THINKING OUTSIDE RCTs

Wanrudee Isaranuwatchai, PhD
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Marcus Tan, MD
Kate Butler
Tony Zhong, MD
Jeffrey S. Hoch, PhD
How a person-level cost-effectiveness analysis from an observational study can show “value for money” of a health intervention?
No conflict of interest that may affect this presentation
Outline

- Observational studies
- Net benefit regression (NBR)
- Case study of breast reconstruction procedures
- Summary
Observational Studies

- Effectiveness
- Validity
- Affordability
- Lack of randomization
- Confounding
- Selection bias
- ...

Propensity score matching
Instrumental variable

Multivariate regression

Concato, Shah, Horwitz. NEJM, 2000; 342; 1887-1892
Net Benefit Regression

HEALTH ECONOMICS
Health Econ. 11: 415-430 (2002)
Published online 31 January 2002 in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/hec.678

Something old, something new, something borrowed, something blue: a framework for the marriage of health econometrics and cost-effectiveness analysis

Jeffrey S. Hoch\textsuperscript{a,}\textsuperscript{*}, Andrew H. Briggs\textsuperscript{b} and Andrew R. Willan\textsuperscript{c}
\textsuperscript{a} Department of Epidemiology and Biostatistics, University of Western Ontario, Canada
\textsuperscript{b} Health Economics Research Centre, University of Oxford, UK
\textsuperscript{c} Department of Clinical Epidemiology and Biostatistics, McMaster University, Canada

Summary

Economic evaluation is often seen as a branch of health economics divorced from mainstream econometric techniques. Instead, it is perceived as relying on statistical methods for clinical trials. Furthermore, the statistic of interest in cost-effectiveness analysis, the incremental cost-effectiveness ratio is not amenable to regression-based methods, hence the traditional reliance on comparing aggregate measures across the arms of a clinical trial. In this paper, we explore the potential for health economists undertaking cost-effectiveness analysis to exploit the plethora of established econometric techniques through the use of the net-benefit framework – a recently suggested reformulation of the cost-effectiveness problem that avoids the reliance on cost-effectiveness ratios and their associated statistical problems. This allows the formulation of the cost-effectiveness problem within a standard regression type framework. We provide an example with empirical data to illustrate how a regression type framework can enhance the net-benefit method. We go on to suggest that practical advantages of the net-benefit regression approach include being able to use established econometric techniques, adjust for imperfect randomisation, and identify important subgroups in order to estimate the marginal cost-effectiveness of an intervention. Copyright © 2002 John Wiley & Sons, Ltd.

Keywords cost-effectiveness analysis using regression; net-benefit framework; cost-effectiveness acceptability curve; economic evaluation; econometrics
Compared to UC, is TX cost-effective?

- ICER = \( \frac{\Delta C}{\Delta E} \)
- Cost-effective = ICER < \( \lambda \)

\( \frac{\Delta C}{\Delta E} < \lambda \)

\( \Delta C < \lambda \Delta E \)

\( 0 < \lambda \Delta E - \Delta C \) (= INB)

- Cost-effective = INB > 0
How to get to INB: Data

\[ NB_i = \lambda E_i - C_i \]

Hoch et al. Health Economics, 2002; 11: 415-430
The regression in NBR – SLR

\[ NB_i = \beta_0 + \beta_1(TX)_i + \varepsilon_i \]

\[ \beta_1 = \overline{NB}_{TX} - \overline{NB}_{UC} \]
\[ = \Delta NB \]
\[ = INB \]
The regression in NBR – MLR

- \( \text{NB}_i = \beta_0 + \beta_1(TX)_i + \sum_{j=1}^{p} \beta_j(X)_{i,j} + \varepsilon_i \)

- \( \beta_1 = \text{INB} = \overline{\text{NB}}_{\text{TX}} - \overline{\text{NB}}_{\text{UC}} \)
  - Adjusted for \( X \)

- Cost-effective:
  - ICER < \( \lambda \) or \( \text{INB} > 0 \)

- \( \beta_1 = \text{INB} \)
Outline

- Observational studies
- Net benefit regression (NBR)
- Case study of breast reconstruction procedures
- Summary
## Case Study

<table>
<thead>
<tr>
<th>Population</th>
<th>All women receiving either DIEP or MS-TRAM between 2008 and 2012 in one hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Deep inferior epigastric perforator (DIEP) flaps</td>
</tr>
<tr>
<td>Comparator</td>
<td>Muscle-sparing transverse rectus abdominis myocutaneous (MS-TRAM) flaps</td>
</tr>
<tr>
<td>Outcome</td>
<td>Patient-reported satisfaction with outcome (BREAST-Q)</td>
</tr>
<tr>
<td>Perspective</td>
<td>Hospital</td>
</tr>
<tr>
<td>Costs</td>
<td>Operating room; hospital stays Medication; allied health care Medical imaging; overhead</td>
</tr>
<tr>
<td>Time horizon</td>
<td>2 years</td>
</tr>
</tbody>
</table>
Objective

- To compare the cost and outcome of DIEP flap to MS-TRAM flap in autologous breast reconstruction from the hospital perspective
Statistical Analysis

- Descriptive analysis
- Net benefit regression
  - Adjusted for age, chemotherapy, radiation, laterality, timing, income, and ethnicity
- Cost-effectiveness acceptability curve (CEAC)
## Descriptive Analysis

<table>
<thead>
<tr>
<th></th>
<th>TX (N = 180)</th>
<th>UC (N = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age ± SD</strong></td>
<td>50.3 ± 8.7</td>
<td>52.7 ± 8.6</td>
</tr>
<tr>
<td><strong>Chemotherapy</strong></td>
<td>106 (59%)</td>
<td>29 (62%)</td>
</tr>
<tr>
<td><strong>Radiation therapy</strong></td>
<td>89 (49%)</td>
<td>30 (64%)</td>
</tr>
<tr>
<td><strong>Household income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low ($0 - $39,999)</td>
<td>23 (13%)</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Medium ($40K - $99,999)</td>
<td>68 (38%)</td>
<td>12 (25%)</td>
</tr>
<tr>
<td>High (≥ $100,000)</td>
<td>89 (49%)</td>
<td>28 (60%)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>139 (77%)</td>
<td>40 (85%)</td>
</tr>
<tr>
<td>Others</td>
<td>41 (23%)</td>
<td>7 (15%)</td>
</tr>
<tr>
<td><strong>Laterality</strong></td>
<td>101 (56%)</td>
<td>16 (34%)</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td>94 (52%)</td>
<td>29 (62%)</td>
</tr>
<tr>
<td><strong>Cost ± SD</strong></td>
<td>$15,344 ± $4,728</td>
<td>$16,681 ± $4,289</td>
</tr>
<tr>
<td><strong>Satisfaction with outcome ± SD</strong></td>
<td>73.8 ± 27.9</td>
<td>71.0 ± 28.6</td>
</tr>
</tbody>
</table>
Net Benefit Regression

- NB from $\lambda$ of $0$ to $50,000$ for each patient
- Run regression models for each $\lambda$

<table>
<thead>
<tr>
<th>Willingness-to-pay (for 1 unit of outcome)</th>
<th>INB (Incremental Net Benefit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda = $0</td>
<td></td>
</tr>
<tr>
<td>$\lambda = $1,000</td>
<td></td>
</tr>
<tr>
<td>$\lambda = $5,000</td>
<td></td>
</tr>
<tr>
<td>$\lambda = $10,000</td>
<td></td>
</tr>
<tr>
<td>$\lambda = $50,000</td>
<td></td>
</tr>
</tbody>
</table>
Probability that DIEP is cost-effective versus willingness-to-pay for 1 more unit of outcome.
Discussion

- Compared to MS-TRAM, DIEP could be an economically attractive option
  - $\lambda$ from $0$ to $50,000$: INB $> 0$
  - $p(TX=CE) \sim 70\%$

- Limitations
  - Single site
  - One perspective
  - One outcome
  - Unknown confounders
There is always A way...

THANK YOU

IsaranuwatcW@smh.ca
Bootstrap adjusted delta C and delta E