HTA and Submissions

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Agenda

• The Decision Problem
• Role of HTA bodies in Canada
  – CADTH, pCODR and INESSS
• Overview of the elements of the HTA submission
  – Clinical package for HTA
  – Economic analysis for HTA
  – Budget impact models
Why HTA?

To support decision-making.

Resources are limited.

New investments mean opportunity costs.

We talk about money, but opportunity costs are measured in other people’s health.
Opportunity Cost

Pick the best description(s):

A. The displaced activity that can no longer be funded if a new investment is made, within a constrained budget;

B. The value of the best activity foregone when a choice needs to be made between possible uses of a constrained budget.

C. The loss of potential gain from other investments when one investment is chosen;

C. What we give up to get the things we want.

What is HTA?

According to WHO:

Health technology assessment is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner.
What is HTA?

Who is HTA (in Canada)?

Not limited to drugs… but will be, for our purposes.
Who makes HTA recommendations?

Clinical and economic reviewers
   – Including clinician experts

HTA expert panels (pERC, CDEC, Conseil)
   - Largely health care practitioners
     - Physicians of various specialties, pharmacists, nurses
   - A health economist
   - 2 public members (patients)
   - Not just technocrats

What guides HTA agencies?

HTA expert panels consider the priorities of payers:
   • Maximizing population health
   • Fiscal prudence

Using HTA values:
   • EBM: the primacy of evidence

The dollars are real… the benefits must be, too.
What does HTA value?

The pCODR deliberative framework:

- Clinical
- Economic
- Patient Values
- Adoption Feasibility

Clinical is the most highly valued quadrant.

How is HTA conducted? (Process)

Submission components:

- Clinical Summary
- Economic Evaluation
- Patient Input
- Budget Impact Analysis

Within a formalized process explicitly framed for each HTA agency (check their websites).
### Patient Input

**Condition and current therapy:**
- Impact of condition on patient
- Patients’ experiences with current therapy
- Impact on caregivers

**Drug under review:**
- Expectations for the new drug (if no experience)
- Experiences with the new drug (clinical trial, compassionate use)

**Any additional information**

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Clinical Summary

Canadian focus!
- Disease background
  - Definitions and descriptions, epidemiology, burden of illness, unmet medical need
- Current Canadian treatment practices
- Clinical evidence to support new therapy
  - Efficacy and safety
- Place in therapy (comparative CLINICAL benefit)
  - In the context of current practice – beyond the RCT

Note: the GVD is only a starting place!

Unmet Medical Need

- Drives prioritization for health care dollars
  - HTA: same speed of process, but possibly a more generous evaluation of clinical data
  - PCPA: ‘top of the pile’
- Documented by treatment guidelines and supported by patient input
  - Commercial features/benefits may not be unmet needs
  - Burden of illness research tells us what we spend but does not tell us if that is the right amount to spend (too high? too low? just right?)
Clinical Evidence: Internal and External Validity

• Methodology issues:
  – study design, statistical plan, conduct of study, duration of observation, inclusion/exclusion criteria

• Outcomes:
  – prefer final vs. intermediate/surrogate
  – align with patient values (especially QOL)
  – statistical vs clinical significance

• Comparator:
  – relevant to current Canadian practice

Clinical Evidence

Your version of the story:
• Support corporate positioning for the drug
  – What is your reimbursement ask?
  – If you seek subgroups – you must provide these data
  – If you have ANY data updates – provide these
  – Goes beyond HC summary, GVD, publications

HTA version of the story:
  – Their primary data sources are: publications, grey literature, treatment guidelines, external clinical experts – not your summary.
IDC/NMA

- If we do not have direct-comparator evidence from RCTs, then we must consider an indirect comparison (IDC) using a network meta-analysis (NMA) to link results from disparate studies.
- Extremely complicated and can be difficult to interpret – often leads to lack of clarity.
- HTA is a tough audience to satisfy for an NMA.
- Essentially, there is no substitute for H2H RCTs.

Linking Submission Components

Price sets the evidence bar and is the reward for the appropriate place in therapy.

Without a clinical story, there is no economic story.
Economic Evidence

- How does that compare with what I’m already doing/paying for?
- Does this investment increase or decrease the total amount of health produced?
- What about the opportunity cost?
- How can we tell?

Defining Health

- Are 10 hip replacements more valuable than 12 knee replacements?
- Should we invest more in genomic testing or pediatric oncology?
- Do we need to increase HPV vaccination rates, or expand mental health facilities?
- Measuring value for money means we need a multidimensional unit of measure.
- At a minimum, we need to account for both duration of life and some estimate of quality of life.
- Hence the creation of the Quality-Adjusted Life Year (QALY).
Quality-Adjusted Life Years

- Combines duration of life with quality of life, (like a KwH), as opposed to just survival (LY).
- Health states are measured on an interval scale whereby 1 represents perfect health, and 0 equals dead. Note that the possibility for states worse than dead also exists.
- Interval scale implies that moving from 0.2 to 0.3 is equivalent to moving from 0.9 to 1.0.
- And that 0.8 is exactly “twice as good” as 0.4.
- This has important equity considerations.

Using QALYs
Pharmacoeconomic Reference Case

- Cost-effectiveness needs 2 ingredients.
- CADTH has recently decided that just about every submission should include a cost-utility analysis (CUA), using QALYs as the outcome.
- CUA is a special form of cost-effectiveness analysis that facilitates decision-making across possible health programs.

Types of Analysis

- Other types of analysis are sometimes permissible, but now only in special cases.
- Cost-effectiveness analysis (CEA) estimates the total costs, with the output expressed in natural units.
- Could be hospitalizations avoided, transplantations saved, days at work gained.
Types of Analysis

• Cost-minimization analysis (CMA) or just cost analysis or cost tables.
• Used when effectiveness is assumed identical. Rarely true, but sometimes the conservative assumption.

• Cost-benefit analysis (CBA) assigns a specific value to health gains. More usually associated with welfarist approaches, but very useful mathematically, and very interesting for research (CV/DCE).

Interpreting Results

• All analyses consider costs
• But not all consider outcomes in the same way

• Most new technologies deliver more health, but at an additional cost.
A Quick Recap

- Decision-makers want to maximize population health
- We measure health in QALYs to allow comparison across investment opportunities
- Most new treatments deliver more health, but at an additional cost.
- We want new investments to create more health than they displace.

Representing Results

- NW: More costly, less effective
- SE: More costly, more effective
- SW: Less costly, less effective
- SE: Less costly, more effective
Types of Models

• When the time horizon is short, we can often use the simplest and most intuitive approach to modeling: the decision tree.
• Read from left to right, the decision tree puts together decision nodes, chance nodes and outcomes to calculate expected costs and outcomes.
• Appropriate for short-term or discrete time analytical problem.
Types of Models

- Consider the following decision tree for prevention of HIV transmission from mother to child:
- The intervention costs $800, but treatment for infected children costs $1500.
- The probability of transmission by untreated mothers is 0.26, and by treated mothers 0.07. However, some women will not accept treatment (p=0.05), incurring no benefits and no additional costs.
Calculations

Expected cost of intervention
= 0.95 x [(0.07 x $2300) + (0.93 x 800)] + 0.05 x [(0.26 x $1500) + (0.74 x $0)]
= $879.25

Expected cost of no intervention = (0.26 x $1500) + (0.74 x $0)
= $390

So intervention costs $480 more

Let us assume that, in case of vertical transmission, the child will expect to enjoy 5 QALYs (due to shortened life expectancy). With no transmission the child will enjoy 40 QALYs.

The expected benefits from intervening can be calculated as:
0.95 x [(0.07 x 5) + (0.93 x 40)] + 0.05 x [(0.26 x 5) + (0.74 x 40)]
= 37.2 QALYs

The expected benefits from not intervening can be calculated as:
[(0.26 x 5) + (0.74 x 40)]
= 30.9 QALYs

ICERs

• So the ICER for this decision tree can be calculated as:
• ($879.25 - $390) / (37.2 - 30.9) = $77.66/QALY

• It all depends on what gets displaced
• WHO recommends a standard approach for LMICs of <3x per capita GDP per DALY averted.
Markov Models

- Better suited to longer-term analysis, e.g. chronic disease, with repeated periods of events/remissions/progressions/etc.
- Uses discrete periods of time and transition probabilities
- Generates a “Markov trace” of results
- Other approaches are also used.

Affordability: Budget Impact

- Forget about the abstract concept of value…
- Can payers afford what you are selling?

- Budget impact analysis is the how you demonstrate the financial effect on the drug plan of the adoption decision

- Methods are highly formalized.
Budget Impact Analysis

• Methods are described by the PMPRB (2007)
• A common baseline period is defined

• We build a Reference Case
• And an Adoption Case

• The difference between the Adoption Case and the Reference Case is the budget impact.

Budget Impact Analysis

• Many organizations use BIAs:
  • Public drug plans
  • Private insurers
  • Cancer agencies
  • Hospitals, clinics, chains, etc.

• The setting determines the scope.
Restricted Purpose and Scope

• BIAs do not try to ascertain value;

• No consideration of:
  • Improved productivity;
  • Reduced LOS;
  • Fewer re-admissions;
  • Fewer follow-up appointments;
  • QALYs or other outcomes;
  • Etc.

• Only spending of direct relevance to the funding silo of the payer.

Calculating the Market Size

<table>
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<tr>
<td>Adoption Case Year 1</td>
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Calculating the Budget Impact

Steps

- Selection of Comparators
- Definition of the baseline period
- Growth parameters
- Costs
- Calculation of Results
- Sensitivity analysis
Comparators

- All relevant comparators, including:
  - Submitted drug;
  - Standard(s) of care or appropriate treatments.
  - No off-label use considered.
- Questions:
  - How should relevant comparators be selected in a crowded therapeutic area, e.g. antidepressants?
  - Are there new treatments on the horizon? What do we know about them?
  - Are all comparators reimbursed in every jurisdiction?
  - Is the SoC consistent across jurisdictions?

Creating the Base-line Period

- Calculation of the baseline period is the first step in modeling:
  - How many prescriptions, and at what cost? (P x Q)
  - So, how do we calculate the baseline period?
- First, we need volume of claims for all appropriate comparators
- 2 basic approaches:
  - Epidemiological (literature searches)
  - Claims-based (IMS Brogan data)
Epidemiological Approach

- Provincial Population
- Prevalence Rate
- % Meet clinical criteria
- Diagnosis Rate
- Treatment Rate

Plan Coverage = Baseline Period Population

Claims-Based Approach

IMS Data on comparators

Standardized to allow comparison

Or

Percentage from indication

= Baseline Period Value (both volume and cost)

= Baseline Period Volume x mean PM dosing
Changes in the Market

• Regardless of whether a claims-based or epidemiological approach is used, the subsequent years of the model will be based on the baseline period and:
  • Anticipated growth rate (requires assumptions);
  • Market penetration of the new drug* (requires assumptions);
  • Displacement rates from existing treatment options* (requires assumptions);
  • Changes in market composition (e.g. genericization, new entrants), (requires assumptions).
  • *Data available from company market research department.

Changes in the Market – Cont’d.

• New drug takes its market from somewhere.
• Market research department will provide information on:
  • **Total** market share attributable to new drug;
  • Displacement rates for each comparator, i.e. percentage of **each** comparator’s market that will be captured.

• Total market share is likely to increase over time.
• Consider possibility of market expansion: e.g. oral RA treatment.
Example of Market Calculations

<table>
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<tr>
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Total budget impact: 1,256,885

Best Practices

- Lots of user inputs;
- Explain what is happening in each calculation;
- Justify assumptions with adequate sources;
- Include all relevant comparators;
- Consider perspective and include all relevant costs
Quality Assurance

- Challenges to efficiently building a good model are many:
  - Reimbursement of comparators may vary by plan;
  - Market capture and displacement is almost always wrong;
  - Fees/mark-ups/co-pays can be structured differently in different jurisdictions;
  - Many drugs have multiple indications, and indication-specific information may not be available;
  - Prices are not transparent on any formulary;
  - Many assumptions incorporated, so many sensitivity analyses are required.

Strategic Implications

- Negotiations are to be expected.
- High budget impact is a serious obstacle to listing, but
- Expenditure caps are sometimes used to provide payer certainty.
- The cap is likely to be based on the budget impact.
Case Examples

- So now that you understand the concept of value…
- Zaxine
- Sovaldi
- Esbriet

Lessons for New Market Access Professionals

- Identify your place in therapy
- At least know where the best value lies (subgroup, disease severity, line of treatment), even if you can’t limit your request to that
- Know your data and know its limits
- Be the bearer of bad news
IN GOD WE TRUST
ALL OTHERS MUST BRING DATA