

EDITOR'S CHOICE

In praise of informed scepticism

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Earlier this year, guidelines from three respected US professional societies advised doctors to give alteplase to patients with acute stroke. The recommendation was based on what the guidelines' authors considered grade A evidence. Yet as Jeanne Lenzer reports (doi:10.1136/bmj.f3830), surveys show that many if not most emergency physicians are sceptical of the benefits and concerned about the harms of alteplase. The published evidence shows reductions in disability but not in mortality, with only two of the 12 randomised trials showing benefit and five having been terminated early because of lack of benefit, higher mortality, and significant increases in brain haemorrhage.

So how did this grade A recommendation occur? Lenzer has found that, as with other clinical practice guidelines before them, these were written by authors almost all of whom had direct or indirect ties with the drug's manufacturer. It is hard not to feel a certain fatigue as I relay this information. Hasn't this been identified before as a major problem with the credibility of guidelines, not least in a thorough and well publicised report by the US Institute of Medicine in 2011? The institute recommended that no authors of guidelines should have financial conflicts of interest, or where this was unavoidable, authors with conflicts should be in the minority.

Lenzer has found that for one of the guidelines recommending alteplase, seven of eight panel members had ties with industry: three had direct relationships with companies that market alteplase, while four had links with an educational foundation wholly funded by industry, whose president and founder was an outspoken advocate for alteplase on acute stroke. The remaining author had resigned from the panel six years earlier.

Meanwhile, emergency physicians find themselves in a difficult position. The guidelines represent the standard of care against which they will be judged in any claims of malpractice. And although the rules on conflict of interest may be tightening, the current standards of care across much of medicine originate with similarly biased guideline panels. Doctors will have to wait for new guidance that they and their patients can trust. Earlier this year, longstanding guidance recommending high dose steroids in acute spinal injury was reversed because of lack of evidence of benefit and clear evidence of harm. In that case too, as Lenzer reports, the initial guidance was tainted with financial conflicts of interest, and physicians were sceptical based on their own clinical experience with the treatment.

So let us put our faith in informed scepticism. And with that in mind, take a look at the unusual proposal launched in this week's *BMJ*, to restore invisible and abandoned trials (RIAT) (doi:10.1136/bmj.f2865). Peter Doshi and colleagues have compiled a dossier of trials that have never been published or have been misreported but for which the data are in the public domain through legal proceedings or freedom of information requests. The list of these trials, on [bmj.com](http://www.bmj.com), makes fascinating reading (www.bmj.com/content/346/bmj.f2865#T1). The RIAT authors are calling for volunteer authors to reanalyse the data, and as we say in the linked editorial (doi:10.1136/bmj.f3601), the *BMJ* and *PLoS Medicine* are the first of what we hope will be a long list of journals keen to publish the results.

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