What is the cost-effectiveness of hepatitis C treatment for injecting drug users on methadone maintenance in New Zealand

Sheerin I G, Green F T, Sellman J D

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
Treatment for hepatitis C virus (HCV) was assessed using either conventional combination therapy (CCT; alpha-interferon combined with ribavirin) or combination therapy with pegylated interferon (PEG) in injecting drug users (IDUs) on methadone maintenance therapy (MMT).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hypothetical cohorts of 1,000 Maori and non-Maori IDUs on MMT.

Setting
The setting was primary care. The economic study was carried out in New Zealand.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
A Markov model was used to model cohorts of patients, changes in their health states, and the effects of MMT and antiviral therapy on morbidity and mortality. Cohorts of 1,000 patients were used. The lifetime horizon was used. Entry to MMT was modelled as a chronic relapsing process with admissions to methadone starting at age 23, with 50% dropping out of treatment in the first year. A subsequent admission to methadone was modelled again with a 50% dropout rate before further entry to treatment, with an average age finally stabilising on methadone of 31 years. The model compared six main treatment options:

- MMT with no treatment for HCV;
- current situation with 5% receiving CCT after stabilising on MMT at age 31;
all eligible patients receive CCT after stabilising on MMT at age 31;
all eligible patients receive CCT after stabilising on MMT at age 26;
all eligible patients receive PEG after stabilising on MMT at age 31; and
all eligible patients receive PEG after stabilising on MMT at age 26.

Outcomes assessed in the review
The authors reported that the model health states and probabilities were described in detail elsewhere (Sheerin et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details).

The following annual transition probabilities were assessed in the review:

- no HCV infection to HCV positive;
- no HCV infection to death;
- HCV positive to no HCV infection;
- HCV positive to chronic HCV;
- HCV positive to death;
- chronic HCV to hepatocellular carcinoma (HCC);
- chronic HCV to compensated liver cirrhosis (LC);
- chronic HCV to death;
- compensated LC to HCC;
- compensated LC to decompensated LC;
- decompensated LC to liver transplant;
- decompensated LC to death;
- HCC to death; and
- liver transplant to death.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

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

Methods used to judge relevance and validity, and for extracting data

Not reported.

**Number of primary studies included**
Seventeen primary studies were included in the review.

**Methods of combining primary studies**
Data from the primary sources were combined, but the methods used were not discussed. In some cases, one study may have been used for a base-case estimate and another for sensitivity limits.

**Investigation of differences between primary studies**
Potential differences between the primary studies were not discussed in the analysis.

**Results of the review**
The annual transition probabilities were as follows:

- no HCV infection to HCV positive, 0.84;
- no HCV infection to death, unspecified;
- HCV positive to no HCV infection, 0.2 to 0.3;
- HCV positive to chronic HCV, 0.7 to 0.8;
- HCV positive to death, unspecified;
- chronic HCV to HCC, 0.001;
- chronic HCV to compensated LC, 0.010 to 0.0221;
- chronic HCV to death, unspecified;
- compensated LC to HCC, 0.015 to 0.020;
- compensated LC to decompensated LC, 0.025 to 0.050;
- decompensated LC to liver transplant, 0.2;
- decompensated LC to death, 0.10 to 0.13;
- HCC to death, 0.5 to 0.8; and
- liver transplant to death, 0.02.

**Methods used to derive estimates of effectiveness**
Assumptions based on published literature and personal communications were used to supplement the transition probabilities.

**Estimates of effectiveness and key assumptions**
The main assumptions were as follows:
excess mortality for Maori was the same as for non-Maori;

IDUs were one-quarter as likely to die while in MMT;

after stabilisation on MMT, 16% per annum dropped out of MMT;

84% had HCV of which 70 to 80% became chronic cases;

25% had persistently normal liver enzymes and did not meet HCV treatment criteria;

non compliance with CCT was 19%;

non compliance with pegylated interferon and ribavirin was 14%;

sustained viral response to CCT was 31% for genotype 1 and 64% for other genotypes; and

sustained viral response to pegylated interferon and ribavirin was 42% for genotype 1 and 80% for other genotypes.

Please refer to the paper for a complete list of assumptions, relating principally to epidemiological factors or modelling assumptions.

**Measure of benefits used in the economic analysis**
The authors used life-years saved (LYS) as their summary measure of benefits.

**Direct costs**
The costing was carried out from the perspective of the New Zealand taxpayer and did not include private costs to the patients. The costs of methadone were calculated from the Christchurch Methadone Programme. These focused on staffing, facilities, and laboratory testing including the cost of the assessment and basic counselling. Prescription costs were taken from a published source specific to New Zealand. As CCT was not funded at that time in New Zealand, an estimate was made from the Australian Pharmaceutical Benefit Schedule. This included the costs of screening, follow up appointments, liver biopsy, laboratory tests and pharmaceuticals. Pegylated interferon costs were assumed to be 20% higher than current costs for conventional CCT. Costs of HCV related liver disease were tracked from the time of commencement of injecting drug use until the last member of the cohort had died. The costs were discounted at rates of 0, 3 and 5%. The price year was 1999/2000 and the costs were inflated using the rate of inflation.

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

**Indirect Costs**
The authors did not estimate the indirect costs and private costs to the patient, which was appropriate for the perspective adopted.

**Currency**
New Zealand dollars (NZ$).

**Sensitivity analysis**
Sensitivity analyses were carried out to assess the impact of altering the transition probabilities in the model and compliance with treatment.
Estimated benefits used in the economic analysis

The results were presented for the base-case only, in which mortality was assumed to be 25% of the mortality rate of IDUs not in MMT. The results were presented as LYS per 1,000 IDUs by differing treatment options.

MMT with no treatment for HCV (MMT only) yielded 2,435 LYS for non-Maori men, 3,697 LYS for Maori men, 4,125 LYS for non-Maori women and 5,315 LYS for Maori women.

The current situation of 5% receiving CCT after stabilising on MMT at age 31 yielded 2,448 LYS for non-Maori men, 3,710 LYS for Maori men, 4,140 LYS for non-Maori women and 5,324 LYS for Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 31 yielded 3,077 LYS for non-Maori men, 4,040 LYS for Maori men, 4,824 LYS for non-Maori women and 5,829 LYS for Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 26 yielded 3,407 LYS for non-Maori men, 4,454 LYS for Maori men, 5,188 LYS for non-Maori women and 6,087 LYS for Maori women.

All eligible patients receiving PEG after stabilising on MMT at age 31 yielded 3,244 LYS for non-Maori men, 4,160 LYS for Maori men, 5,050 LYS for non-Maori women and 5,983 LYS for Maori women.

All eligible patients receiving PEG after stabilising on MMT at age 26 yielded 3,619 LYS for non-Maori men, 4,611 LYS for Maori men, 5,483 LYS for non-Maori women and 6,304 LYS for Maori women.

Cost results

The results related to the net cost (not discounted) of MMT and HCV treatment for the different strategies for a cohort of 1,000 IDUs. Please refer to the paper for a complete breakdown of the costing results.

MMT only cost NZ$36,329,355 non-Maori men and NZ$41,645,639 for non-Maori women.

The current situation of 5% receiving CCT after stabilising on MMT at age 31 cost NZ$36,421,667 for non-Maori men and NZ$41,741,949 for non-Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 31 cost NZ$38,541,276 for non-Maori men and NZ$40,227,567 for non-Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 26 cost NZ$28,352,553 for non-Maori men and NZ$32,866,868 for non-Maori women.

All eligible patients receiving PEG after stabilising on MMT at age 31 cost NZ$40,122,562 for non-Maori men and NZ$42,004,981 non-Maori women.

All eligible patients receiving PEG after stabilising on MMT at age 26 cost NZ$29,424,111 for non-Maori men and NZ$34,143,254 non-Maori women.

Synthesis of costs and benefits

The results related to the cost per LYS (discounted at 3%) for the different strategies for a cohort of 1,000 IDUs. Please refer to the paper for a complete breakdown of the costing results.

MMT only cost NZ$14,920 (NZ$25,397) per LYS for non-Maori men and NZ$10,096 (NZ$25,035) for non-Maori women.

The current situation of 5% receiving CCT after stabilising on MMT at age 31 cost NZ$14,880 (NZ$25,406) per LYS for non-Maori men and NZ$10,084 (NZ$25,047) for non-Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 31 cost NZ$12,527 (NZ$25,038) per LYS for non-
Maori men and NZ$8,339 (NZ$24,377) for non-Maori women.

All eligible patients receiving CCT after stabilising on MMT at age 26 cost NZ$8,323 (NZ$18,534) per LYS for non-Maori men and NZ$6,336 (NZ$18,602) for non-Maori women.

All eligible patients receiving PEG after stabilising on MMT at age 31 cost NZ$12,368 (NZ$25,505) per LYS for non-Maori men and NZ$8,318 (NZ$24,757) non-Maori women.

Sensitivity analyses revealed that at the mid-range estimates of disease progression and at the upper rate of disease progression, the cost-effectiveness of HCV treatment had a similar order of magnitude to the base-case model.

Authors’ conclusions
On the basis of incremental cost-effectiveness ratios, the provision of conventional combination therapy (CCT; alpha-interferon plus ribavirin) to methadone patients is cost-effective, even though sustained response rates are lower than those for pegylated interferon combined with ribavirin (PEG).

CRD COMMENTARY - Selection of comparators
The authors compared treatment for HCV using CCT (alpha-interferon plus ribavirin) or PEG (pegylated interferon plus ribavirin). Different treatment strategies associated with the two technologies were assessed, one of which represented current practice. Both technologies were reported to be relatively new to the authors' setting. In addition, neither was funded by the public health system at the time of the study, thus providing the ideal motive to assess their cost-effectiveness.

Validity of estimate of measure of effectiveness
Few details of the review of published literature were reported. However, the authors did report that details of the model are reported elsewhere, and this account may well provide further information concerning the review. It was likely that systematic review methodology was not employed as the review aimed to populate a model and, therefore, sources that provided data appropriate for the model parameters were most likely found.

Validity of estimate of measure of benefit
The number of LYS was used as the summary measure of health benefits. This measure enables broad comparisons with other health technologies.

Validity of estimate of costs
The costing was carried out from the perspective of the New Zealand taxpayer. All categories of cost relevant to this perspective were included in the analysis. The costs to the patient and broader costs to society were not relevant to this perspective. A breakdown of the cost estimates, including unit costs, was not reported although the authors presented extensive cost results for the various treatment strategies and sub-populations. This would not enable the analysis to be easily reworked for other settings. The costs were treated deterministically and a sensitivity analysis was not conducted to test variability in the data. Discounting was appropriately carried out, as the costs were incurred over more than two years, and the costs were appropriately inflated to 1999/2000 levels. This improves the reproducibility of the results.

Other issues
The authors were able to draw comparisons between their own study and those of other authors, suggesting the results are more conservative compared with other research, and between their cost-effectiveness results and other treatments currently funded in New Zealand. The issue of generalisability of the results to other settings was not explicitly
addressed, although the nature of the analysis means that the model might easily be repopulated with data for alternative settings, thus enabling authors to estimate the impact of treatments in their own settings. The authors provided a range of base-case and sensitivity analysis results for a range of treatment strategies and sub-populations. In one sense the authors tried to achieve too much from this single study. Hence, the results might have had more impact and greater clarity if they had been presented separately. The conclusions drawn accurately reflect the scope of the analysis and relate well to the stated aims. A valuable discussion was provided of the context of the results and the barriers to improving treatment, and how these barriers might be overcome. Limitations to the study were not discussed.

**Implications of the study**
The authors clearly advocate the wider introduction and funding of the study technologies into the wider New Zealand market and recommend "ongoing analysis in order to assess cost-effectiveness as new therapies become available".

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**Other publications of related interest**

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