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Letters

New BMJ policy on economic evaluations

Response of NHS Economic Evaluation Database Research Team

Editor—We, the NHS Economic Evaluation Database Research Team, agree with Smith that economic evaluations should contain comprehensive reporting of both clinical effectiveness and economic analysis and that the BMJ is right to implement this new policy.1 How the clinical trial results (which inform the economic evaluation) are obtained is often paramount to the understanding and quality of the economic analysis conducted.2

Research reports are included and abstracted in full on the NHS Economic Evaluation Database (www.york.ac.uk/inst/abstracted in full on the NHS Economic Evaluation Database Research Team, agree with Smith that economic evaluations should contain comprehensive reporting of both clinical effectiveness and economic analysis and that the BMJ is right to implement this new policy.1 How the clinical trial results (which inform the economic evaluation) are obtained is often paramount to the understanding and quality of the economic analysis conducted.2

Firstly, the pertinent concern is surely to ensure that economic evaluations should contain economic results. The findings of focus group research in UK health authorities. Value Health 2002;5:71-8.

2 Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ 1996;313:275-83.

Will the BMJ return clinical trials if submitted without any economic results?

Editor—The implications of the BMJs new policy for economic evaluations are unclear.1

Firstly, a lag often exists between the clinical and economic results, making simultaneous submission difficult. Typically, clinicians are eager to disseminate important clinical results immediately. For example, the extracorporeal membrane oxygenation (ECMO) trial was among the first research projects to incorporate economic evaluation in its design from the outset. The preliminary clinical results were written up and fast tracked to the Lancet before I was even employed to continue the economic evaluation.2

The economic evaluation was published in the BMJ years later, having required the clinical evidence in its analysis and appropriate sensitivity analyses and having undergone delay to publication.3

Would it have benefited anyone to withhold dramatic clinical results until the economic results were ready? Clinical results are often more generalisable to an international audience than the concurrent economic results. The limitations of any clinical information in the absence of economic evidence should be made explicit. The pertinent concern is surely to ensure relevant policy makers exercise restraint until the full information is available.

Secondly, no incentive is given in the BMJ policy for clinicians to change their practice. Presumably clinicians send results to the Lancet for higher impact factors and wider dissemination. If economists cannot persuade colleagues to submit the clinical paper alongside the economic paper to the BMJ, they will resort to submitting results to economic journals for which a different style for different specialist audiences would be required, ensuring even poorer dissemination to clinical audiences and policy makers.

Finally, your editorial emphasised strong support for keeping clinical and economic results together, and Smith told us to send “somebody else your clinical results and us your economic results, and we will send them back, politely.” May I therefore ask, politely, is the converse also true? Will you return clinical trials if submitted without any economic results?

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Economic evaluations should be judged on scientific merit

Editor—Health economists have been grateful for the BMJs hitherto supportive stance towards the publication of economic evaluations. The proposed new policy not to publish economic evaluations unless also offered the clinical results is disappointing and misjudged.1

Firstly, this policy denies the fact that, although clinical and economic results from a trial are both components of an overall evaluation, they also have many differences, often including the funding agencies supporting them, the researchers, and the timescale over which they are performed and published. Perhaps most importantly, important trials are often prepared for an international audience, but economic evaluations usually relate to specific healthcare systems; large trials may generate the need for several country specific economic evaluations.

These differences justify researchers in choosing to submit clinical and economic
results to different journals, and entitle journals to use different criteria when deciding whether to publish or reject. Consequently, as in other disciplines, research findings that are closely related and possibly interdependent often appear in different journals. That poses no great problem to readers, especially in the era of electronic publication championed by the BMJ.

Secondly, what is the likely effect of this policy? Researchers aim to publish where no one will forgo an opportunity to publish. A new policy on economic evaluations will certainly affect the outcome of economic analyses of clinical trials and other clinical studies. If the policy is indeed more scientifically important papers, leaving non-trial based economic analyses and data-free “think pieces.” This is hardly the route to improving the journal's impact on the adoption of new treatments or technologies.

Smith admits this new policy owes something to petulance but nevertheless defends it as reasonable. We think it is unreasonable and ask him to reconsider.

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We are currently involved in economic analyses of several large trials whose clinical results have recently been published in other journals, including the Lancet. If adopted, this policy will deny us the opportunity to have our scientific research results considered for publication by the BMJ.

1 Smith R. New BMJ policy on economic evaluations. BMJ 2002;325:1124 (16 November.)


Economic evaluations are often based on many studies

Editor—I understand the reasons for the new policy on publishing economic evaluation studies, but it is not clear how this will apply to many of the best evaluations that are based on reviews of many randomised controlled trials and other clinical studies, and use modelling to assess outcomes and cost effectiveness. There is no reason to exclude such studies.

If the new policy is to work it is important also for the BMJ to ensure that its processes of review and decision making are joined up in terms of the different components of studies. Too often in the past when pairs of papers were submitted or when a single paper reported the overall results of a study the reviewing of the economics has been weak. Smith's editorial raises the point that publishing clinical outcomes without economic ones is really incomplete evaluation. I look forward to results of high quality clinical trials being rejected for want of a proper economic evaluation.

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3 Smith R. New BMJ policy on economic evaluations. BMJ 2002;325:1124 (16 November.)

Will the Lancet play ball?

Editor—The debate ensuing from the BMJ's new policy on publication of economic evaluations is interesting. Smith made several important practical points, but we believe that some broader strategic issues still remain.

Thankfully, major research funders in the United Kingdom increasingly require that economic evaluation be an integral part of the design of a clinical trial. In many ways the BMJ's decision is the natural extension of this philosophy. The risk is, however, that unless other major journals follow suit the policy will damage the dissemination of cost effectiveness information.

The collaboration between clinicians and health economists is often delicate. The pressures that this new policy will place on this relationship will have implications for long term cooperation. Given the pressure to publish rapidly in high impact journals to secure long term funding, the interests of clinical and economic researchers will not always coincide.

An immediate effect of this policy for those of us participating in multidisciplinary research is the need to agree publication strategies at the outset of a project. It may be that a process similar to the Lancet's protocol pre-approval could facilitate these discussions by providing confidence that high quality clinical trials including an economic evaluation will be acceptable to the major journals.

Unless all researchers accept the need for the simultaneous publication of clinical and economic results, cost effectiveness information may be confined to more specialist journals which are rarely seen by the clinical community. The best solution would be for the major journals to agree that clinical trials designed to inform policy decisions must include a high quality economic evaluation. We would be interested to know the Lancet's thoughts on this issue.

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It is important for our research careers to be able to publish in high impact journals.

1 Smith R. New BMJ policy on economic evaluations. BMJ 2002;325:1124 (16 November.)

2 Electronic responses to: New BMJ policy on economic evaluations. bmj.com 2002. bmj.com/cgi/content/full/325/7373/1124#responses (accessed 14 Feb 2003.)

Self help smoking cessation in pregnancy

Programmes for smoking cessation can work

Editor—Moore et al show that giving smoking cessation booklets to pregnant women does not help them stop smoking. But the intervention offered to pregnant smokers in this study was not based on previously available evidence that adding booklets to face to face advice does not improve smoking cessation rates and that more intensive interventions are needed to help pregnant smokers stop smoking.

Nevertheless, a recent meta-analysis indicates that individually tailored materials produced by computers increases by 80% the odds of stopping smoking compared with receiving no materials. Because computer tailored programmes are based on the relevant personal characteristics of each smoker, participants may be more interested in reading these documents and prepared to...
apply the advice included. Consequently, individually tailored documents are 1.36 times more effective than booklets in helping smokers stop smoking. In addition, most available computer tailored programmes include a follow up, which is an essential element in the treatment of addictions.

Tobacco dependence is a chronic condition with relapses and often needs prolonged treatment. It is a serious condition that is unlikely to be treated with booklets alone. But computer tailored programmes can be a useful adjunct to pharmaco-therapy and to advice given by doctors and midwives. By using new information technology (internet, text messages on cell phones, etc), these programmes can reach large numbers of smokers at a low cost. Because the prevalence of smoking among pregnant women has increased sharply in many European countries in recent years, and few doctors and midwives are trained in treating tobacco dependence, there is an urgent need to assess the efficacy of computer tailored smoking cessation programmes in pregnant smokers.

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Competing interests: J F Etter developed an effective computer tailored smoking cessation programme, available in four languages at no charge.

What does work in Doncaster

Entorr—In their editorial describing the interim smallpox guidelines for the United Kingdom Harling et al ask how countries lacking the public health infrastructure to respond to outbreaks and without vaccine supplies would be able to control an outbreak of smallpox.1

Confronted with the threat of intentional release of biological agents, the World Health Organization advocates dual use investment in public health infrastructure to strengthen outbreak intelligence and verification, support the response to an outbreak, maintain an emergency vaccine reserve, and provide public health information. In 2002 the World Health Assembly urged countries to share expertise, supplies, and resources, and asked WHO to develop collective mechanisms to contain or mitigate the impact of such a global health threat.2

WHO advocates investment in global infrastructure for outbreaks such as smallpox

Entorr—In their editorial describing the interim smallpox guidelines for the United Kingdom Harling et al ask how countries lacking the public health infrastructure to respond to outbreaks and without vaccine supplies would be able to control an outbreak of smallpox. WHO recognises that countries may wish to identify key workers and immunise them to allow a rapid response to a smallpox outbreak. It is in keeping with WHO policy for countries to devise and implement such a plan in line with their own assessment of national infrastructure and needs.

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Poly specific snake antivenom may help in antivenom crisis

Entorr—In Africa snakebites cause thousands of deaths annually and much permanent physical disability, but the supply of antivenom, the only specific treatment, is threatened by commercial pressures and privatisation. This has been caused over the
past few years by the cessation of antivenom manufacture by Behringwerke in Germany, greatly reduced production by Aventis Pasteur in France, and the threat to continued production by Africa’s sole remaining producer, the African Health Laboratory Service in Johannesburg.

Without antivenom, human suffering and death from snake bite are increasing, especially in west Africa. Only conservative treatment is possible, or the use of ineffective antivenoms manufactured in Asia or dangerous traditional remedies.

In February 2001 a workshop held by the World Health Organization identified interregional collaboration as the only short-term solution.4 Colombia’s national institute for public health responded by offering to develop a prototype pan-African polyspecific antivenom.

Venoms from nine species of Echis, Bitis, and Naja were selected as being medically the most important in Africa (a mamba antivenom is being developed separately). Horses were hyperimmunised with 15 African venoms using the Colombian institute’s standard protocol. The neutralising potency of the equine antiserum in WHO standard preclinical assays against five intravenous pooled venoms was sufficiently high to justify the purification of the crude antiserum to produce a definitive antivenom.5

In preclinical tests this antivenom showed good neutralising potency against the venoms covered by the African Health Laboratory Service’s polyspecific antivenom. The new antivenom also neutralised the venoms of saw scaled vipers (genus Echis) (ED50, 14.3 μl/mouse) as effectively as both the African Health Laboratory Service’s Echis antivenom (12.8 μl/mouse) and Micropharm’s Echis ocellatus Fab fragment antivenom (13.0 μl/mouse).6 Unlike these two monospecific antivenoms, the pan-African antivenom powerfully neutralises the venom of Bitis arietans (1.5 μl/mouse) and has moderate activity against Naja naja oivitiens venom (73.0 μl/mouse). These species cause most severe snakebites in Africa.

Another polyspecific African antivenom (developed in Costa Rica) and a new Micropharm monospecific E ocellatus Fab fragment antivenom are undergoing preclinical testing. These three antivenoms will be compared by randomised controlled trials in Nigeria.

Letters

Randomised controlled trial for twin delivery

Entorr—The article by Smith et al is a timely retrospective cohort study, in which the possible benefit of planned caesarean section for twins is suggested.1 A meta-analysis of available studies did not show any appreciable difference in neonatal outcomes, but pointed out that available data are mainly level 2, being based largely on retrospective cohort studies.2

On the basis of these data and data from the Atee Nova Scotia perinatal database, we have estimated the potential risk of vaginal delivery of twins at 32 weeks or older carries a risk of perinatal mortality or serious morbidity of about 4%. To show a reduction in this to 2% requires 2500 patients (power 80%, alpha error 0.05, two sided). On the basis of our experience with the term breech trial we believe that such a trial is possible, and with support from over 175 centres we have submitted such a proposal to the Canadian Institutes for Health Research. We caution against any radical change in practice without strong evidence from a well designed randomised controlled trial. Any centre that is interested should contact our group at jon.barrett@swchs.on.ca

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for The Twin Birth Study Collaborative Group

Challenges for myocardial infarction should be precise

Entorr—Savage and Channer highlight a serious problem in their editorial on managing acute myocardial infarction.3 Doctors are under increasing pressure to reduce door to needle times to below 30 (possibly 20) minutes and often now delegate this task to thrombolytic nurses. Such nurses are accountable for the door to needle time and are often blamed if the targets of national service frameworks are not met. Often delay occurs in calling a thrombolytic nurse, such that the nurse has very little time thinking if he or she is to stay within the target.

Everyone involved should know that statistics on door to needle times should apply only to those patients in whom the diagnosis is definite and no possible contraindication exists. If potential problems are identified with either the diagnosis or a potential contraindication the clock should stop ticking. The thrombolytic nurse should then have ready access to someone with the experience and knowledge to weigh the risks and benefits in an individual patient. Although any decision should be made as

Thrombolysis with recombinant streptokinase in Cuba

Entorr—Analysis of the causes of the low rate (21%) of thrombolysis for acute myocardial infarction in England and Wales described by Mayor would be interesting.1 In Cuba thrombolysis with home manufactured recombinant streptokinase has been widespread since 1993. When this procedure was introduced nationwide, the overall proportion of patients receiving treatment was a little above 50%.

The main reason why thrombolysis was not given was largely because patients arrived at hospital more than 12 hours after the onset of symptoms. Other causes were non-ST elevation and contraindications for thrombolysis, such as possible causes of bleeding.2 The management system for patients has, however, become more efficient, with patients arriving earlier. Also doctors in emergency departments are more acquainted with the product, so currently the rate of thrombolysis is around 50% nationwide and even 70% in some units.

The report also says that streptokinase should not be given twice because of the formation of anti-streptokinase antibodies. We found that almost all patients had low titres of anti-streptokinase antibodies before thrombolysis; they increased rapidly after treatment but then started to fall.3 After six months the average anti-streptokinase titre was roughly still enough to neutralise the thrombolytic activity in plasma achieved with the 1.5 million unit dose. After one year the titres had almost returned to pretreatment values. Given these data, we think that streptokinase can be given again after a case-by-case analysis of risk and benefit until six months after the first administration and surely after one year.

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Checklists for myocardial infarction should be precise

Entorr—Savage and Channer highlight a serious problem in their editorial on managing acute myocardial infarction.3 Doctors are under increasing pressure to reduce door to needle times to below 30 (possibly 20) minutes and often now delegate this task to thrombolytic nurses. Such nurses are accountable for the door to needle time and are often blamed if the targets of national service frameworks are not met. Often delay occurs in calling a thrombolytic nurse, such that the nurse has very little time thinking if he or she is to stay within the target.

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1 Mayor S. NICE recommends greater use of thrombolics in acute myocardial infarction. BMJ 2002;325:1057. (9 November.)
quickly as possible, sufficient time should be allowed to avoid hasty or ill considered decisions. Delays in calling the thrombolysis nurse or junior doctor should be minimised. Every hospital in the United Kingdom has a different checklist for assessing patients. Is it not time for a nationally agreed list of relative and absolute contraindications to thrombolysis? Such a list should be precise and specific in its statements, not simply say uncontrolled hypertension. In addition, in some groups of patients the benefits of thrombolysis are higher and the complications are worth risking. Other groups of patients may have less potential benefit and therefore need a more cautious strategy. Thus users of the checklist require easy access to expert opinion.

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Results of audit of psychiatrists’ practice when copying letters to patients

<table>
<thead>
<tr>
<th>Letter sent to patient</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copy of general practitioner’s letter</td>
<td>73</td>
</tr>
<tr>
<td>None</td>
<td>3</td>
</tr>
<tr>
<td>General practitioner’s letter with at least one omission</td>
<td>17</td>
</tr>
</tbody>
</table>

Parts omitted

- History or examination details: 14
- Diagnosis: 3
- Prognosis: 6
- Reason for omission: 14
- Fear of distressing patient: 14
- Other concerns: 6

We have also received copies of referral letters from his paediatric doctor to consultants and heads of other hospital departments, the local education authority in support of continuing provision of home tuition, and examination boards in support of “special arrangements” for GCSE examinations.

Occasionally, errors in letters have occurred, but we are in a position to pick up these and have them corrected. Administrative errors have also occurred—I am told, through the use of temporary secretarial staff. This has resulted in follow up letters being sent to the wrong general practitioner at the wrong surgery and to an unnamed special educational needs coordinator at the wrong school, evidenced by the list of copied recipients at the foot of our copies of these letters.

For parents of young people who are unable to access mainstream education because of long term illnesses such as myalgic encephalomyelitis/chronic fatigue syndrome the difficulties in maintaining effective liaison between school, specialist educational needs coordinator, educational welfare officer, home tuition coordinator, general practitioner, hospital consultant, community paediatrician, and local education authority can be serious. In addition, some families also deal with social services and child and adolescent mental health services, as well as having input from the connections service.

For many it can be a communications nightmare on top of an already challenging situation. Anything that helps to improve liaison, such as receiving copies of hospital letters, is to be welcomed, and I would advise all parents to ask for copies of these letters if they do not already receive them.

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Employing users who turn back into patients is difficult

Editor—Simpson and House conducted a systematic review of involving users in the delivery and evaluation of mental health services.1

I have certainly found employing users to be a positive experience. However, one difficulty not mentioned in the paper is that of subsequently treating these people as patients again when they relapse.

The move from patient to colleague is comparatively easy compared with the transition back to that of patient, particularly if the Mental Health Act is needed.

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1 Simpson EL, House AO. Involving users in the delivery and evaluation of mental health services: systematic review. BMJ 2002;325:1265-9. (30 November.)