Ten highest ranked research questions by importance and feasibility combined
Table 10. Infrastructure gaps ranked by importance and feasibility combined

C – Program Delivery Research

Table 11. Ten highest ranked research questions by importance and feasibility combined
Table 12. Infrastructure gaps ranked by importance and feasibility combined

Note: The number of respondents may vary from one question to another.

A – Fundamental Research

Table 7. Ten highest ranked research questions by importance and feasibility combined

Question	Label	Importance	Feasibility	Total (n = 40)
A11	Economic burden of HPV disease	4.51	4.21	8.72
A10	Identity of vaccinated in screening	4.23	4.00	8.23
A7	Cost of screening vs prevention	4.35	3.83	8.18
A12	Cost of F/P/T databases & linkages	4.30	3.84	8.14
A5	Clinical progression of disease	4.03	3.76	7.79
A13	Distribution of HPV in Aboriginal pop	3.94	3.84	7.78
A1	Transmission/acquisition of HPV	3.92	3.58	7.50
A8	Psychosocial burden of disease	3.42	3.74	7.16
A3	Incidence of co-infection	3.60	3.40	7.00
A2	Prevalence/duration of infection	3.39	3.26	6.65

Table 8. Infrastructure gaps ranked by importance and feasibility combined
(note: there were 9 infrastructure gaps identified for fundamental research)

Gap	Label	Importance	Feasibility	Total (*n* = 40)
A14	Accessibility of P/T databases for modeling	4.63	3.82	8.45
A17	Network of different disciplines	4.21	4.07	8.28
A16	Define acceptable conflict of interest levels	4.21	4.04	8.24
A15	Capacity of epi/eco modelling	4.29	3.71	8.00
A19	NACI equivalent in cancer screening	3.97	3.94	7.92
A18	Sentinel units for viral surveillance	3.73	3.80	7.53
A20	Task Force on Preventive Health Care	3.63	3.40	7.03
A22	Peer-review process for models	3.11	3.05	6.16
A21	Legislation to implement/monitor progress	3.34	2.18	5.52

B – Intervention Research

Table 9. Ten highest ranked research questions by importance and feasibility combined

Question	Label	Importance	Feasibility	Total (*n* = 41)
B2	Immunogenicity of 2-dose schedule	4.64	4.24	8.88
B19	Impact on screening programs	4.85	4.00	8.85
B7	Co-administration with other vaccines	4.66	4.11	8.76
B1	Effectiveness of a 2-dose schedule	4.53	3.97	8.50
B15	Impact of vaccines on genotypes	4.37	3.97	8.34
B21	Impact on non-cervical cancers	4.40	3.68	8.08
B3	Correlates of protection	4.45	3.58	8.03
B16	Risk of disease other than types 16 & 18	4.30	3.73	8.03
B9	Immunocompromised population	4.28	3.61	7.89
B22	Incidence of adverse events following immunization	4.24	3.59	7.82

Table 10. Infrastructure gaps ranked by importance and feasibility combined
(note: there were 4 infrastructure gaps identified for intervention research)

Gap	Label	Importance	Feasibility	Total (*n* = 41)
B25	CIHR RFPs that focus on multi-disciplines	4.16	3.74	7.89
B26	Linkages between vaccine & cancer registries	4.68	3.02	7.70
B24	Linkage of registries across Canada	4.29	2.59	6.88
B23	Registries of all HPV-related diseases	3.70	2.60	6.30

C – Program Delivery Research

Table 11. Ten highest ranked research questions by importance and feasibility combined

Question	Label	Importance	Feasibility	Total (*n* = 37)
C1	Most efficient way to deliver HPV program	4.86	4.14	9.00
C8	KAB in recipients, providers, parents	4.54	4.41	8.95
C6	Vaccine program delivery costs	4.84	4.09	8.92
C9	How to promote vaccine	4.64	4.14	8.78
C3	Vaccine program's effect on screening	4.58	3.86	8.44
C2	How to get best coverage of vaccine	4.47	3.94	8.41
C10	Optimal schedule	4.40	3.86	8.26
C7	Catch-up program cost-effective/feasible	4.42	3.76	8.17
C5	Will vaccine impact pop who get cancer	4.31	3.56	7.87
C13	Ethical/legal issues with data linkage	3.94	3.69	7.63

Table 12. Infrastructure gaps ranked by importance and feasibility combined
(note: there were 8 infrastructure gaps identified for program delivery research)

Gap	Label	Importance	Feasibility	Total (*n* = 38)
C22	CIC HPV working group	4.23	4.09	8.32
C19	Environmental scan of acceptability studies	3.71	4.39	8.10
C15	Articulation of goal of the program	4.18	3.87	8.04
C16	Collaboration between Cancer/NACI – national guidelines	4.34	3.69	8.04
C20	Research funding for social science	4.14	3.52	7.66
C18	Impact of minors' consent	3.61	3.78	7.39
C17	HPV testing with screening	3.80	3.53	7.33
C21	Environmental scan: sexual debut & school leaving	3.68	3.59	7.26

3. Results by Participant Demographics

Participants were asked to categorize themselves by primary field of work, primary role, primary affiliation and primary specialization (see report for definitions of these categories). These are termed “subgroups” below.

Combined Results

Table 13. Ten highest ranked research questions by importance and feasibility combined for all participant subgroups

Table 14. Ten highest ranked infrastructure gaps by importance and feasibility combined for all participant subgroups

A – Fundamental Research

Table 15. Ten highest ranked research questions for importance and feasibility combined by field of work

Table 16. Infrastructure gaps ranked for importance and feasibility combined by field of work

B – Intervention Research

Table 17. Ten highest ranked research questions for importance and feasibility combined by field of work

Table 18. Infrastructure gaps ranked for importance and feasibility combined by field of work

C – Program Delivery Research

Table 19. Ten highest ranked research questions for importance and feasibility combined by field of work

Table 20. Infrastructure gaps ranked for importance and feasibility by field of work

Combined Research Components (A,B,C), by Primary Field of Work

Table 21. Ten highest ranked research questions for importance and feasibility combined for vaccinologists

Table 22. Ten highest ranked research questions for importance and feasibility combined for cancer experts

Table 23. Ten highest ranked research questions for importance and feasibility combined for STI experts

Table 24. Ten highest ranked infrastructure gaps for importance and feasibility combined for vaccinologists

Table 25. Ten highest ranked infrastructure gaps for importance and feasibility combined for cancer experts

Table 26. Ten highest ranked infrastructure gaps for importance and feasibility combined for STI experts

Table 13. Ten highest ranked research questions for importance and feasibility for all subgroups
(research components A, B, C combined)

Question	Label	Primary field of work			Primary role			Primary affiliation			Primary specialization			All
		Vaccinology *n* = 13	Cancer *n*= 13	STI *n* = 11	Decision maker *n* = 5	Expert *n* = 14	Researcher *n* = 20	University *n* = 20	Government organization *n* = 15	Other *n* = 4	Clinician *n* = 16	Epidemiologist *n* = 13	Other *n* = 10	*n* = 41
C1	Most efficient way to deliver HPV program	9.17	9.00	8.89	9.25	8.92	9.06	8.94	9.15	9.00	8.80	9.09	9.25	9.00
C8	KAB in recipients, providers, parents	9.33	9.18	8.30	9.00	8.54	9.33	9.16	8.77	9.00	9.40	8.00	9.33	8.95
C6	Vaccine program delivery costs	9.03	8.70	8.90	9.50	8.77	8.89	8.73	9.01	9.67	8.87	8.60	9.44	8.92
B2	Immunogenicity of 2-dose schedule	9.46	8.41	8.45	8.80	9.00	8.79	9.32	8.25	9.00	9.20	8.85	8.38	8.88
B19	Impact on screening programs	8.62	9.00	8.82	8.60	8.71	9.01	8.95	8.67	9.00	8.68	8.85	9.10	8.85
C9	How to promote vaccine	9.23	8.73	8.60	9.00	8.85	8.87	8.88	8.77	9.33	8.87	8.35	9.22	8.78
B7	Co-administration with other vaccines	9.54	8.50	8.20	8.60	8.93	8.72	9.18	8.30	8.75	9.26	8.31	8.49	8.76
A11	Economic burden of HPV disease	8.29	8.83	8.82	8.50	8.49	8.93	8.41	9.18	8.75	8.28	9.00	9.05	8.72
B1	Effectiveness of a 2-dose schedule	8.74	8.50	8.09	9.40	8.07	8.55	8.61	8.33	8.50	8.46	8.38	8.70	8.50
C3	Vaccine program's effect on screening	8.25	8.55	8.56	8.50	8.38	8.59	8.33	8.54	9.33	8.20	8.55	8.75	8.44

Note: The number of respondents may vary from one question to another.

Table14. Ten highest ranked infrastructure gaps for importance and feasibility for all subgroups
(research components A, B, C combined)

		Primary field of work			Primary role			Primary affiliation			Primary specialization			
Gap	Label	Vaccinology *n* = 13	Cancer *n*= 13	STI *n* = 11	Decision maker *n* = 5	Expert *n* = 14	Researcher *n* = 20	University *n* = 20	Government organization *n* = 15	Other *n* = 4	Clinician *n* = 16	Epidemiologist *n* = 13	Other *n* = 10	All *n* = 41
A14	Accessibility of P/T databases for modeling	8.67	8.38	8.24	8.80	8.62	8.18	8.28	8.59	8.50	8.15	8.67	8.50	8.45
C22	CIC HPV working group	8.43	7.93	8.35	9.67	8.59	7.81	7.83	9.27	8.67	7.85	9.20	8.38	8.32
A17	Network of different disciplines	8.12	8.26	9.01	8.00	8.53	8.30	8.55	8.37	7.33	8.33	8.49	8.07	8.28
A16	Define acceptable conflict of interest levels	8.62	7.70	8.43	7.20	7.34	9.09	7.82	8.62	8.75	8.69	7.58	8.20	8.24
C19	Environmental scan of acceptability studies	8.64	7.72	7.47	10.00	7.69	8.03	7.54	8.83	8.33	7.78	8.29	8.44	8.10
C15	Articulation of goal of the program	8.38	7.83	8.00	8.75	7.80	8.18	7.98	8.24	8.33	8.06	7.82	8.33	8.05
C16	Collaboration betw Cancer/NACI – national guidelines	8.72	7.64	7.78	9.00	7.86	7.96	8.08	8.46	6.00	7.89	8.20	8.19	8.04
A15	Capacity of epi/eco modelling	8.00	7.70	8.18	7.25	8.06	8.09	7.44	8.62	8.25	7.17	8.33	8.78	8.00
A19	NACI equivalent in cancer screening	7.66	8.58	7.80	8.25	7.38	8.44	7.68	8.77	7.25	7.54	8.15	8.38	7.92
B25	CIHR RFPs that focus on multi-disciplines	8.08	7.67	8.00	7.00	8.21	7.83	8.15	8.00	6.00	8.13	8.18	7.33	7.89

Note: The number of respondents may vary from one question to another.

A – Fundamental Research

Table 15. Ten highest ranked research questions for importance and feasibility combined by field of work

Question	Label	Importance	Feasibility	Total
Vaccinology (*n* = 13)				
A10	Identity of vaccinated in screening	4.58	4.10	8.68
A11	Economic burden of HPV disease	4.13	4.17	8.29
A12	Cost of F/P/T databases & linkages	4.18	4.00	8.18
A13	Distribution of HPV among Aboriginal pop	4.40	3.78	8.18
A7	Cost of screening vs prevention	4.10	3.83	7.93
A5	Clinical progression of disease	3.83	3.73	7.56
A1	Transmission/acquisition of HPV	3.82	3.42	7.23
A3	Incidence of co-infection	3.64	3.36	7.00
A8	Psychosocial burden of disease & Tx	3.18	3.67	6.85
A9	Migration/ethnicity effect on prevention	3.55	3.17	6.71
Cancer (*n* = 13)				
A7	Cost of screening vs prevention	4.77	4.23	9.00
A11	Economic burden of HPV disease	4.75	4.08	8.83
A12	Cost of F/P/T databases & linkages	4.58	3.80	8.38
A5	Clinical progression of disease	4.00	4.00	8.00
A10	Identity of vaccinated in screening	4.00	4.00	8.00
A1	Transmission/acquisition of HPV	4.00	3.69	7.69
A8	Psychosocial burden of disease & Tx	3.69	3.69	7.38
A13	Distribution of HPV in Aboriginal pop	3.40	3.90	7.30
A3	Incidence of co-infection	3.45	3.27	6.73
A2	Prevalence/duration of infection	3.75	2.85	6.60
STI (*n* = 11)				
A11	Economic burden of HPV disease	4.55	4.27	8.82
A12	Cost of F/P/T databases & linkages	4.40	3.75	8.15
A7	Cost of screening vs prevention	4.40	3.73	8.13
A1	Transmission/acquisition of HPV	4.18	3.82	8.00
A10	Identity of vaccinated in screening	4.09	3.80	7.89
A13	Distribution of HPV among Aboriginal pop	3.91	3.90	7.81
A5	Clinical progression of disease	4.18	3.55	7.73
A8	Psychosocial burden of disease & Tx	3.70	4.00	7.70
A3	Incidence of co-infection	3.50	3.44	6.94
A4	Distribution of HPV in population	3.82	3.10	6.92

Note: The number of respondents may vary from one question to another.

Table 16. Infrastructure gaps ranked for importance and feasibility combined by field of work
(note: there were 9 infrastructure gaps identified for fundamental research)

Gap	Label	Importance	Feasibility	Total
	Vaccinology (*n* = 13)			
A14	Accessibility of P/T databases for modeling	5.00	3.67	8.67
A16	Define acceptable conflict of interest levels	4.33	4.29	8.62
A17	Network of different disciplines	3.83	4.29	8.12
A15	Capacity of epi/eco modelling	4.17	3.83	8.00
A19	NACI equivalent in cancer screening	3.91	3.75	7.66
A22	Peer-review process for models	3.73	3.58	7.31
A18	Sentinel units for viral surveillance	3.50	3.75	7.25
A20	Task Force on Preventive Health Care	3.60	3.27	6.87
A21	Legislation to implement/monitor progress	3.40	2.33	5.73
	Cancer (*n* = 13)			
A19	NACI equivalent in cancer screening	4.25	4.33	8.58
A14	Accessibility of P/T databases for modeling	4.38	4.00	8.38
A17	Network of different disciplines	4.17	4.09	8.26
A15	Capacity of epi/eco modelling	4.25	3.45	7.70
A16	Define acceptable conflict of interest levels	4.15	3.55	7.70
A20	Task Force on Preventive Health Care	3.92	3.45	7.37
A18	Sentinel units for viral surveillance	3.46	3.54	7.00
A21	Legislation to implement/monitor progress	2.82	2.23	5.05
A22	Peer-review process for models	2.17	2.83	5.00
	STI (*n* = 11)			
A17	Network of different disciplines	4.73	4.29	9.01
A18	Sentinel units for viral surveillance	4.45	4.27	8.73
A16	Define acceptable conflict of interest levels	4.00	4.43	8.43
A14	Accessibility of P/T databases for modeling	4.60	3.64	8.24
A15	Capacity of epi/eco modelling	4.40	3.78	8.18
A19	NACI equivalent in cancer screening	3.90	3.90	7.80
A20	Task Force on Preventive Health Care	3.30	3.45	6.75
A22	Peer-review process for models	3.45	2.82	6.27
A21	Legislation to implement/monitor progress	3.91	2.00	5.91

Note: The number of respondents may vary from one question to another.

B – Program Delivery Research

Table 17. Ten highest ranked research questions for importance and feasibility combined by field of work

Question	Label	Importance	Feasibility	Total
Vaccinology (*n* = 13)				
B7	Co-administration with other vaccines	4.85	4.69	9.54
B2	Immunogenicity of 2-dose schedule	5.00	4.46	9.46
B1	Effectiveness of a 2-dose schedule	4.83	3.91	8.74
B15	Impact of vaccines on genotypes	4.45	4.18	8.64
B19	Impact on screening program's	4.62	4.00	8.62
B9	Immunocompromised population	4.46	3.77	8.23
B3	Correlates of protection	4.69	3.38	8.08
B22	Incidence of vaccine-associated adverse events	4.30	3.73	8.03
B21	Impact on non-cervical cancers	4.23	3.67	7.90
B6	Intradermal/transcutaneous immunization	3.85	3.92	7.77
Cancer (*n* = 13)				
B19	Impact on screening *programs*	5.00	4.00	9.00
B1	Effectiveness of a 2-dose schedule	4.42	4.08	8.50
B7	Co-administration with other vaccines	4.58	3.92	8.50
B2	Immunogenicity of 2-dose schedule	4.50	3.91	8.41
B21	Impact on non-cervical cancers	4.54	3.69	8.23
B18	Safety of the adjuvants	4.54	3.58	8.12
B22	Incidence of adverse events following immunization	4.40	3.70	8.10
B16	Risk of disease other than types 16 & 18	4.23	3.77	8.00
B6	Intradermal/transcutaneous immunization	4.25	3.64	7.89
B13	Herd immunity levels	4.42	3.30	7.72
STI (*n* = 11)				
B15	Impact of vaccines on genotypes	4.64	4.30	8.94
B19	Impact on screening programs	4.91	3.91	8.82
B16	Risk of disease other than types 16 & 18	4.50	4.09	8.59
B2	Immunogenicity of 2-dose schedule	4.36	4.09	8.45
B7	Co-administration with other vaccines	4.60	3.60	8.20
B3	Correlates of protection	4.64	3.55	8.18
B10	Vaccine response among HPV infected	4.40	3.73	8.13
B1	Effectiveness of a 2-dose schedule	4.27	3.82	8.09
B21	Impact on non-cervical cancers	4.30	3.64	7.94
B11	Immunogenicity in Aboriginal women	4.00	3.70	7.70

Note: The number of respondents may vary from one question to another.

Table 18. Infrastructure gaps ranked for importance and feasibility combined by field of work
(note: there were 4 infrastructure gaps identified for intervention research)

Gap	Label	Importance	Feasibility	Total
	Vaccinology (*n* = 13)			
B26	Linkages betw vaccine & cancer registries	4.85	3.62	8.46
B25	CIHR RFPs that focus on multi-disciplines	4.25	3.83	8.08
B24	Linkage of registries across Canada	4.45	2.64	7.09
B23	Registries of all HPV-related diseases	3.91	3.00	6.91
	Cancer (*n* = 13)			
B25	CIHR RFPs that focus on multi-disciplines	3.75	3.92	7.67
B26	Linkages betw vaccine & cancer registries	4.50	3.00	7.50
B24	Linkage of registries across Canada	4.33	3.08	7.41
B23	Registries of all HPV-related diseases	3.08	2.15	5.23
	STI (*n* = 11)			
B25	CIHR RFPs that focus on multi-disciplines	4.45	3.55	8.00
B23	Registries of all HPV-related diseases	4.60	2.82	7.42
B26	Linkages betw vaccine & cancer registries	4.82	2.18	7.00
B24	Linkage of registries across Canada	4.09	2.18	6.27

Note: The number of respondents may vary from one question to another.

C – Program Delivery Research

Table 19. Ten highest ranked research questions for importance and feasibility combined by field of work

Question	Label	Importance	Feasibility	Total
Vaccinology (*n* = 13)				
C8	KAB in recipients, providers, parents	4.67	4.67	9.33
C9	How to promote vaccine	4.82	4.42	9.23
C1	Most efficient way to deliver HPV program	4.83	4.33	9.17
C6	Vaccine program delivery costs	4.67	4.36	9.03
C2	How to get best coverage of vaccine	4.75	4.25	9.00
C10	Optimal schedule	4.55	4.08	8.63
C7	Catch-up program cost-effective/feasible	4.58	3.82	8.40
C3	Vaccine program's effect on screening	4.33	3.92	8.25
C14	Linking sexual health programs to vaccines	4.18	3.82	8.00
C13	Ethical/legal issues with data linkage	4.17	3.75	7.92
Cancer (*n* = 13)				
C8	KAB in recipients, providers, parents	4.82	4.36	9.18
C1	Most efficient way to deliver HPV program	4.91	4.09	9.00
C9	How to promote vaccine	4.73	4.00	8.73
C6	Vaccine program delivery costs	5.00	3.70	8.70
C3	Vaccine program's effect on screening	4.91	3.64	8.55
C7	Catch-up program cost-effective/feasible	4.36	3.78	8.14
C10	Optimal schedule	4.20	3.90	8.10
C2	How to get best coverage of vaccine	4.36	3.64	8.00
C11	Cold chain of vaccines	3.91	4.00	7.91
C5	Will vaccine impact pop who get cancer	4.27	3.36	7.64
STI (*n* = 11)				
C6	Vaccine program delivery costs	4.80	4.10	8.90
C1	Most efficient way to deliver HPV program	4.89	4.00	8.89
C9	How to promote vaccine	4.70	3.90	8.60
C3	Vaccine program's effect on screening	4.67	3.89	8.56
C2	How to get best coverage of vaccine	4.56	3.88	8.43
C8	KAB in recipients, providers, parents	4.20	4.10	8.30
C5	Will vaccine impact pop who get cancer	4.56	3.56	8.11
C10	Optimal schedule	4.40	3.60	8.00
C12	Health gains in non-targeted groups?	4.20	3.50	7.70
C7	Catch-up program cost-effective/feasible	4.11	3.44	7.56

Note: The number of respondents may vary from one question to another.

Table 20. Infrastructure gaps ranked for importance and feasibility combined by field of work
(note: there were 8 infrastructure gaps identified for program delivery research)

Gap	Label	Importance	Feasibility	Total
	Vaccinology (*n* = 13)			
C16	Collaboration betw Cancer/NACI – national guidelines	4.64	4.08	8.72
C19	Environmental scan of acceptability studies	4.09	4.55	8.64
C22	CIC HPV working group	4.13	4.30	8.43
C15	Articulation of goal of the program	4.30	4.08	8.38
C20	Research funding for social science	4.45	3.70	8.15
C21	Environmental scan: sexual debut & school leaving	3.90	3.73	7.63
C18	Impact of minors' consent	3.13	4.10	7.23
C17	HPV testing with screening	3.73	3.45	7.18
	Cancer (*n* = 13)			
C22	CIC HPV working group	4.13	3.80	7.93
C15	Articulation of goal of the program	4.10	3.73	7.83
C19	Environmental scan of acceptability studies	3.50	4.22	7.72
C18	Impact of minors' consent	4.25	3.40	7.65
C16	Collaboration btw Cancer/NACI – national guidelines	4.09	3.55	7.64
C20	Research funding for social science	4.00	3.45	7.45
C17	HPV testing with screening	3.91	3.45	7.36
C21	Environmental scan: sexual debut & school leaving	3.60	3.27	6.87
	STI (*n* = 11)			
C22	CIC HPV working group	4.25	4.10	8.35
C15	Articulation of goal of the program	4.18	3.82	8.00
C16	Collaboration betw Cancer/NACI – national guidelines	4.11	3.67	7.78
C17	HPV testing with screening	4.11	3.50	7.61
C19	Environmental scan of acceptability studies	3.27	4.20	7.47
C20	Research funding for social science	3.90	3.30	7.20
C21	Environmental scan: sexual debut & school leaving	3.27	3.56	6.83
C18	Impact of minors' consent	3.50	3.17	6.67

Note: The number of respondents may vary from one question to another.

Combined Research Components (A, B, C), by Primary Field of Work

Table 21. Ten highest ranked research questions for importance and feasibility combined for vaccinologists

Question	Label	Importance	Feasibility	Total (*n* = 13)
B7	Co-administration with other vaccines	4.85	4.69	9.54
B2	Immunogenicity of 2-dose schedule	5.00	4.46	9.46
C8	KAB in recipients, providers, parents	4.67	4.67	9.33
C9	How to promote vaccine	4.82	4.42	9.23
C1	Most efficient way to deliver HPV program	4.83	4.33	9.17
C6	Vaccine program delivery costs	4.67	4.36	9.03
C2	How to get best coverage of vaccine	4.75	4.25	9.00
B1	Effectiveness of a 2-dose schedule	4.83	3.91	8.74
A10	Identity of vaccinated in screening	4.58	4.10	8.68
B15	Impact of vaccines on genotypes	4.45	4.18	8.64

Table 22. Ten highest ranked research questions for importance and feasibility combined fo cancer experts

Question	Label	Importance	Feasibility	Total (*n* = 13)
C8	KAB in recipients, providers, parents	4.82	4.36	9.18
A7	Cost of screening vs prevention	4.77	4.23	9.00
B19	Impact on screening programs	5.00	4.00	9.00
C1	Most efficient way to deliver HPV program	4.91	4.09	9.00
A11	Economic burden of HPV disease	4.75	4.08	8.83
C9	How to promote vaccine	4.73	4.00	8.73
C6	Vaccine program delivery costs	5.00	3.70	8.70
C3	Vaccine program's effect on screening	4.91	3.64	8.55
B1	Effectiveness of a 2-dose schedule	4.42	4.08	8.50
B7	Co-administration with other vaccines	4.58	3.92	8.50

Table 23. Ten highest ranked research questions for importance and feasibility combined for STI experts

Question	Label	Importance	Feasibility	Total (*n* = 11)
B15	Impact of vaccines on genotypes	4.64	4.30	8.94
C6	Vaccine program delivery costs	4.80	4.10	8.90
C1	Most efficient way to deliver HPV program	4.89	4.00	8.89
A11	Economic burden of HPV disease	4.55	4.27	8.82
B19	Impact on screening programs	4.91	3.91	8.82
C9	How to promote vaccine	4.70	3.90	8.60
B16	Risk of disease other than types 16 & 18	4.50	4.09	8.59
C3	Vaccine program's effect on screening	4.67	3.89	8.56
B2	Immunogenicity of 2-dose schedule	4.36	4.09	8.45
C2	How to get best coverage of vaccine	4.56	3.88	8.43

Table 24. Ten highest ranked infrastructure gaps for importance and feasibility combined for vaccinologists

Gap	Label	Importance	Feasibility	Total (*n* = 13)
C16	Collaboration betw Cancer/NACI – national guidelines	4.64	4.08	8.72
A14	Accessibility of P/T databases for modeling	5.00	3.67	8.67
C19	Environmental scan of acceptability studies	4.09	4.55	8.64
A16	Define acceptable conflict of interest levels	4.33	4.29	8.62
B26	Linkages btw vaccine & cancer registries	4.85	3.62	8.46
C22	CIC HPV working group	4.13	4.30	8.43
C15	Articulation of goal of the program	4.30	4.08	8.38
C20	Research funding for social science	4.45	3.70	8.15
A17	Network of different disciplines	3.83	4.29	8.12
B25	CIHR RFPs that focus on multi-disciplines	4.25	3.83	8.08

Table 25. Ten highest ranked infrastructure gaps for importance and feasibility combined for cancer experts

Gap	Label	Importance	Feasibility	Total (*n* = 13)
A19	NACI equivalent in cancer screening	4.25	4.33	8.58
A14	Accessibility of P/T databases for modeling	4.38	4.00	8.38
A17	Network of different disciplines	4.17	4.09	8.26
C22	CIC HPV working group	4.13	3.80	7.93
C15	Articulation of goal of the program	4.10	3.73	7.83
C19	Environmental scan of acceptability studies	3.50	4.22	7.72
A15	Capacity of epi/eco modelling	4.25	3.45	7.70
A16	Define acceptable conflict of interest levels	4.15	3.55	7.70
B25	CIHR RFPs that focus on multi-disciplines	3.75	3.92	7.67
C18	Impact of minors' consent	4.25	3.40	7.65

Table 26. Ten highest ranked infrastructure gaps for importance and feasibility combined for STI experts

Gap	Label	Importance	Feasibility	Total (*n* = 11)
A17	Network of different disciplines	4.73	4.29	9.01
A18	Sentinel units for viral surveillance	4.45	4.27	8.73
A16	Define acceptable conflict of interest levels	4.00	4.43	8.43
C22	CIC HPV working group	4.25	4.10	8.35
A14	Accessibility of P/T databases for modeling	4.60	3.64	8.24
A15	Capacity of epi/eco modelling	4.40	3.78	8.18
B25	CIHR RFPs that focus on multi-disciplines	4.45	3.55	8.00
C15	Articulation of goal of the program	4.18	3.82	8.00
A19	NACI equivalent in cancer screening	3.90	3.90	7.80
C16	Collaboration betw Cancer/NACI – national guidelines	4.11	3.67	7.78

Note: The number of respondents may vary from one question to another.

4. Ranking of All Identified Research Questions (*n* = 49) and Infrastructure Gaps (*n* = 21)

Table 27. All research questions ranked for importance and feasibility

Question	Label	Importance (*n* = 41)	Feasibility (*n* = 40)	Total (*n* = 41)
C1	Most efficient way to deliver HPV program	4.86	4.14	9.00
C8	KAB in recipients, providers, parents	4.54	4.41	8.95
C6	Vaccine program delivery costs	4.84	4.09	8.92
B2	Immunogenicity of 2-dose schedule	4.64	4.24	8.88
B19	Impact on screening programs	4.85	4.00	8.85
C9	How to promote vaccine	4.64	4.14	8.78
B7	Co-administration with other vaccines	4.66	4.11	8.76
A11	Economic burden of HPV disease	4.51	4.21	8.72
B1	Effectiveness of a 2-dose schedule	4.53	3.97	8.50
C3	Vaccine program's effect on screening	4.58	3.86	8.44
C2	How to get best coverage of vaccine	4.47	3.94	8.41
B15	Impact of vaccines on genotypes	4.37	3.97	8.34
C10	Optimal schedule	4.40	3.86	8.26
A10	Identity of vaccinated in screening	4.23	4.00	8.23
A7	Cost of screening vs prevention	4.35	3.83	8.18
C7	Catch-up program cost-effective/feasible	4.42	3.76	8.17
A12	Cost of F/P/T databases & linkages	4.30	3.84	8.14
B21	Impact on non-cervical cancers	4.40	3.68	8.08
B3	Correlates of protection	4.45	3.58	8.03
B16	Risk of disease other than types 16 & 18	4.30	3.73	8.03
B9	Immunocompromised population	4.28	3.61	7.89
C5	Will vaccine impact pop who get cancer	4.31	3.56	7.8
B22	Incidence of adverse events following immunization	4.24	3.59	7.82
A5	Clinical progression of disease	4.03	3.76	7.79
A13	Distribution of HPV in Aboriginal pop	3.94	3.84	7.78
B10	Vaccine response among HPV infected	4.25	3.43	7.68
B18	Safety of the adjuvants	4.20	3.48	7.67

Table 27. All research questions ranked for importance and feasibility *(continued)*

Question	Label	Importance (*n* = 41)	Feasibility (*n* = 40)	Total (*n* = 41)
C13	Ethical/legal issues with data linkage	3.94	3.69	7.63
B20	Impact on Tx & F/U of CIN1 lesions	4.06	3.55	7.61
B6	Intradermal/transcutaneous immunization	3.95	3.63	7.58
C11	Cold chain of vaccines	3.76	3.77	7.53
A1	Transmission/acquisition of HPV	3.92	3.58	7.50
B13	Herd immunity levels	4.19	3.31	7.50
B11	Immunogenicity in Aboriginal women	3.79	3.64	7.43
C12	Health gains in non-targeted groups?	3.86	3.41	7.27
C14	Linking sexual health programs to vaccines	3.82	3.43	7.25
B4	Vaccines interchangeability	3.90	3.34	7.24
A8	Psychosocial burden of disease	3.42	3.74	7.16
C4	Will other behaviours change with immunization	3.92	3.17	7.08
A3	Incidence of co-infection	3.60	3.40	7.00
A2	Prevalence/duration of infection	3.39	3.26	6.65
B17	Background rate of unrelated events	3.50	3.11	6.61
A9	Migration/ethnicity effect on prevention	3.49	3.10	6.59
B14	Natural infection as a booster	3.58	2.83	6.40
B8	Vaccine in pregnancy	3.59	2.62	6.21
A6	Epidemiology of warts in Canada	2.89	3.15	6.04
A4	Distribution of HPV in population	3.19	2.68	5.86
B5	Both vaccines in sequential schedule	2.82	2.57	5.38
B12	Impact of estrogen on immune response	2.42	2.62	5.04

Note: The number of respondents may vary from one question to another.

Table 28. All research infrastructure gaps ranked for importance and feasibility

Gap	Label	Importance (*n* = 40)	Feasibility (*n* = 41)	Total (*n* = 41)
A14	Accessibility of P/T databases for modeling	4.63	3.82	8.45
C22	CIC HPV working group	4.23	4.09	8.32
A17	Network of different disciplines	4.21	4.07	8.28
A16	Define acceptable conflict of interest levels	4.21	4.04	8.24
C19	Environmental scan of acceptability studies	3.71	4.39	8.10
C15	Articulation of goal of the program	4.18	3.87	8.05
C16	Collaboration betw Cancer/NACI – national guidelines	4.34	3.69	8.04
A15	Capacity of epi/eco modelling	4.29	3.71	8.00
A19	NACI equivalent in cancer screening	3.97	3.94	7.92
B25	CIHR RFPs that focus on multi-disciplines	4.16	3.74	7.89
B26	Linkages betw vaccine & cancer registries	4.68	3.02	7.70
C20	Research funding for social science	4.14	3.52	7.66
A18	Sentinel units for viral surveillance	3.73	3.8	7.53
C18	Impact of minors' consent	3.61	3.78	7.39
C17	HPV testing with screening	3.80	3.53	7.33
C21	Environmental scan: sexual debut & school leaving	3.68	3.59	7.26
A20	Task Force on Preventive Health Care	3.63	3.40	7.03
B24	Linkage of registries across Canada	4.29	2.59	6.88
B23	Registries of all HPV-related diseases	3.70	2.60	6.30
A22	Peer-review process for models	3.11	3.05	6.16
A21	Legislation to implement/monitor progress	3.34	2.18	5.52

Note: The number of respondents may vary from one question to another.