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 Jönsson and Weinstein (1997).

- 'Test of interaction' approach Cook *et al* (2002).

- 'Regression' approach Willke *et al* (1998), Koopmanschapp *et al* (2001).

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 (ie, *clustering*).

- Ignoring 'centre effects' may lead to p-values too small, biased estimates and misleading confusions (Localio *et al*, 2001).

ANALYTICAL APPROACH

- 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
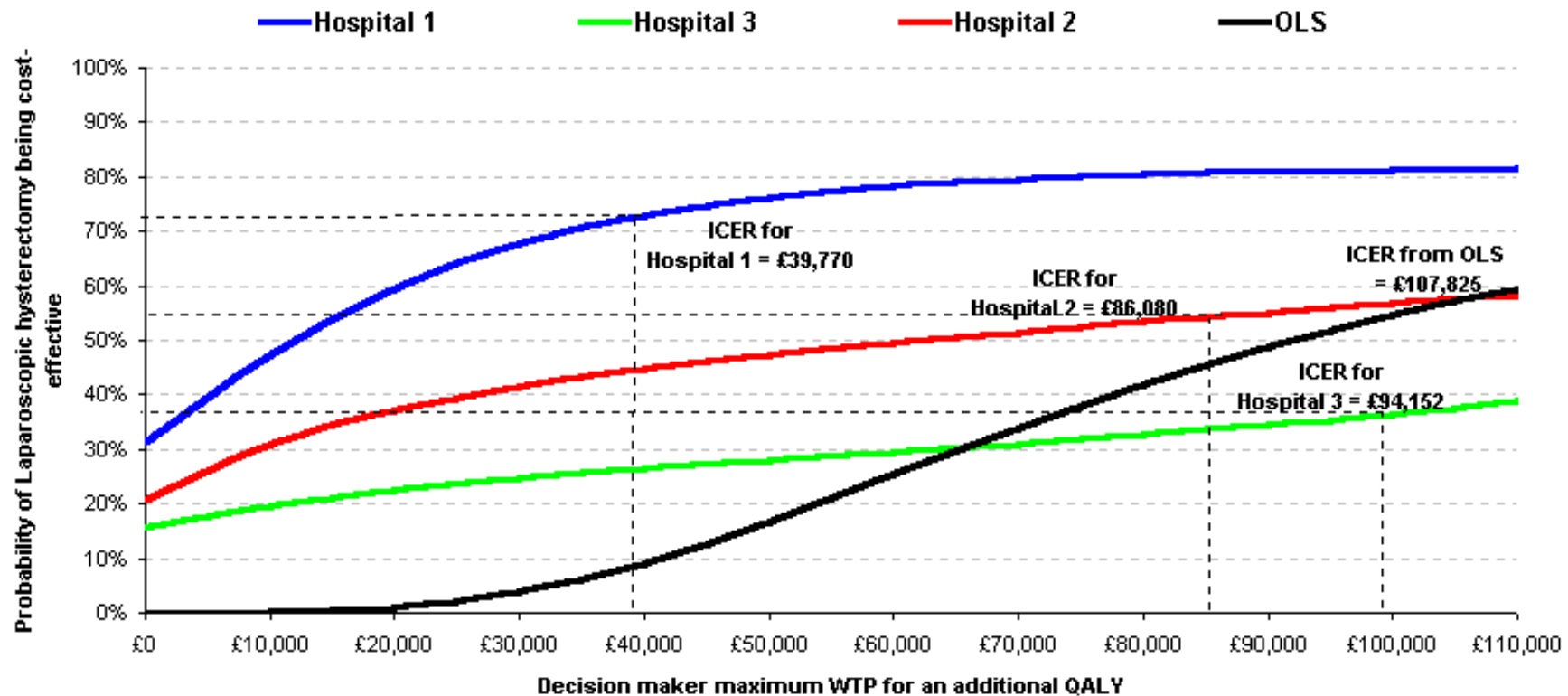
DESIGN CONSIDERATIONS FOR FUTURE MULTINATIONAL EVALUATIONS

- Selection of countries in multinational trials.

- Selection of centres in trials.

- Collection of centre-level variables.

- Selection of resource items for costing.

SELECTION OF COUNTRIES

- 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?

SELECTION OF CENTRES IN TRIALS

- 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?

COLLECTION OF COUNTRY AND CENTRE LEVEL VARIABLES

- 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

SELECTION OF RESOURCE ITEMS FOR COSTING

- 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

	Costs (US$)						
	Germany	Italy	France	Sweden	UK	Australia	Spain
Procedure costs							
Burr holes	130	77	216	*372*	365	711	72
Chest tubes	87	210	*150*	175	*201*	120	93
Central nervous system shunt	1148	1749	617	371	357	699	*526*
Craniofacial procedures	*350*	*471*	*628*	693	*843*	888	*673*
Cranioplasty	*590*	794	*1059*	*1557*	*1420*	*1197*	*1134*
Debridement of brain	824	357	740	1386	2247	717	552
Dialysis	*153*	206	*275*	*404*	*368*	*310*	*294*
Elevation of skull fracture	367	357	483	693	377	*505*	336
Evacuation of lesion	506	357	493	1386	476	*722*	705
Filtration for renal failure	*248*	*334*	*441*	*655*	*597*	759	234
Gastroscopy	*106*	245	63	347	*256*	156	*204*
Gastrostomy (procedure)	79	*148*	361	*290*	*264*	*223*	95
Humeral shaft fracture	*287*	*386*	106	*757*	1904	*582*	21
Intracranial drainage	273	432	*340*	175	365	389	259
Laparotomy (exploratory)	130	209	301	866	462	573	492
Lobectomy	*544*	830	*977*	1040	569	2251	705
Peritoneal lavage	*38*	117	*69*	*102*	*93*	23	34
Removal of bone flap	506	357	411	175	408	1650	332
Replacement of bone flap	809	604	524	*1203*	526	1308	616
Shunt placement	*642*	1749	*1152*	260	2087	*1302*	580
Spine operation	*1125*	1515	*2019*	*2970*	*2708*	*2283*	*2164*
Splenectomy	249	389	*483*	*711*	*648*	*547*	*518*
Swan-Ganz monitor	*207*	335	*371*	*546*	*498*	*420*	317
Superficial laceration	16	31	20	175	154	*68*	36
Tracheostomy	151	120	301	347	256	1105	132
Per diem costs							
Daily intensive care unit	445	601	774	1231	1159	945	876
Daily intermediate care unit	*169*	304	301	573	315	207	*324*
Daily routine care unit	134	187	350	267	173	159	236
Daily rehabilitation unit	140	324	210	336	*384*	186	464

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.