The value of evidence: a re-analysis of the use of steroids in head injury
Retrospective case study: the CRASH trial

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PURPOSE

The value of clinical research lies in improving treatment decisions to improve health. Research proposals need to demonstrate this value to obtain funding. Funding is limited and so there is a need to prioritise among potentially valuable research designs. We aimed to show how formal, quantitative assessments of cost-effectiveness and the value of further evidence can improve the process of research prioritisation by identifying research designs that offer the greatest improvement in health.

THE CASE STUDY

Decision problem (in 2000)
Should public funds be used to investigate the effect of steroids for treating severe traumatic brain injury?

Disease burden
- 10-20 severe TBI per 100,000 population
- Leaving approx 1 in 3 dead and 1 in 3 disabled

Intervention
- Cheap, generic, no private sponsor
- Variable use in practice (12-64% of ICUs)
- Uncertain effectiveness

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RESULTS

Figure 6. Uncertainty in the effect of steroids on number of TBI patient years lived in full health annually in the UK
Area of coloured square shows probability of health years lived within range specified.

Incorporating impact on health related quality of life and life expectancy changes optimal decision based on current evidence because steroids associated with increased risk of vegetative state or severely disabled
- Don’t choose steroids as expect reduction in number of health years lived for TBI sufferers
- Decrease in QALY gain is positive compared to no steroids
- Error probability ~25%

Figure 7. Uncertainty in the effect of steroids on number of person years lived in full health annually in the UK
Area of coloured square shows probability of health years lived within range specified.

Incorporating impact on health service resource use shows that steroids would increase costs and displace other health-generating activities
- Don’t choose steroids as expect reduction in number of health years lived overall in UK
- Risk that true health gain is positive compared to no steroids
- Error probability ~10%

Figure 5. Decision analytic model

Specifies logical mathematical relationship between multiple sources of evidence
Probabilistic analysis reflects joint impact of uncertainty from all sources of evidence

VALUE OF EVIDENCE

Is more evidence valuable?
Compare health gains with decision based on current evidence to one with reduced overall uncertainty
- Answer is yes: additional evidence could prevent forgoing of potential health gains from steroids

What type of evidence is required?
Examine contribution of each input parameter to overall uncertainty
- Answer is more information on the numbers left dead, vegetative or severely disabled would reduce decision uncertainty
- More information on health related quality of life, life expectancy or resource use would not be valuable as would not reduce decision uncertainty

How much evidence is required?
Compare costs of research study to value of expected reduction in decision uncertainty
- Benefits of CRASH trial design recruiting 20,000 patients expected to exceed cost
- Smaller study could have achieved same value of reduction in decision uncertainty

What is required to change clinical practice?
Need some assessment of factors that influence clinicians’ decisions
- Size of CRASH trial and unexpected results ensured high profile
- Would other means to change practice represent better value for money?

Should research be prioritised?
Compare the net health gains of proposed research studies
Requires that alternative proposals be compared on same basis

DISCUSSION

Despite the potential to aid decisions about the use of research resources, formal methods of economic evaluation are not widely used. This contrasts with the increasing use of economic evaluation in reimbursement decisions. The discrepancy may be due to the separation of institutions with the remit for making reimbursement decisions from those responsible for commissioning research even though the objectives underlying both policy decisions are the same, i.e. to improve overall population health. Using cost-effectiveness analysis to estimate the impact of research designs on overall health adds value to the research prioritisation process by enabling:

(i) comparison of all competing proposals on the same basis;
(ii) efficient, transparent and accountable allocation of funds;
(iii) optimisation of research design to ensure that further evidence directly addresses decision uncertainty.

Limitations:
- Requires development of cost-effectiveness analysis at research proposal stage rather than reimbursement assessment
- Formal methods may not capture all things of interest (e.g. value of establishing network of researchers in reducing costs of future trials)

REFERENCES

