Cost-effectiveness and meta-analysis of clinical evidence of drugs and medical devices for use on the NHS

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Summary

• PenTAG & NICE
• Modelling cost-effectiveness
• Examples of statistical issues;
  1. Extrapolation of patient survival from trials
  2. Adjustment for drug treatment switching in trials
  3. Meta-analysis of trial outcomes
PenTAG

- Peninsula Technology Assessment Group, Peninsula College of Medicine & Dentistry Univ. Exeter & Plymouth (currently !)
- Based in Veysey Building, Exeter
- One of 9 academic groups assessing;
  - clinical effectiveness,
  - cost-effectiveness
  of drugs and medical devices for NICE
NICE

• National Institute for Health and Clinical Excellence

• Set up under Tony Blair to control spending on expensive treatments, e.g. cancer drugs.
New drugs can give patients with blood cancer months of extra life. So why are thousands denied them?

... NICE had previously ruled in October 2006 that patients with myeloma were not eligible for the drug because it was not considered cost-effective, although its clinical effectiveness was undisputed.

...
The campaigners argued that NICE's initial rejection of Velcade was based mainly on the grounds of cost rather than efficacy, and that this decision was therefore 'perverse and unfair', particularly as the cost of the drug was only just over the £30,000 threshold for NHS drugs. (The NHS has a financial cut-off at £30,000 per person per year; more expensive drugs are not considered cost-effective.)

Cost-effectiveness modelling

- Attach costs and patient benefits to each health state
- Patient benefit “utility” on [0,1] scale
Stats issue 1: Extrapolation

- Cost-effectiveness affected by mean survival = area under curve
Stats issue 2: Treatment switching

• Problem;
  – New drug more effective, hence some patients switch to new drug
  – Common problem: substantially biases cost-effectiveness

• Solution;
  – Need to adjust for switching
  – Censoring people when they switch biases
  – No agreed “best” method used to adjust
Stats issue 2: Example of adjustment

- Trial of new drug vs. placebo for stomach & bowel cancer
- Problem: 84% placebo patients switched to new drug
- Pfizer adjusted survival for placebo patients;
  - What would survival have been if had not switched?
  - Assumption: survival improved proportionally from start new drug to death
Before adjusting

**Sunitinib (N=243)**
- Median 72.7 weeks
- 95% CI (61.3, 83.0)

**Placebo (N=118)**
- Median 64.9 weeks
- 95% CI (45.7, 96.0)

Hazard Ratio = 0.876
- 95% CI (0.679, 1.129)
- p = 0.306
After adjusting

Overall Survival Probability (%)

Time (weeks)

Sunitinib (N=243)
Median 72.7 weeks
95% CI (61.3, 83.0)

Placebo (N=118)
Median* 39.2 weeks
95% CI (28.0, 54.1)
Hazard Ratio =0.529
95% CI** (0.296, 1.130)
p=0.306

Hazard Ratio =0.505
95% CI** 0.388-0.658
P=<0.0001

NICE recommended use of sunitinib on NHS
Stats issue 3: Meta analysis

Example 1

Which of drugs A, B or C is most cost-effective?

Example 2
RPSFT method

Trial Model

Trial & model

BSC arm

Sunitinib arm