Module 5 – Examples & getting projects funded

Centre for Health Policy
Melbourne School of Population and Global Health

UKPDS: Case study

• United Kingdom Prospective Diabetes Study was one of the first large RCTs to include economic evaluation

• Reported in September 1998

• Of the 40 publications since publication of the main study results, around 10 have had a health economic focus

• Continued collaboration 15 years on

Blood Glucose & Blood pressure Study: Aims

To determine the cost per Quality Adjusted Life Year (QALY) gained of three UKPDS policies:

• Intensive blood glucose control: Is intensive blood glucose control with sulphonylurea, or insulin, cost-effective in preventing clinical complications in people with Type 2 Diabetes?

• Metformin: Is intensive blood glucose control with Metformin in overweight patients cost-effective in preventing complications?

• Tight blood pressure control: Is tight blood pressure control cost-effective in preventing complications?

Main economic evaluation

Comparison: Intensive versus conventional blood glucose and blood pressure control policies in Type 2 diabetic patients

Data: Patient level data on costs and outcomes from UKPDS

Outcome measure: Quality adjusted life years

Time period: Within study effects extrapolated over lifetime (median follow-up 10 years for Blood Glucose and 8.4 years for Blood Pressure Trial)

Perspective: UK health care system

Result: Incremental cost per QALY gained in 2004 £s (£1 = 1.5 Euros)
Costs and resource use

- **Therapy**
  - Drug doses (antidiabetic, antihypertensive, other)
  - Tests (blood glucose, HbA1c)
  - Standard practice (cost of implementing UKPDS policies in a general health care setting)

- **Complications:**
  - Hospital admissions (length of stay, diagnosis)
  - Non-inpatient services (home, clinic & telephone contacts with GPs, nurses, dieticians, etc.)

- Cost of complications is modelled over each patient’s lifetime

### Costs: Blood pressure study

<table>
<thead>
<tr>
<th>Item</th>
<th>Low tight</th>
<th>Tight</th>
<th>Mean cost (SD)</th>
<th>Difference (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensive treatment</td>
<td>1,217</td>
<td>1,029</td>
<td>11.39</td>
<td>3.84 (92.49, 225.9)</td>
</tr>
<tr>
<td>Cost of implementation</td>
<td>1,215</td>
<td>1,027</td>
<td>12.02</td>
<td>3.97 (92.52, 225.9)</td>
</tr>
<tr>
<td>Total cost of treatment</td>
<td>2,032</td>
<td>1,056</td>
<td>14.52</td>
<td>3.97 (92.52, 225.9)</td>
</tr>
<tr>
<td>Without hospitalisation costs</td>
<td>4,544</td>
<td>5,358</td>
<td>5.155</td>
<td>3.23 (192.0, 225.9)</td>
</tr>
<tr>
<td>Hospitalisation costs</td>
<td>2,116</td>
<td>5,358</td>
<td>2.144</td>
<td>3.23 (192.0, 225.9)</td>
</tr>
<tr>
<td>Total cost</td>
<td>3,652</td>
<td>10,717</td>
<td>3.817</td>
<td>3.23 (192.0, 225.9)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>23,778</td>
<td>28,258</td>
<td>3.78</td>
<td>3.23 (192.0, 225.9)</td>
</tr>
<tr>
<td>Total cost</td>
<td>26,995</td>
<td>33,050</td>
<td>3.78</td>
<td>3.23 (192.0, 225.9)</td>
</tr>
<tr>
<td>Total cost</td>
<td>33,050</td>
<td>33,050</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

### Unit costs

<table>
<thead>
<tr>
<th>Item</th>
<th>Unit cost for year</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin (800 mg/500 mg daily)</td>
<td>0.015/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Chlorpropamide (200 mg/250 mg daily)</td>
<td>0.019/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Glimepiride (1 mg daily)</td>
<td>0.020/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Glibenclamide (10 mg daily)</td>
<td>0.020/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Sulphonylureas (50 mg daily)</td>
<td>0.020/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U100)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U50)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U20)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U10)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U5)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U2)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
<tr>
<td>Insulin (U1)</td>
<td>0.07/0.01</td>
<td>Drug cost 2004</td>
</tr>
</tbody>
</table>

### Simulating lifetime outcomes

- **Estimating Outcomes**
  - Estimate QALYs for people with Type 2 diabetes, based on profile of complications of each patient over their remaining lifetime
  - Use UKPDS Outcomes Model which is based on an integrated set of parametric proportional hazard models to predict absolute risk of first occurrence of seven major diabetes-related complications, using:
    - patients’ characteristics (e.g. age and sex)
    - time varying risk factors (e.g. HbA1c)
### Total outcomes

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean (SD) conventional</th>
<th>Mean (SD) intensive</th>
<th>Mean difference (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive BG</td>
<td>16.35 (8.36)</td>
<td>16.62 (8.35)</td>
<td>0.27 (-0.48, 1.03)</td>
</tr>
<tr>
<td>Metformin</td>
<td>16.44 (8.49)</td>
<td>17.32 (7.94)</td>
<td>0.88 (-0.54, 2.29)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>13.71 (8.00)</td>
<td>14.16 (7.81)</td>
<td>0.45 (-0.70, 1.60)</td>
</tr>
</tbody>
</table>

### Cost-utility results

<table>
<thead>
<tr>
<th>Intervention more effective, more costly</th>
<th>Intensive blood glucose control with sulphonylurea/insulin £6000 per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention more effective, less costly</td>
<td>Intensive blood glucose control with metformin £2000 per QALY</td>
</tr>
<tr>
<td>Intervention less effective, less costly</td>
<td>Tight blood pressure control £4000 per QALY</td>
</tr>
</tbody>
</table>

**INCREMENTAL QALYs**

- £4,000
- £2,000
- £0
- £2,000
- £4,000

**INCREMENTAL COST**

- £2,000
- £4,000

Costs & QALYs discounted at 3.5% p.a.

### Initial outputs

Three economic evaluations alongside the RCT:

- Two in BMJ
- One in Diabetologia

**Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41)**

Alison Grant, Philip Clarke, Andrew Farrar, Barry Holman, and Robert Durrer on behalf of the United Kingdom Prospective Diabetes Study Group.

**Abstract**

Objective To compare the cost effectiveness of conventional versus intensive blood glucose control in type 2 diabetes, and the cost effectiveness of the policy features required using intensive the intensive blood glucose control in type 2 diabetes.

**Methods**

Conventional and intensive blood glucose control in type 2 diabetes.

**Conclusions**

Conventional blood glucose control was less costly and less effective, and intensive blood glucose control was more costly and more effective.

### Policy paper: Cost of implementation

- Cost of implementation of the program in the UK
- Published in the BMJ 2002

Implementing intensive control of blood glucose concentration and blood pressure in type 2 diabetes in England: cost analysis (UKPDS 65)

Alison Grant, Philip Clarke, Andrew Farrar, Barry Holman, on behalf of the United Kingdom Prospective Diabetes Study (UKPDS) Group.

**UKPDS – describes a simulation model for projecting QALYs for people with diabetes**

- Used over 150 research groups world-wide
- 270 citations
- Used by more 180 other research groups
Other ways to collaborate

**DiGEM Study**
- RCT of blood glucose monitoring in people with Type 2 diabetes not using insulin
- Conclusion of main study: “At 12 months the differences in HbA1c level between the three groups (adjusted for baseline HbA1c level) were not statistically significant (P=0.12).”
- EQ5D administered at baseline & 12 months

<table>
<thead>
<tr>
<th>Table 1: Mean (standard error) of HbA1c, mean difference (95% confidence interval) per patient within each group and mean difference between baseline and 12-monthly follow-up in the three groups.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>Standard care</td>
<td>9.13 (0.23)</td>
</tr>
<tr>
<td>Less intensive individual group</td>
<td>9.15 (0.23)</td>
</tr>
<tr>
<td>More intensive individual group</td>
<td>9.13 (0.23)</td>
</tr>
</tbody>
</table>

**LDS study**
- Large RCT of statins/ fibrates in people with Type 2 diabetes, ended early due to withdrawal of Cerivastatin
- SF-36 items administered to 4,051 individuals at baseline alongside clinical measure include assessment of visual acuity
- Examined the association between visual acuity and quality of life
- Only paper ever published using the trial data

**FIELD study**
- Large RCT of the use of Fibrates to lower cholesterol in people with diabetes
- Non-significant primary outcomes
- Looked at relationship between EQ-5D scores predicting events
- Demonstrated that scores further stratified risk over and above that used in CVD risk prediction equations

**AusHeart**
- Australian Hypertension and Absolute Risk Study involving 322 general practitioners who each collected clinical data on 15–20 patients aged 55 year
- Consented to have their information linked with Medicare data
- Also collected income data & household structure
- First Australian study to combine socio-economic data with clinical & MBS/PBS information
- Showed large health inequality, but even use of out-of-hospital Medicare benefits across income groups

**Developing country application**
- Approached by investigators of RCT of Malaria treatments in PNG
- Extrapolated to get estimate in terms of life years saved
- The most cost-effective treatment option was $58 per life year saved
To determine the costs and cost-effectiveness of an early childhood home visiting program delivered to families in socio-economically disadvantaged areas of Sydney, Australia during 2007-2010.

The cost of HB intervention in the clinical study over 2 years was $1309 per child (2012 AUD).

The incremental cost-effectiveness ratio was $4230 per unit BMI avoided.


Collaboration & Funding

**Reasons to Collaborate**

- Collaboration represents trade between researchers
- Clear gains as it allows people to specialize, but there must be gains from trade
- Only four reasons to collaborate and so each party must be exchanging:
  - Data
  - Money
  - Skills
  - Enjoyment of academic interaction

**Collaboration: Ingredients for Success**

1. In theory grant collaborations should work as both parties have a common goal – high quality publications
2. Clear understanding of roles and responsibilities on project
3. If you want people to do a hard day’s work – you need to pay them!
4. If things become difficult - try to think of it from the other researcher’s perspective

**Investigators**

- Chief investigator usually required for a typical economic evaluation alongside a clinical study (0.05 to 0.1FTE)
- Smaller applications may be fine with an AI (many health economists are already on maximum number NHMRC grants)
- Role as CI for economics is specific so don’t rule out more junior economists (i.e. Senior Research Fellows/ Associate Professors)
  - Can always use more junior economist as CI with Professor as AI
  - Can use AI with named researcher

**Research Input**

- Economic evaluation alongside a clinical study
  - PSP4 Experienced postdoctoral researcher (i.e. a researcher who would normally be considered as a named investigator on the research application and/or approaching the NHMRC CDA scheme or equivalent
    - $82,551 p.a.
  - Occasionally a salary for CI economist if relatively junior (RF/SRF) and not on fellowship
  - Could justify PSP3 if simple application
Examples of role for CI

“CIX has made a major contribution to the planning and design of the health economic evaluation of this program. In doing so CIX has also provided input into overall research design, outcome measures and follow-up periods. CIX will be primarily responsible for overseeing and supervising the economic evaluation/modelling and associated manuscripts, with contributions to the overall study management.”

Role/justification of funding for PSP4

• “A research fellow with significant experience in economic evaluation and modelling is required for this project. They will be required to coordinate appropriate collection of both clinical study data on key outcomes related to the economic modelling and to translate and prepare this data in a format suitable for the economic modelling. They will take the lead in the design and collection of cost data through embedding processes within the study conduct and administrative databases. They will coordinate the capture of downstream health costs associated with the relevant disease states. They will be responsible with direction from CIX for the economic modelling. Model validation and calibration will be required to ensure model outputs are consistent with known patterns of mortality and disease progression in Australia. Extensive one-way and multiway including probabilistic sensitivity analyses will be conducted by the research fellow and with oversight and direction from CIX and they will be responsible for the presentation of results and preparation of manuscripts.”

Example budgets - salary

<table>
<thead>
<tr>
<th></th>
<th>Simple (PSP3)</th>
<th>Standard (PSP4)</th>
<th>Complex (PSP4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>0.1</td>
<td>6,989</td>
<td>0.2</td>
</tr>
<tr>
<td>Year 2</td>
<td>0.1</td>
<td>6,989</td>
<td>0.2</td>
</tr>
<tr>
<td>Year 3</td>
<td>0.5</td>
<td>34,946</td>
<td>0.6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>48,924</td>
<td></td>
</tr>
</tbody>
</table>

*Illustrative examples only - requirements may change significantly depending on specifics of a research proposal

Other possible budget items

• Access costs for PBS/MBS data – Varies from $5000 to $10,000
• Travel to investigator meetings
• Specialist software e.g. TreeAge for economic modelling

Greatest challenges

• Appropriate match of CI/AI and finding one who has not filled all their NHMRC project places
• Engaging economist early increases chances of finding one with capacity
• Looking to set up a “Health Economics/ Clinical researchers eHarmony” website
• Long-term collaborations work best.

Final observations

• Need to engage early with a health economist to scope the task and help design the study
• Focus on collecting data where there are likely to be differences between groups
• Be true to the data when undertaking the analysis and adopt “conservative assumptions” when required.
• Be prepared to change your beliefs if evidence disproves your hypothesis