ISSUES AND PITFALLS RELATED TO ESTIMATING THE COST OF INTERVENTION IN APPLYING COST-EFFECTIVENESS MODELS FROM DEVELOPED COUNTRIES TO DEVELOPING COUNTRIES

Henry Glick
Division of General Internal Medicine
University of Pennsylvania
www.uphs.upenn.edu/dgimhsr

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THE PROBLEM

- Transferring estimates of cost impacts of medical therapies from one country to another in general, and -- more specifically -- from countries with more developed economies to countries with less developed economies faces a number of difficulties

- Concerns about the transferability of estimated cost impacts revolve around a number of issues. Three commonly cited issues are:
  1) Differences in absolute and relative prices for medical service use (i.e., price weights or unit costs);
  2) Differences in practice patterns (i.e., accessibility; medical service use; etc.); and
  3) The interaction between practice pattern and outcome
    - The fact that medical service use can affect outcome and outcome can affect medical service use

QUESTIONS THAT NEED ANSWERING

- While it is generally recognized that the transferability of estimates of mean cost differences from one setting to another may be affected by setting-specific differences in price weights and medical service use, little is known about the relative importance of these two factors

- Q1: Among countries with reasonably homogeneous economic conditions, is it more important to account for country-specific differences in price weights when translating results, or is it more important to account for differences in medical service use?

- Q2: Is anything known about the relative importance of these variables when translating results between countries with heterogeneous conditions?
While our main focus today has to do with decision models, some of the best evidence about the relative importance of these factors comes from economic assessment conducted as part of multinational clinical trials.

- These trials collect data on resource use, price weights, and epidemiology.
- They allow one to evaluate the relative impacts of price weights, resource use, and epidemiology on the transferability of data from one setting to another.

**EXAMPLE #1. INTERNATIONAL SUBARACHNOID HEMORRHAGE TRIAL**

- Phase III trial conducted in nine European countries, Australia and New Zealand that accrued 1023 patients.
- Most of the utilization data and all of the outcome data (death) were collected prospectively as part of the clinical trial.
- Economists in six countries -- within regions with reasonably homogeneous economic conditions -- conducted hospital-based costing studies that yielded estimates of average variable costs.
- The six countries selected included 84% of the trial patients.
- The evaluation of the impact of variation in price weights, resource use, and epidemiology was based on data from 5 of these 6 countries (the sixth was excluded due to low enrollment in the trial).

**IMPACT OF PRICE WEIGHTS VS OTHER VARIATION**

Cost per death averted (subanalysis using data from 5 countries) *

<table>
<thead>
<tr>
<th>Country</th>
<th>Price Weights</th>
<th>Country Specific Costs †</th>
<th>Country Specific Costs and Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46,818</td>
<td>5,921</td>
<td>11,450</td>
</tr>
<tr>
<td>2</td>
<td>57,636</td>
<td>91,906</td>
<td>60,358</td>
</tr>
<tr>
<td>3</td>
<td>53,891</td>
<td>90,487</td>
<td>244,133</td>
</tr>
<tr>
<td>4</td>
<td>69,145</td>
<td>93,326</td>
<td>181,259</td>
</tr>
<tr>
<td>5</td>
<td>65,800</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Overall</td>
<td>45,892</td>
<td>45,892</td>
<td>45,892</td>
</tr>
</tbody>
</table>

† Country-specific resource use × Country-specific price weights

** New therapy dominates

EXAMPLE #2. REVIEW OF TRANSFERABILITY OF RESULTS FROM ECONOMIC EVALUATIONS IN 44 MULTINATIONAL STUDIES

- Drummond and colleagues reviewed the "main causes of variation in study results from place to place"

- Conducted a literature review using OHE-HEED and NHSEED to identify 46 European studies with inter-country comparisons
  - In current presentation, 2 studies omitted because they had "detailed data from only one country, with negligible information about other countries"

- "Classified studies by extent of generalizability (based on size of difference in results and importance for decision-making)"
  - More generalizable: Observed differences in ICERS unlikely to change adoption decision
  - Less generalizable: Observed differences in ICERS likely to change adoption decision

Authors’ conclusion: "...the amount of variation you find depends on the amount the analyst allows (in study design or analysis)"
EXAMPLE #3. IMPORTANCE OF PRICE WEIGHTS WHEN COUNTRIES HAVE HETEROGENEOUS ECONOMIC CONDITIONS *

- International antibiotic trial
- Valued trial-wide medical services by use of country-specific price weights:

<table>
<thead>
<tr>
<th>Country</th>
<th>Average cost difference</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed countries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2588</td>
<td>1104</td>
</tr>
<tr>
<td>2</td>
<td>2441</td>
<td>1746</td>
</tr>
<tr>
<td>3</td>
<td>2899</td>
<td>1548</td>
</tr>
<tr>
<td>Developing country</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1091</td>
<td>329</td>
</tr>
</tbody>
</table>

* Unpublished data

- Price weights appear to have an important effect on cost-effectiveness when countries have heterogeneous economic conditions

APPROACHES TO STATISTICAL EVALUATION OF TRANSFERABILITY

- In the clinical trial setting, two approaches for addressing confidence about transferability are currently making their way into the literature
  - Hypothesis tests of homogeneity
  - Multi-level random-effects model shrinkage estimators
- These approaches rely on having data from the different countries
- To be useful in the models setting, one will either need to compare primary data from the settings or one will need to develop models capable of second-order Monte Carlo simulation

HYPOTHESIS TESTS OF HOMOGENEITY

- Evaluate the homogeneity of the results from the different countries
  - If there is no evidence of heterogeneity (i.e., a nonsignificant p-value for the test of homogeneity), and if one believes the test was powerful enough to rule out economically meaningful differences in costs, then one cannot reject the ability to transfer data
  - If there is evidence of heterogeneity, then the method indicates one should not transfer data without adjustment

ESTIMATION

- The second method uses multi-level random-effects model shrinkage estimation to provide more precise estimates of country-specific results than are yielded by separate -- and naive -- analysis of each country's costs and effects
  - Borrow information from the mean estimate to add precision to the center/country-specific estimates


LIMITATIONS

- Have focused mainly on point estimates, and less on whether one can be confident that price weights, resource use, and epidemiology have different impacts on transferability
- Would expect evaluation of country-specific resource use would appear to be more variable than evaluation of country-specific price weights because the former analysis breaks the overall sample into smaller subgroups while the latter analysis does not
  - Breaking a larger group into smaller subgroups leads to more variability in the outcome

CONCLUSIONS

- Transferring estimates of cost impacts of medical therapies from one country to another may be problematic because of differences in price weights, differences in practice patterns, and the interaction between practice pattern and outcome
- There is some initial evidence that when transferring data between countries with homogenous economic conditions, accounting for differences in medical service use may be more important than accounting for differences in price weights
- Accounting for differences in both price weights and medical service use is probably more important when transferring estimates from developed to developing countries