should not deceived ourselves, or people who trust our recommendations. There is no gold standard evidence that acupuncture improves pain or anything else. The BMA report is quite simply wrong.

R A Moore consultant biostatistician, should be heard @pox.ac.uk

H J McQuay professor of pain relief

A D Oldman research associate

L E Smith research associate

Pain Research and Nuffield Department of Anaesthetics, University of Oxford, The Churchill, Oxford OX3 7LJ


Is approval of acupuncture for back pain really evidence based?

Editor—The BMA has concluded that acupuncture should be made more widely available to British people through the NHS and that general practitioners should receive training in it.2 The association seems to base its conclusion on three things: evidence showing that “acupuncture is more effective than placebo” for back pain, nausea and vomiting, migraine and dental pain; the fact that 47% of general practitioners have arranged for their patients to receive acupuncture; and the wish of 46% of those professionals to receive training in acupuncture in order to treat their patients.1

The evidence on the effectiveness of acupuncture in the treatment of back pain seems to have been misinterpreted. The Cochrane Collaboration Back Review Group has published a major systematic review of the Efficacy of Acupuncture in low back pain.3 This review followed a rigorous methodology and an exhaustive search for information. Its results indicated poor research methods and contradictory results from studies of acupuncture in low back pain. The review was therefore inconclusive and could not serve as a basis for recommending acupuncture. This was consistent with the results of past systematic reviews4 and with a randomised trial that compared the effectiveness of acupuncture with that of massage and self care education.5

Although scientific evidence in this respect has not changed much in several years, public and medical opinion seem to have changed. The establishment of a double standard for the approval of a treatment technique, bowing to the pressure of public opinion and not taking into account evidence based recommendations, is harmful to the public’s health and to the economy of the NHS. In time it could also be harmful to the treatment approved with the lower standard and to the credibility of its practitioners and the institutions that recommend it.

Clinical practice is not always based on scientific evidence and the search for an efficient use of resources. Many years ago patients were convinced of the effectiveness of leeches for the treatment of infectious diseases, doctors prescribed them, and apothecaries sold them. Nevertheless, despite public demand and medical interest, evidence of the efficacy, safety, and cost effectiveness of the treatment was lacking. This lesson from the past should be kept in mind.

Francisco M Kovacs president

Maria Teresa Gil del Real coordinator

Kovacs Foundation, Scientific Department, Palma de Mallorca 07102, Spain

mgt@kovacs.org

The authors are members of the management committee of the COST B4 programme on unconventional medicine.

1 Silvert M. Acupuncture wins BMA approval. BMJ 2000; 321:11, 1 July.


Lung cancer and passive smoking

Turning over the wrong stone

Editor—In their reanalysis of the epidemiological evidence on lung cancer and smoking Copas and Shi1 assert that after allowing for publication bias the apparent average excess risk of lung cancer from passive smoking2 would drop from 24% to 15%. Despite the lack of supporting data,2 we are asked to believe solely on the basis of statistical inference that such data must be hiding under a stone. They are, however, turning over the wrong stone.

More important than publication bias is the underestimation of risk that occurs when these studies assess exposure solely on the basis of whether non-smokers either lived or did not live with a smoker,3 when other exposure exists.

Where other exposure is common—for example, in childhood, in social situations, or in the workplace—the risk of lung cancer may be seriously underestimated. Spouses of non-smokers exposed in other circumstances will be misclassified as non-exposed, contaminating the referent group, and attenuating the risk estimate. For example, Hackshaw et al estimate that the odds ratio would have been 1.42 (95% confidence interval 1.21 to 1.66) if those with spousal exposure alone were compared with those who were truly unexposed.4 By comparison, in a recent meta-analysis of risk associated with workplace exposure, Wells found an estimated relative risk of 1.39 (1.15 to 1.68) for the five studies meeting basic study quality standards.5 Repace and Lowrey found that when both workplace exposure and an unexposed referent group were taken into account in the American Cancer Society study of passive smoking and lung cancer, a population relative risk of 1.2 increased to 1.7.6

Repace and Lowrey modelled the risk of workplace exposure, estimating the average relative risk at 2.0 for office workers in the United States in the 1980s. This result is consistent with a value reported by Reynolds et al for women with 30 or more years of workplace exposure—namely, at ages at which lung cancer mortality begins to become significant.7 Moreover, all of these analyses focus on average risk. Repace et al estimated that individuals at the 95th centile—for example, those experiencing high smoker density and low air exchange—have an exposure, and a risk, as much as four times as high as those at the median. This result is commensurate with observations of dose8 and risk.9

Turning over stones may indeed alter the estimated risk, but turning over the right stone indicates that in the original meta-analysis, the actual passive smoking–lung cancer risk is underestimated, not overestimated.

Kenneth C Johnson senior epidemiologist

Environmental Risk Assessment and Case Surveillance Division, Cancer Bureau, Laboratory Centre for Disease Control Health Protection Branch Health Canada, Ottawa, Ontario, Canada

K IA 0L2

Kerl J C, Johnson@hc-sc.gc.ca

James Repace health physicist

Repace Associates, SecondHand Smoke Consultants, Bowie, MD 20720, USA

repace@eros.com

Competing interests: None declared.


Increased risk is not disputed

Editor—In their paper on lung cancer and passive smoking, Copas and Shi say that in our review of passive smoking and lung cancer there is clear evidence of publication bias and that allowing for this substantially lowers the estimate of relative risk (which we reported as 1.24 before correction for other biases and confounding and 1.26 after correction).1,2 Neither is correct.

It is proposed that large studies will tend to be published regardless of their result but small studies published only if they are positive (publication bias). As Copas and Shi point out, studies with a large standard error (indicating a small study) tend to be
associated with a large relative risk (correlation coefficient 0.35, \( P = 0.03 \)), implying that there may be some unpublished small negative studies. An indication of the size of the effect can be obtained by restricting the analysis to those studies with smaller standard errors which are less susceptible to increase publication bias. If the six studies with the largest standard errors (>0.5) are excluded there is no evidence for an association between standard error and relative risk (correlation coefficient 0.15, \( P = 0.48 \)) and the estimate of risk is 1.22; even if the 12 studies with the largest standard errors (>0.4) are excluded the estimate is 1.23; neither is materially different from the estimate based on all 37 studies (1.24). This indicates that the effect of unpublished studies is likely to be negligible.

There is further evidence against material publication bias in that 32 of the 39 studies reported non-significant results and in 16 (41%) the authors had either concluded that there was no effect (13) or that the evidence was inconclusive (3), suggesting that the passive smoking literature is one with a strong tendency for positive results to be published while negative results remain unpublished.

Even if one accepts the calculations of Copas and Shi, their relative risk estimate, which assumes that as many as 20% of all studies are unpublished, is 1.15, not substantially different from our own estimate (1.26) and well within the confidence interval on our result (1.06 to 1.47). Even under the extreme assumption that 40% of studies were not published their estimate (1.11) would still be consistent with ours. Copas and Shi do not dispute that there is an increased risk of lung cancer due to passive smoking nor do they seriously challenge our estimates of its magnitude.

Allan Hackshaw lecture a.hackshaw@mds.qmw.ac.uk

Malcolm Law reader Nicholas Wald professor Wolfson Institute of Preventive Medicine, Department of Environmental and Preventive Medicine, London EC1M 6BQ

Competing interests: None declared.


Nothing new was said

Editor—My reaction to this paper is a big yawn. Copas and Shi think that there is evidence of publication bias against small studies that reach the negative conclusion that second hand smoke causes lung cancer. This is nothing new, nor is the analysis they present (based on something called a funnel plot).

Copas and Shi agree that a meta-analysis of the published studies on passive smoke may be lung cancer should show a significant increase in risk of 1.24. They compute that if only 60% of the studies that have ever been done were published and that the remaining 40% of studies that were done but never published—and that no one has ever heard of—were all negative, then the increase in risk would only be 1.11 and not significant.

There is no evidence that these studies were ever done. Our investigation suggests that there is no publication bias.

Copas and Shi also point out that if only 70% of the studies were published, and all the unpublished studies showed no elevation in risk, then the pooled risk would be 1.13 and significant (\( P = 0.052 \)).

So, you could argue that they proved that, while failure to publish negative studies would lower the true risk of lung cancer associated with passive smoking, under any reasonable guess at how much “unpublished” research there was, there would still be an increase in risk. But despite the fact that many people have tried to find these unpublished studies, no one has been able to find them. The root of the industry would make sure we knew about them.

What Copas and Shi say is that if several people did studies that found no effect of passive smoking and lung cancer and found no increase in risk, and we suddenly knew about these papers, then our estimate of how much the risk was increased would be smaller. But the risk would still be increased.

The real killer from second hand smoke is heart disease, not lung cancer. Heart disease kills about 10 times more people than lung cancer. Not even the tobacco industry has contested the evidence on asthma.

So… what’s the big deal?

Stanton A Glantz professor of medicine University of California, San Francisco, CA 94145-0150, USA glantz@medicine.ucsf.edu

Competing interests: None declared.


Scalas for visual test of publication bias are unfair

Editor—Funnel plots can be useful to detect publication and related bias. The funnel plot in the review of the epidemiological studies of passive smoking and lung cancer by Copas and Shi is, however, biased.1 In the absence of publication bias the plot can be assumed to be symmetrical only if relative risks are plotted on a logarithmic scale. The scale used by Copas and Shi is on a linear scale and will give the visual impression of publication bias even when there is none. Studies indicating that exposure to passive smoking increases the risk of lung cancer will spread out on the graph because the relative risk may range from 0.0 to infinity; in contrast studies showing a reduction in risk will be compressed in the range of 1.0 to zero. Visual interpretation of the data is therefore not possible by using the scale presented.

Christopher Cates general practitioner Manor View Practice, Bushey Health Centre, Bushey WD2 2NN, chrisrates@email.msn.com

Competing interests: None declared.


Authors’ reply

Editors—We thank the respondents for their comments on our paper. We agree with Johnson and Repace that the truth will be hiding under stones. Some of these stones (causes of bias) were considered in the earlier review by Hackshaw et al. They found that some stones give an increase in risk, others a decrease, and that on aggregate they tend to cancel out. What we have done is to add one more stone (publication bias) and use it to redo their calculation of the overall risk. It is not the wrong stone, just one of several stones.

Johnson and Repace start their letter by asserting that we claim that the excess risk decreases from 24% to 15%. We have not come up with a single best estimate. This is impossible without making assumptions that cannot be proven one way or the other. All our unpublished studies are there. Our conclusion is that at least some publication bias is needed to explain the trend in the funnel plot, and that allowing for even a small amount of study selection can give a substantially lower figure.

The paper by Bero et al, which we did refer to in our paper, suggests that there is no publication bias.1 We would emphasise the word “suggest”—neither their arguments nor the fact that no unpublished papers have been found mean that none exists. Our analysis does not dispute that the risk is increased; the question is by how much. Neither do we claim that the unpublished papers were all negative. We can say nothing at all about them, just that there may be a pool of studies from which the ones in the review are a selection. Our method lets the funnel plot tell us how much bias there may have been in this selection.

Just because more people die of heart disease than of lung cancer does not necessarily mean that there are more deaths attributable to passive smoking. A rather similar review by He et al, who are looking at studies of passive smoking and heart disease, comes up with a relative risk of 1.28.2 Thus, in relative terms, the elevation of risk is fairly similar.

In their letter, Hackshaw et al point out that most of the range of estimates we discuss is within their confidence band. Publication bias is another source of statistical uncertainty but, unlike ordinary sampling variability, acts in the downward direction only. Whatever confidence range is given, it tends to be just the single figure which is remembered. If there is good reason to think this is an overestimate, then surely this needs to be pointed out.

Finally, Cates is right in pointing out that we did not use logarithmic scales in our funnel plot. We decided to plot the raw figures so they could be compared more easily with the various values of relative risk discussed in the earlier article by Hackshaw et al. But this is
Quality of randomised controlled trials in head injury

Trials in head injury are more complex than review suggests

Editor—The review by Dickinson and colleagues shows a remarkably narrow view of research in head injury and virtually ignores the need to match the design to the research question. Historically, many clinical trials have been underpowered, but the authors' premise that the main aim of head injury trials should be to detect changes of “a few per cent” in the rate of death or disability does not apply, for example, to phase I/II trials in the acute stage nor to the later interventions used in many of their reviewed trials. The authors might find it useful to reread the article “Why do we need some large, simple randomised trials?” by Yusuf et al (note the word “some” in the title).

Several factors influence the relevant effect size and hence the size of the trial. Such factors include the size of the population, the variability of the intervention, and the ability to carry out useful secondary analyses. In severe head injury trials not only are they practicable and likely to be expensive, and therefore evidence of a substantial effect is required if budget holders are to be persuaded to support them. The focus on a 10% benefit has reflected a perception that funding could be obtained for a treatment that benefits 1 person in 10. However, even this may be optimistic. Despite the 13% benefit obtained from nimodipine treatment in sub-arachnoid haemorrhage,1 corresponding to a number needed to treat of eight, clinicians have had difficulties in gaining funding for the routine use of this drug. The effectiveness in individual patients is also relevant.

Dickinson and colleagues say that unfamiliarity among ethicists and committees and investigators with the idea of randomisation without consent obstructs recruitment. This is erroneous and displays a dangerously superficial attitude towards a complex area. What urgently needs to be clarified is the legal framework in which research in incompetent adults takes place. Recent legislation in the Scottish parliament contained no provision for an exception to the requirement to obtain informed consent. Equally it is not clear that any legal framework exists to allow research without consent in the rest of the United Kingdom.

The authors highlighted inadequately funding as one obstacle that has prevented large randomised controlled trials of widely practicable treatments for head injuries. The corresponding author is an applicant to the Medical Research Council for substantial funding for developing the CRASH study2 into a full scale trial, a study that is in part supported by the manufacturer of the agent under trial. In view of this, and his apparently strong position on this issue,3 it may be found surprising that no competing interests were declared.

Gordon D Murray professor of medical statistics
Department of Community Health Sciences,
Epidemiology and Statistics, University of
Edinburgh, Edinburgh, EH8 9AG
Gordon.Murray@ed.ac.uk

Graham M Teasdale professor of neurosurgery
University Department of Neurosurgery, Institute
of Neurological Sciences, Southern General Hospital,
Glasgow G51 4TF

Competing interests: As director of a charitable organisation, the European Brain Injury Consor-
tium, Professor Murray has been active in providing statistical advice to several pharmaceutical compa-

ties on the design, conduct, and analysis of clinical trials in head injury—namely, Bayer, Cambridge Neuroscience, Novartis, Pharmos, SmithKline Bee-

cham, and Synthelabo. In addition to extensive declared interests in head injury (BMJ 2000;230:1631-5), Professor Teasdale was a co-applicant to the Medical Research Council and a member of the steering committee for the pilot phase of the CRASH study but is not an applicant for funding for the full phase and has withdrawn from the steering committee.


Authors’ reply

Editor—We are pleased that Murray and Teasdale agree that clinical trials in head injury have been too small and that some large simple randomised controlled trials are needed. To date, there have been no such studies in head injury.

We are grateful to Professor Murray and Teasdale for identifying yet another obstacle to conducting large trials in head injury, the idea that to obtain funding a treatment must benefit at least 1 person in 10. There is no rational basis for the establishment of such a decision rule. Many factors impact on the decision to provide a treatment but considerations of efficiency require that priority is given to treatments that provide the greatest benefit per unit of cost. Even expensive treatments that benefit fewer than 1 person in 10 might be worth funding if the intervention offers an overall net welfare gain. In head injury, with high rates of long term disability, such a situation might easily occur.

When the effect size is large even small trials may be able to detect it. However, Murray and Teasdale fail to appreciate that both the size and the precision of the estimated treatment effect must be taken into account in therapeutic decision making. Large trials, with larger numbers of outcome events, provide more precise estimates of treatment effect. Thus, a true treatment effect is likely to be close to what has been observed. Imprecise estimates of even large treatment effects from poor quality trials make clinical and funding decisions difficult.

We agree that the legal framework in which research in incompetent adults takes place needs to be clarified. Given that such senior investigators as Murray and Teasdale are unclear on this issue, we hope that we might be forgiven for suggesting that less experienced investigators also find this issue problematic.

In our paper we openly and publicly make the scientific argument for some large simple randomised trials in head injury. We openly and publicly acknowledge that the same scientific argument underpins the Medical Research Council’s CRASH trial (corticosteroid randomisation after significant head injury), the first large simple randomised controlled trial in head injury. Open scientific argument in the pages of a medical journal does not constitute a conflict of interest and we are surprised that Murray and Teasdale think otherwise.

Finally, we would point out that the CRASH trial is sponsored by the Medical Research Council and not the manufacturers of the agent under trial. The manufacturers have donated the drug for the trial to the Medical Research Council, but the design, management, and conduct of the trial are entirely independent of them.

Ian Roberts senior lecturer in epidemiology
Ian.Roberts@ich.ucl.ac.uk

Frances Bunn review group coordinator, Cochrane Injuries Group
Reinhard Wentz information specialist, Cochrane Injuries Group

Phil Edwards research fellow
Child Health Monitoring Unit, Institute of Child Health, University College London, London
WC1N 1EH

Competing interests: None declared.

If in doubt, declare competing interests

Editor—Five years ago it was unusual for contributors to medical journals to declare competing interests even though they often had them. Now, increasingly, contributors do declare them, but there continues to be confusion over when to declare.

The BMJ started its campaign on competing interests by asking authors to declare any sort of competing interest, be it personal, political, religious, or whatever. Now we concentrate on financial competing interests because they are easier to define and there is stronger evidence that they matter.

A number of journals and other chose not to declare that they had applied to the Medical