Health Economics, health care payers, guidelines and the inherent tension: Can they ever agree?

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Outline:

• To outline the principles of health economics and its use in health care priority setting
• Interpreting the results of economic evaluations: policy makers, and guideline groups
• Affordability vs cost-effectiveness and what else matters besides health outcomes and costs
• Influencing policy-makers: How to reduce tension between government payers and guidelines producers moving forward?
Objectives:

- Case studies

- KDIGO
Glucose testing strips in diabetes

67 year old woman, with Type 2 Diabetes and Albuminuria; follow-up visit

No hypoglycemic episodes. BP 126/80

Medications; metformin (500 mg bid), glyburide (2.5 mg bid) and Ramipril (5 mg daily).

A1c high (8.6%): You recommend watching diet, exercise and increasing glyburide to 5 mg bid.

You request she monitor her blood sugar intermittently during the day and request follow-up in few months.
Sevelamer for hyperphosphatemia
(First line)

76 year old man with ESRD on hemodialysis.

Comorbidities; CHF and cardiovascular disease; Below the knee amputation.

Medications; calcium carbonate (500 mg) AC-supper, one-alpha 0.5 ug daily.

Labs; Calcium 2.24 mmol/l, phosphate 2.15 mmol/l and PTH 196 pmol/l.

Receives meals on wheels therefore difficult to stick to renal diet and refuses Dietician.

Being aware of a recent meta-analysis, you recommend sevelamer 1600 mg, tid AC meals.
Sevelamer for hyperphosphatemia (second line therapy)

76 year old man with ESRD on hemodialysis.

Comorbidities; CHF and severe cardiovascular disease; below the knee amputation.

Medications; calcium carbonate (1250 mg tid), AC-meals, one-alpha 0.5 ug daily.

Labs; Calcium 2.54 mmol/l, phosphate 2.35 mmol/l and PTH 696 pmol/l.

Receives meals on wheels therefore difficult to stick to renal diet and refuses Dietician.

Being aware of a recent meta-analysis, you recommend sevelamer 1600 mg, tid AC meals.
Is health economics relevant to health care providers?

The goal of health care providers is to:
- Improve care, and improve length and quality of life

The goal of health care-policy makers is to:
- Improve care, and improve length and quality of life – subject to a fixed budget.
“I will apply, for the benefit of the sick, all measures which are required”
Objectives:

- Basic principles of health economics
What is economic evaluation?

Comparative analysis of alternative courses of action in terms of both their costs and consequences.

Opportunity cost, scarcity of resources, and choice.
Funding diabetes nurses or sevelamer in ESRD

Diabetes nurses help with blood sugar control.
  Reduces eye and kidney complications.
  Annual costs $150,000 per clinic.

Sevelamer (vs calcium) in ESRD as first line therapy:
  Lowers vascular calcification
  Impact on mortality (?)
  $4,500 annually
3 types of economic evaluation:

Cost- effectiveness analysis.

Cost- utility analysis.

Cost- benefit.
What is the role of economic evaluation within health care priority setting?

Improved clinical outcomes

KDIGO

Increased costs
An example:
Glucose testing strips in diabetes
Self-monitoring for patients with Type 2 Diabetes (not using insulin): Background

- Self-monitoring of blood glucose is recommended for patients who are not using insulin (Canadian Diabetes Association guidelines).

- $350 million per year in Canada

- ~50% of the total expenditure on blood glucose test strips is for patients with type 2 diabetes who are not using insulin.

CMAJ, Jan. 12, 2010, 182(1)
Self-monitoring for patients with Type 2 Diabetes (not using insulin): Effectiveness

- 7 RCTs, enrolling a total of 2270 patients with type 2 diabetes managed with oral antidiabetes agents or lifestyle measures.
- Compare self-monitoring of blood glucose (and education) with no self-monitoring.
- Average number of tests 1.29 per day ($0.73 per test strip).
- The pooled difference in A1C was in favour of self-monitoring (weighted mean difference –0.25%, 95% confidence intervals [CI] –0.36% to –0.15%).
Self-monitoring for patients with type 2 diabetes not using insulin

**Table:** Cumulative incidence of diabetes-related complications over 40 years

<table>
<thead>
<tr>
<th>Condition</th>
<th>Overall % (95% CI)</th>
<th>1 Chronic Condition Only % (95% CI)</th>
<th>2+ Chronic Conditions % (95% CI)</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>36.58</td>
<td>36.21</td>
<td>0.38</td>
<td>266</td>
</tr>
<tr>
<td>Heart failure</td>
<td>17.64</td>
<td>17.20</td>
<td>0.44</td>
<td>228</td>
</tr>
<tr>
<td>Stroke</td>
<td>16.34</td>
<td>16.14</td>
<td>0.20</td>
<td>500</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>2.29</td>
<td>2.21</td>
<td>0.08</td>
<td>1299</td>
</tr>
</tbody>
</table>

**Cost per QALY:** $110,000
How to interpret a cost-effectiveness ratio:

<table>
<thead>
<tr>
<th>Cost/QALY ratio</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;$20,000</td>
<td>Strong evidence for adoption and appropriate utilization.</td>
</tr>
<tr>
<td>$20,000-100,000</td>
<td>Moderate evidence for adoption and appropriate utilization.</td>
</tr>
<tr>
<td>&gt;$100,000</td>
<td>Weak evidence for adoption.</td>
</tr>
</tbody>
</table>
Using Effectiveness and Cost-effectiveness to Make Drug Coverage Decisions
A Comparison of Britain, Australia, and Canada

Fiona M. Clement, PhD
Anthony Harris, MA, MSc
Jing Jing Li, BPharm, BCom
Karen Yong
Karen M. Lee
Braden J. Manns, MD, MSc

Context National public insurance for drugs is often based on evidence of comparative effectiveness and cost-effectiveness. This study describes how that evidence has been used across 3 jurisdictions (Australia, Canada, and Britain) that have been at the forefront of evidence-based coverage internationally.

Objectives To describe how clinical and cost-effectiveness evidence is used in coverage decisions both within and across jurisdictions and to identify common issues in the process of evidence-based coverage.

JAMA 2009
Figure: Ranked cost per QALY where a cost per QALY was felt to be relevant to decision-making ("committee’s best guess ICER")

KDIGO
Back to self-monitoring: How to interpret the results?

High quality systematic review shows small changes in HbA1C, which translate into small changes in clinical events noted in the economic evaluation.

Improvements in clinical outcomes are uncertain.

Baseline cost per QALY ~$110,000 – higher than most interventions we pay for in Canadian health care.
Other factors policy makers consider when setting priorities

Life saving intervention versus gain in life expectancy.
Impact on quality of life.
Is the treatment for a large or small number of people?
Is the treatment for older or younger patients?
Is the treatment for those with good or poor baseline health?
Will it be successful – clinical uncertainty?
Equality of access to therapy.
Political priorities
What is the budget impact / affordability?
Policy recommendation:

- Most adults with type 2 diabetes using oral antidiabetes drugs (without insulin) do not require routine blood glucose monitoring. Periodic testing may be needed for select patients, such as those with acute illness, changes to drug therapy, and those at high risk of hypoglycemia.

- Limited funding across Canada
How might a guideline group interpret the same results?

2008 Canadian Diabetes Guidelines:
- Self monitoring in routinely recommended for use in patients with diabetes not using insulin

2018 Canadian Diabetes Guidelines:
- More nuanced use recommended.
Sevelamer for hyperphosphatemia
(First line or Second line or ?)
### Sevelamer vs. Calcium

#### KDIGO

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Sevelamer</th>
<th>Calcium salts</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total Events</td>
<td>Total Weight</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M-H</td>
<td>Random</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleyer 1999</td>
<td>0</td>
<td>40</td>
<td>40</td>
<td>Not estimable</td>
</tr>
<tr>
<td>BRCG Study 2008</td>
<td>1</td>
<td>62</td>
<td>6</td>
<td>0.12 [0.02, 0.51]</td>
</tr>
<tr>
<td>CARE Study 2004</td>
<td>0</td>
<td>50</td>
<td>0</td>
<td>Not estimable</td>
</tr>
<tr>
<td>CARE-2 Study 2008</td>
<td>3</td>
<td>100</td>
<td>7</td>
<td>0.44 [0.12, 1.66]</td>
</tr>
<tr>
<td>Hervas 2003</td>
<td>2</td>
<td>18</td>
<td>2</td>
<td>1.22 [0.19, 7.64]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>260</td>
<td>262</td>
<td>19.8%</td>
<td>0.43 [0.13, 1.38]</td>
</tr>
</tbody>
</table>

Total events 6 17
Heterogeneity: Tau² = 0.34; Ch² = 2.87, df = 2 (P = 0.24); I² = 30%
Test for overall effect: Z = 1.42 (P = 0.15)

#### 1.1.2 Sevelamer versus calcium carbonate

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Sevelamer</th>
<th>Calcium carbonate</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total Events 12</td>
<td>Total Weight 22</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M-H</td>
<td>Random</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Di Iorio 2012</td>
<td>12</td>
<td>107</td>
<td>22</td>
<td>0.54 [0.28, 1.03]</td>
</tr>
<tr>
<td>Ferrara 2008</td>
<td>0</td>
<td>44</td>
<td>0</td>
<td>Not estimable</td>
</tr>
<tr>
<td>INDEPENDENT-HD Study 2013</td>
<td>28</td>
<td>232</td>
<td>100</td>
<td>0.28 [0.19, 0.41]</td>
</tr>
<tr>
<td>Koivu 2005</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Sadek 2003 (2)</td>
<td>1</td>
<td>21</td>
<td>3</td>
<td>0.33 [0.04, 2.56]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>420</td>
<td>427</td>
<td>36.6%</td>
<td>0.35 [0.22, 0.56]</td>
</tr>
</tbody>
</table>

Total events 41 125
Heterogeneity: Tau² = 0.00; Ch² = 7.78, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 2.42 (P = 0.00001)

#### 1.1.3 Sevelamer versus calcium salts (calcium acetate and calcium carbonate)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Sevelamer</th>
<th>Calcium salts (calcium acetate and calcium carbonate)</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total Events 284</td>
<td>Total Weight 303</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M-H</td>
<td>Random</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Block 2005</td>
<td>11</td>
<td>60</td>
<td>23</td>
<td>16.6%</td>
</tr>
<tr>
<td>Chertow 2002</td>
<td>16</td>
<td>99</td>
<td>6</td>
<td>10.1%</td>
</tr>
<tr>
<td>DRCOR Study 2007</td>
<td>267</td>
<td>1053</td>
<td>276</td>
<td>18.5%</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>1212</td>
<td>1218</td>
<td>43.6%</td>
<td>0.85 [0.57, 1.27]</td>
</tr>
</tbody>
</table>

Total events 284 303
Heterogeneity: Tau² = 0.06; Ch² = 3.47, df = 2 (P = 0.18); I² = 42%
Test for overall effect: Z = 0.79 (P = 0.43)

Total (95% CI) 1892 1907 100.0% 0.54 [0.32, 0.93]

Total events 331 445
Heterogeneity: Tau² = 0.41; Ch² = 45.11, df = 8 (P < 0.00001); I² = 82%
Test for overall effect: Z = 2.21 (P = 0.03)
Test for subgroup differences: Ch² = 8.11, df = 2 (P = 0.02), I² = 75.3%

**Footnotes:**
(1) In Navaneethan et al., 2011, these values are nested under “Sevelamer versus calcium acetate”.
(2) These values were found in the publication yet not included in the analysis in Navaneethan et al., 2011.
Economic evaluation of sevelamer in patients with end-stage renal disease

Braden Manns\textsuperscript{1,2,3}, Scott Klarenbach\textsuperscript{3,4}, Helen Lee\textsuperscript{1}, Bruce Culleton\textsuperscript{2}, Fiona Shrive\textsuperscript{1} and Marcello Tonelli\textsuperscript{3,4,5,6}
Cost-effectiveness of first line sevelamer use (lifetime time horizon (in CAN$))

<table>
<thead>
<tr>
<th>Model</th>
<th>Strategy</th>
<th>Marginal cost</th>
<th>Marginal effectiveness (QALYs)</th>
<th>Incremental cost per QALY gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>Calcium-based phosphate binders</td>
<td>$33 000</td>
<td>0.21</td>
<td>$157 500</td>
</tr>
<tr>
<td>(Primary care)</td>
<td>Sevelamer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>Calcium-based phosphate binders</td>
<td>$17 000</td>
<td>0.00</td>
<td>Sevelamer dominated</td>
</tr>
<tr>
<td>(Cost minimization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td>Calcium-based phosphate binders</td>
<td>$64 000</td>
<td>0.50</td>
<td>$127 000</td>
</tr>
<tr>
<td>(Mortality over time)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 4</td>
<td>Calcium-based phosphate binders</td>
<td>$27 000</td>
<td>0.097</td>
<td>$287 100</td>
</tr>
<tr>
<td>(Mortality by age)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What about second line use?
How might a policy maker interpret the results?

Variable coverage decision by policy makers across Canada:

- No funding
- Fund as first line therapy
- Fund as second line therapy who have developed hypercalcemia on calcium-based binders
2017: KDIGO guidelines
• We suggest lowering elevated phosphate levels toward the normal range (2C)
• Avoid hypercalcemia
• Restrict the dose of calcium based phosphate binders
Objectives:

- Influencing policy-makers
Influencing policy-makers: Answer 2 Questions honestly

Does the intervention you’re considering really work?

What are the resource implications of the new treatment?
Influencing policy-makers:

Focus on areas with the best quality clinical data (low uncertainty)

What are the downstream implications on cost – and were they measured in trials, or can they be reliably estimated?

Is the cost per QALY high because of the impact of dialysis costs?
Finding common ground with health care payers

Clinical practice guidelines should take cost into account – KDIGO √

Focus implementation efforts on higher risk populations

Formularies that consider costs can help you care for your patients in a cost-conscious manner, while still providing the vast majority of “effective” therapies.

Developing local guidelines which your care can be consistent with
- Anemia protocol
- Order sets that guide physician care
QUESTIONS

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Thank you