

These letters are selected from rapid responses posted on [bmj.com](http://bmj.com). Selection is usually made 12 days after print publication of the article to which they respond.



**bmj.com** To submit a rapid response go to any article on [bmj.com](http://bmj.com) and click “respond to this article”

# LETTERS



DAVID PARKER/SPL

## WITHDRAWAL OF SIBUTRAMINE

### Editorial is judgment in advance of the facts

Williams's negative, even nihilistic, approach to obesity treatment and to sibutramine in particular is ill judged and inaccurate.<sup>1</sup> His editorial seems to be based mainly on the limited data from the Sibutramine Cardiovascular Outcomes Trial (SCOUT) released by the European Medicines Agency, and perhaps data not in the public domain. It would have been better to await full details of the trial findings before writing an editorial.

To say that the trial has left a “mess of data that are impossible to interpret”<sup>1</sup> is wrong. We, the Executive Steering Committee, delayed the final closure of the database expressly to ensure that the data collection is as robust as that of other cardiovascular trials. We are now analysing for publication unique data on the impact of therapeutic weight loss in obese people.

The cardiovascular effects of sibutramine are complex: for most patients in SCOUT it reduced blood pressure during a six week active run-in,<sup>2</sup> as well as increasing HDL cholesterol.<sup>3</sup> SCOUT was not “an act of faith”<sup>1</sup> but required by the European regulatory authorities when sibutramine received its product licence. To say that no other manufacturer signed up for such a long study is also not true: Sanofi-aventis did just this for rimonabant until its withdrawal (CRESCENDO trial).

Williams is dismissive of small percentages of weight loss: the newly published SIGN guidelines,<sup>4</sup> among others, contradict him. He seems twice to endorse the concept of a magic bullet for obesity, which few in the discipline subscribe to because of the well known complexities of neural defences against body weight loss.<sup>5</sup>

Most involved doctors hope for progressive advances in treatment strategies, perhaps akin to hypertension treatment. Sibutramine withdrawal needs to be considered carefully once all the data are formally published. Given the need for better obesity treatments, a more appropriate editorial would have been in order.

**Nick Finer** consultant endocrinologist and honorary professor, University College Hospitals London, London WC1T 7DN [n.finer@ucl.ac.uk](mailto:n.finer@ucl.ac.uk) On behalf of the Executive Steering Committee of the Sibutramine Cardiovascular Outcome Trial (SCOUT): Ian Caterson, Walmir Coutinho, Luc Van Gaal, Aldo Maggioni, Christian Torp-Pedersen, Arya Sharma, and Philip James.

**Competing interests:** The authors are members of the SCOUT Executive Steering Committee, for which they have received payment from Abbott. In addition NF, IC, WC, LVG, AS, and CT-P have received lecture fees from Abbott.

- 1 Williams G. Withdrawal of sibutramine in Europe. *BMJ* 2010;340:c824. (9 February.)
- 2 Torp-Pedersen C, Caterson I, Coutinho W, Finer N, Van Gaal L, Maggioni A, et al; SCOUT Investigators. Cardiovascular responses to weight management and sibutramine in high-risk subjects: an analysis from the SCOUT trial. *Eur Heart J* 2007;28:2915-23.
- 3 James WP, Astrup A, Finer N, Hilsted J, Kopelman P, Rössner S, et al; STORM Study Group. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *Lancet* 2000;356:2119-25.
- 4 Scottish Intercollegiate Guidelines Network. Management of obesity. Guideline No 115. February 2010. Available at: [www.sign.ac.uk/guidelines/fulltext/115/index.html](http://www.sign.ac.uk/guidelines/fulltext/115/index.html).
- 5 Adan RA, Vanderschuren LJ, la Fleur SE. Anti-obesity drugs and neural circuits of feeding. *Trends Pharmacol Sci* 2008;29:208-17.

Cite this as: *BMJ* 2010;340:c1346

### Author's reply

Finer and colleagues' spirited letter might stimulate a wider and long overdue debate on the lasting benefits of the modest reduction in fat mass achievable with any of the anti-obesity drugs in clinical practice.

For an obese adult weighing 70 kg aged 20 who gains 30 kg of fat through adult life, a 10% loss of weight lasting two years is only a 3% reduction in the total excess fat carried until the age of 60. Whether such drug induced weight loss prolongs life or reduces the cardiovascular damage of obesity is still not known.<sup>1</sup> This crucial question could be answered by long term trials in which all participants are followed up to death (not the intention of SCOUT or CRESCENDO), and provided that the drug has no intrinsic impact on the cardiovascular system. Sibutramine clearly has intrinsic sympathomimetic effects, causing tachycardia and hypertension in some patients.<sup>2</sup>

Thus the cause of the excess cardiovascular risk in the pre-terminal analysis of SCOUT cannot be determined, and this outcome is uninterpretable.

Ideally, a magic bullet that is effective, safe to be given for life, and cheap should be possible. Orlistat, “the only drug specifically licensed for use in obesity”,<sup>1</sup> probably falls short of this mark, even if given for longer than its licensed duration. We shall never know how good orlistat is because the necessary lifelong study will never be done. Meanwhile, obesity gains momentum so fast that whatever we are doing to stop it is not working.

As my editorial shows, I think that the idea of a magic bullet is untenable because of physiology and human nature. Sibutramine is just the latest in a long line of drugs that had to be withdrawn because of risk or inefficacy. The writing on the wall is all too clear; perhaps standing back a little would allow Finer and colleagues to see what it's trying to tell us.

**Gareth Williams** professor of medicine, Faculty of Medicine and Dentistry, University of Bristol, Bristol BS10 5NB [gareth.williams@bristol.ac.uk](mailto:gareth.williams@bristol.ac.uk)

**Competing interests:** GW previously (up to 2003) had support for preclinical and clinical research, accepted honorariums to speak at meetings, and acted as a paid scientific and medical adviser to various drug companies, including the manufacturers of sibutramine.

- 1 Scottish Intercollegiate Guidelines Network. Management of obesity. Guideline No 115. February 2010. Available at: [www.sign.ac.uk/guidelines/fulltext/115/index.html](http://www.sign.ac.uk/guidelines/fulltext/115/index.html).
- 2 McNulty SJ, Ur E, Williams G, for the Multicenter Sibutramine Study Group. A randomised trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care* 2003;26:125-31.

Cite this as: *BMJ* 2010;340:c1349

### Magic bullets now uncontrolled

With the loss of sibutramine, Williams advocates surrender because we have only one drug—orlistat—to face the rising tide of obesity.<sup>1</sup> He makes no comment on another sinister development. Although prescription drugs are carefully monitored, fraudulent claims for obesity cures are no longer controlled in the UK.

Before 2008, the Trade Descriptions Act (TDA) enabled trading standards officers to prosecute vendors of antiobesity products for which false claims were made. I acted as expert witness to many such prosecutions at which substantial fines were imposed on the vendors. In May 2008, the Consumer Protection against Unfair Trading Regulations (CPUTR) replaced the TDA, after which any complaints about false claims for medicinal products had to be processed by a call centre—Consumer Direct. This centre was mainly to help consumers to get refunds after

unsatisfactory purchases, and it did not assist in prosecutions for misleading claims for health products.

Recently I have noted a spate of advertisements for fat furnaces, slimming patches, fat magnets, metabolism spurs, and so on. These claims have already been found to be misleading under the TDA. A search using freedom of information law showed no such prosecutions have occurred since 2008 under CPUFR.

Williams may not be aware that dietary advice without drugs can be as effective as orlistat. But of course advice on lifestyle change cannot compete with unfettered false claims for magic bullets.

**John S Garrow** retired physician, Rickmansworth, Hertfordshire  
WD3 7DQ.johngarrow@aol.com

**Competing interests:** JSG is a longstanding member of HealthWatch, a registered charity for treatment that works.

1 Williams G. Withdrawal of sibutramine in Europe. *BMJ* 2010;340:c824. (9 February.)

Cite this as: *BMJ* 2010;340:c1351

## DOCTORS ON THE FRONT LINE

### Time for a civilian front line?

War changes medicine: how will the wars in Iraq and Afghanistan change the management of trauma in civilian life?<sup>1</sup>

The original AcBCDE approach to trauma management—airway with cervical spine immobilisation, breathing, circulation, disability, exposure—has needed in these conflicts to become cABC (catastrophic bleeding, airway, breathing, circulation).<sup>1</sup> Increasing sport activities and high speed road traffic collisions have led to more patients with multiple injuries and severe haemorrhage being treated in emergency departments in developed countries. Aggressive blood resuscitation and control of coagulopathy are often paramount but seem not to fit well with the AcBCDE approach. We in emergency departments should therefore be flexible and adapt algorithms to the clinical needs, just like doctors on the front line.<sup>1</sup>

As well as shock packs and a low threshold for using O negative blood, the design of emergency departments and trauma centres needs to be changed to minimise the distance from the receiving unit to operating theatres and imaging centres. In Macdonald's article the chain of care starts on the field with robust prehospital care and continues in a centre where a single multidisciplinary team awaits the patient with operating theatres and imaging centres nearby. This should be our objective for emergency departments.

I wonder when such effective coordination and condensed communication between teams will be attained, with patients being stabilised

outside hospital before transfer straight to an operating theatre-imaging centre without passing Go.

**Janos P Baombe** doctor, Emergency Department, Manchester Royal Infirmary, Manchester M13 9WL baombejp@yahoo.co.uk  
**Competing interests:** JPB is an ATLS instructor.

1 Macdonald H. Doctors on the front line. *BMJ* 2010;340:c379. (18 February.)

Cite this as: *BMJ* 2010;340:c1318

## SSRIS AND TAMOXIFEN

### Why condemn fluoxetine?

In their editorial promoting the CYP2D6 inhibition hypothesis as the explanation for the important interaction between paroxetine and tamoxifen, Andersohn and Willich use the hypothesis alone to justify the statement that, "for safety reasons, coprescription of fluoxetine and tamoxifen in women with breast cancer should be avoided until additional evidence becomes available."<sup>1</sup> But in one study, fluoxetine of all the antidepressants studied, had the lowest, if not statistically significant, all cause mortality during tamoxifen treatment.<sup>2</sup> And another study found that fluoxetine also had one of the lowest (not statistically significant) recurrence rates in oestrogen receptor positive breast cancer of all common CYP2D6 inhibiting drugs.<sup>3</sup>

Drug interactions are complex, and moving beyond the evidence with such a recommendation could cause unnecessary concern. Apart from paroxetine, the present evidence base raises no concern of increased risk of breast cancer occurrence or mortality.

**Michael J Jenkinson** consultant physician, Queen Elizabeth The Queen Mother Hospital, Margate, CT9 4AN  
michael.jenkinson@ekht.nhs.uk

**Competing interests:** None declared.

- 1 Andersohn F, Willich SN. Interaction of serotonin reuptake inhibitors with tamoxifen. *BMJ* 2010;340:c783. (8 February.)
- 2 Kelly CM, Juurlink DN, Gomes T, Duong-Hua M, Pritchard KI, Austin PC, et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study. *BMJ* 2010;340:c693.
- 3 Ahern TP, Pedersen L, Cronin-Fenton DP, Sorensen HT, Lash TL. No increase in breast cancer recurrence with concurrent use of tamoxifen and some CYP2D6-inhibiting medications. *Cancer Epidemiol Biomarkers Prev* 2009;18:2562-4.

Cite this as: *BMJ* 2010;340:c1319

### Authors' reply

Our recommendations and those of others (full reference details of which are available in the response on bmj.com) to avoid coprescribing fluoxetine and tamoxifen are not based on a hypothesis alone, as indicated by Jenkinson,<sup>1</sup> but on the growing evidence of a central role for cytochrome P450 2D6 (CYP2D6) in the efficacy of tamoxifen. A marked reduction in plasma concentrations of endoxifen during cotreatment with the strong CYP2D6 inhibitors paroxetine or

fluoxetine has been demonstrated.<sup>2,3</sup> A recent study on genetically determined variation in CYP2D6 activity also indicated the importance of unimpaired CYP2D6 metabolism for tamoxifen efficacy.<sup>4</sup> The increased risk of death from breast cancer during cotreatment with paroxetine reported by Kelly and colleagues is in line with these findings.<sup>5</sup>

If a drug needs bioactivation via CYP2D6, it is reasonable to avoid cotreatment with all strong inhibitors of this enzyme until their safe concurrent use has been shown. In Kelly and colleagues' study, and in the case-control study cited by Jenkinson,<sup>6</sup> the confidence intervals of the risk estimates for fluoxetine were wide, so they did not exclude a clinically relevant increase in risk. In the light of these data, a "presumption of innocence" with respect to fluoxetine seems inappropriate and may cause unacceptable harm. Instead, convincing evidence for the safe concurrent use of fluoxetine and tamoxifen is needed before current recommendations are revised.

**Frank Andersohn** senior research associate  
frank.andersohn@charite.de

**Stefan N Willich** professor and director, Institute for Social Medicine, Epidemiology, and Health Economics, Charité University Medical Centre, 10098 Berlin, Germany

**Competing interests:** FA declared no competing interests. SNW served as a consultant for Sanofi-Aventis.

- 1 Andersohn F, Willich SN. Interaction of serotonin reuptake inhibitors with tamoxifen. *BMJ* 2010;340:c783. (8 February.)
- 2 Borges S, Desta Z, Li L, Skaar TC, Ward BA, Nguyen A, et al. Quantitative effect of CYP2D6 genotype and inhibitors on tamoxifen metabolism: implication for optimization of breast cancer treatment. *Clin Pharmacol Ther* 2006;80:61-74.
- 3 Stearns V, Johnson MD, Rae JM, Morochio A, Novielli A, Bhargava P, et al. Active tamoxifen metabolite plasma concentrations after coadministration of tamoxifen and the selective serotonin reuptake inhibitor paroxetine. *J Natl Cancer Inst* 2003;95:1758-64.
- 4 Schroth W, Goetz MP, Hamann U, Fasching PA, Schmidt M, Winter S, et al. Association between CYP2D6 polymorphisms and outcomes among women with early stage breast cancer treated with tamoxifen. *JAMA* 2009;302:1429-36.
- 5 Kelly CM, Juurlink DN, Gomes T, Duong-Hua M, Pritchard KI, Austin PC, et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population-based cohort study. *BMJ* 2010;340:c693.
- 6 Ahern TP, Pedersen L, Cronin-Fenton DP, Sorensen HT, Lash TL. No increase in breast cancer recurrence with concurrent use of tamoxifen and some CYP2D6-inhibiting medications. *Cancer Epidemiol Biomarkers Prev* 2009;18:2562-4.

Cite this as: *BMJ* 2010;340:c1321

**bmj.com podcast**

podcasts.bmj.com/bmj/2010/02/12/transmuting-tamoxifen

## OSTEONECROSIS OF THE JAW

### Note on dental procedures

Dental advice in the case of osteonecrosis of the jaw and bisphosphonate treatment needs clarification.<sup>1</sup>

The broad term "dental procedure" could cause confusion among doctors. There are multitudes of dental procedures and many are perfectly safe in patients taking high



dose bisphosphonates. Indeed, some dental procedures in this group of patients, such as restorations or root canal treatment, are to be positively encouraged if the alternative is extraction of the tooth.<sup>2</sup>

A more accurate term for interventions to be avoided in these patients might be surgical procedures involving the mandibular or maxillary bone.

**Michael N Pemberton** consultant in oral medicine, University Dental Hospital of Manchester, Manchester M15 6FH  
mike.pemberton@manchester.ac.uk

**Competing interests:** None declared.

- 1 Khan A. Osteonecrosis of the jaw and bisphosphonates. *BMJ* 2010;340:c246. (2 February.)
- 2 Fedele S, Kumar N, Davies R, Fiske J, Greening S, Porter S. Dental management of patients at risk of osteonecrosis of the jaws: a critical review. *Oral Dis* 2009;15:527-37.

Cite this as: *BMJ* 2010;340:c1317

## EVALUATING COMPLEX INTERVENTIONS

### Health improvement programmes: really too complex to evaluate?

Imagine an intervention whose effects vary within and between individuals and depend on subtle interactions between deliverers and recipients, and in which exposure is uncertain. Given this complexity, who would contemplate conducting a randomised controlled trial? In fact, all these issues must be dealt with in drug or therapeutic trials, as well as in more obviously complex interventions.<sup>1</sup>

Mackenzie and colleagues describe the problems of a specific intervention—Keep Well—to argue that randomised controlled trials are inappropriate or impossible for evaluating most health improvement interventions.<sup>2</sup> In doing so, they ignore the many successful randomised controlled trials of health improvement interventions that suggest this intervention type is not a special case,<sup>3,4</sup> and misrepresent the MRC guidance for the development and evaluation of complex interventions.<sup>5</sup>

Keep Well has many features that make evaluation difficult, but shifting the focus of evaluation from effectiveness towards implementation is a mistake. Why should

decision makers want to know about implementation, populations reached, or impact on practice unless they know whether the intervention is effective? Such questions are highly pertinent, but only in the context of good information about outcomes.

The MRC guidance is pragmatic in recommending randomised controlled trials. It warns researchers to beware of blanket statements prescribing specific methods for settings, and draws attention to successful and useful applications of a range of non-experimental approaches. The guidance also recognises that rigid protocols are often impractical, and emphasises the need for theoretically informed process evaluations. It is misleading and unhelpful to class it as part of a powerful “lobby for controlled trial designs.”<sup>1</sup>

**Lyndal Bond** associate director, MRC/CSO Social and Public Health Sciences Unit, Glasgow G12 8RZ lbond@sphsu.mrc.ac.uk

**Peter Craig** programme manager, MRC Population Health Sciences Research Network, Glasgow G12 8RZ

**Matthew Egan** senior investigator scientist

**Kathryn Skivington** pre-doctoral fellow

**Hilary Thomson** senior investigator scientist, MRC/CSO Social and Public Health Sciences Unit, Glasgow G12 8RZ

**Competing interests:** None declared.

- 1 Bond L, Craig P, Egan M, Skivington K, Thomson H. Rapid response. MRC guidelines and the evaluation of health improvement programmes: are health improvement programmes really too complex to assess their effectiveness? *bmj.com* 2010. www.bmj.com/cgi/eletters/340/feb01\_1/c185#231555
- 2 Mackenzie M, O'Donnell C, Halliday E, Sridharan S, Platt S. Do health improvement programmes fit with MRC guidance on evaluating complex interventions? *BMJ* 2010;340:c185. (1 February.)
- 3 Kinmonth A, Wareham NJ, Hardeman W, Sutton S, Prevost AT, Fanshawe T, et al. Efficacy of a theory-based behavioural intervention to increase physical activity in an at-risk group in primary care (ProActive UK): a randomised trial. *Lancet* 2008;371:41-8.
- 4 Rosen L, Manor O, Engelhard D, Sucker D. In defense of the randomized controlled trial for health promotion research. *Am J Public Health* 2006;96:1181-6.
- 5 Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:979-83.

Cite this as: *BMJ* 2010;340:c1332

### What is and what could be



Mackenzie and colleagues confuse a range of different issues when evaluating a community wellness programme.<sup>1</sup> Whatever the problems of randomisation and standardisation, all kinds of detailed monitoring would provide some valuable research data, even with

imperfections. For example, different projects used different methods to contact their target population groups.<sup>1</sup> How did they do it and what was the response rate? This information would tell us something about getting responses to initiatives of this kind.

I have never met anyone in the NHS who argues that every drug is 100% effective, but those involved in community initiatives seem generally convinced that their interventions work and so evaluation is not high on their agenda. This often stems, legitimately, from a concern to help disadvantaged groups. But if resources are limited, we need to find the best ways of helping, not assume that we already know.

Existing established services frequently collect almost no good quality data. As a result, we would still be stuck with potentially ineffective services if we evaluated new ideas effectively. The culture of data collection and evaluation is also poorly developed, making data collection on new initiatives harder.

Services to improve population wellness should be evaluated as thoroughly as possible. Then, even if some limitations apply to the approach and methods, we are doing the best we can to learn what works and what does not. If we measure what happens in multi-site initiatives—a natural experiment—we will be better equipped to decide on the priority of these services relative to others.

**Peter A West** health economist, York Health Economics Consortium, University of York, York pa.west@blueyonder.co.uk

**Competing interests:** PAW is a health economist and health service researcher who has attempted to evaluate a range of community interventions, usually without much success.

- 1 Mackenzie M, O'Donnell C, Halliday E, Sridharan S, Platt S. Do health improvement programmes fit with MRC guidance on evaluating complex interventions? *BMJ* 2010;340:c185. (1 February.)

Cite this as: *BMJ* 2010;340:c1340

## IMPROVING RESEARCH

### Publications shouldn't be key to advancement

“The tide of low quality, low impact prognosis research” could be applied to many areas of clinical research.<sup>1</sup> But what causes so much poor quality research? The answer is simple: publications are fundamental to advancement in medicine. Application forms ask for a list of publications and CVs are assessed on publications, regardless of quality. This attitude is reinforced throughout medical training. Thus, excellent trainees who are passionate about treating patients, but less passionate about research, are forced to publish.

Trainees learn important lessons about critical appraisal by performing research—a skill



important for all trainees. But do trainees need to design and complete a high quality research project? This is not the same as being able to design and complete good quality audits. Audit and research are often grouped together. Audit is fundamental for all clinicians to improve local practice.

However, I suggest that the royal colleges take a new approach to teaching trainees about research. Instead of learning about research ad hoc, often relaying bad habits, validated paths should be open to all trainees. A well structured course teaching the principles and practice of research that ends in a supervised project is an obvious choice. Trainees who are not gifted in research could then “tick the research box” without feeling pressure to publish. And those interested in future research could be taught the importance of integrity and quality.

Perhaps the recent *BMJ* cover title “Get them while they’re young” would be a good motto as we try to improve the quality of research.

John A Ford registrar, North Shore Hospital, Auckland  
johnalexanderford@gmail.com

Competing interests: None declared.

- 1 Hemingway H, Riley RD, Altman DG. Ten steps towards improving prognosis research. *BMJ* 2009;339:b4184. (30 December.)

Cite this as: *BMJ* 2010;340:c1322

## GUIDELINE DEVELOPMENT

### Missing published and unpublished data in guidelines

The varying perspectives in the debate on guideline development are warranted discussions that should continue.<sup>1,2</sup> The two concepts of guideline development outlined below should be considered before guideline release.

Firstly, does the guideline include current published data? The American Diabetes Association (ADA) released its *Standards of Medical Care in Diabetes* in January 2010.<sup>3</sup> The guideline proposes to consider the use of aspirin, but in November 2009 a meta-analysis of randomised controlled trials in diabetes concluded that, compared with placebo, aspirin did not significantly reduce the risk of major cardiovascular events (relative risk 0.90, 95% confidence interval 0.81 to 1.00), cardiovascular mortality (0.94, 0.72 to 1.23), or all cause mortality (0.94, 0.82 to 1.05).<sup>4</sup> The 2010 ADA guideline did not mention the meta-analysis.

Secondly, are government agency data reviewed for newly approved drugs? Such a review would allow authors to find

unpublished trials. More than half of the trials to support approval of new molecular agents approved for sale in the US between 1998 and 2000 remained unpublished after five years. Most unpublished trials were considered to be negative.<sup>5</sup> Similarly, 40% of trials submitted to the Swedish drug regulatory authority have not been published.<sup>6</sup>

These two questions raise doubt about the validity of even the most rigorously developed guidelines.

G Elliott Cook assistant professor,  
LECOM School of Pharmacy, Erie, PA 16509, USA  
ecook@lecom.edu

Competing interests: None declared.

- 1 Grol R. Has guideline development gone astray? Yes. *BMJ* 2010;340:c306. (29 January.)
- 2 Gibbons RJ, Antman EM, Smith SC. Has guideline development gone astray? No. *BMJ* 2010;340:c343. (29 January.)
- 3 American Diabetes Association. Standards of medical care in diabetes—2010. *Diabetes Care* 2010;33:s11-61.
- 4 Berardis GD, Sacco M, Strippoli GF, Pellegrini F, Graziano G, Tognoni G, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. *BMJ* 2009;339:b4531.
- 5 Lee K, Bacchetti P, Sim I. Publication of clinical trials supporting successful new drug applications: a literature analysis. *PLoS Med* 2008;5:e191.
- 6 Melander H, Ahlqvist-Rastad J, Meijer G, Beermann B. Evidence based medicine—selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications. *BMJ* 2003;326:1171-3.

Cite this as: *BMJ* 2010;340:c1337

## RESPONSE

### Steven L Shafer responds to Jeanne Lenzer

Lenzer describes how *Anesthesia & Analgesia* handled an article when alert readers noted an error in the tables and the authors were unable to find their original spreadsheets.<sup>1</sup> As editor in chief of the journal, I analysed the published tables and concluded that the error was likely in the calculation of the confidence intervals. In correspondence with Lawrence Saidman, correspondence editor of *Anesthesia & Analgesia* and former editor in chief of *Anesthesiology*, the authors disclosed the loss of their data<sup>2</sup> and I noted that the “findings stand, albeit weakly.”<sup>3</sup> Lenzer’s query from the *BMJ* in February 2009 was the first correspondence of any kind received by the editorial board about our 2007 editorial decision not to retract the article.

How should a journal respond when data are lost? The era of written laboratory notebooks has passed. This problem will likely recur because investigators archive data on spreadsheets hosted on their laptop computers. As Harvey Marcovitch, former chair of the Committee on Publication Ethics, observed, “The data having gone missing is not satisfactory ... but the best

approach is always one of transparency.”<sup>1</sup> I agree: the authors had to disclose the loss of their data.<sup>2</sup>

Should the article be retracted? Retraction sends a strong message about authors’ responsibility for archiving data. Had the article touted a new drug, device, or procedure, we would have retracted it. However, the article raised an important safety concern, subsequently verified,<sup>4</sup> that mortality might increase after transfusion of old blood. We allowed the article to stand, “albeit weakly,” in the interest of patient safety, and to encourage repetition of the study.

Journals have neither the authority nor the resources to investigate questions that arise about the conduct of research. That responsibility lies with academic institutions. In January 2009 we were informed that the article’s conclusions were inconsistent with a previous abstract by the authors. Without the original data these differences could not be explained, so the article was retracted.

Learning from this experience, *Anesthesia & Analgesia* now requires identification of

an “archival author” who is responsible for safekeeping data after publication.<sup>5</sup>

Our decision in this case is not a precedent for how journals should handle loss of research data. Rather, we highlight the importance of carefully examining the available data, considering all options, and making a responsible editorial decision that weighs the implications of all possible courses of action.

Steven L Shafer editor in chief, *Anesthesia & Analgesia*, professor of anesthesiology, Columbia University, Columbia University Medical Center, 622 W 168th St, PH 5-505 New York, NY 10032-3725, USA

sshaffer@anesthesia-analgesia.org

Competing interests: SLS is editor in chief, *Anesthesia & Analgesia*.

- 1 Lenzer J. Journal retracts article about age of transfused blood three years after publication. *BMJ* 2009;338:b2057. (20 May.)
- 2 Basran S, Frumento RJ, Cohen A, Lee S, Du Y, Nishanian E, et al. Authors’ reply. *Anesth Analg* 2007;104:1597.
- 3 Shafer SL. Occam’s razor. *Anesth Analg* 2007;104:1597-8.
- 4 Koch CG, Li L, Sessler DI, Figueroa P, Hoeltge GA, Mihaljevic T, et al. Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 2008;358:1229-39.
- 5 2009 *Anesthesia & Analgesia* guide for authors. *Anesth Analg* 2009;109:217-31. Available at: www.aeditor.org/GuideforAuthors.pdf

Cite this as: *BMJ* 2010;340:b3920