Pharmacoeconomics and Management in Pharmacy X

[John Vella B.Pharm.(Hons.) M.Sc.(Pharmacoeconomics)]

News review

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Academic bias

As part of the Australian National Research Assessment, the nation's 133 most senior academic economists participated in a voting process that assigned quality ratings to almost a thousand journals of economics. The ratings were applied on the nation's 975 academic economists' publications retroactively by a number of institutions for a variety of purposes. The government used them to rank Universities and to distribute research funds. And Universities used them in hiring decisions, and the determination of salaries and publication bonuses. This study investigates the determinants of voting decisions. We find that voters are influenced by objective measures of journal quality. However, *we also find strong evidence that, other things equal, voters assign the highest possible quality rating to journals in which they have published. They also overstate the quality of journals to which they have special access while understating the quality of journals that fall primarily in the fields of expertise of their 842 non-voting colleagues, or in which these non-voting colleagues have published.*

Freakonomics blog

- This study proves that academics are positively biased towards the journals that publish their research
- They exhibit negative approaches to those that publish work from competing researchers
- They also overstate the quality of the journals to which they have special access

Overdosed America

- A well-written book by Dr. John Abramson
- Dr. Abramson is an MD in the US, with years of practice as a family doctor, and a teaching post at Harvard University
- He wrote this book in an effort to inform the public at large about the manner in which the pharmaceutical industry and the market for medicines has changed

A monopoly in all senses

- Dr. Abramson argues a very persuasive thesis, and presents facts to back up his statements
- He shows the reader how the average medical professional has very little free time to devote to information gathering and continuing education
- The little snippets gathered are usually delivered by company reps, with the appropriate bias

Cox-2 conspiracy?

- An example is that of Celebrex, a cox-2 inhibitor, & one of the top selling drugs in the US
- It is touted as a superior product, and yet the book reveals that it is no better than naproxen, a much older and cheaper alternative
- Studies in favour of the product were paired with weaker comparators and stopped when convenient

A long way to go!

Pharmacoeconomic methods influence only 13 hospital formulary system decisions: Survey

Published on June 7, 2010 at 7:11 AM · No Comments

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Pharmacoeconomic methods rank low as a decision influencer on formulary cha according to a new survey released today by the Society of Hospital Medicine and the American Society of Health-System Pharmacists (ASHP). Respondents that only 13 percent of formulary system decisions made by Pharmacy and The (P&T) committees in hospitals is influenced by pharmacoeconomic methods.

The findings in the new report are based on a survey of 319 ASHP members tha either directors of pharmacy or members of ASHP's Pharmacy Practice Manager Section.

Pharmacoeconomic methods evaluate the value of effects compared to the cos pharmaceutical products when making decisions on changes to the formulary s Hospital formularies identify medications and medication-use policies used withi particular hospital. Decisions on the management of a formulary system have a significant impact on the quality and safety of patient care.

PE knowledge

- The study demonstrates the low take-up of PE as an integral part of decision making
- The fact that cost concerns are stated separately exhibits the lack of proper knowledge and understanding of the subject
- The concept of outcome based evaluation and treatment is still in its infancy

Critique of a PE journal article

Background facts (i)

- “only 1% of the articles in medical journals are scientifically sound”[1]
- There are perhaps 30,000 biomedical journals in the world, and they have grown steadily by 7% a year since the seventeenth century[2]

- [1] Professor David Eddy, Duke University
- [2]Dr. Richard Smith, BMJ editor

Background facts (ii)

- Critical reviews of papers in medical journals have consistently found that about 50% of published articles used incorrect statistical methods
- can lead to invalid results and inappropriate conclusions. A conservative estimate is that about 25% of medical research is flawed because of incorrect conclusions drawn from confounded experimental designs and the misuse of statistical methods[1]

- [1] Zolman, 1993

Background facts (iii)

- Also, the bias generally favors the treatment over the control
- “Why are errors so common? Put simply, much poor research arises because researchers feel compelled for career reasons to carry out research that they are ill equipped to perform, and nobody stops them.”[1]

- [1] Altman, 1994

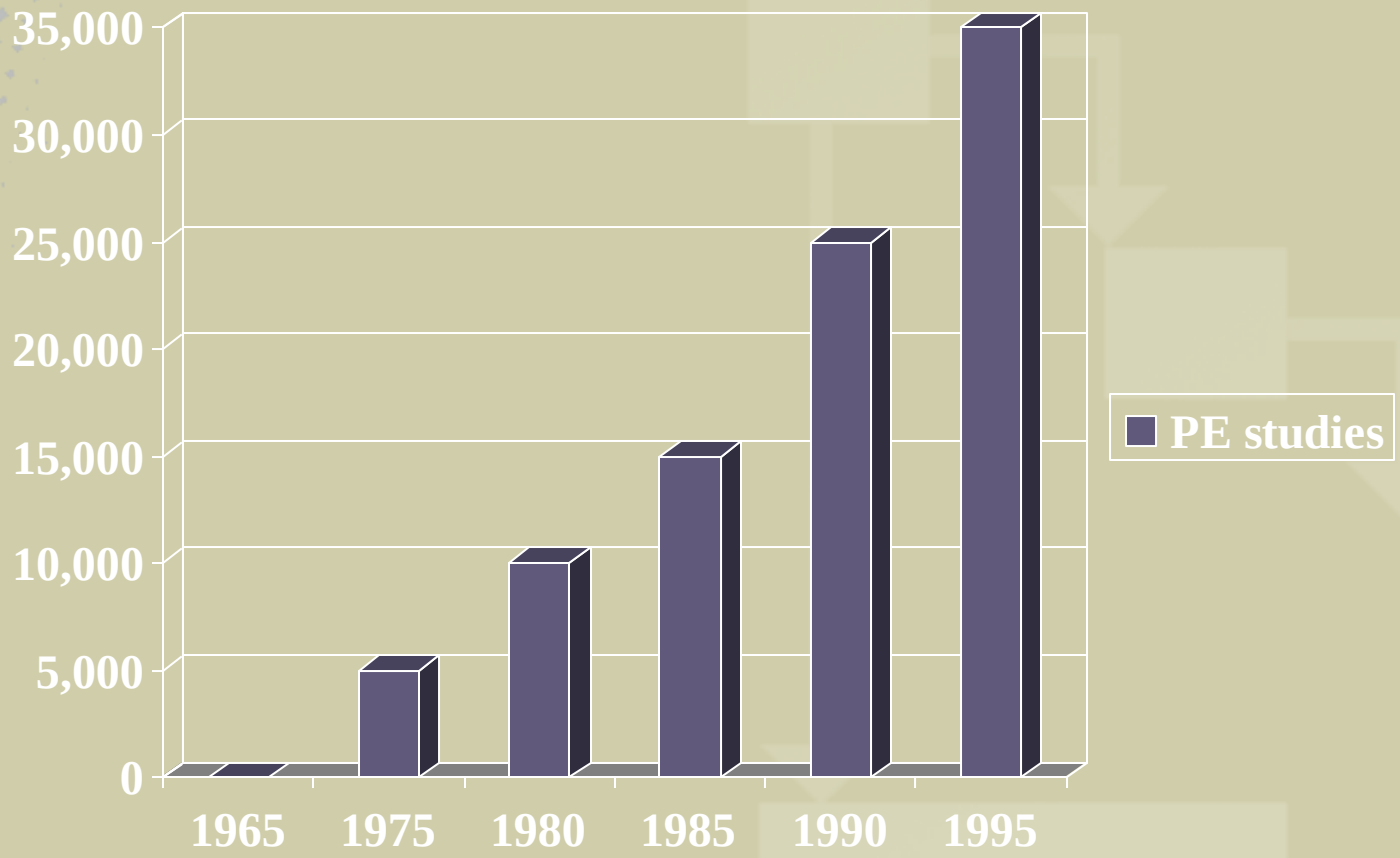
Background facts (iv)

- Researchers often use of the wrong techniques (either willfully or in ignorance)
- Use the right techniques wrongly
- Misinterpret their results
- Report their results selectively
- Cite the literature selectively
- Draw unjustified conclusions

Journal articles (i)

- Tens of thousands of articles are out there
- Electronic media has increased accessibility
- It is imperative that poor articles are discarded and good quality research appreciated and referenced
- No study is perfect; thoroughness is balanced with the practicality of the research

Quantity of available studies



Journal articles (ii)

- It is imperative to evaluate research findings in the light of their validity and general application
- That is, findings reported must be based on valid methodology and data and results can be extrapolated to general populations, without the need for protocol controlled environments

Journal Articles (iii)

- If a study is carefully reviewed to ensure that the author(s) included all meaningful components of an economic evaluation, the likelihood of finding credible and useful results is higher
- This lecture will highlight the basic rules to follow when evaluating an economic study[1-2]

- [1]Adapted from Rascati K, Essentials of Pharmacoeconomics
- [2]Adapted from Say L, Critical Appraisal of Research Reports

Journal Articles (iv)

- Review of more than 4200 published medical reports in about 30 journals(many of them prestigious e.g. BMJ, JAMA, NEJM, Lancet) in terms of scientific adequacy of study designs, data collection and statistical methods *(Williamson, 1986)*
- – only 20% of 4235 research reports met the validity
- criteria
- – ~80% of those inadequately designed and analysed
- had reported positive findings whereas ~ 25% of those
- with adequate designs reported positive results

Basic points

- Is the article relevant to current needs?
- Are the results valid?
- Can they be applied to general practice?

Title: Is the Title Appropriate?

Randomised controlled trial comparing cost effectiveness of general practitioners and nurse practitioners in primary care

P Venning, A Durie, M Roland, C Roberts, B Leese

Title: Is the Title Appropriate?

- Can we make out what type of PE study was carried out?
- Is it a CMA, CEA, CUA, or CBA?
- Is the author stating his biases in the manner in which the title is worded?
- Is the journal a respectable peer-reviewed and often quoted one?

Title: Is the Title Appropriate?

- In this case the study is clearly identified as an RCT, meaning that strict protocols were in place
- The type of PE approach is not specified
- However, the setting (primary care) is indicated
- No bias is present in the title statement
- The BMJ is one of the top medical journals in which to have a paper accepted

Is a Clear Objective Stated?

The aim of this study was to compare the process, outcome, and costs of care given by general practitioners and nurse practitioners for patients requesting a same day appointment in 20 general practices. This group of patients was chosen because a high proportion would be likely to agree to randomisation as they would not have a strong preference for one practitioner who was already involved in their ongoing care.

Is a Clear Objective Stated?

- Does the author(s) clearly state the aim and objectives at the beginning of the study?
- A well designed PE evaluations sets out its targets early on, revealing that the relevant groundwork has been diligently carried out
- Flawed research will tend to be vague in where it wants to get, and how it will get there

Is a Clear Objective Stated?

- The extract shown before was taken from the second paragraph of the article
- The manner in which the study will be carried out is clearly defined, as is the setting
- The rationale for adopting a particular approach is also argued

Is a Clear Objective Stated?

- E.g. of a weak study title:

- An analysis of the cost of anti-hypertensive treatment in the elderly

Is the study design appropriate?

The study took place in 20 geographically dispersed practices in England and Wales. Table 1 shows the location, list size, and number of general practitioner partners in the practices recruited. Ethical approval was obtained for the 20 practices from local research ethics committees. Each practice employed a nurse who had completed a one or two year nurse practitioner training programme at diploma, BSc, or MSc level. The median length of time the nurses had been qualified as nurse practitioners was 3 (range 1-5) years and the median time as registered nurses was 22 (9-35) years. Each nurse practitioner had been seeing patients as first point of contact for at least two years.

Is the study design appropriate?

- When comparing interventions or treatments, it is imperative to draw a comparison to the best alternative available
- Drawing parallels to *weaker* alternatives falsely strengthens results
- E.g. comparing a new cox-2 inhibitor to aspirin will inordinately favour the compound

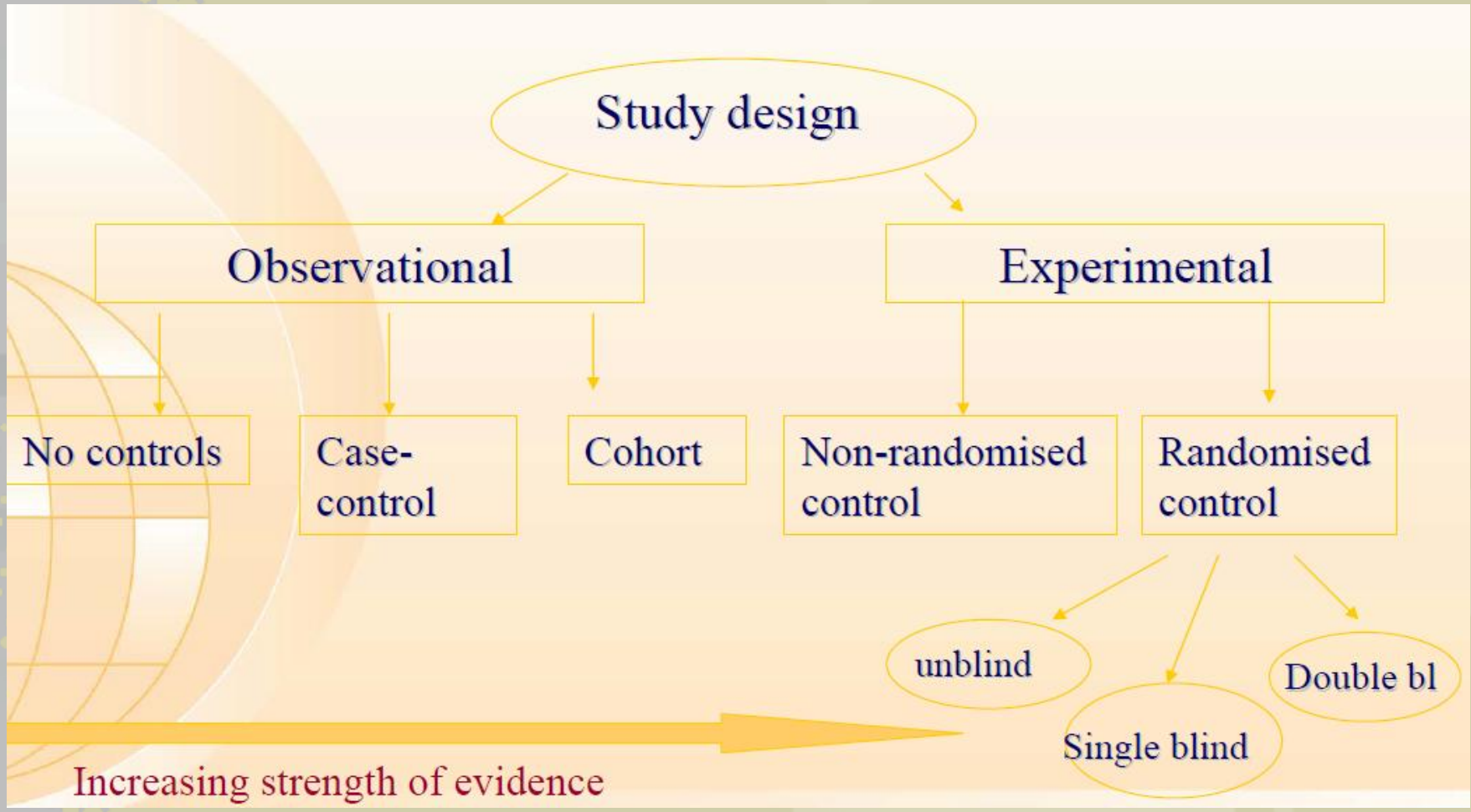
Is the study design appropriate?

- The same study compared the effectiveness of nurse practitioners to GPs
- This is an appropriate choice
- Small sample sizes, and short empirical time-frames are the sign of a weak study design

Is the study design appropriate?

- E.g. Jupiter had 17,802 subjects over a median follow-up period of 1.9 years
- Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin
- One of the largest recent studies on statins

Evaluate the strength of the design



Study design

- The previous slide demonstrates that the ‘strongest’ evidence is provided by studies based on a double blind, randomised experimental study
- This is also known as an RCT, or Randomised Controlled Trial and is the gold standard for clinical trials

Types of RCTs (i)

- Classified by study design.
- Parallel-group – each participant is randomly assigned to a group, and all the participants in the group receive (or do not receive) an intervention
- Crossover – over time, each participant receives (or does not receive) an intervention in a random sequence

Types of RCTs (ii)

- Split-body – separate parts of the body of each participant (e.g., the left and right sides of the face) are randomised to receive (or not receive) an intervention
- Cluster – pre-existing groups of participants (e.g., villages, schools) are randomly selected to receive (or not receive) an intervention

Types of RCTs (iii)

- Factorial – each participant is randomly assigned to a group that receives a particular combination of interventions or non-interventions (e.g., group 1 receives vitamin X and vitamin Y, group 2 receives vitamin X and placebo Y, group 3 receives placebo X and vitamin Y, and group 4 receives placebo X and placebo Y)

Types of RCTs (iv)

- The advantages of proper randomisation in RCTs include:
- It eliminates bias in treatment assignment, specifically selection bias and confounding.
- It facilitates blinding (masking) of the identity of treatments from investigators, participants, and assessors.

Types of RCTs (v)

- It permits the use of probability theory to express the likelihood that any difference in outcome between treatment groups merely indicates chance.

Results (i)

- Are the statistics clear and relevant?
- Is the appropriate level of significance quoted?
- A p value of < 0.05 is considered to be the statistical level of acceptability for quoted results
- This means that the results will be replicated in 95% of the general population as compared to the sample studied

Results (ii)

- Has ethical approval been obtained for any patient involvement?
- This is vital, as the case with the MMR and autism controversy in the UK
- The children studied were included without the permission of their guardians or of the hospital administrators
- Chaos for a number of years in the immunisation schedules

Discussion (i)

- Should start off with a statement confirming or denying the initial hypothesis
- Focus should be on the inherent biases and limitations
- The results should be brought into the contextual perspective, that is their relevance to the body of knowledge on the subject matter should be emphasised

Discussion (ii)

- Comparisons to other studies are useful and can be utilised to increase the import of results
- Are the citations presented in a standard format?
- Is the list of contributors reasonable –twenty authors for a small study?

Discussion (iii)

- Conflict of interest –any financial / administrative relationships with institutions related to the outcome of interest
- Take as an example the recent admission by high ranking WHO administrators involved in the Avian/Swine Flu campaigns that they had vested interests in major multinational pharmaceutical companies

Skill summary (i)

- Describe what critical appraisal means and why it is needed
- Identify which information to seek in which sections of a research article
- Be familiar with the important characteristics of a study to be systematically searched in the article (think systematically when reading a research article)

Skill summary (ii)

- Be aware of the checklists and be able to use them to appraise different study designs
- Take on board the points raised and utilise them when producing original work
- Always keep in mind that the whole system of research and the advancement of knowledge is based on an interconnected web of published and referenced work

Skill summary (iii)

- Aware that being able to differentiate the mediocre from the good and outstanding increases the value and solidity of the whole academic knowledge base
- In the field of PE this is all the more important as certain researchers take advantage of the fact that the novelty of the specialty allows them to produce sub-standard and/or misleading work

Checklist (i)

- Use the internet: it is a free and limitless source
- Pick your sources well: only quote journals or peer-reviewed sites that are frequently mentioned within their field of expertise
- Download copies of all references utilised in research

Checklist (ii)

- Follow references around, that is, track down frequently quoted authors and look up more work by them
- File your saved work systematically, otherwise you will never find what you need when you need it
- Learn to scan articles before reading them: assimilate the main points and decide whether it is worth going further

Checklist (iii)

- Once you have identified the main authorities in a particular area you are researching, look up the people they reference and get hold of their work
- If you are not able to find a particular reference, contact the original author

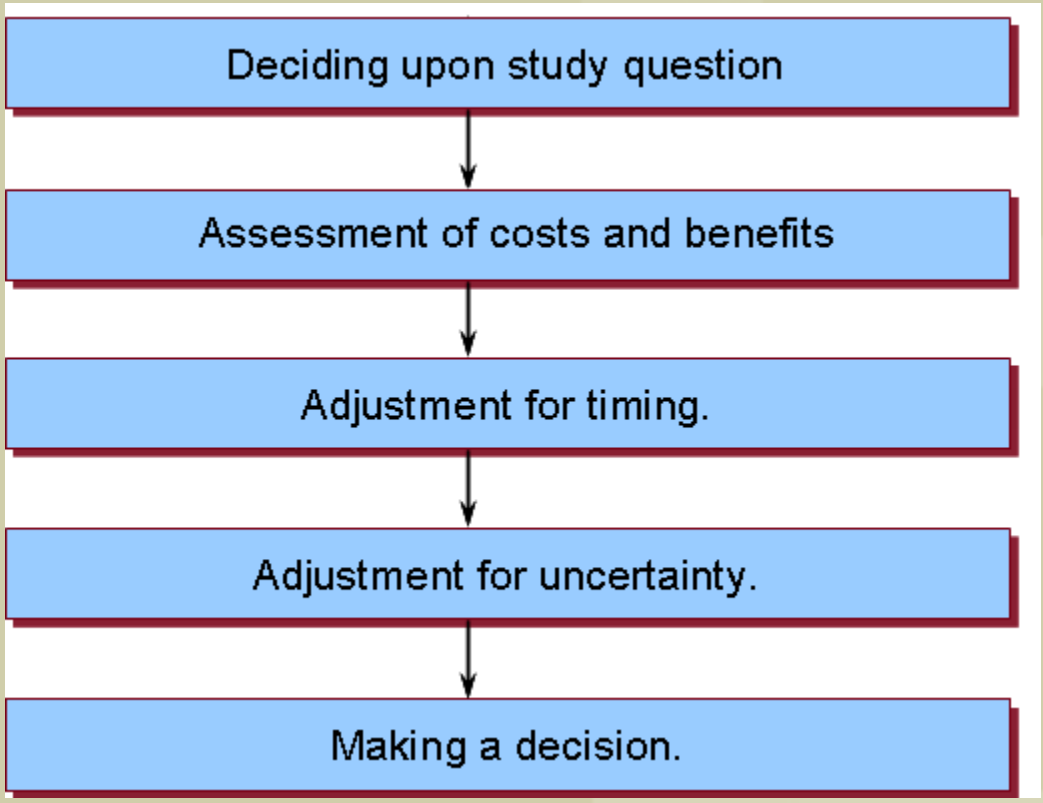
Summary

- The fact that an article has made it to publication does not mean that it is worthwhile
- Critical appraisal of research is vital so as to decide on what to absorb and what to discard when carrying out further study in the field of interest

Designing a PE study and preparing it for publication[1]

[1] Extracted from a presentaion byNelly BIONDI ,South African Centre of Epidemiological Modelling and Analysis (SACEMA), Makerere University, 21th July 2009

Stages in economic evaluation



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.

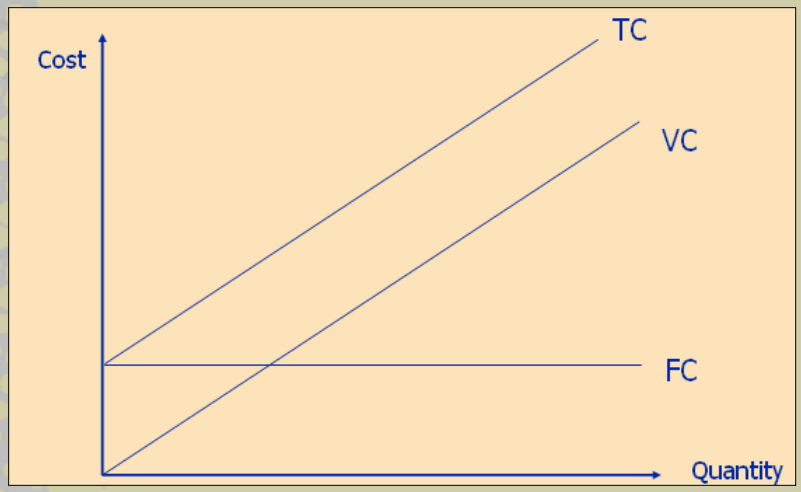
Assessment of costs

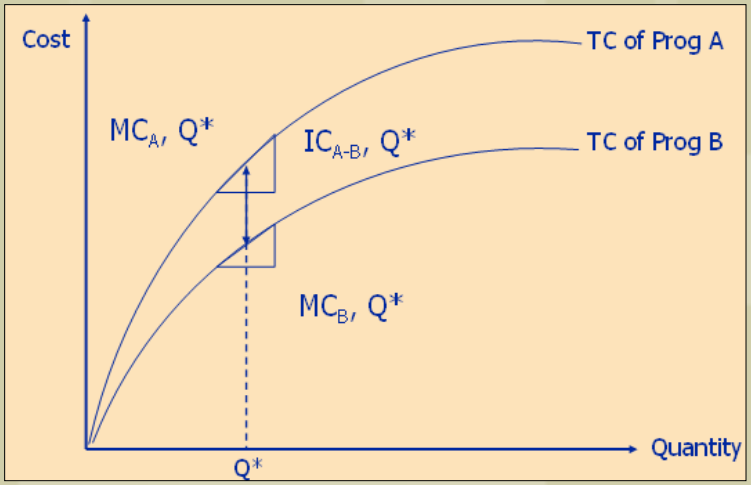
Overview of costing process:

- Identification of costs
  - *Cost type*: direct vs indirect vs intangible.
  - *Cost category*: programme, patient.
  - *Organizational level*: national, regional, district.
  - *Input category*: capital vs recurrent.
  - *Intervention activities*: planning, administration, media, training.
  - *Time*: start-up vs post-implementation.
  - *Funding*: national govt vs NGO vs donor.

Assessment of costs

- Measurement
  - Measure in natural physical units (e.g. hours of labour time).
  - Fixed, variable and total costs.
  - Average versus marginal costs.
  - Marginal versus incremental costs.





Assessment of costs

Table 1: Number of cases detected & costs of screening with sequential guaiac tests

Number of tests	Total cases detected	Total costs (£)	Average cost per case detected (£)
1	65.9496	77,511	1,175
2	71.4424	107,690	1,507
3	71.9003	130,199	1,811
4	71.9385	148,116	2,059
5	71.9417	163,141	2,268
6	71.9420	176,331	2,451

(For a population of 10,000, costs include stool tests and barium-enema examinations on those found positive)

From Neuhauser and Lewicki (1975)

Table 2: Changes in cases detected and in costs of sequential guaiac tests

Number of tests	Additional cases detected	Additional costs (£)	Marginal cost (additional cost per additional case detected (£)
1	65.9496	77,511	1,175
2	5.4956	30,179	5,492
3	0.4580	22,509	49,150
4	0.0382	17,917	469,534
5	0.0032	15,024	4,724,695
6	0.0003	13,190	47,107,214

Assessment of costs

- Valuation
  - Market prices (e.g. wage rates) used unless strong belief they do not reflect opportunity cost (e.g. volunteers).
  - Local currencies vs international currencie.
  - Adjustments for price inflation.

- Calculation
  - Multiply unit of measurement by unit cost (e.g. 2 hours of time at $5 per hour = $10 labour cost).

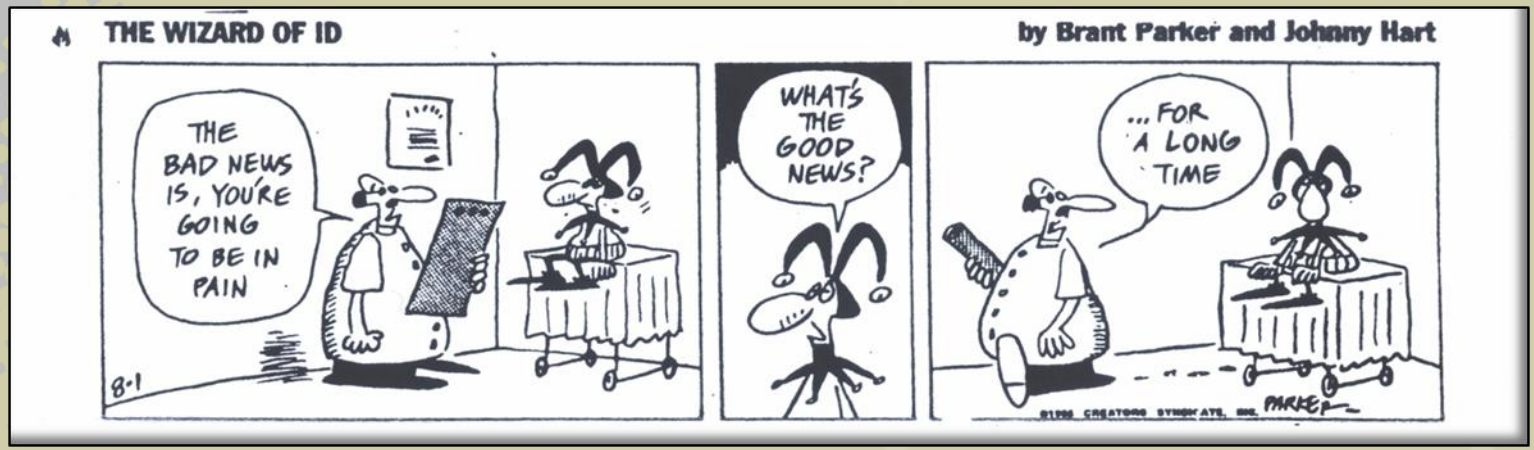
Assessment of health effects

Overview of the process:

- Identification
  - Which outcome measure is employed depends on the objective of the evaluation.
  - This then determines the type of evaluation.

- Measurement
  - Measure *effectiveness* not *efficacy*.
  - Measure (count) in natural physical units.
  - Measure *final* not *intermediate outcomes*.

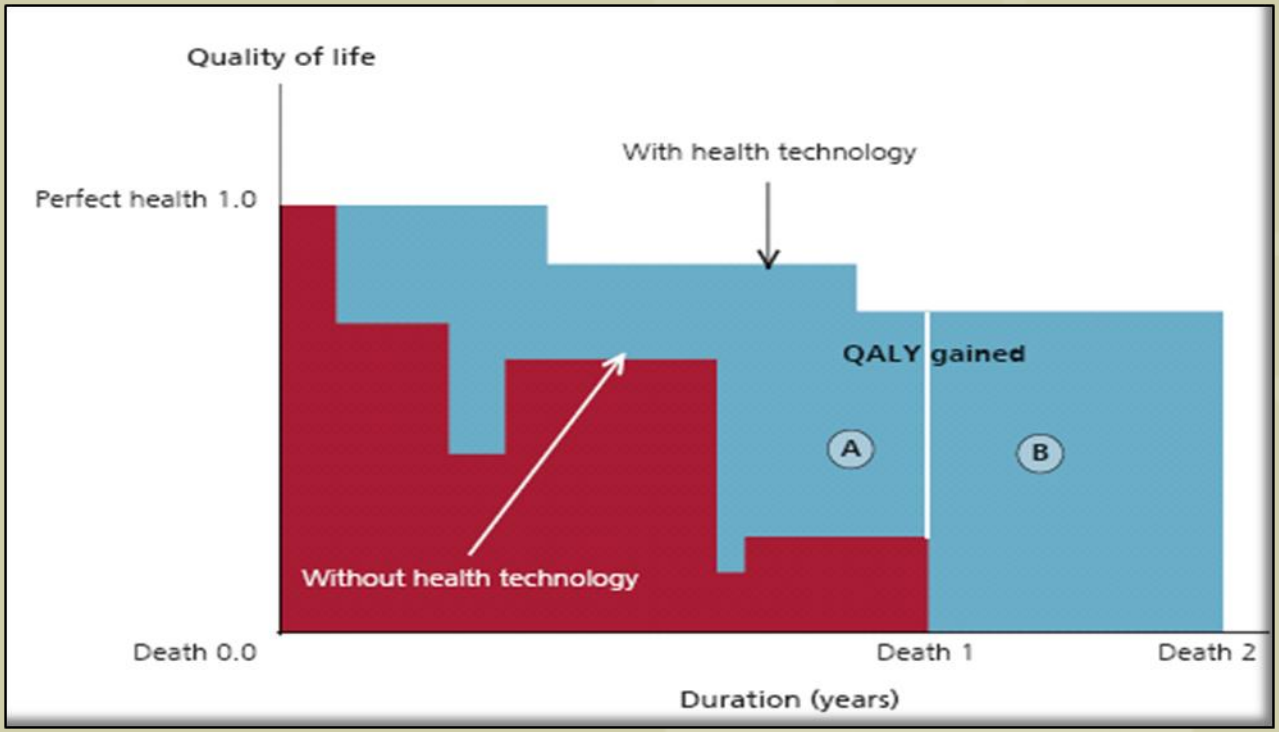
Assessment of health effects



- Valuation *if appropriate*
  - Value is determined by benefits sacrificed elsewhere (see opportunity cost again).
  - Valuation either in terms of:
    - Utility (e.g. QALY, DALY, HYE)
    - Money (e.g. WTP)

Assessment of health effects

Zoom on the concept of QALY:



Adjusting 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.

- Annuitization of capital costs
  - Capital costs represent an investment at start-up in an asset which is used and depreciated over time.
  - Annualise the initial capital outlay over the useful life of asset.

Sensitivity analysis

- Process of **assessing the robustness** of an economic evaluation by considering the effects of uncertainty.

- Consists in:
  - Identifying the (uncertain) variables.
  - Specifying the plausible range over which they should vary.
  - Recalculating results, usually based on:
    - One-way analysis
    - Multi-way analysis
    - Extreme scenario analysis
    - Threshold analysis.

A review of the different types of PE evaluations[1]

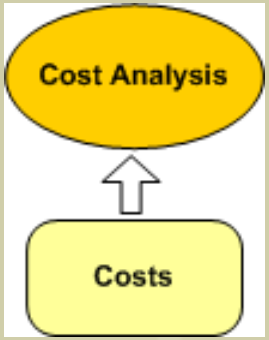
[1] Extracted from a presentaion byNelly BIONDI ,South African Centre of Epidemiological Modelling and Analysis (SACEMA), Makerere University, 21th July 2009

Basic types of economic evaluation

- Cost minimization Analysis (CMA)
- Cost-effectiveness Analysis (CEA)
- Cost-utility Analysis (CUA)
- Cost-benefit Analysis (CBA)

Cost minimization Analysis

- Specific type of analysis in which the outcomes of the 2 (or more) healthcare interventions are **assumed equal**.
- Therefore economic evaluation is based solely on comparative costs.



- Result: least cost alternative.

Cost-effectiveness Analysis

- In CEA, outcomes are measured in **natural or physical units** (e.g. heart attacks avoided, deaths avoided…).

- **Only one** domain of outcomes can be explored at a time.

- Result: cost per unit of consequence (e.g. cost/LY gained)

Cost-effectiveness Analysis

- Decision rule:

  Two programmes **A** (comparator) and **B.**

  - If Outcome **B** = Outcome **A** => Compare costs (CMA).
  - If Outcome **B** > Outcome **A** and Cost **B** < Cost **A**, **B** is dominant.
  - If Outcome **B** > Outcome **A** and Cost **B** > Cost **A**, we have to make a decision.

- In order to make a decision on which intervention to choose, a **cost-effectiveness ratio** (CER) should be calculated.

Cost-effectiveness Analysis

- The most commonly CERs used are the:
  - Average cost-effectiveness ratio (ACER)

$$ACER = \frac{Cost\ B}{Effectiveness\ B}$$

  - Incremental cost-effectiveness ratio (ICER)

$$ICER = \frac{\Delta Cost\ B - Cost\ A\ \Delta}{\Delta Effectiveness\ B - Effectiveness\ A\ \Delta}$$

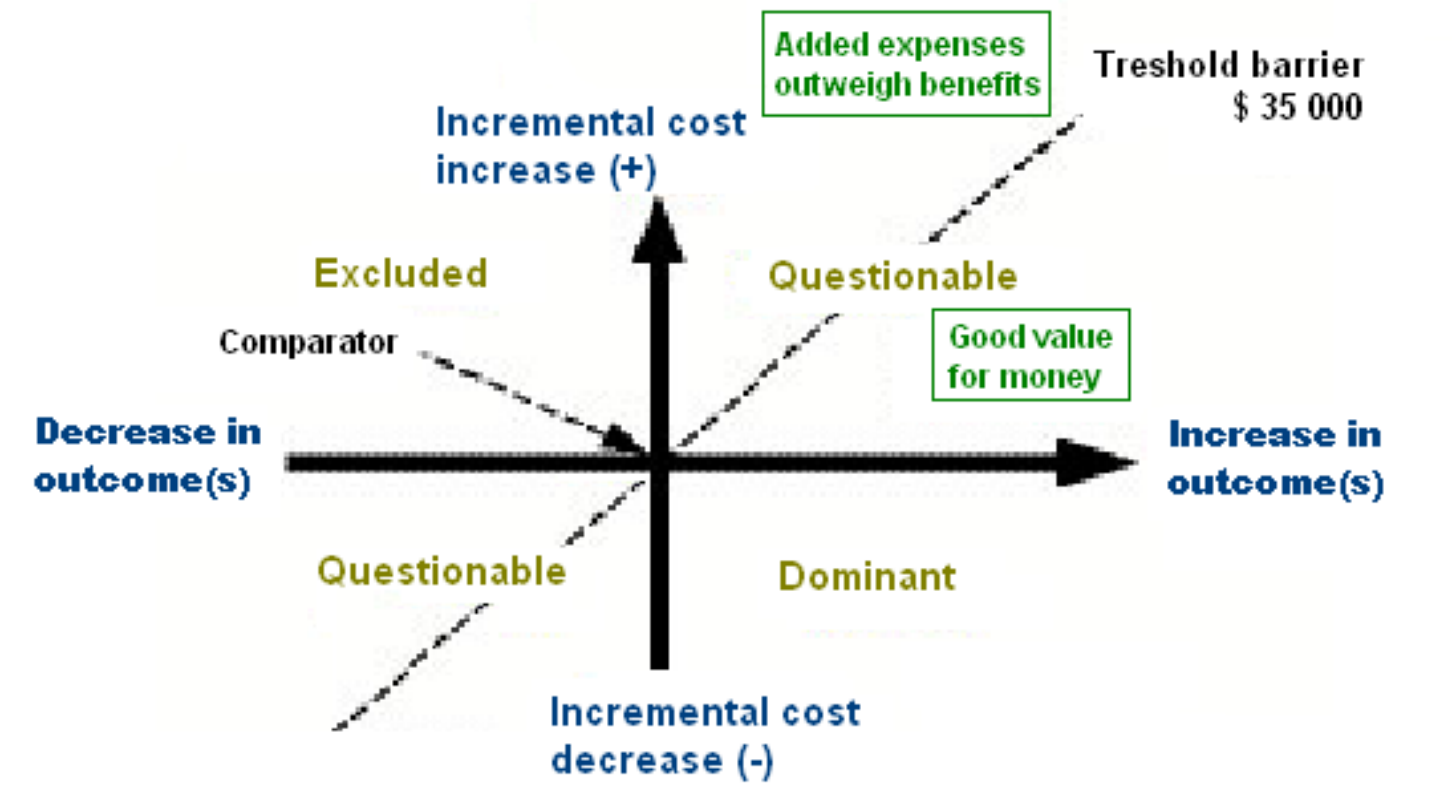
- The next question is : *Is the intervention "cost-effective"?*

Cost-effectiveness Analysis

- There is no ‘magic’ cut-off number that establishes whether or not an intervention is ‘**cost-effective**’.
- It will depend on what is termed the decision maker’s ‘**ceiling ratio**’.
- The ceiling ratio can be inferred from the amount that decision-makers are **willing to pay.**
- To make a decision:
  - If ICER of the program ≤ ceiling ratio → adopt the program
  - If ICER of the program > ceiling ratio → do not adopt the program

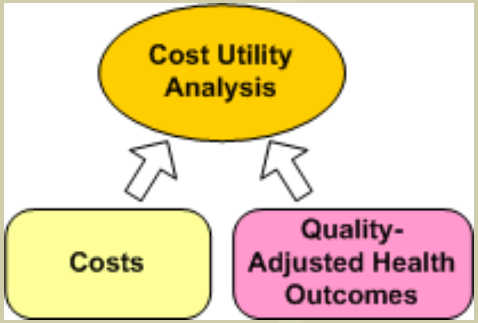
Cost-effectiveness Analysis

- The cost-effectiveness acceptability Plane:



Cost-utility Analysis

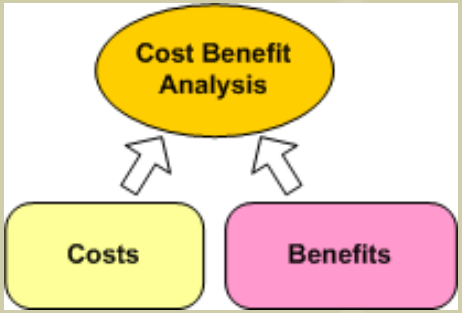
- In CUA, the outcomes are measured in **healthy years**, to which a value has been attached.
- CUA is **multidimensional** and incorporates considerations of quality of life as well as quantity of life using a common unit.



- Result: Cost per unit of consequence (e.g. cost/QALY).

Cost-benefit Analysis

- CBA try to value the outcomes **in monetary terms**, so as to make them commensurate with the costs.



- Result: Net benefit or cost-benefit ratio.

- CBAs rarely used in health care.

Summary

Type of Analysis	***Costs***	***Consequences***	***Result***
Cost Minimisation	Money	Identical in all respects.	Least cost alternative.
Cost Effectiveness	Money	Different magnitude of a common ***measure*** eg., LY's gained, blood pressure reduction.	Cost per unit of consequence eg. cost per LY gained.
Cost Utility	Money	Single or multiple effects not necessarily common. ***Valued*** as "utility" eg. QALY	Cost per unit of consequence eg. cost per QALY.
Cost Benefit	Money	As for CUA but ***valued*** in money.	Net £ cost: benefit ratio.