Potential conflicts of interest – none
Pharmacoeconomics: from policy to science
– Why the need for pharmacoeconomics?
– Common approaches in pharmacoeconomic evaluations
– How pharmacoeconomic evaluations inform decision-making

Workshop 1: Designing a pharmacoeconomic evaluation

Workshop 2: Decision-making based on pharmacoeconomic evidence

Seminar II Summary
Resource Allocation in Healthcare

• Budget constrained health care systems
  – Taxation
  – Insurance

• Systems without a budget constraint
  – Budgets increase to accommodate new ‘valuable’ technologies

• Mixed systems
  – Budget constraints (perhaps time limited)
  – Partial increase in budget to accommodate new technologies
The ‘Economic’ Problem in Healthcare

- Finite resources for health care
- ↑ costs of health care
  - Labour intensive
  - Expensive technologies
  - New drugs
- ↑ demand for health care
  - Demographics
  - ↑ expectations
The Concept of Opportunity Costs

New Technologies
- Health gain
- Additional costs

Budget constrained healthcare system

Displaced Services
- Health forgone
- Resources released
Key Questions

- Can it work?
  - Efficacy

- Does it work?
  - Effectiveness

- Should it be used, given other demands on a fixed budget?
  - Economics
Overall Aim of Evaluation

• Help decision-makers maximise health gain (technical efficiency) given constraints
• Provide clear signals to industry regarding likely return on investment
Economic evaluation is... 

“The comparative analysis of alternative courses of action in terms of both their costs and consequences in order to assist policy decisions” (Drummond et al, 1997)

A means of comparing the virtues (benefits) and vices (costs) of different ways of doing things
Spotting Pharmaconomic Evaluations

- Is there a comparison of two or more alternatives?
- Are both costs and consequences examined?
- If not – the study is not a pharmacoeconomic evaluation but may be:
  - description of costs or outcomes
  - evaluation of efficacy or effectiveness
  - cost analysis
Stages of an Economic Evaluation

1. Define study question
   (Perspective, alternatives, form of evaluation)

2. Identify, measure and value all relevant costs and consequences

3. Adjust for differential timing

4. Apply decision rule and undertake sensitivity analyses

5. Make recommendations to decision makers
Deciding upon the study question

• Identifying the problem and aims of evaluation
  • What is the problem?
  • Why is this problem important?
  • What aspects of the problem need to be explained?

• Choosing the alternative options
  • Describing the interventions accurately
  • Defining the counterfactual intervention (comparator)

• Defining the audience
  • Defining the info needs of the audience
  • Considering how the audience will use the study results
Deciding upon the study question

- Defining the perspective of the study
  - Patient / Providers / Payers / Healthcare system / Society
  - Choosing a perspective depends on the audience

- Defining the time frame and analytic horizon
  - Analytic horizon > Time frame

- Choosing the study format
  - Prospective / Retrospective / Model
  - Depends on data, time and resources available
# Types of Economic Evaluation

<table>
<thead>
<tr>
<th>Cost Evaluation Types</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness, CEA</td>
<td>A common measure in natural units, different magnitudes – e.g. life years gained, mmHg change</td>
</tr>
<tr>
<td>Utility, CU</td>
<td>Single or multiple effects valued as “utility” – quality adjusted life years gained</td>
</tr>
<tr>
<td>Minimisation, C(_{\text{MIN}})</td>
<td>Identical in all aspects</td>
</tr>
<tr>
<td>Benefit, CBA</td>
<td>Monetary</td>
</tr>
<tr>
<td>Consequence, CCA</td>
<td>Multiple</td>
</tr>
</tbody>
</table>
Cost–effectiveness Analysis (CEA)

- If outcomes are not identical but are commensurate: $C_B/E_B > C_A/E_A$, then select A
  - lower cost per unit of output

- E.g.
  - Smoking cessation programme (outcome – number of quitters)
  - Treatments for heart conditions or cancer (outcome – years of life gained).
  - Treatments to improve the quality of life (outcome – quality of life scale)
Cost Utility Analysis (CUA)

- If outcomes are multi-dimensional
  - i.e. \( U_A = f(E_a, E_b, \ldots) \) and \( U_B = g(E_a, E_b, \ldots) \),
  - \( C_B/U_B > C_A/U_A \), then select A
  - lower cost per unit of output

- Multi-attribute quality of life (QoL) where:
  \[
  QoL = f\{\text{physical capacities and limitations, pain, social isolation, anxiety, depression, feelings, etc.}\}
  \]
Cost Minimisation Analysis (CMA)

• If outcomes are identical (i.e. non-inferior) \( C_B > C_A \), then select A
  
  - lower cost for given outcome

• E.g.
  
  - Post-stroke rehabilitation: home vs. hospital (outcome – delivery of physiotherapy)
  
  - Monitoring of blood pressure: self- vs. clinic (outcome – BP measurement)
Types of Costs

Total Cost
- Direct Cost
- Indirect Cost (Loss of Productivity)
- Intangible Cost (Anxiety, pain or suffering)

Direct Cost
- Direct Medical Cost
- Direct Non-medical Cost (Patient out of pocket expenses)

Indirect Cost
- Fixed Cost (Capital, overheads)
- Semi-fixed Cost (Staff)
- Variable cost (Drugs, disposable equipment)

Intangible Cost
- What perspective?
Measuring Costs – Precision

Most precise

**Micro-costing**
Each component of resource use (for example, laboratory tests, days of stay by ward, drugs) is estimated and a unit cost derived for each case-mix group.

**Case-mix group**
Gives the cost for each category of case or hospital patient. Takes account of length of stay. Precision depends on the level of detail in specifying the types of cases.

**Disease-specific per diem (or daily cost)**
Gives the average daily cost for treatments in each disease category. These may still be quite broad (for example, orthopaedic surgery).

**Average per diem (or daily cost)**
Averages the per diem over all categories of patient. Available in most health care systems.

Least precise

*Drummond et al, 2005*
Outcomes

• Change in health status
  – Lives saved
  – Life-years gained
  – Measures of functioning
  – Cases avoided (preventive interventions)

• Change in perceived health status
  – Subjective measures of quality of life
  – Adjustment of perceived risk
Assessment of health effects
Quality Adjusted Life Years (QALYs)

- Weighting each remaining year of an individual’s life by the expected quality of life
- For example:

A 70 year old man is expected to live for another 20 years, but between the age of 80 and 90, due to a variety of illnesses, we expect his quality of life to be only half the quality of his life prior to this

\[
(10 \text{ yrs } \times 1 \text{ QALY/year}) + (10 \text{ yrs } \times 0.5 \text{ QALY/year}) = 15 \text{ QALYs}
\]
Incremental cost–effectiveness ratio (ICER)

{\text{ICER}} = \frac{\text{Cost}_A - \text{Cost}_B}{\text{Effect}_A - \text{Effect}_B}

- Comparative
- Cost per unit of effectiveness (CEA)
- Cost per life–years gained (CEA)
- Cost per quality–adjusted life–years gained (CUA)
An Example

<table>
<thead>
<tr>
<th></th>
<th>Hip Replacement</th>
<th>No Hip Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life (health utility)</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Cost of procedure</td>
<td>£15,000</td>
<td>£0</td>
</tr>
</tbody>
</table>

ICER = \( \frac{£15,000 - £0}{0.7 \times 15 - 0.5 \times 15} \) = £5000 per QALY

Assumes that hip replacement patient lives for average of 15 years after intervention
Incremental costs

Incremental life-years

Difference in costs

Difference in life-years
New treatment more costly

Old treatment dominates

New treatment more effective but costly

New treatment less costly but less effective

New treatment less effective

New treatment less costly

New treatment dominates
Incremental Cost-effectiveness Plane

Old treatment dominates

New treatment more effective but costly

New treatment less costly but less effective

New treatment dominates

New treatment less costly

New treatment more costly

Ceiling Ratio e.g. £20,000 per QALY
Incremental (marginal) vs Average Analysis?

- An analysis of different doses of a cholesterol lowering drug shows that 80mg per day gives a cost effectiveness of £25,000 per life-year gained (LYG)
- 40mg per day gives £15,000 per LYG
- So it’s probably worth giving 80mg where possible as the extra LYG costs only £10,000?
- Well...
80 mg

£25,000 per life-year gained

40 mg

£15,000 per life-year gained

Costs

Life-year gained
40 mg £15,000 per life-year gained
80 mg £25,000 per life-year gained
£85,000 per life-year gained
Incremental cost–effectiveness = what is the additional cost to achieve the additional effectiveness
Adjust for Timing – Discounting

• Prefer to have benefits now and bear costs in the future – ‘time preference’
• Rate of time preference is termed ‘discount rate’
• To allow for differential timing of costs (and benefits) between programmes all future costs (and benefits) should be stated in terms of their present value using discount rate.
• Thus, future costs given less weight than present costs.
Uncertainty and Variability

- **Overall variability between patients**
  - Observed variability within a sample of patients in, e.g. costs and outcomes
  - Reflected in standard deviations associated with a mean value
- **Parameter uncertainty**
  - Imprecision in our estimates of, e.g. mean costs or outcomes
  - Reflected in standard error of the mean
- **Sub-group heterogeneity**
  - ‘Base-line’ characteristics ‘explain’ a proportion of overall variability between patients (e.g. age, sex)
  - E.g. mean cost of an MI may differ between young and old
- **Structural (model) uncertainty**
  - Uncertainty regarding modelling assumptions
Pharmacoeconomic Evaluation

• Synthesis of available evidence: RCT, observational studies, opinion
• Extrapolation from surrogate to final endpoints
• Extrapolation over time
• Indirect comparisons
• Correction of suspected biases
• Requires assumptions and judgement
• Extrapolation = uncertainty
Iterative Approach to Economic Evaluation

Figure 1. Five stages in an iterative approach to the economic evaluation of health technologies

- **Stage 1**: Identify decision problems
- **Stage 2**: Synthesis and modelling given available evidence
- **Stage 3**: Setting of research priorities
- **Stage 4**: Primary research (e.g. RCTs)
- **Stage 5**: Synthesis and modelling with updated evidence

**Preferred funding basis for economic evaluation**

- Trial-based CEA / measurement
- Trial with synthesis and modelling

*Sculpher et al; Health Economics 2006
Boyd et al; Drug Dev Res 2010*
Policy Decision – questions for a new technology

• Does it actually work?
  – Is it better than the existing technology?
  – “better” means more output, but how is output to be measured?

• Can we afford to pay for it?
  – How much will it cost?
  – Is it worth spending more on this technology?
  – Is it worth transferring resources from another health care area to pay for this new technology?
# International Guidelines on Health Technology Assessment

<table>
<thead>
<tr>
<th></th>
<th>Published PE Recommendations</th>
<th>PE Guidelines</th>
<th>Submission Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td>South Africa</td>
<td>Brazil</td>
<td></td>
</tr>
<tr>
<td><strong>America-Centre and South</strong></td>
<td>Brazil, Cuba, México</td>
<td>Canada</td>
<td></td>
</tr>
<tr>
<td><strong>America-North</strong></td>
<td>United States</td>
<td>Taiwan, South Korea</td>
<td>Israel, Thailand</td>
</tr>
<tr>
<td><strong>Asia</strong></td>
<td>China Mainland</td>
<td>Baltic (Latvia, Lithuania, Estonia)</td>
<td>England &amp; Wales, Finland, Poland, Scotland</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td>Austria, Denmark, Hungary, Italy, Russian Federation, Spain</td>
<td>Belgium, France, Germany, Ireland, The Netherlands, Norway, Portugal, Slovak Republic, Sweden</td>
<td></td>
</tr>
<tr>
<td><strong>Oceania</strong></td>
<td>New Zealand</td>
<td>Australia</td>
<td></td>
</tr>
</tbody>
</table>
Variation in how HTA is used in decision making

Increasing use of formal quantifications of trade-offs

Limited quantification
- Examples: Germany, France, US
- Focus on individual effects
- Possible interest in costs, not pharmacoeconomics

Greater use of quantification
- Examples: the UK, Sweden
- Interested in pharmacoeconomics
- Use of QALYs

The future?
- UK value-based pricing
- Weights to QALYs: severity, unmet needs, end of life
The National Institute for Health and Care Excellence

“NICE is the independent organisation in the UK responsible for providing national guidance to the NHS and the wider public health community on the promotion of good health and the prevention and treatment of ill health”

• England and Wales, April 1999
• Northern Ireland, July 2006
A Brief History of NICE

2010: 460 staff and a budget of £78m

- Clinical guidelines
- Interventionsal Procedures
- Public health
- QOF
- Quality standards

Technologies
The NICE Technology Appraisal Process

- Selection
- Assessment
- Appraisal
The NICE Process – Selection

• Not all licensed drugs selected
• NICE has key role in topic selection
• Criteria:
  – Impact on health
  – Impact on costs
  – Urgency
  – National priorities (recent predominance of cancer therapies)
The NICE Process – Assessment

• Scope sets up questions to be addressed

• Key elements of the assessment:
  – Systematic review of clinical and economic evidence
  – Cost-effectiveness analysis
  – Critical review of manufacturer submissions
The NICE Process – Assessment

Multiple Technology Appraisals

– Several related technologies (longer review)
– Initiation to guidance about 52 weeks
– Undertaken by academic groups
– Company submissions typically include systematic review and model

Single Technology Appraisals

– Change in 2006 in face of criticism about slowness
– Relates mainly to new pharmaceuticals
– Manufacturers provide all assessment (clinical review and cost-effectiveness model)
– Academic evidence review group critically reviews submission
The NICE Process – Appraisal

- Appraisal Committee
- Assessment Reports
- Manufacturer Submissions
- Patient Organisation Submissions
- Professional Submissions
- Patient Witnesses
- Expert Witnesses
The NICE Appraisal Committee Members

- Public Health Experts (x 2)
- Clinical Nurse Specialist
- Commissioning Executives (x 4)
- General Practitioner
- Health Economists (x 3)
- Statisticians (x 2)
- Clinical Pharmacologist (x 2)
- Pharmaceutical Industry (x 2)
- Lay Representative (x 2)
- CHAIR (Radiologist)
- Clinical Experts

Committee A – 28 members
The NICE Process – Decisions

- Unconditional positive guidance
- Conditional positive guidance (on particular patient characteristics)
- Negative guidance
- Recommended only in research
- Opportunity for appeal
- Decisions reviewed in the future
NICE Decision Considerations

• Weighs up benefits of technology under assessment against what’s currently available
• Takes into account:
  - any undesirable side effects
  - the effects of refusing NHS availability
  - impact of treatment on length and quality of life
  - net cost to the NHS
  - the impact of treatment on NHS resources
<table>
<thead>
<tr>
<th>Element of health technology assessment</th>
<th>Reference case</th>
<th>Section providing details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defining the decision problem</td>
<td>The scope developed by the Institute</td>
<td>5.2.5 &amp; 5.2.6</td>
</tr>
<tr>
<td>Comparator</td>
<td>Therapies routinely used in the NHS, including technologies regarded as current best practice</td>
<td>5.2.5 &amp; 5.2.6</td>
</tr>
<tr>
<td>Perspective on costs</td>
<td>NHS and PSS</td>
<td>5.2.7 to 5.2.10</td>
</tr>
<tr>
<td>Perspective on outcomes</td>
<td>All health effects on individuals</td>
<td>5.2.7 to 5.2.10</td>
</tr>
<tr>
<td>Type of economic evaluation</td>
<td>Cost-effectiveness analysis</td>
<td>5.2.11 &amp; 5.2.12</td>
</tr>
<tr>
<td>Synthesis of evidence on outcomes</td>
<td>Based on a systematic review</td>
<td>5.3</td>
</tr>
<tr>
<td>Measure of health effects</td>
<td>QALYs</td>
<td>5.4</td>
</tr>
<tr>
<td>Source of data for measurement of HRQL</td>
<td>Reported directly by patients and/or carers</td>
<td>5.4</td>
</tr>
<tr>
<td>Source of preference data for valuation of changes in HRQL</td>
<td>Representative sample of the public</td>
<td>5.4</td>
</tr>
<tr>
<td>Discount rate</td>
<td>An annual rate of 3.5% on both costs and health effects</td>
<td>5.6</td>
</tr>
<tr>
<td>Equity weighting</td>
<td>An additional QALY has the same weight regardless of the other characteristics of the individuals receiving the health benefit</td>
<td>5.12</td>
</tr>
</tbody>
</table>

HRQL, health-related quality of life; NHS, National Health Service; PSS, personal social services; QALYs, quality-adjusted life years.
The cost-effectiveness threshold

• “The appropriate threshold to be used is that of the opportunity cost of programmes displaced by new, more costly technologies”

• If most plausible estimate is below £20,000 per QALY gained: cost-effective use of NHS resources

• Above £20,000: are there benefits not captured by the QALY? Has quality of life aspect been adequately measured?

• Above £30,000: “... need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources”

Appraising life-extending, end of life treatments

“the impact of giving greater weight to QALYs achieved in the later stages of terminal diseases, using the assumption that the extended survival period is experienced at the full quality of life anticipated for a healthy individual of the same age”
NHS end-of-life drugs rule change

Drugs which give terminally ill patients a few extra months to live have a better chance of being approved on the NHS under new rules.

The National Institute for Health and Clinical Excellence (NICE) is to extend the threshold at which the drugs are deemed cost-effective.

But this will only be in certain

The NHS has a finite pot of money for treatments
End of life criteria

• The treatment is indicated for patients with a short life expectancy, normally <24 months

• There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared to current NHS treatment

• The treatment is licensed or otherwise indicated for small patient populations
Other Threshold Exceptions

- **Severity of the underlying illness**
  When ICERs are equivalent, society would give priority to the expensive relief of a serious condition compared with relatively inexpensive relief of a mild discomfort.

- **Stakeholder persuasion**
  When symptoms are poorly reflected in clinical trials or inadequately reflected in the measure of health-related quality of life used.

- **Significant innovation**
  When the technology produces a substantial, demonstrable and distinct benefit, that may not have been adequately captured in the measure of health-related quality of life used.

- **Disadvantaged populations**
  E.g. poorer people and ethnic minorities.

- **Children**
  Society would generally favour ‘the benefit of the doubt’ being afforded to sick children.
Implications of NICE Decision

• PCTs are legally bound to fund within 3 months of a positive decision
• NICE is often criticised as a “penny pinching” body to guard NHS budgets
• King’s Fund estimated NICE decisions added a net cost of £1022m to NHS budget between 2003/4 and 2006/7
• Meeting the cost of these decisions is one of the reasons PCTs often use to justify over spending
What NICE does well:

• Goes beyond HTA, provides a “front end” for the evidence produced by HTA and to integrate it with policy

• In the UK are they integrated with decision making, legally binding, national in scale and put into practice in a system with a single payment

• “NICE’s success may owe more to its setting within a single payer health system with a constrained budget than it does to anything unique about its methods”
Criticisms of NICE

- Threshold
  - Too high
  - Too low
- Disinvestment
- Patient Perspective
- Non submission
Threshold

  - A 2-year project, funded by the NIHR and MRC Methodology Research Programme
  - Aimed to develop methods to estimate the NICE cost–effectiveness threshold using routinely available data
  - “The central or ‘best’ threshold is estimated to be £18,317 per QALY”
  - Recommended additional weight for health benefits in diseases which impose a large health burden and/or where there are wider social benefits for patients and/or carers
Researchers claim NHS drug decisions 'are flawed'

By Jane Dreaper
Health correspondent, BBC News

The formula used by the NHS to recommend which drugs should be funded is "flawed" and should be scrapped, researchers say.

The European Commission-funded study tested the assumptions of the system used by NICE (the National Institute for Health and Clinical Excellence).
Value based pricing:

- There is currently no link between clinical guidelines, HTA and medicines pricing
- UK Government committed to changing Pharmaceutical Price Regulation Scheme (PPRS) to ensure better use of NHS resources
- Basic idea is that the price of a medicine should be related to cost effectiveness based on clinical evidence
- All branded medicines would be evaluated against alternatives including generics
Industry sets price initially

Evidence gathered on clinical effectiveness

Comparison made with therapeutic value of alternatives

Cost effectiveness established

Reimbursement to NHS/industry dependent on clinical value