Controversy

Mass influenza vaccination in Ontario: Is it worthwhile?

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Articles under the Controversy flag appear in the form of a debate. Dr. Schabas (page 36) and Dr. Demicheli were each asked to present their view of the mass vaccination program being carried out against influenza in Ontario. Rebuttals follow on pages 40 and 41.

The recent decision of the Ontario government to make the influenza vaccine available at no charge to all its citizens for the forthcoming "influenza season" may produce mixed reactions.[1] This decision involves the extension of the current vaccination policy (of actively offering the vaccine to elderly and ill people with a high probability of developing serious complications and dying) to healthy adults, regardless of their risk status.

Influenza is a global disease with a high societal burden, but the decision calls into question the rules of evidence-based decision-making, which are still largely undefined in this particular field of public health.

Before embarking on public health vaccination campaigns of whole populations, a set of fundamental questions must first be answered:[2]

- Is the condition or the disease to be prevented important?
- Do we know enough about the incidence, the natural history and the burden of this disease to reasonably forecast the likely impact of immunization?
- Does the vaccine work? (That is, is it effective in preventing clinical cases of influenza?)
- Is the vaccine safe and acceptable? (That is, does it have adverse effects and, if so, are they localized or systemic and of short or long duration?)
- Does the vaccine make the best use of resources available compared with doing nothing or other preventive activities?

The clinical and societal importance of influenza is usually taken for granted. Nevertheless, looking at the epidemiology of the disease and comparing it with other conditions, our knowledge of influenza appears only limited and indirect. The incidence and distribution of laboratory-confirmed cases of influenza A and B are only available from small samples, whereas information on the population distribution of influenza is based on a syndromic definition of cases usually known as influenza-like illness (ILI). The actual proportion of influenza A and B cases among ILI cases is not well known, but the few available studies indicate a modest proportion of probably less than 10%, regardless of age group.[3–6] The same considerations apply to outcomes such as mortality, hospital admissions and other complications that are conventionally measured in terms of "excess" incidence when epidemic and nonepidemic periods are compared. Thus, our knowledge comprises estimates of the generic impact of ILI during epidemic periods, but we do not know what share of the problem is directly caused by influenza A and B viruses. This greatly limits the value of studies that estimate comparatively the population impact of the vaccine.

The question of effectiveness is probably best answered by means of clinical trials or, whenever possible, by systematic reviews and meta-analysis of groups of trials such as those prepared and assembled in the Cochrane Library. In the case of the influenza vaccine, a systematic review of 20 randomized trials of the effects of the vaccine in healthy adults[7] shows that inactivated parenteral vaccines have an efficacy of 68% (95% confidence interval [CI] 49%–79%) in reducing virologically confirmed cases but only of 24% (95% CI 14%–33%) in reducing clinical (ILI) cases. Thus, only 1 of 4 vaccinated adults will acquire protection against the clinical illness. The use of the vaccine significantly reduces time off work, but the size of this effect (0.4 days) is not clinically relevant.

The rates of complication caused by influenza in these trials were very low, and the few trials that considered this as an outcome did not show a significant reduction in such rates through vaccination. The impact of the vaccine on admissions to hospital was assessed by only one trial that showed a favourable impact of the vaccine.

These findings are partly at odds with the conclusions reported in a previous meta-analysis of evidence for the effect of immunization on elderly people,[8] which showed greater clinical effectiveness, thus supporting the present worldwide policy of vaccinating only elderly people and other high-risk groups.

Questions about the safety of vaccines can only partly be answered by clinical trials, because possible long-term effects and rare adverse effects can only be assessed by means of observational studies carried out for longer periods of time (so-called "postmarketing" studies). In the case of influenza, both clinical trials and other types of studies show that safety does not appear to be a particular problem with any of the available vaccines. Millions of doses of influenza

vaccine are administered each year, and the current vaccines appear to be well tolerated. Serious or life-threatening adverse effects are rare.[9] However, the decision to extend the influenza vaccination program to a whole population may mean that safety issues will become of crucial importance. A study of young, healthy adults[7] in which the acceptability of influenza vaccination was assessed, by calculating individual preferences using a cost–utility study design, revealed that vaccines have such low population effectiveness and numerous local, trivial adverse effects that the trade-off was unfavourable.[10] This finding may have been partly influenced by the timing of this exercise, which was carried out in an interepidemic period when memories of the latest ILI peak were fading.

Finally, we turn to the issue of efficiency. The evidence strongly favours vaccines as the best way to prevent influenza A and B in healthy adults.[10] But do vaccines represent the best use of resources? The Ontario announcement quotes a cost–benefit study indicating a net benefit of about $40 per vaccination.[1] A study of British soldiers, based on 3 Cochrane reviews and a systematic review of the economics of influenza prevention, shows that the cost of preventing a clinical case of influenza was about Can$6200.[10] Which of the 2 studies are we to base our decisions on?

One of the few areas of consensus in the discipline of health economics concerns the difficulty inherent in generalizing results from single studies and the impossibility of transferring economic evaluations from one social context to another.[11] The growing economic literature on influenza vaccination shows (as frequently happens in the economics of vaccines) conflicting results for different studies and the existence of major methodological problems, suggesting the need for extreme caution in interpreting their conclusions.[12]

Given the quality of the information available and the cost of universal vaccination, the Ontario decision is probably not destined to be emulated elsewhere. We may, however, be tempted to consider this attempt as an experiment, a sort of pilot project. Unfortunately, the level of uncertainty that still surrounds the problem of influenza prevention is so high that the consequences of this decision, even if properly monitored and evaluated, will probably raise many new questions and leave the crucial ones unanswered.

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