Potential cost-effectiveness of a preventive hepatitis C vaccine in high risk and average risk populations in Canada

Krahn M D, John-Baptiste A, Yi Q, Doria A, Remis R S, Ritvo P, Friedman S

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
A policy of universal vaccination with a hepatitis C (HCV) vaccine was examined in two groups. One was a high-risk group, such as injection drug users (IDUs) who were human immunodeficiency virus (HIV) or HCV negative at the time of vaccination. The other was a low-risk group, such as 12-year-old school children.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised two hypothetical cohorts of individuals, HIV or HCV negative IDUs and 12-year-old school children.

Setting
The setting was primary care and the community. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 1979 and 2003. The cost data were obtained from studies published between 1995 and 2002. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' opinions.

Modelling
A Markov model was constructed to examine the economic and clinical consequences of the universal HCV vaccination strategy (in the two hypothetical cohorts of individuals) in comparison with no vaccination. Individuals were followed until all members of the cohort had died. The cycle length was one year. A simplified structure of the model and the health states included in the analysis were reported. The health states included different liver fibrosis stages (from no fibrosis to liver cirrhosis), decompensated cirrhosis, hepatocellular carcinoma, liver transplant and liver-related death. HCV prognosis was a function of liver fibrosis stage and HCV serologic status. Following the model, HCV-infected individuals initially had no fibrosis but progressed over time to more severe fibrosis stages. Antiviral therapy (ribavirin plus interferon) halted disease progression. Individuals who developed liver cirrhosis could develop decompensated liver disease or hepatocellular carcinoma and could either die from these complications or require a liver transplant. Progression was unidirectional and no regression was modelled.
Outcomes assessed in the review
The outcomes estimated from the literature were:

vaccine compliance;

HCV and HIV incidence and mortality;

the transition probabilities across health states;

the probabilities of treatment with combination therapy;

the probabilities of sustained response to combined treatment; and

utility values associated with health states.

Study designs and other criteria for inclusion in the review
A systematic review of the literature was carried out to identify relevant primary studies. No information on the design of the primary studies and patients' characteristics was given. The utility weights came from a study involving a sample of 200 HCV patients with all levels of disease severity.

Sources searched to identify primary studies
Clinical inputs were derived from a systematic review of MEDLINE, manual searches of bibliographies of identified articles, reviews of conference proceedings, studies by the investigators, and the investigators' files.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Thirty primary studies provided evidence.

Methods of combining primary studies
The primary estimates were pooled by calculating a weighted average. The weight was the inverse of the variance for the transition probability or number of patients in the study.

Investigation of differences between primary studies
Not stated.

Results of the review
The probability of vaccine compliance was 0.90 in the general population and 0.51 (range: 0.51 - 0.88) among IDUs.

The HCV incidence rate (per 100,000/year) in the general population was 7.4 (range: 7.4 - 16.3). Age-specific HCV incidence rates were also reported.

The HCV incidence rate among IDUs was 0.145 per person/year. The HIV incidence rate among IDUs was 0.01 per
person/year. The ratio of IDU mortality to general population mortality was 14.3.

The ratio of IDU HIV+ mortality to all IDU mortality was 2.5.

The probability of treatment with combination therapy depended on disease stage and ranged from 0.052 to 0.800.

Similarly, the probability of sustained response to combined treatment depended on disease stage and ranged from 0.208 to 0.432.

The utility weights were as follows:

Canadian population norms (sustained virological response, spontaneous resolution, never infected), 0.930 (range: 0.928 - 0.932);

mild or moderate chronic hepatitis, 0.73 (range: 0.64 - 0.83);

compensated cirrhosis, 0.74 (range: 0.66 - 0.83);

decompensated cirrhosis, 0.69 (range: 0.52 - 0.85);

liver transplantation, 0.70 (range: 0.63 - 0.77);

hepatocellular carcinoma, 0.51 (range: 0.26 - 0.76);

sustained virological responder, 0.77 (range: 0.63 - 0.77);

disutility of interferon therapy, 0.14 (range: 0.05 - 0.30);

utility associated with HIV infection, 0.80; and

utility associated with ongoing injecting drug use, 0.65.

Transition probabilities were also reported.

**Methods used to derive estimates of effectiveness**

Some assumptions were made to derive estimates of effectiveness. In particular, HCV vaccine efficacy was a conservative estimation based on the efficacy of other vaccines (such as hepatitis B vaccine).

**Estimates of effectiveness and key assumptions**

The vaccine response rate was 0.90.

The vaccine efficacy was 0.80.

The annual loss of immunity was 0.025.

Cessation of injection drug use was assumed to have been 1.0 in the age group 20-29 years, 0.74 in the age group 30-39, 0.4 in the age group 40-49, 0.09 in the age group 50-69, and 0 for individuals older than 70 years.

**Measure of benefits used in the economic analysis**

The summary benefit measure used was the quality-adjusted life-years (QALYs). These were obtained using a modelling approach. Quality of life and survival data were combined to calculate the QALYs. The utility weights were derived from a published study where the Health Utilities Index Mark 3 questionnaire was used. The short-term impairment in quality of life (disutility) associated with combination antiviral therapy was elicited using the EQ-5D. Lifetime cases of HCV and lifetime HCV-related deaths were also reported. Discounting was performed and an annual
discount rate of 3% was applied.

**Direct costs**
The authors stated that a societal perspective was adopted, but only direct medical costs appear to have been included in the analysis. The health services included in the economic evaluation were vaccine costs and administration, combination treatment, annual management of HCV (stage-dependent), and the treatment of HIV infection. The unit costs were not presented separately from the quantities of resources used because most costs were reported as macro-categories. The costs were estimated from published sources and a cost-to-charge ratio of 1.62 was used to convert estimated charges into actual costs. The resource use data were not reported. Discounting was relevant, as the costs were incurred over a long timeframe, and an annual rate of 3% was applied. All the costs were inflated to 2003 values using the Consumer Price Index for health and personal care.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the economic evaluation.

**Currency**
Canadian dollars (Can$). The costs were converted to Can$ at the purchasing power parity conversion rate. The exchange rate from US dollars ($) to Can$ was $1 = Can$1.31.

**Sensitivity analysis**
One- and two-way sensitivity analyses were carried out to assess the impact of variations in clinical and economic model inputs on the model results. A Monte Carlo simulation was also used to determine the confidence intervals (CIs) for expected costs, QALYs and cost-utility ratios.

**Estimated benefits used in the economic analysis**
In the cohort of IDUs, there were 460 lifetime cases of HCV (per 1,000), 139 lifetime HCV-related deaths (per 1,000) and 18,786 QALYs with vaccination, and 708, 227 and 17,202, respectively, with no vaccination. The vaccination strategy thus led to a reduction of 248 HCV cases and 88 deaths, and an increase of 1.584 QALYs.

In the cohort of average-risk 12-year-olds, there were 380 lifetime cases of HCV (per 100,000), 88 lifetime HCV-related deaths (per 100,000) and 26,558 QALYs with vaccination, and 560, 161 and 26,550, respectively, with no vaccination. The vaccination strategy thus led to a reduction of 180 HCV cases and 73 deaths, and an increase of 0.008 QALYs.

**Cost results**
The expected costs with and without vaccination were, respectively, Can$33,490 and Can$33,889 among IDUs (vaccination cost-saving), and Can$176 and Can$32 among average-risk 12-year-olds (difference Can$144; range: 76 - 211).

**Synthesis of costs and benefits**
An incremental cost-utility ratio was calculated to combine the costs and QALYs of vaccination in comparison with no vaccination.

Among IDUs, vaccination was dominant over no vaccination because it was more effective (+ 1.584 QALYs; 95%
confidence interval, CI: 0.431 - 3.100) and less costly (-Can$399).

Among average-risk 12-year-olds, the incremental cost per QALY gained with vaccination over no vaccination was Can$18,000 (95% CI: 7,000 - 66,700).

The sensitivity analysis showed that the cost-effectiveness of vaccination held to variations in all model inputs among high-risk individuals. However, in the average-risk scenario, the cost-effectiveness of vaccination was sensitive to HCV incidence, vaccine cost and the age of vaccination, although, in general, the cost per QALY remained below the threshold of Can$50,000.

The probabilistic sensitivity analysis suggested that vaccination was cost-effective. In particular, for the IDU population, the CI for the cost per QALY was -Can$740 to Can$340, while among average-risk 12-year-old individuals the CI for the cost per QALY was Can$6,949 to Can$66,691.

**Authors’ conclusions**

A hepatitis C (HCV) vaccine, even of moderate efficacy, would be cost-saving among high-risk individuals and cost-effective in low-risk populations.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparator was appropriate because no vaccination represented the actual standard care. In fact, no HCV vaccine is actually available. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from published data and the authors’ opinions. A systematic review of the literature was performed to identify the primary studies. However, limited information on the design and characteristics of the primary studies was provided. Thus, it was not possible to assess the quality and robustness of the primary sources. No inclusion criteria were used in the selection of the primary studies. Further, there were few details of the methods used to extract the data from each study and to combine the primary estimates were reported. Given the lack of data, a key assumption was made on vaccine efficacy. However, the issue of uncertainty was extensively addressed in the sensitivity analysis.

**Validity of estimate of measure of benefit**

QALYs were used as the summary benefit measure, which was appropriate because they capture the impact of survival and quality of life in a single measure. Discounting was applied, as recommended by Canadian guidelines. Utility adjustments were derived from the literature and information on the source of the data was reported. QALYs are comparable with the benefits of other health care interventions.

**Validity of estimate of costs**

The costs included were not consistent with the perspective adopted in the study. The authors stated that a societal perspective was used, but the indirect costs were not included in the economic evaluation. There was limited information on the unit costs and quantities of resources used. A detailed breakdown of the cost items was not provided, as some costs were presented as macro-categories, and this limits the possibility of replicating the results of the study in other settings. The source of the cost data was reported. The costs were treated deterministically in the base-case, but the cost estimates were varied in the sensitivity analysis. The price year was reported, which aids deflation exercises in other time periods. Discounting was relevant and was appropriately carried out.

**Other issues**

The authors did not make extensive comparisons of their findings with those from other studies. In terms of the issue of the generalisability of the study results to other settings, the authors stated that the transferability of their conclusions
depends on the degree to which the HCV epidemiology and HCV health care costs in other countries are similar to those of Canada. In particular for the general population, the cost-effectiveness of vaccination depends on the local burden of disease, the cost of caring for individuals with HCV infection and, notably, the cost of reaching vaccinees and administering the vaccine.

The authors noted some limitations of their analysis. Such limitations were mainly related to the speculative nature of some assumptions, owing to the fact that an HCV vaccine does not actually exist in the market. Moreover, the study did not capture the full benefits of vaccination such as preventing secondary and tertiary infection in non-cohort members.

Implications of the study
The study results supported the development of an HCV vaccine for the prophylaxis of high-risk individuals. The vaccine might also be cost-effective in individuals at average-risk of HCV.

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Other publications of related interest


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