# Randomised Controlled Trials in Mental Health- AFFIRM Short Course

## Economical Evaluation in Randomised Controlled Trials

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Thanks to Professor Sarah Byford



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**AFFIRM** AFrica Focus on Intervention Research for Mental Health

# Economical Evaluation Aims

Collecting economic data at the same time as evidence for effectiveness.

Outline of key preparatory design elements

- Objectives of economic evaluation

- Design of trial based economic evaluations

- How are data measured and valued

- Analysis and reporting of data

- Advantages of trial based economic evaluations

# Economics

*"The central concern of economics is
how to use available resources best when
these resources are insufficient to meet
total needs"*
Robinson BMJ, 1993;307:994-996

So, economics is concerned with resource allocation

# Theory of welfare economics

- To set priorities with limited resources need
  - → costs and benefits

- Economics is the study of welfare/wellbeing

- Societal perspective

- Concerned with the impact of an action on the whole of society, not just the individuals directly involved

- Effects may be negative (costs) or positive (benefits)

- Aim to ensure total benefits outweigh total costs

# Economic evaluation

- Devoting resources to one service means forgoing the benefits that would have arisen by funding another

- Choices must be made

- Economics is concerned with making these choices in a **rational**, **explicit** and **transparent** manner

- Economic evaluation defined as the **comparative** analysis of **alternative** courses of action in terms of both **costs** and **consequences**

- Basic tasks are to **identify**, **measure**, **value** and **compare** all relevant costs and consequences

| Methods of economic evaluation | Costs | Consequences |
|---|---|---|
| Cost-effectiveness | £ | Disease-specific scale |
| Cost-consequences | £ | Range of disease-specific scales |
| Cost-utility | £ | Generic measure of utility e.g. QALYs |
| Cost-benefit | £ | £ |
| Cost-minimisation | £ | None, assumed equal |
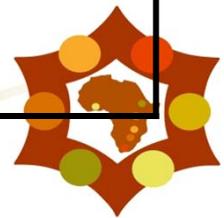
# What are the objectives of economic evaluation?

- Concerned with 2 quantities
  - The additional cost of a new treatment compared with the existing alternative
  - The addition health benefits
- If all the costs and outcomes relevant to this comparison can be measured, they can then be averaged across all patients in the treatment (t) or the control (c) group to obtain mean cost *C and* mean effect *E for each group.*
- the cost effectiveness of the new treatment compared with the alternative
  - the incremental cost effectiveness ratio (ICER) will simply be the difference in costs divided by the difference in effects:
    ICER=*Ct−Cc/Et−Ec=ΔC/Δ*

# Figure: The cost effectiveness plane
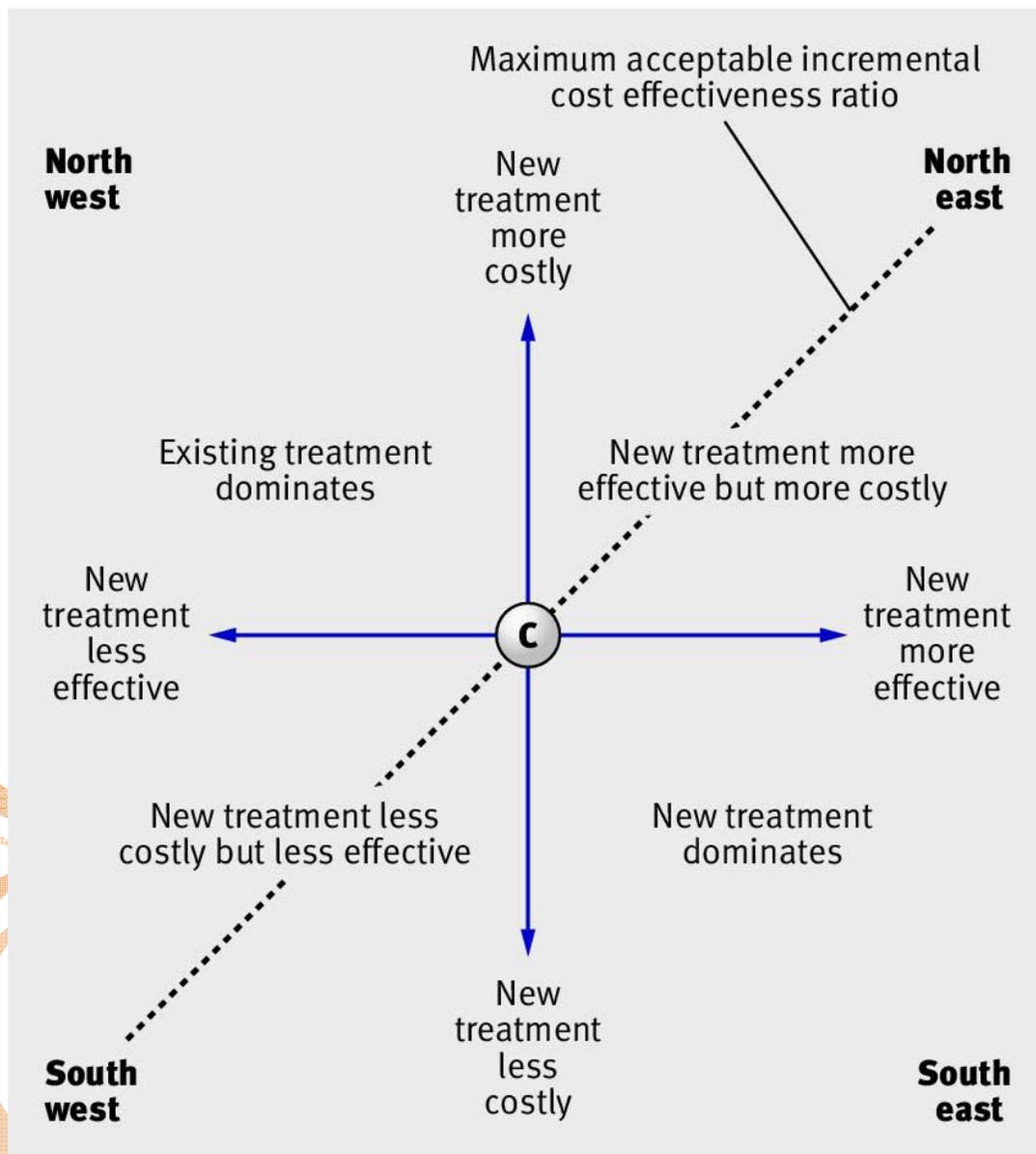


The x axis shows the difference in effectiveness between the new treatment and the comparator and the y axis shows the difference in cost. The slope of the line from any point on the figure to the origin is the incremental cost effectiveness ratio

# Design of trial based economic evaluations

- Collaboration between trialists and health economists
  - SOPS, data collection and informed consent procedures.
- Where possible, the robust instruments and procedures used for economic data collection should be pilot tested for
  - efficiency, clarity, and ease of use.
- Pragmatic trials offer analysts an opportunity to evaluate the cost effectiveness of an intervention under real world conditions,
  - comparison of the intervention of interest with current practice, and follow-up under routine conditions.
- Pragmatic trials designed primarily to answer questions about safety and efficacy,
  - the generalisability of the economic results may be impaired by tight inclusion criteria and treatment protocols or by the absence of a "usual care" arm.
- No sample size for economical outcomes
  - Economists therefore focus on estimating cost and effect differences and assessing the likelihood that an intervention is cost effective, rather than testing a particular hypothesis concerning cost effectiveness.

# How are data measured and valued?

- Use of resources

- Valuation of resource use

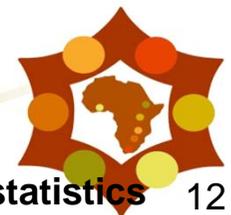- Measurement and valuation of outcomes
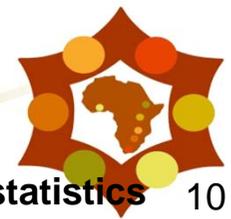
# 1. Use of resources

- The resources used by patients (eg as hospital admissions, consultations, and types of drugs administered) are normally recorded for each patient over the trial follow-up.

- The categories of resource use that are included in the study will be determined by the perspective of the analysis—whether it is confined to the healthcare system (sometimes referred to as the payer) or includes broader societal costs.

- The system perspective would typically include direct medical care, including
  - the intervention itself, treatment of any side effects or complications, and follow-up care to the intervention or the underlying condition.

- Use of many resources can normally be recorded on trial case report forms with little or no extra burden

- When data are collected through patient or carer questionnaires, researchers have to balance recall bias against completeness of sampling information
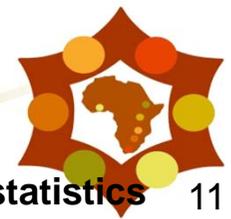
# 2. Valuation of resource use

- The total cost for an individual patient participating in a trial is the product of the quantity of each resource item they use and the unit cost of each item. Unit costs should theoretically be based on the economic notion of opportunity cost, which represents the value of the resource in its most highly valued alternative use.

- Standard unit costs are often applied across all patients and trial centres, but non-standardised unit costs may be appropriate if the relative prices of factors such as labour and equipment vary between trial centres, especially in multinational trials.

- All costs should be valued at the same price date, with adjustment using healthcare specific inflation indices when necessary.

- Economic evaluations based on multinational trials should convert costs into a common currency by using purchasing power parity adjustments.

# 3. Measurement and valuation of outcomes

- The preferred outcome measure for many health economists, and many reimbursement agencies, remains the quality adjusted life year (QALY), a preference based measure of health outcome that combines length of life and health related quality of life.

- To estimate QALYs patients typically complete at different time points a generic health related quality of life questionnaire with pre-existing preference weights that can be attached to each health state—for example EQ-5D the Health Utilities Index and the SF-6D

- The QALY is a measure of the value of health outcomes. Since health is a function of length of life and quality of life, the QALY was developed as an attempt to combine the value of these attributes into a single index number.

- The basic idea underlying the QALY is simple: it assumes that a year of life lived in perfect health is worth 1 QALY (1 Year of Life × 1 Utility value = 1 QALY) and that a year of life lived in a state of less than this perfect health is worth less than 1.
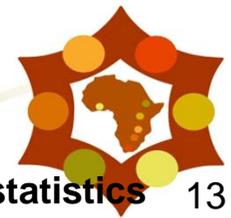
# Analysis and reporting of data

- Discounting

- Dealing with skewed, missing data

- Handling uncertainty

- Longer term extrapolation

# 1. Discounting

- Trial based economic evaluations often measure and value costs and outcomes over several years of patient follow-up. In this situation costs and outcomes that occur after the first year of follow-up are typically reduced by a discount factor so that they can be fairly compared.

- Some economists have argued for applying different discount rates to future costs and health outcomes, but NICE recommends that economic evaluations should discount both costs and outcomes at an annual rate of 3.5%

- Sensitivity analyses that test the effects of differential discount rates on costs and outcomes are recommended

# 2. Dealing with skewed, missing data

- Skewness
  - Data are often skewed due to few patients use very high amounts of resource
  - Zero inflated
  - Violate the assumptions of standard statistical test
  - Bootstrapping
  - Analyses for normal distributions may be appropriate in large samples (eg GLM)
  - For QALYS may be important to adjust fr baseline difference sin heath status

- Missing data
  - Impute or draw on methods to predict missing data in the modelling
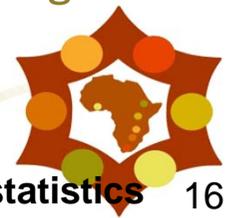
# 3. Handling uncertainty

- Sampling (or stochastic) uncertainty
  - usually reported as a CI
- depends on variation in both the numerator (incremental cost) and the denominator (incremental effectiveness) of the incremental cost effectiveness ratio.
  - problems: denominator (the effect difference) may be zero
  - problems: negative value might represent improved outcomes and lower costs be careful!
- Heterogenity in the trial population
  - explored by formulating a new benefit value for each patient from the observed costs and effects, and then constructing a regression model with a treatment variable and covariates such as age, sex and disease severity
- Methodological uncertainity
  - issues such as appropriate discount rate or cost perspective
  - explore through standard sensitivity analyses
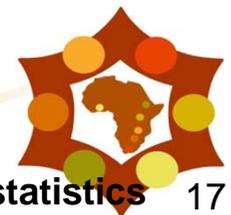
# 4. Longer term extrapolation

- Cost effectiveness observed within a trial may be substantially different from what would have been observed with continued patient follow-up:
  - for example, the benefits of reducing fatal outcomes typically continue well beyond the end of the trial.

- Consequently, extrapolation of cost effectiveness over an extended period, **often a lifetime**, is considered important.

- However, unbiased estimation of long term cost effectiveness may require more **complex models of the disease process**, accompanied by information on the cost and utility of interventions and complications.

- **Trial based economic evaluations that use patient level data** have important advantages in permitting the construction of such models and permitting them to be validated.

# Complexities in mental health

- Broad perspective
- Multi-agency involvement
- Complex interventions
- Significant data collection burden
- Multiple outcomes
- Inadequate quality of life scales
- Highly skewed costs - implications for sample size and statistical analysis

$\Rightarrow$ Complex problems, complex interventions
$\Rightarrow$ Complex evaluations

# Summary points

1. Economic evaluation is increasingly used to inform the regulatory and reimbursement decisions of government agencies

2. Evaluations conducted alongside randomised controlled trials provide access to data on individual patients

3. This enables a wide range of analytical techniques—for example, to examine the relation between events of interest and health related quality of life

4. Designing a rigorous trial based economic evaluation requires close collaboration between trialists and health economists from the outset of the trial

5. We have outlined key issues concerning the design, conduct, analysis, and reporting of economic evaluations based on randomised trial with individual patient data are outlined

# References

- Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart G. *Methods for the economic evaluation of health care programmes , 3rd ed. Oxford University Press, 2005.*

- 2 National Institute for Health and Clinical Excellence. *NICE guide to the methods of technology appraisal . NICE, 2008.*

- Petrou S and Gray A. *Economic evaluation alongside randomised controlled trails: design, conduct , analysis and reporting. BMJ 2011;342:d1548 doi: 10.1136/bmj.d1548*