Economics Notes

Economic modelling before clinical trials

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Clinical trials can be expensive and technically difficult to execute. Ideally, before a trial is undertaken three questions require answering. Firstly, what is the amount of clinical uncertainty within a given area. Secondly, what is the likely achievable benefit from a given trial relative to some other alternative use of the research resources. Thirdly, given that a trial is indicated, what should its size and design be?

The first question is usually resolved through the use of a prior systematic review of the literature. Indeed, major funding agencies such as the Medical Research Council (MRC) ask whether a systematic review has been undertaken when funding decisions are made. The second issue regarding the likely benefit relative to cost is not usually considered.[1] However, the inclusion of some economic modelling during the early design stages of a trial can inform not only the scale of the potential benefit of the proposed research relative to cost but can also help answer the third question on key trial design decisions.

Economic input into research funding decisions tends to be limited to cost of illness studies, which are used either implicitly or explicitly to encourage research into health areas which present a high financial cost to society.[2] However, cost of illness studies cannot fully inform funding decisions and cannot aid trial design. A better method is to use the economic evaluative techniques of cost effectiveness, cost utility, or cost benefit analysis.[3]

As an example, Parsonnet and colleagues undertook an economic evaluation of screening for *Helicobacter pylori* to prevent gastric cancer before the start of any clinical trial.[4] Their rationale was that any randomised trial of screening would need to be extremely large, lengthy, and consequently expensive. Before undertaking such a large scale enterprise it would be useful to know whether, given a clinically plausible reduction in cancer, screening is likely to be economically efficient compared with no screening. Furthermore, the study sought to determine which segment of the population screening should be aimed at. The study concluded that screening the population (particularly men) aged 50-70 was cost effective given the assumption of a 30% decrease in gastric cancer. Therefore, a trial should be designed to detect at least a 30% reduction in cancer among 50-70 year olds.[4] Similarly, a pretrial economic evaluation by Buxton and Townsend supported the MRC's decision to fund a large trial of hormone replacement therapy.[5]

In a slightly different approach Torgerson et al made the explicit assumption that a trial for preventing hip fractures in elderly women should be undertaken, and they sought to identify potentially the most cost effective intervention.[6] After comparing seven possible preventive strategies they concluded that a single annual vitamin D injection would potentially be the most cost effective method of prevention. Indeed, if the preventive strategy led to a 20% fall in hip fractures among treated women, this would lead, on average, to a healthcare cost saving of £100 per treated person.[6]

In another study Gillespie et al showed that economic modelling could be used to inform the size of a trial testing new hip prostheses and indeed whether a trial should take place at all.[7] For instance, a new prosthesis costing twice as much as a current prosthesis but only leading, at best, to a 20% reduction in prosthetic failure would not justify a trial or licensing. On the other hand, a new prosthesis which cost 20% more than current devices but led to a 50% reduction in prosthetic failure would justify a trial, which if undertaken over five years would require 5516 participants.[7]

As well as informing decisions on whether to undertake a trial and of which intervention, prior economic modelling can also guide what data to collect. For example, though there have been several economic evaluations of hormone replacement therapy[8] there have been no large long term trials of the hormone. Existing evaluations suggest that quality of life gains due to hormone replacement therapy and losses because of any breast cancer effects are critical to its relative cost effectiveness.[8] Therefore, any large scale trial of hormone replacement therapy would be well advised to collect quality of life data on the drug's short term effects and on the effects due to breast cancer.

Clinical trials are expensive and it is wasteful of research resources to evaluate technologies which, no matter how effective, cannot be relatively cost effective. Economic modelling carried out before a trial is designed and funded will aid trialists to choose the best research solution and should increase the efficiency of research.

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4 Parsonett J, Harris RA, Hack HM, Owens DK. Modelling cost effectiveness of Helicobacter pylori screening to prevent gastric cancer: a mandate for clinical trials. *Lancet* 1996;348:150-4.
5 Buxton M, Townsend J. Cost effectiveness scenario analysis for a proposed trial of hormone replacement therapy. *Health Policy* 1997;39:181-94.
6 Torgerson DJ, Donaldson C, Reid DM. Using economics to prioritise research: a case study of randomised trials for the prevention of osteoporosis. *J Health Services Res Policy* 1996;1:141-6.
7 Gillespie WJ, Pekarsky B, O'Connell DL. Evaluation of new technologies for total hip replacement: economic modelling and clinical trials. *J Bone Joint Surg* 1995;77B:528-33.
8 Torgerson DJ, Reid DM. The economics of osteoporosis and its treatment. *Pharmacoeconomics*: 1997;11:126-38.

Endpiece

Not a good start

A happy childhood has spoiled many a promising life.

Robertson Davies (1913-95), *What's bred in the bone*, London: Penguin, 1986