DESIGN CONSIDERATIONS IN MULTINATIONAL ECONOMIC EVALUATIONS

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OUTLINE OF PRESENTATION

- The dilemma posed by multinational studies.
- An additional complication.
- Possibilities for multilevel modelling.
- Design implications for future multinational evaluations.
THE DILEMMA POSED BY MULTINATIONAL STUDIES

- Factors, varying from place to place, may impact on cost-effectiveness.
- Data needs to be gathered from a range of healthcare systems with different information systems and accounting conventions.
- Resource use data collected alongside multinational clinical trials cannot simply be pooled.
OPTIONS FOR THE ANALYST

- Model, using the clinical data alone.
- Develop strategies to transfer economic data from one setting to another, or to analyse multinational economic clinical trials.
WHY NOT MODEL USING THE CLINICAL DATA ALONE?

- Some decision makers prefer to see trial-based economic evaluations.
- A trial is a good vehicle for collecting patient-level resource use data (despite all the problems!).
STRATEGIES TO ANALYSE MULTINATIONAL ECONOMIC CLINICAL TRIALS

- ‘Relative resource reduction’ approach

- ‘Test of interaction’ approach
  Cook et al (2002).

- ‘Regression’ approach
AN ADDITIONAL PROBLEM

- Multinational clinical trials not only involve several countries, they may involve several clinical centres within a country.
- Patients within a centre are more similar (in respect of treatment patterns) than those from different centres (i.e., clustering).
- Ignoring ‘centre effects’ may lead to p-values too small, biased estimates and misleading confusions (Localio et al., 2001).
Multilevel models explicitly account for the hierarchical structure of the data (level-3: country; level-2: hospital; level-1: patients).

Allow a more accurate assessment of the cost-effectiveness of alternative strategies, producing accurate parameter estimates.

Facilitates the exploration of variability of cost-effectiveness results by location-related factors such as country, centre, clinician.
CASE STUDY: THE EVALUATE TRIAL

- Multicentre RCT comparing laparoscopic-assisted (n=573) versus abdominal hysterectomy (n=286).
- Total of 25 English centres with 528 patients in total.
- Median follow-up of 12 months.
- Follow up: baseline, 6-week, 4 and 12 months.
- Cost analysis from UK NHS perspective.
- Health outcomes in terms of QALYs.
ACCEPTABILITY CURVES

Graph showing the probability of laparoscopic hysterectomy being cost-effective for different hospitals and the decision maker's maximum WTP for an additional QALY.

- Hospital 1: £39,770
- Hospital 2: £86,080
- Hospital 3: £94,152
- OLS: £107,825

Key points:
- ICER for Hospital 1 = £39,770
- ICER for Hospital 2 = £86,080
- ICER for Hospital 3 = £94,152
- ICER from OLS = £107,825
DESIGN CONSIDERATIONS FOR FUTURE MULTINATIONAL EVALUATIONS

- Selection of countries in multinational trials.
- Selection of centres in trials.
- Collection of centre-level variables.
- Selection of resource items for costing.
Currently this is based on political expediency or logistical reasons.

Should the selection of countries take account of the level of similarity of healthcare systems?

Are there natural groupings of countries that can be analysed together?
Currently this is based on recruitment potential, the need to involve key investigators or logistical reasons.

Should an attempt be made to select ‘typical’ centres, or to recruit a representative sample of centre types?
These could be used as covariates in the multilevel model.

Potential variables depend on the type of trial but could include:

- **Country level**
  - % GDP spent on health
  - reimbursement system for hospitals.
  - payment method for physicians

- **Centre level**
  - bed occupancy
  - teaching status
  - range of clinical specialties

- **Patient level**
  - age
  - gender
  - disease severity
  - socio-economic status
Current methods of selection are unclear, but level of detail probably reflects the level of funding for the economic study.

With increased detail the need for imputation of unit costs increases (Schulman *et al*, 1998).
Table 1: Reported Procedure and Per Diem Costs for Study Countries

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<thead>
<tr>
<th></th>
<th>Germany</th>
<th>Italy</th>
<th>France</th>
<th>Sweden</th>
<th>UK</th>
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</table>

Actual costs are in plain text; market-basket imputed costs are in bold/italic text.

POINTS TO NOTE

- Selection of resource items should take account of the availability of financial data.
- A ‘multi-layered’ approach might be advisable.
- A standardised protocol for generating unit costs is advisable but only minimises (rather than solves) the problem of variability in financial systems.
CONCLUSIONS

- Progress has already been made in tackling the methodological challenges posed by multinational studies.
- The role of multilevel modelling should be explored further.
- The analysis of multinational economic clinical trials could be assisted by thinking more carefully about the design of these studies.