Parachute approach to evidence based medicine

As obvious as ABC

EDITOR—I strongly oppose the proposition of Potts et al.¹ For all the difficulties of doing high quality randomised controlled trials of some research questions, or in challenging settings, making arbitrary decisions about the “obviousness” of the effectiveness of interventions based on observational evidence cannot be the way forward. This point is well made by the readers with expert knowledge who have already responded about the specific examples described by Potts et al.²

Other readers have criticised the naïveté of the argument but seem to accept the underlying sentiment that the world should not always wait for evidence from randomised controlled trials. This point of view presupposes some method, or criteria, for judging obviousness of effectiveness and merits further consideration.

I propose that deciding an intervention is obviously beneficial on the basis of non-randomised evidence requires benefit that clearly outweighs all possible adverse effects (whether frequent and mild, or rare and severe); benefit that could not be explained by bias; and an intervention that is obviously beneficial in all contexts in which it will be applied.

Increasingly, researchers talk about the value of an intervention—the extent to which an intervention does more good than harm.³ Judging value can be extremely difficult. Those who cite the example of the obviousness of the benefits of penicillin often forget that some people may have a serious or fatal allergic reaction to this drug. Historically, even randomised controlled trials have tended to report adverse effects less well than benefits. Although non-randomised or uncontrolled studies may raise the alarm about possible adverse effects, measuring or attributing harm on the basis of these sources of evidence is often difficult. Even when harm is obvious, judging value usually requires quantitative estimates of benefit and harm which the decision maker can regard with equal trust.

There is some evidence about the possible size of bias in non-randomised studies. In prospective studies designed as randomised controlled trials but where concealment of randomised allocation was not done (or

where reviewers were unclear about what was done), bias leads on average to exaggeration of effects by 30%⁴; since some studies with uncertain concealment of allocation will have been unaffected, the true effect of lack of concealment is almost certainly larger. In other examples, such as the effect of hormone replacement therapy on cardiovascular disease, biases in non-randomised studies seem to have led to a doubling/halving of the effect size found in randomised controlled trials. Interestingly, controversy still exists among topic experts

about possible reasons for the differences in the effects of hormone replacement therapy observed in such trials and non-randomised studies.⁵ Other biases, such as publication and outcome reporting biases, are expected to be worse for non-randomised evidence.

Advocates of the obvious effects of an intervention need to be confident about its benefits in all contexts. Once a decision has been made that an intervention has obvious benefits, its widespread implementation will act to prevent further evaluation.

So next time something seems obvious, see if it passes the ABC test.

Barnaby C Reeves reader in epidemiology
Clinical Trials and Evaluation Unit, University of Bristol, Bristol Royal Infirmary, Bristol BS2 8HW
barney.reeves@bristol.ac.uk

Competing interests: BCR is a co-convenor of the Cochrane Non-Randomised Studies Methods Group and reviewed the original manuscript of Potts et al.

- 1 Potts M, Prata N, Walsh J, Grossman A. Parachute approach to evidence based medicine. *BMJ* 2006; 333:701-3. (30 September.)
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Arguments are easily refuted

EDITOR—Potts et al's various anecdotes purport to show the futility and danger of attempting to minimise bias in evaluating health care interventions.¹ Fortunately, with widespread access to good quality summa-

ries of evidence, their arguments can be refuted easily. For example, a quick check in *Clinical Evidence* reassures us that misoprostol is no more effective than placebo and has significant adverse effects.² With regard to male circumcision, the authors suggest that it was wrong to undertake trials to assess effectiveness. Yet they also acknowledge that circumcision can have complications. Were we to ignore the possibility that the intervention may cause harm in the rush to implementation? The authors also suggest that compliance is not an issue, which is not clear from the papers they cite.³ Do they propose to make male circumcision compulsory?

William McGuire associate professor
Department of Child Health, Australian National University, Canberra, ACT 2605, Australia
william.mcguire@act.gov.au

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Summary of other responses

The article by Potts et al sparked heated international debate.¹ Many took issue with the parachute analogy, which they perceived as flawed, inappropriate, superficial, outdated, or mere sophistry—although only a few correspondents mentioned that it had been taken from a spoof article.

The ethical aspect of randomised controlled trials was mentioned as important for patient safety. Many understandably criticised the fact that the authors had chosen resource poor settings to illustrate their point, and not only because this implies discrimination or double standards. To cite Lelia Duley, professor of obstetric epidemiology in Leeds, “the appropriate evidence can potentially have even more dire consequences in poor countries, where health services resources are even more scarce and overstretched than in rich countries.” And many cited examples to illustrate where “good science” without trials had not had the desired good outcomes. Two out of the three interventions used as examples were criticised on grounds of their effectiveness. Simon Gates, principal research fellow at Warwick Medical School, thought that the authors cited literature selectively for all three examples and had not based their conclusions on an overview of the evidence.

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Two respondents wholeheartedly agreed with the authors. David Hawker, a retired general practitioner/anaesthetist from Bodmin, thinks we have become “star-struck” by the need for randomised controlled trials and that this thinking may “severely hinder the good.” And A Breck Mackay from Australia criticises evidence based medicine itself in its current form as faulty owing to underlying assumptions that need to be re-evaluated.

Others agree with certain aspects of the reasoning in the article. Gautham Suresh, associate professor of paediatrics in the United States, is among those who maintain that it is crucial always to use the highest level of evidence in choosing interventions and be explicit about this choice, but he agrees with the authors in that “one should not always wait for the highest possible evidence before acting.” This point of view is largely supported by Oliver Boney, senior house officer in general medicine in Luton, who emphasises that randomised controlled trials remain the gold standard of evidence based medicine precisely because of the inherent unreliability of observational studies.

Miles Witham, clinical lecturer at Dundee University, concludes that the authors have made a compelling case for more controlled trials, not fewer—and the sooner the better. And while Matthew Green, senior house officer general surgery in Frimley Park, agrees that some treatments may need to be introduced without the benefit of full randomised controlled trials of effectiveness, he points out that this throws up questions about accountability, authority, and follow-up.

Oxfordshire general practitioner Richard Lehman in his journal blog on *bmj.com* concluded: “This article is so bad it may actually do some good.”² Enough said.

Birte Twisselmann assistant editor (web)
BMJ

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MRI in predicting curative resection of rectal cancer

See *Research* p 779

New dilemma in multidisciplinary team management

EDITOR—Tumour shrinkage by preoperative chemoradiotherapy is now an everyday reality, and pathological complete responses are not uncommon.¹ A “new dilemma” is posed by the apparent complete disappearance of cancer on magnetic resonance imaging, and often clinically, after chemoradiotherapy. A delay of six to 10 weeks is usual before operating—a time perceived as a “window of opportunity,” as regrowth in the irradiated area is believed inevitable.

This concept has been challenged by a series by Habr-Gama et al.² Altogether 360 patients with T3 and T4 rectal cancer (or T2 when considered for abdominoperineal resection) were treated with preoperative chemoradiotherapy.³ Ninety nine patients (28%) classified as clinical complete responders at eight weeks after completion of chemoradiotherapy were managed by surveillance alone. Only 2% in this observation group have died of cancer in a follow-up extending for up to 10 years, whereas local recurrence occurred in just five patients, all amenable to successful salvage surgery.

We propose to open accrual into a pilot study of observation for complete responders, as assessed on magnetic resonance imaging at four weeks after completing chemoradiotherapy. This will be administered at the Pelican Centre and largely delivered at the Royal Marsden Hospital. Magnetic resonance imaging, whose excellence in accurately predicting surgical mesorectal margins has been shown by the MERCURY group,^{4,5} will be central to this study's intensive follow-up, in addition to regular clinical and sigmoidoscopic assessment.

Specialised primary surgery, backed by magnetic resonance imaging based selection for preoperative chemoradiotherapy, will continue to be the cornerstone of management. Nevertheless, our fundamental understanding of modern cancer treatment for all solid tumours demands that this group of complete responders be properly investigated. Furthermore, if the experience of Habr-Gama et al is confirmed, several hundred patients with rectal cancer in the United Kingdom each year may one day be spared the necessity for major surgery.

R J Heald surgical director
Completeresponse@pelicancancer.org

Brian D P O'Neill clinical oncology research fellow
Brendan Moran consultant surgeon
Pelican Cancer Foundation, Basingstoke
RG24 9NA

Gina Brown consultant radiologist
Ara W Darzi honorary consultant
Andrew C Wotherspoon consultant histopathologist
David Cunningham consultant medical oncologist
Diana M Tait consultant medical oncologist
Royal Marsden NHS Foundation Trust, London
SW3 6JJ

Competing interests: None declared.

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Does post-neoadjuvant MRI have a role?

EDITOR—In the MERCURY study, magnetic resonance imaging incorrectly predicted tumour in the margin in 27 patients.¹ Twenty one of these had neoadjuvant therapy in the form of chemoradiation.¹ This is important, as recently many rectal cancers are now treated with neoadjuvant therapy.

The preliminary results from our data for a study assessing the outcomes of neo-adjuvant therapy for rectal cancers also show that the post-neoadjuvant staging scans do not accurately match in a sizeable proportion of patients with the final histological stage. This requires further comparison with results from other studies and centres. This discrepancy is thought to be related to the post radiotherapy scarring associated with the downsizing of the tumour, which may cause difficulty in interpretation of the scans.

As neoadjuvant therapy is quite commonly used to treat rectal cancers, it might be something that needs to be studied, to ascertain the importance of conducting post-treatment scans. These may have little if any role as most patients would have surgery irrespective of the scan results, except those who show a complete response to treatment, which is quite rare.

Durgesh S Rajee research fellow
Whittington Hospital, London N19 5NF
durgeshraje@hotmail.com

Competing interests: None declared.

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Defining a “window of opportunity” for laparoscopic surgery

EDITOR—The MERCURY Study Group provides clear evidence that preoperative magnetic resonance imaging can accurately predict surgical resection margins,¹ and its work in particular, has already led to a paradigm shift in the preoperative investigation and treatment of rectal cancer, at least in the United Kingdom.

This is at least implicitly acknowledged in that both previous letters focus on magnetic resonance imaging in the increasingly common scenario of assessment after neoadjuvant chemoradiotherapy. Heald et al propose a pilot study of observation rather than major surgery for complete responders as assessed on magnetic resonance imaging at four weeks after chemoradiotherapy.

Over the past three years, our experience has been that, in addition to clinical and sigmoidoscopic examination, serial magnetic resonance imaging can be of value after chemoradiotherapy in documenting an ongoing response beyond the conventional four to six weeks interval before surgery.² In 30 consecutive patients with locally advanced rectal cancer, we repeated magnetic resonance scans at four weekly intervals to optimise the timing of surgery at maximal response, the median time for

which was 12 weeks (range 8 to 15 weeks). In the pilot study proposed by Heald et al, no information would be available on the time frame during which response might still be seen, as those patients who did not achieve complete response at four weeks would presumably proceed immediately to definitive surgical resection.

Although it is open to conjecture whether this lengthened gap may increase the number of patients obtaining radiological or pathological complete response, it has allowed us to perform laparoscopic total mesorectal excision for most patients, the feasibility and short term safety of which we recently reported.³

We agree with Heald et al's concept of a "window of opportunity" after chemoradiotherapy, but the window is bigger than commonly believed, and the opportunity it affords may be to offer more patients the choice of minimally invasive surgery.

Bruce F Sizer *consultant in clinical oncology*
bruce.sizer@essexrivers.nhs.uk
Essex County Hospital, Colchester CO3 3NB

Tan Arulampalam *consultant surgeon*

Ralph Austin *consultant surgeon*

Nicola Lacey *consultant radiologist*

Don Menzies *consultant surgeon*

Roger Motson *consultant surgeon*
Colchester General Hospital, Colchester CO4 5JL

Competing interests: None declared.

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Obesity is a wake up call for developing world too

EDITOR—The ABC article on obesity by Haslam et al is equally a wake up call to the developing world, which is gradually being affected by the epidemic of obesity.¹ Sri Lanka is no exception. However, unlike developed countries, Sri Lanka has a prevalence of 29% of being underweight among children and a prevalence of 30% of anaemia among women and children under 5.² Implications of an epidemic of obesity may overburden a health system that is expected to cater for an increasing burden of non-communicable diseases due to the epidemiological and demographic transition.

The prevalence of obesity was estimated to be 20.3% in men and 36.5% in women in four provinces in Sri Lanka, the highest prevalence being in the more urbanised Western Province.³ In another study in the most urbanised district, Colombo, the prevalence of obesity was estimated to be 32.2% among adults.⁴

Obesity is increasing owing to demographic changes, urbanisation, and life style changes that took place during the past decade or so. Most of the risk factors are behaviour related and hence influenced by urbanisation and unhealthy life styles, such as a move from the traditional Sri Lankan diet to a fast food culture and low physical activity.⁴ The urban and rural differences in the two extremes of obesity and starvation have been summarised on bmj.com.⁵

Public health authorities in Sri Lanka must wake up to take measures to contain the impending epidemic of obesity before it further overburdens the health budget of this lower middle income country.

Pushpa Ranjan Wijesinghe *post doctoral fellow in community medicine*
Epidemiological Unit, Ministry of Health, Sri Lanka
Gunathilake@khalasa.com

Competing interests: None declared.

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Belittlement and harassment of medical students

Is a source of medical education

EDITOR—From the moment a medical student wanders out of the cosy lecture theatre and is unleashed into the hospital, the habitual embarrassment begins. Where would we be without the terrifying words "Student doctors? Don't all look down; why don't you report the x ray?" or "Surgical sieve? Ring any bells?"

The constant questioning does feel like harassment because that is what it is. Through this Socratic method of teaching, teachers are wearing us down, exhausting us until our thoughts are clarified and any faulty reasoning is exposed.¹ This forces us to think systematically and act practically like "real" doctors. Getting it wrong can make you feel belittled, but that is common in life. My friends belittle me when I get something wrong in a pub quiz. It is the exposure and loss of certainty that we equate with humiliation, although this can arise simply from feeling inadequate.

Unfortunately, as stated by Frank et al,² a minority of malicious doctors use teaching as a forum to humiliate, upset, and even torment medical students. Although bullying

has no place in the NHS, my overriding concern is that current bad press could censor current Socratic teaching methods and prevent invaluable education on the ward and in clinics.

The spectrum of teachers may be wide, but this dynamic, interactive teaching method can be very effective when done well. So to the depressed and belittled medical student, bear in mind: what doesn't kill you may just stop you from killing the patient.

Golnar Aref-Adib *medical student*
University of Nottingham Medical School, Queen's Medical Centre, Nottingham NG7 2UH
goly@doctors.org.uk

Competing interests: None declared.

- 1 Socratic teaching. www.cutsinger.net/socratic.html. University of North Carolina. James Cutsinger's Department of Religious Studies.
- 2 Frank E, Carrera JS, Stratton T, Bickel J, Nora LM. Experiences of belittlement and harassment and their correlates among medical students in the United States: longitudinal survey. *BMJ* 2006;333:682-4. (30 September.)

Remedial training—ethics and sensitivity

EDITOR—Roig recommends that medical students be instructed in ethical writing to avoid plagiarism.¹ He believes that when we internalise and apply its basic principles, this will reduce plagiarism and generalise to other areas of scientific research and personal conduct.

Frank et al speak of the teaching of ethics and call for more sensitivity (in the context of addressing bullying and harassment) and think that if the medical profession is serious about creating a satisfied workforce and about teaching students to behave ethically with colleagues and patients, teachers must behave in an ethically appropriate and sensitive way.²

I understand the sentiment but wonder at the efficacy of teaching ethics (to those probably established in their ethical practices) and requesting sensitivity (of those perceived to be insensitive). Would it also be useful to focus more intensely on ethics, confidence, and collegiality in medical school admissions?

P A Geis
11955 Millstone Court, Loveland, OH 45140, USA
jorge1907@aol.com

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