How Do We Use HTA and Real-World Evidence to Implement “Reassessments” Effectively?

An Academic View of Real World Economic Evidence: The pie’s the limit

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Think like an Academic Health Economist...

- We have *scarce resources*.
- Not everything *worth* doing is *worth* doing well.
- Only collect more evidence if the *value* exceeds the cost.

How Do We Use HTA and Real-World Evidence to Implement “Reassessments” Effectively? Judiciously
Key steps, all necessary.

Step 0
- Develop research questions about value of care

Step 1
- Produce the evidence

Step 2
- Review the evidence (to inform policy)

Step 3
- Use the evidence (to make policy)
- Use the policy to change practice

Step 4
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Examples:
What could possibly go wrong?
Many attempts have been made to estimate the cost effectiveness of these treatments for multiple sclerosis. Analyses have produced cost effectiveness estimates ranging from over £1m per quality adjusted life year (QALY) gained to cost saving.\textsuperscript{4-9} Owing to major flaws in the modelling of the clinical course of multiple sclerosis, efficacy, discontinuation of treatment, mortality, and the analysis of uncertainty, none of these estimates can be considered robust.\textsuperscript{8} The Cost Effectiveness of Multiple Sclerosis Therapies Study Group was commissioned by the National Institute for Clinical Excellence to undertake this economic assessment in
“To be truly independent, the scientific advisory group should resemble the data monitoring committee of a clinical trial. Without such independence, hard decisions, such as recommending a price reduction or closure of the scheme, are unlikely to be made.

**Fig 3** Impact of time horizon on cost effectiveness
What are the lessons more generally for patient access schemes? One is that financially based schemes are preferable to those based on outcomes. Outcome based schemes should probably be avoided if at all possible. For those that do go ahead, it is vital to ensure appropriate governance given the inevitable conflicts of interest. Since a robust control group is essential, policy oriented randomised clinical trials may be required. Monitoring and evaluation of outcomes must be independent of the companies involved. Transparency is essential, involving annual reports, access to data, and rights to publish. Any of these might have helped avoid the current fiasco.

Continuing the scheme is unjustified

Christopher McCabe and colleagues examine the claims behind the decision not to reduce drug costs in the multiple sclerosis risk sharing scheme

Since 2002 people in England with multiple sclerosis have been able to access disease modifying drugs through a risk sharing scheme. The scheme was set up after the National Institute for Health and Clinical Excellence (NICE) recommended that the drugs should not be used in the NHS because of doubts about their effectiveness and high price. It suggested instead that the Department of Health could work with the manufacturers to make the treatments available to NHS patients in a cost effective manner—that is, at a lower price.

Under the terms of the scheme interferon beta (Avonex, Betaseron, and Rebif) and glatiramer acetate would be made available to NHS patients in the context of a study monitoring disease progression. The data were to be reviewed at two year intervals. If the observed benefit was less than that predicted by the model NICE had commissioned from the Sheffield School of Health and Related Research (SCHRARR), which four of us worked on, the drug price would be reduced to achieve a target cost effectiveness ratio of £36 000 (€40 000; $54 000) per quality adjusted life year (QALY).

Since the start of the scheme, 5583 patients meeting the Association of British Neurologist criteria for benefit are less, and less than zero if the treatment is better than predicted. Expected benefit is derived from a historical Canadian cohort followed up over 25 years, and disability was assessed with the extended disability status scale. The scheme established a tolerance range of 20% for the deviation score within which the treatments would be deemed to have performed as expected. The primary analysis reports a deviation score of 113%. This means that disease progression of treated patients was greater than expected for untreated patients. Patients who received the drugs are likely to have benefited from fewer relapses, but the drugs have not prevented any disability, and therefore the manufacturers would need to pay the NHS to use the drugs to make them cost effective.

Lack of action

Although the monitoring team concludes that there is no evidence these treatments are cost effective, it also argues it would be “premature, at this stage, to reach any decision about re-pricing the drugs without further follow-up and analyses.” It gives three reasons for this view: the validity of estimate the effect of treatment. However, the literature on the severity of the disease suggests that although the disease is increasing in incidence, it may be less aggressive, rather than more so, in recent cohorts. This may be due to ascertainment bias, and the prudent presumption would be no change. An assumption of increasingly aggressive disease cannot be supported, and continuing with the scheme will not provide additional evidence of this.

What if the costs and utilities used in the model are wrong?

The SCHRARR model applies the same costs and utilities to both treated and untreated patients in the same disease state—with the exception of the drug cost. The effect of inaccuracies in these data on estimated cost effectiveness depends on a divergence in the distribution of the treated and untreated cohorts across the scale used to measure disability. However, the observed treated patients do not diverge from the modelled untreated patients, so changing the costs and utility data used in the analysis cannot affect the estimates of cost effectiveness.
Step 1 Challenges: Building and Nurturing capacity
(who will do the analysis?)
“Providing those answers will be the new job Bernie O’Brien who received a $3-million grant from the MOH to evaluate what he calls the latest medical “toys.”

The Ministry has provided doctors and hospitals with $12 million for the new drug-eluting stents on the proviso that they agree to participate in O’Brien’s research study on the economic benefits of them.

“BUT PART OF OUR JOB IS TO QUESTION, ‘SHOULD WE ALWAYS BE PAYING FOR THE LATEST TWIST IN THE TECHNOLOGY?’”

explains O’Brien. “It does provide a better image and it may be more sensitive and specific, but does it change outcomes for patients?” He says the evidence that this is cost-effective is absent. As a result, the Ministry has launched a roll out of PET scanners, and will fund at least two randomized controlled trials.

He explains that many of these new technologies are like new toys. “Hospitals and doctors will always want the brightest and the best,” says O’Brien, “but part of our job is to question, ‘should we always be paying for the latest twist in the technology?’ It’s like buying the latest DVD player. Compared to the basic model of a DVD is it really worth paying more?”

and muscle tissue in detail while the patient is alert. The traditional computed tomography (CT) scan shows only structural details within the brain.

One of the questions we need to ask is if PET scanning in diagnostic work results in better decisions and better patient outcomes,”
How will the people who will do this, learn to do this?

Who will have ‘hands on’ experience?
Step 2 Challenges: Will the evidence be reviewed?
Time matters
Can’t just do the work and hope someone will appreciate it.
Step 3 Challenges:
After the recommendation, will it be used?
EBP Herceptin Update

Executive Summary

2013 marks the second-year anniversary of the establishment of the Evidence Building Program (EBP). This program was introduced to provide time-limited coverage for cancer drugs in situations where data is collected to answer an evidence gap, to evaluate clinical benefit, and to confirm overall value. The objective of the EBP is to collect real-world data on cancer drugs where there is emerging or evolving evidence and a strong suggestion of clinical benefit, while current evidence is insufficient to support a permanent funding decision. Data collected through the EBP will be evaluated and will inform a final funding decision by the Executive Officer of Ontario Public Drug Programs.

Herceptin (trastuzumab), was approved as the first drug in the EBP, for use with chemotherapy to treat breast tumours of less than or equal to 1 cm in diameter that are node negative and HER2 positive. Since May 2011, 137 patients in Ontario have received or are receiving Herceptin through the EBP.

Presented below is a program summary of patients who have completed or are enrolled in EBP Herceptin during the period from May 2011 to March 2013, all of whom have met the eligibility criteria as established by the program.

As only two years have elapsed since the program, it is not yet possible to verify if the benefits and harms from giving Herceptin to this group of women are comparable to women with larger tumors. This data collection is ongoing, and sufficient information is expected to be available by 2016 to inform a permanent funding decision.
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Room 203

Room 204
Economic evidence in an uncertain world: The final frontier

Jeffrey S. Hoch, PhD

“Every politician knows that, any time you pit a suffering young mom against the phrase ‘cost-benefit analysis,’ it’s no contest.”
Getting Past PowerPoint Slides and Putting Real-World Evidence Into Action

Panellists: Jessica Arias, Program Manager, Cancer Care Ontario; Jaclyn Beka, Health Economist and Manager, Pharmacoeconomics Research Unit, Cancer Care Ontario; Angie Wong, Director, Ontario Public Drug Programs, Ministry of Health and Long-Term Care; Dr. Kelvin Chan, Medical Oncologist, Sunnybrook Health Sciences Centre Odette Cancer Centre

In 2010, Ontario implemented public funding for azacitidine for myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). While the trial protocol used a seven-consecutive-day schedule, two additional dosing schedules were funded because most hospitals lacked the ability to follow the seven-day regimen. As a condition of funding, Cancer Care Ontario (CCO) agreed to conduct a prospective study to evaluate all three dosing schedules for effectiveness. CCO developed and implemented a process to collect real-world evidence (RWE) from cancer centres and hospitals administering azacitidine. The data collection and analysis, done in collaboration with a research team, was completed in 2016 and the findings have been presented at various tables, including a health technology assessment (HTA) committee. The conclusions and implications are currently being studied by CCO and the Ministry of Health and Long-Term Care. As an example of a successful collaboration that involved prospective data collection, analysis, and use of RWE to inform decision-making, the azacitidine evaluation has generated a series of "lessons learned" relevant to public payers interested in growing RWE capacity in cancer care. The azacitidine analysis will be used as a case study by this panel, which comprises a health services researcher, a HTA panel expert, a health economist, a representative from a cancer agency, and payer representatives. Speakers will examine the components of an RWE framework that are most relevant to them, such as: how to identify uncertainty and develop research questions; how to manage data collection, sharing, and analysis; and how the results of RWE analyses can be used to inform decision-making on drug funding.
Key parts of RWE…

Do it
- How will it be done?
- Who’s “buy in” is needed?

Read it
- A new recommendation submission?
- A new recommendation?

Use it
- A new decision?
- How could this be win/win?
Is this Win / Win?  

Price too low?  

Price too high?
Where should Academics focus?

- What needs to be analyzed?
- How to obtain it?
- How to analyze it?
- Power(?)

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But is it *more valuable* to all parties to find out?

If so, let’s get it done!

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**IT IS WISER TO FIND OUT THAN TO SUPPOSE.**

*MARK TWAIN*
Think like an Academic Health Economist…

How Do We Use HTA and Real-World Evidence to Judiciously Implement “Reassessments” Effectively?

- Calculate value in terms of *changing the decision*.
  - If there is low chance you made the wrong decision or
  - If there is low cost from making the wrong decision
    - Then what is the benefit of more evidence?
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