

An analytical framework for immunization programs in Canada

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Abstract

Recent years have seen an increase in the number of new vaccines available on the Canadian market, and increasing divergence in provincial and territorial immunization programs as jurisdictions must choose among available health interventions with limited funding. We present an analytical framework, which we have developed to assist in the analysis and comparison of potential immunization programs. The framework includes 58 criteria classified into 13 categories, including the burden of disease, vaccine characteristics and immunization strategy, cost-effectiveness, acceptability, feasibility, and evaluability of program, research questions, equity, ethical, legal and political considerations. To date this framework has been utilized in a variety of different contexts, such as to structure expert presentations and reports and to examine the degree of consensus and divergence among experts, and to establish priorities. It can be transformed for a variety of other uses such as educating health professionals and the general public about immunization.

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1. Introduction

At an ever-increasing pace, new vaccines are being developed, licensed, and commercialized in Canada due to initiatives of pharmaceutical companies. New products are evaluated by the National Advisory Committee on Immunization, which determines the optimal conditions of use of the vaccine in the epidemiological context of Canada [1]. Other expert committees such as the Canadian Task Force on the Periodic Health Examination [2] or the Committee to Advise on Tropical Medicine and Travel [3] may also produce recommendations or guidelines for health professionals. Integration of a new vaccine into a publicly-funded immunization program is the responsibility of provinces and territories, and each jurisdiction decides which products will be purchased and offered free of charge to certain target groups. Decision-making

structures and processes for immunization vary greatly between Canadian provinces and territories, and it has been observed that decision-making criteria may vary between different vaccines in the same jurisdiction [4]. This lack of standardization and reproducibility in the vaccine evaluation process has negative consequences on the homogeneity and equity of immunization programs across Canada [5]. To help improve this situation, in the context of the development of a National Immunization Strategy [6,7], an analytical framework has been developed to allow comprehensive and systematic evaluation of all factors which should be considered before making decisions regarding the pertinence of new immunization programs.

2. Development of the framework

The first step in the framework development was to contact key scientific and public health experts involved in the planning of immunization programs across Canada. A se-

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ries of names were provided by the Chief Medical Officers of Health or their equivalents in all Canadian provinces and territories. A questionnaire was sent to these persons asking what factors were important in recent decisions regarding publicly-funded immunization programs in their jurisdiction. They were also invited to provide information regarding the structures and processes for program planning.

A total of 23 questionnaires were received. This includes group responses for New Brunswick, Ontario, Alberta, British Columbia, and Nova Scotia. All provinces and territories except for Nunavut and the Yukon were represented. Responses representing potential decision-making criteria were entered into an Excel database and factors identified in three publications were also added [8–10], to reach a total of 194 items. Multiple mentions of the same criteria were eliminated as were different wordings representing the same concept (i.e. vaccine price and vaccine cost). The list was returned to participants for validation and tested in expert committee meetings. This produced a total of 58 different criteria, which were grouped into 13 categories, inspired by the work by White and Mathias [10]. The final version of the framework is presented in the Appendix.

3. Content of the framework

3.1. Burden of disease

In a public health perspective, the burden of disease is an important factor to set priorities. Vaccines were first developed to prevent frequent and deadly diseases such as smallpox, diphtheria, tetanus, infant pertussis, poliomyelitis, or measles, and the relevance of the programs implemented during the 20th century cannot be questioned. However, new vaccines developed during the last ten years are targeting less frequent or less severe conditions, and investments for their prevention have to be weighted against other competing health priorities. The need to justify new programs led to epidemiological studies aiming to assess precisely the health and economic impact of vaccine preventable diseases in Canada, including varicella [11–13], pneumococcal infections in children [14,15], serogroup C meningococcal disease [16], and adolescent pertussis [17–19].

3.2. Vaccine characteristics

Efficacy and safety are the main criteria in the initial evaluation of a new product. When the decision was made in Quebec to use the new serogroup C conjugate meningococcal vaccine instead of the polysaccharide vaccine to control an outbreak in 2001, the high effectiveness in young children of the former and its capacity to induce long-term memory were critical arguments [4]. When acellular pertussis vaccines were introduced in Canada, safety above all other considerations was decisive for their immediate adoption [20].

3.3. Immunization strategy

Sometimes, public health objectives can be attained via different immunization strategies, and the control of influenza is a good illustration. A universal vaccination program was implemented in Ontario, in 2000, while a “high-risk” approach is still used in the other provinces [21]. Unfortunately, the relative cost-effectiveness of the two strategies has not yet been evaluated.

3.4. Cost-effectiveness

With the increasing cost of vaccine products, cost-effectiveness analyses are needed to justify new programs, especially because long-term, recurrent expenditures are involved. In Canada, the first economic analysis was performed for the influenza vaccination of health care workers in 1991 [22]. Presently, this type of information is systematically requested and cost-effectiveness analyses have been produced for the two-dose measles program [23], the adult pneumococcal program [24], the varicella program [25,26], the infant pneumococcal [27–29] and serogroup C meningococcal programs [16]. Although not always cost-saving, immunization programs generally compare well with other health interventions [30,31]. It seems, however, that the absolute cost of a program is perceived to be more important than the predicted marginal cost-effectiveness ratios in the short-term perspective of some decision-makers.

3.5. Acceptability

The demand for a new program is a very powerful argument for decision-makers at the political level. Consider for example the case of serogroup C meningococcal disease, which generates a lot of anxiety in the population and attracts enormous media attention, due to the unpredictable, rapid onset of this disease and its serious consequences. A survey in Quebec in 2002 found that 86% of respondents felt that the conjugate vaccine should be included in the routine childhood immunization series [32]. Support for a vaccine against (pneumococcal) pneumonia was 60%, and only 41% for a vaccine against chickenpox. Despite the fact that the varicella program is the most favourable program from an economic point of view [25,26], and also that the greatest disease reduction can be achieved from a program using the seven-valent pneumococcal conjugate vaccine [28], a routine one-dose meningococcal program was introduced in Quebec in 2002. No decision has been made yet for the other two vaccines.

3.6. Feasibility

The best immunization strategies have no value if they are impossible to carry out in practice. Past experience has

shown that it is always easier to implement a new vaccine if it is combined with an existing vaccine or if it may be administered in the same visit as another vaccine. This was indeed the case for the replacement of the live oral polio vaccine by the inactivated combined injectable polio vaccine [1]. In certain cases, practical aspects require vaccine doses to be given which are not strictly necessary. An example is the second dose of the mumps vaccine at the same time as the indispensable second dose of measles vaccine and the less indispensable second dose of rubella vaccine [1].

3.7. Ability to evaluate

All immunization programs must be evaluated in terms of their safety and population effectiveness. In addition, public health authorities must be accountable to taxpayers. In Quebec, there is a well-established tradition of including an evaluative component in all new immunization programs. The usefulness of this type of investment was demonstrated after the mass serogroup C meningococcal immunization campaign in Quebec (using the polysaccharide vaccine) in 1992–1993, in which post-implantation studies alerted of the poor performance of this vaccine in young children and the short duration of protection [4].

3.8. Research questions

New immunization programs are often implemented before important scientific questions can be resolved. A current example is the fact that the duration of protection given by the type C meningococcal conjugate vaccine given at 12 months of age is not yet known [33], while this program aims to prevent invasive meningococcal infections until adulthood. In contrast, uncertainty about scientific questions may block adoption of a program. For example, uncertainty about the impact of a varicella immunization on the incidence of shingles in the adult population [34] is a factor, which has delayed implementation of this program in several provinces.

3.9. Equity

Applying principles of equity applied to immunization in Canada should mean that vaccines are freely accessible to populations, which can benefit from them. The supposedly universal nature of Canadian health care is often cited as an example to follow for other countries. Problems of access to vaccines occurred with the first varicella vaccine in Canada, which had to be stored frozen. This caused several problems for the distribution network, particularly in outlying regions. During the Canadian Varicella Consensus Conference in 1999, availability of a refrigerator-stable vaccine was considered as a *sine qua non* criterion for adoption of a universal program [35]. Fortunately, the pharmaceutical companies in-

volved rapidly met this challenge and refrigerator-stable varicella vaccines were quickly developed and commercialized [1].

3.10. Ethical considerations

In Canada, there are no mandatory immunizations, and regulations regarding immunization in schools or workplaces allow exemptions in certain cases, or are challenged if no exemptions are allowed [36]. Important measures have been taken by public health authorities to supply the best possible information on vaccine products and to ensure informed choices by the populations, via publications, Internet sites, or information sheets given during visits for vaccinations [1].

3.11. Legal considerations

In the practice of curative medicine, certain medications are often used in a manner different than that originally recommended by the manufacturer and defined in the original licensure of the product. The principle of freedom of practice in treatment is harder to apply in the areas of prevention and publicly-funded immunization programs. For example, mounting evidence indicates that a single dose of the hepatitis A vaccine gives good long-term protection and that the marginal effectiveness of the second dose is quite low [37]. Therefore, implementation of a one-dose hepatitis A vaccination program could be considered as a cost-effective option. With resources saved by this program, it would theoretically be possible to invest in other programs to maximize health benefits for the population. However, this type of approach has the potential problem of legal action in the case of vaccine failures.

3.12. Conformity of programs

In Canada, there is much variation in publicly-funded vaccination programs between jurisdictions which are not justified by epidemiological factors [6]. The lack of standardization of programs could have negative consequences, for example when a vaccination strategy increases the age of infection (and therefore the severity of disease) for the non-vaccinated population. This is the case for varicella [38].

3.13. Political considerations

Also, it is important to consider political aspects of immunization programs, which can involve political benefits or risks. Mass meningococcal immunization programs had political benefit in Quebec as they responded to demands from the public and also attenuated much negative media coverage of disease outbreaks [4]. Political risks and problems are present in the case of pre-exposure smallpox vaccination in the United States for certain workers, which has caused much disagreement and debate [39], while in Canada discussions

Table 1

Desirability of immunization programs against serogroup C meningococcal disease, varicella and pneumococcal disease according to different criteria (percentage of maximal score), as assessed by the Population Health Immunization Subcommittee (PHIS) and by the *Comité sur l'Immunisation du Québec (CIQ)*

Criteria	Serogroup C meningococcal disease (%)	Varicella (%)	Pneumococcal disease (%)
Disease characteristics and burden	73 64	87 59	93 91
Vaccine characteristics	78 82	70 69	82 78
Immunization strategies	84 79	76 72	66 88
Social and economic costs and benefits	61 54	74 56	74 34
Feasibility and acceptability	90 86	51 64	82 72
Ability to evaluate	79 93	71 88	69 86
Research questions	64 68	62 56	65 75
Other considerations including equity, politics and legal issues	68 77	61 65	71 72
Overall, this program should be publicly-funded	72 79	85 78	84 94

Conversion method: percentage of maximal score = $[(0 \times \text{response very low desirability} + 1 \times \text{response low desirability} + 2 \times \text{response intermediate desirability} + 3 \times \text{response high desirability} + 4 \times \text{response very high desirability}) / 4 \times \text{number of responders}] \times 100\%$. Number of participants = 21 for PHSC, and 8 for CIQ. CIQ responses include aggregated percentages for categories 5–6, and 9–13 of the framework.

in this area are quite laborious, especially given our political structure.

4. Use of the framework

In Quebec, the framework has been used to structure the reports on the pertinence of control programs against varicella [40], pneumococcal [41], and serogroup C meningococcal disease [42]. The framework was also used in consensus-building and prioritization conferences that were carried out with the Health Canada Population Health Immunization Subcommittee, on February 25, 2002, in Toronto, and with the “Comité sur l'Immunisation du Québec” on March 14, 2003, in Longueuil (Quebec). First, the relative merits of the three programs were presented to participants, using each of the criteria included in the framework. Participants were then asked to mark the desirability of each program using a five-item Likert scale, ranging from very high to very low desirability. Results are presented in Table 1, and expressed as a percentage of the maximal score. Congruence in the opinion of the two groups is striking, although there are a few exceptions (i.e. burden of varicella, and cost-effectiveness of the three programs). This observation suggests that the use of the framework increases the reliability in decision-making. Feedback from participants also brought the suggestion that the general categories of the framework be adapted into educational tools for teaching health professionals and informing the public about immunization programs.

5. Conclusion

Starting from published material and the experience of Canadian scientists and public health professionals, a series of essential questions has been developed and the elements which should be analyzed in the planning of publicly-funded immunization programs are presented. The proposed analytical framework may be utilized to structure a report or a presentation on the pertinence of a new program, or can structure discussions and consensus-building activities in expert committees. It can also serve as a tool for teaching and public education. The framework has proven to be a useful tool to build awareness and encourage more thorough and systematic evaluation of potential immunization programs. However, to have a more significant impact on decision-making in Canada, this tool must be integrated into a larger process of organizational change which integrates aspects of this tool into appropriate structures and processes which will meet the needs of decision-makers in their various contexts in a timely manner. This requires sustained, multiple and ongoing interactions among those involved in immunization program planning in Canada, combined with the will and resources for improving this process in the coming years.

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Appendix A. List of criteria included in the analytical framework for evaluating immunization programs

1 Burden of disease

Question 1: 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, of 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.

2 Vaccine characteristics

Question 2: 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 manufactures, 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 adverse events, contraindications, precautions.

- 2.11 Potential interaction with other vaccines.

- 2.12 Potential impact of immunization program on resistance to antibiotics and antivirals.

3 Immunization strategy and program

Question 3: Is there an immunization strategy which allows 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.

4 Cost-effectiveness of program

Question 4: Is it possible to obtain funding for the program and are cost-effectiveness indices comparable to those of other health care interventions?

- 4.1 Vaccine cost which is determined, among other factors, by the number of companies distributing the vaccine in Canada and their marketing strategy.
- 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 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 to other vaccines and other health care interventions.

5 Acceptability of vaccine program

Question 5: 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.

6 Feasibility of program

Question 6: 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, ...).
- 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.

7 Ability to evaluate programs

Question 7: 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 Availability of information systems for monitoring reduction of disease incidence, complications, sequelae, and mortality.
- 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.

8 Research questions

Question 8: Have important research questions affecting implementation of the program been adequately addressed?

- 8.1 Main uncertainties concerning effects of vaccine and impacts of program.
- 8.2 Ongoing and planned research projects in the fields of vaccine development, immunogenicity, efficacy and safety.
- 8.3 Need for research to assist evaluation, planning and decision-making regarding this particular program and proposals to meet these needs in a timely manner.
- 8.4 Need for a pilot immunization program.

9 Equity of the program

Question 9: 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.

10 Ethical considerations

Question 10: 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.

11 Legal considerations

Question 11: 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).

12 Conformity of program

Question 12: Does the planned program conform to those planned or implemented elsewhere (other regions, countries)?

- 12.1 Conformity of new program with planned or existing programs in other jurisdictions and countries.

13 Political considerations

Question 13: 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.

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