



The Hospital for Sick Children
Technology Assessment at SickKids (TASK)

**SYSTEMATIC REVIEW OF THE COST-EFFECTIVENESS
OF INFLUENZA IMMUNIZATION PROGRAMS: A
CANADIAN PERSPECTIVE**

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REPORT HIGHLIGHTS

The Report Highlights consists of a summary of the full report with the same name and should be evaluated in conjunction with the full report and its appendices. Full documents are available for download

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Conflicts of Interest

During the timing of writing this technical report, ET was an employee of AstraZeneca Canada.

Introduction

Commonly referred to as “the flu,” seasonal influenza is an acute viral respiratory infection affecting 10% to 20% of Canadians each year [1]. In response to the seasonal influenza threat, each province and territory in Canada offers its own approach to immunizing their residents. These publically funded programs are “universal” or “targeted.” A universal program provides publically funded vaccine for all residents; a targeted program uses specific criteria so that only certain groups receive publically funded vaccine. While there have been economic evaluations to assess the cost-effectiveness of alternative program designs, there has been no comprehensive reviews of the literature. It remains unclear whether a targeted or universal program provides more benefit and value for money. Policy makers require evidence to consider what program design is optimal under budget constraints to best protect the population against influenza.

Key Messages

- Each province and territory in Canada has designed and adopted its own approach to immunizing their respective populations. These publically funded programs can be “universal” or “targeted.”
- Evidence is unclear as to whether a targeted program or a broader universal program provides more benefit and value for money.
- While the quality of the included studies was strong overall, there were some weaknesses, such as clarity in definitions of vaccine efficacy, justifications in study design, and discounting.
- Effects of herd immunity was not specified in many economic evaluations.
- From the societal perspective and in many cases the health care system perspective, seasonal influenza vaccination was found to be a cost-effective strategy across several population subgroups.
- As of June 2015, influenza immunization policies differ across Canada, with six provinces (AB, SK, MB, ON, NS, NL) and all three territories offering universal influenza immunization programs and three provinces (BC, QC, NB) providing targeted influenza immunization programs.

Objectives

The primary research objective was to systematically review and appraise the quality of published economic evaluations of influenza immunization, describe their scope and diversity, and discuss and determine the cost-effectiveness in specific population subgroups. A secondary research objective was to highlight, compare and contrast the various influenza immunization policies across Canada.

Methods

Systematic Review

The literature in citation databases (MEDLINE, EMBASE), in the biomedical and health economic field, and grey literature sources were systematically searched. Specific inclusion and exclusion criteria were developed to ensure literature relevance. Results of the search were reviewed to identify relevant studies meeting all inclusion/exclusion criteria and quality appraisal was performed.

Quality Appraisal

Each study was examined and appraised using the Scottish Intercollegiate Guidelines Network (SIGN) quality appraisal tool for economic evaluations [2] and supplemented with five additional vaccine specific questions, created and adapted based on guidance from the *WHO Guide for Standardization of Economic Evaluations of Immunization Programmes* [3]. Data were extracted from each economic evaluation including payer perspective, time horizon, study design, discounting, and costs and health outcomes for intervention and comparator groups.

Results

Systematic Review

The study selection process is depicted in Figure 1. Using the search strategy, 4786 studies were identified. After removal of 565 duplicates, 4221 titles were screened for eligibility. A total of 4113 studies were removed based on title screening and 68 studies were removed based on abstract screening, resulting in 41 relevant studies for review and quality appraisal. The analytical technique used most frequently among these economic evaluations was the CBA which comprised 20 of the included evaluations. CUAs were used in 19 of the studies and CEAs were performed in two studies. All studies took a societal, health care system, individual, or third party payer perspective with some studies adopting multiple perspectives.

Quality Appraisal

Based on the quality appraisal, ten low quality studies were excluded resulting in 31 high quality studies [4-34]. Table 1 presents results from the SIGN checklist and Table 2 presents results from the additional vaccine related questions.

Clarity on sources and key definitions were the main driver of lower quality. Excluded studies lacked refined definitions of populations, vaccine efficacy, health outcomes, or perspective taken in the analysis. Some studies also did not provide a full incremental economic evaluation. When considering more logistical considerations of vaccination, the studies were generally descriptive and clear about the administration of the vaccine; however most of the studies were not specific with regard to herd immunity.

Discussion

Certain population subgroups that reflect different degrees of risk and cost-effectiveness emerged from the literature: children and adolescents, pregnant and postpartum women,

healthy working adults, and high risk patients. The economic evaluations included were conducted from the societal, public health payer, and third party health payer perspectives, generally considered appropriate and useful for policy makers.

While the quality of the included studies was strong overall, there were some significant weaknesses that the appraisal revealed, such as clarity in definitions of vaccine efficacy, justifications in study design, and discounting. Questions regarding vaccine administration, wastage, and herd immunity should be considered and it was found that despite the importance of indirect protection in vaccination, most studies were not specific with regard to herd immunity.

Vaccinating pregnant women was generally found to be cost-effective. For children and adolescents, all included studies agreed that compared to no vaccination, vaccination is more effective in improving health outcomes, but depending on the age and risk of the children, cost-effectiveness varied as the age of children increased. Overall, vaccinating older children was less cost-effective as seen across all of the studies, regardless of risk. Younger children tended to derive more benefit from the influenza vaccine than older children and as a result, increased age was associated with an increased cost per unit of health benefit gained.

For high risk adults, there was a mix of different results depending on population characteristics and model inputs. For high risk adults, groups with a pre-existing risk of complications were examined. It was found that vaccinating working age cancer patients was extremely cost-effective from the societal perspective and that vaccinating health care workers and adults with underlying illnesses was cost-effective from the perspective of the health care system. Results for healthy working age adults were mixed. This subgroup is large and diverse relative to the other subgroups and the health outcomes of infection are generally not as overtly severe. Overall, the results in healthy working age adults support vaccination, but in several studies the results were sensitive to model inputs such as assumed vaccine efficacy, rate of uptake, and lost productivity. Additional studies are likely necessary.

Essential factors in the study findings are the perspective taken in the analyses, model inputs specific to each economic evaluation, and the age-associated risk of infection and illness severity of the subgroup.

The policy analysis indicated that as of June 2015 immunization policies differed across Canada. Six provinces (AB, SK, MB, ON, NS, NL) and all three territories offer universal influenza immunization. Among the groups of provinces offering targeted programs, there were differences with some provinces including certain high risk groups while others did not. It may be more cost-effective, pragmatic and politically expedient to effect coverage for high risk target groups by offering a universal, rather than a targeted program.

Conclusions

From the societal perspective and in many cases the health care system perspective, seasonal influenza vaccination was found to be a cost-effective strategy. Vaccinating pregnant and postpartum women compared to only vaccinating high risk pregnant and postpartum women was generally cost-effective. If indirect protection from mother to neonate was considered in the analysis, vaccination was cost-effective or in some cases, a dominant strategy. Similarly, vaccinating all children and adolescents against seasonal influenza was generally cost effective, with robust evidence for infants, toddlers, and adolescents. If indirect protection from children to parents, caregivers, and household was considered in the analysis, vaccination was cost-effective or in many cases, a dominant strategy. The cost-effective evidence for vaccinating healthy working age adults (18 to 64 years old) was mixed and sensitive to inputs based on geographic location, vaccine efficacy, and valuation of lost productivity. Overall, universal mass immunization programs were favoured as a cost-effective strategy. Programmatic considerations such as administration, and incremental uptake rates were important to the sensitivity of the results.

Influenza immunization policies differ across Canada. Offering universal influenza immunization may be more effective and equitable for all Canadians if provincial programs evolve into a national immunization strategy.

Figure 1: Flow Diagram of Study Selection Process

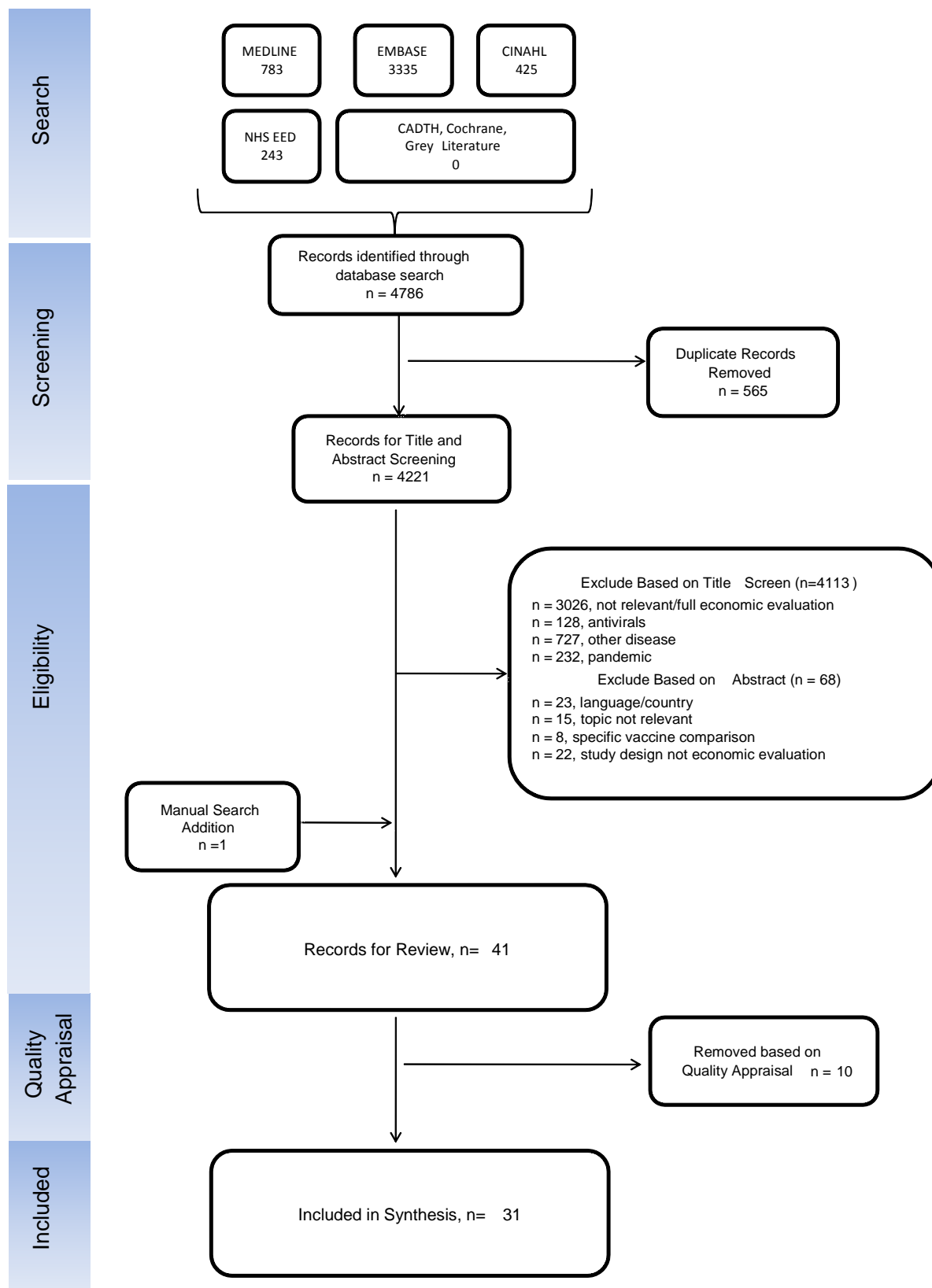


Table 1: Quality appraisal results based on the SIGN checklist (n=31)

Scottish Intercollegiate Guidelines Network (SIGN)	Yes	No	Can't Say
(1) The study addresses an appropriate and clearly focused question	41	0	0
(2) The economic importance of the question is clear	37	1	3
(3) The choice of study design is justified	5	35	1
(4) All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately	30	5	6
(5) The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately	29	3	9
(6) If discounting of future costs and outcomes is necessary, it been performed correctly	10	29	2
(7) Assumptions are made explicit and a sensitivity analysis performed	33	4	4
(8) The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes	36	3	2
(9) The results provide information of relevance to policy makers	32	6	3

Table 2: Quality appraisal results based on additional vaccine related questions (n=31)

Additional Vaccine Questions	Yes	No	Can't Say
(1) Details of vaccine administration were clearly stated	32	5	4
(2) Was an appropriate definition of vaccine efficacy/effectiveness provided and referenced?	34	6	1
(3) Were vaccine safety and adverse events considered?	24	13	3
(4) Vaccine wastage was considered in the study	4	30	7
(5) Indirect effects such as community or herd immunity are considered in the conclusions	6	26	9

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