Letters

Representation of authors and editors from poor countries

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Observed publication bias may reflect who is funding research

EDITOR—Despite research in tropical medicine being undertaken in countries from low human development index, authorship and editorial opinion remain with countries from higher development index. This unfair trend observed by Keiser et al demands to be addressed and overturned.[1]

This observed bias may arise because countries of high human development index fund the bulk of research in tropical medicine.[2 3] Authors from these countries have prepared the grant applications, taken principal investigator status, and believe that they should take primary or terminal authorship. Researchers from low human development index countries can break this cycle only if they can obtain international funding themselves or are allowed authorship by the principal investigators. It seems this is rarely extended to the collaborators in tropical countries, even though they are the ones practically conducting the study.

If such generosity in authorship and mentorship were provided, this would enable researchers from low human development index countries to become successful principal investigators, obtain funding, and be invited to the editorial board of respected journals. Keiser et al could have examined the funding source of the published research articles against authorship country of origin to see if this was confounding.

We are sure that these publication biases are not just restricted to tropical medicine. Consequently, we strongly advocate this approach be delivered uniformly across all clinical disciplines to support research and researchers in countries of low human development index, who are concurrently tackling substantial healthcare inequalities and unremitting disease,[4] and deservedly need greater support.

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1 Keiser J, Utzinger J, Tanner T, Singer BH. Representation of authors and editors from countries with different human development indexes in the leading literature on tropical medicine: survey of current evidence. *BMJ* 2004;328:1229-32. (22 May.)
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Partnerships may well be unequal

EDITOR—The findings by Keiser et al with regard to poor representation of countries with a low human development index on the boards of international journals in tropical medicine is not surprising.[1] They have done well to highlight this disparity in an area where local knowledge is key. It would also be interesting to examine whether there was notable overlap between different boards. In other words, did the developing country members consist of "the usual suspects"?

Underinvestment in research and health care in many developing countries undoubtedly accounts for some of the disparity. Yet the issues of wider power dynamics play a part. For example, the authors call for more research partnership between richer and poorer nations, but the question is whether you can have a partnership of unequals. With most of the funding for research coming from the wealthier countries of the West, it is extremely difficult, and perhaps impossible, for the research agenda not to be dictated by them and for the richest of the "fruits" not to go to them. Perhaps the innovative scheme by the Wellcome Trust to help establish researchers in tropical medicine from developing countries and to support their careers may improve the situation.

Similarly, the existence of African Journals On Line (supported by the International Network of the Availability of Science Publications) and other such initiatives may help foster relationships between researchers in different countries. That said, improved public and private sector funding of research from within developing countries must also be encouraged.

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Quality medical research from poor countries could be privileged in high impact journals

EDITOR—Keiser et al highlight the obvious under-representation of authors and editors from countries with low human development indexes in prestigious tropical medicine journals.[1] This shows the paradox of the greater burden of tropical disease afflicting people living in the underdeveloped world being studied, then published, by researchers in countries with a high development index.

Great obstacles confront researchers who live and work in countries that are poor in resources, and where diseases are prevalent, in conducting and publishing medical research into diseases of poverty.[2] These inequities are exacerbated by poor dissemination of and reduced access to quality medical research among clinicians in countries where these diseases are endemic.[3] This may be ameliorated by allowing duplicate publication in local journals or forums of difficult to access articles from prestigious journals with high local relevance, for a lesser cost or for free.[4] Journal space in high impact journals could be quarantined for articles on locally relevant medical research conducted by researchers from less developed countries. Publications could be actively solicited or commissioned from researchers who live and work in such countries in special focus issues.

Although quality clinical research flow from countries rich in research to countries poor in research is limited,[5] the reverse also occurs. Awareness of health issues pertaining to less developed countries among

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clinicians in the developed world could be improved by increased presence of article summaries and links to publications of note originating from less developed countries within sections such as Journal Watch.

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1 Keiser J, Utzinger J, Tanner T, Singer BH. Representation of authors and editors from countries with different human development indexes in the leading literature on tropical medicine: survey of current evidence. *BMJ* 2004;328:1229-32. (22 May.)
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Raised cardiac troponins

Troponins seem to be sensitive but not specific

EDITOR—The initial statement in Ammann et al's editorial on raised cardiac troponins, "Troponin T and troponin I are highly sensitive and specific markers of myocardial injury," is contradicted by a later statement: "In sepsis, for example, cardiac troponins are raised in up to 85% of patients in the absence of any acute coronary syndromes."[1]

Although troponins are clearly highly sensitive for acute coronary syndromes, and therefore valuable for risk stratification in patients presenting with classic cardiac chest pain, the real issue is the specificity of troponin assays when randomly applied in general medical admissions units to patients presenting as unwell (and not necessarily with cardiac syndromes). Given a high false positive rate in non-cardiac conditions—sepsis syndromes, eclampsia, and others—their specificity must be suspect.

Not unusually, an admitting junior doctor merrily "ticks all the boxes" on the clinical chemistry form and the patient (who clearly has pneumonia, without cardiac chest pain, and with a pristine electrocardiogram) has a raised troponin T concentration. Although this result does not necessarily imply a coexistent (clinically unsuspected) acute coronary syndrome, it does have prognostic implications for the pneumonia.

For my personal "missing from the list of diseases associated with raised troponins" diagnosis, I offer dermatomyositis.

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1 Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins. *BMJ* 2004;328:1028-9. (1 May.)

Troponin is raised in pre-eclampsia

EDITOR—In their editorial on raised cardiac troponins Ammann et al omit an important cause of increased troponin concentration in obstetric medicine—gestational hypertension and pre-eclampsia.[1]

Fleming et al showed fivefold higher median values for cardiac troponin I in pre-eclamptic women than in normotensive pregnant women.[2] These median values were above those which would be indicative of significant myocardial damage. Awareness of this becomes important in women with severe pre-eclampsia complicated by pulmonary oedema, the pathogenesis of which is likely to be multifactorial related to capillary leak, hypoalbuminaemia, hypertension, and global left ventricular dysfunction. It is also important as the other commonly used marker of myocardial ischaemia, the MB isoenzyme of creatine kinase, is raised in around a third of normal pregnant women on the first postpartum day after vaginal delivery.[3]

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1 Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins. *BMJ* 2004;328:1028-9. (1 May.)
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Brief lifestyle interventions for hypertension

Opportunity to provide useful information has been missed

EDITOR—Little et al address an important topic in their trial of dietary advice for patients with a single high blood pressure reading in primary care.[1] Robust evidence from randomised controlled trials of the effectiveness of nurse led hypertension management in primary care is lacking.[2] No mention is made of a possible cluster effect of different practices, neither do the authors clarify whether randomisation was balanced within practices. Neither nurses assessing outcomes nor patients were blinded to the intervention arm.


PENNY GRET/ARS

The entry assessment of blood pressure does not follow guidelines from the British Hypertension Society (neither does that at six months), which indicates that at least two measurements (1-2 minutes apart) should be taken on each occasion.[3] The patients enrolled would probably have had normal blood pressure and therefore would have been less likely to respond to treatment, since the blood pressure response to any treatment is greater the higher the blood pressure.

A reduction of sodium intake to <100 mmol/day (or to <6 g salt) would be expected to reduce systolic blood pressure by 2-8 mm Hg.[3] Low sodium salt achieved a reduction in sodium to potassium ratio of 0.32 (95% confidence interval 0.08 to 0.56). This is comparable to the changes seen in older patients with a higher blood pressure.[4] Nevertheless, a 1.3 mm Hg lower systolic blood pressure at one month and 1.4 mm Hg at six months is observed, although this does not reach significance.

This is exactly the effect on blood pressure to be expected from that change in the ratio of sodium to potassium in younger people with normal blood pressure.[5] The study was probably underpowered to detect such a difference. The modest rise in the anxiety score at one month (not sustained at six months) with low sodium salt is difficult to interpret since the trial was not double blind.

The outcome of this trial could have been predicted by a scrupulous examination of the study design. An opportunity to provide useful information has been missed.

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1 Little P, Kelly J, Barnett J, Dorward M, Margetts B, Warm D. Randomised controlled factorial trial of dietary advice for patients with a single high blood pressure reading in primary care. *BMJ* 2004;328:1054-7. (1 May.)
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Authors' reply

EDITOR—Cappuccio's suggestions do not explain the results. Nurses measured blood pressure by using semi-automated monitors (minimising measurement bias) and gave structured advice in all groups (minimising placebo effect[1 2]). Any bias is likely to favour the active interventions, and there was no evidence of this.

General practitioners and nurses were asked to refer patients after two to three readings, using appropriate cuff sizes on a single occasion—the group targeted for non-pharmacological advice according to guidelines from the British Hypertension Society. After a few weeks the baseline blood pressure (the mean of three readings on the second occasion) was 153/93 mm Hg, similar to the previous smaller Dutch study (158/91 mm Hg), which indicated that low

sodium salt was effective.[3] When patients with a baseline diastolic blood pressure above 90 mm Hg (n = 171) were selected the estimate for the low salt group was – 1.16 mm Hg (95% confidence interval – 3.5 to 1.18). When patients older than 60 (n = 94—a similar power to the Dutch study) were selected the estimate was 0.001 mm Hg (– 3.17 to 3.17).

Robust standard errors, allowing for clustering, were almost identical (slightly lower)—as expected with individual randomisation and a highly structured approach.

There are two likely reasons for the lack of effect: low sodium salt is not very effective, and in a pragmatic trial the control group are not constrained to a constant diet and know that they aren't getting low salt—and thus may be more motivated to change diet in response to basic advice (as we observed). Hence even among elderly patients and those with more definite hypertension the effect may be less than expected. To balance blinded "efficacy" trials we also need evidence from pragmatic open trials designed to look at the effect of advice in everyday practice—where patients' behaviour is rather more realistic.

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1 Little PS, Williamson I, Warner G, Gould C, Kinmonth AL, Gantley M. An open randomised trial of prescribing strategies for sore throat. *BMJ* 1997;314:722-7.
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Treatment of hepatic encephalopathy

It's not lactulose

Editor—Als-Nielsen et al systematically reviewed randomised trials using lactulose or lactilol for hepatic encephalopathy,[1] which has been warranted for some time. We agree that non-absorbable disaccharides have been introduced into clinical practice without any convincing evidence base but question the authors' conclusion, that there is insufficient evidence to determine whether non-absorbable disaccharides are of benefit to patients with hepatic encephalopathy. Surely, this comprehensive review shows clearly that lactulose is ineffective for treatment of hepatic encephalopathy, rather than there being insufficient evidence.

Furthermore, the results of this study have several important implications.

Firstly, what should comprise standard medical treatment for hepatic encephalopathy? Lactulose should no longer be included, but strict attention should be paid to treating the precipitating factors, with correction of dehydration, electrolyte and acid base imbalance,[2] constipation, and infection.[3]

Secondly, we make a plea for placebo controlled trials: no restriction should be imposed on the conduct of placebo controlled studies on ethical grounds.

Thirdly, the interorgan metabolism of ammonia should be revisited and the recent studies showing the important roles of the small intestine, muscle, and kidneys in regulating the blood concentrations of ammonia considered.[4]

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1 Als-Nielsen B, Gluud L, Gluud C. Non-absorbable disaccharides for hepatic encephalopathy: systematic review of randomised trials. *BMJ* 2004;328:1046-50. (1 May.)
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Authors' reply

Editor—We do not agree that our Cochrane review clearly shows that lactulose is ineffective. The fact that we found no evidence of effect does not imply that there is evidence of no effect.[1] It is difficult to prove that a treatment has no effect.[1]

A survey of 989 abstracts of Cochrane reviews showed that inappropriate claims of no effect were made in 240 (22.5%) abstracts.[2] In our review, we found that high quality trials found no significant effect of lactulose on the risk of no improvement of hepatic encephalopathy (relative risk 0.92, 95% confidence interval 0.42 to 2.04). The confidence interval indicates that we cannot exclude that lactulose may benefit (reduce the risk of no improvement by up to 58%). On the other hand, lactulose may also harm (increase the risk of no improvement by up to 104%). Our meta-analysis is based on only two trials with a total of 46 patients. Accordingly, our analysis has low power to detect clinically beneficial or harmful effect.

A consequence of claiming no effect would be that further research assessing the effect of lactulose is unnecessary. We find that a large, randomised, parallel, double blind trial is warranted. It would be interesting to compare lactulose, another laxative (magnesium or sorbitol) prepared to appear and taste like non-absorbable disaccharides, and a placebo of similar taste and appearance but without a cathartic effect (such as glucose).

We agree that lactulose should not be part of standard treatment of hepatic encephalopathy, and that placebo controlled trials are mandatory in this field, where none of the current treatments has proved clinically effective.

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Competing interests: None declared.

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2 Alderson P. Absence of evidence is not evidence of absence. *BMJ* 2004;328:476-7. (28 February.)

Patient organisations in ME and CFS seek only understanding

Editor—To compare general practitioners' attitudes to patients with chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) and those with irritable bowel syndrome was disappointing in the study by Raine et al.[1] Particularly disappointing was that the study was conducted in the months after the chief medical officer recognised—with considerable attendant publicity—the severity and impact of chronic fatigue syndrome or myalgic encephalomyelitis on the lives of those affected.[2]

One outcome of the study was that pressure groups were perceived as influencing clinical encounters, making it harder to legitimise the symptoms. That the authors labelled patients' organisations "pressure groups" was interesting in itself.

The organisations cover a range of views on the illness and the solutions needed. This organisation carries out an information role for patients and professionals and provides a range of services no different from that of any other medium sized charity (www.afme.org.uk). We campaign vigorously of course for recognition of chronic fatigue syndrome and myalgic encephalomyelitis and for funding to remedy years of neglect in this field.

We are not "antidoctor" and our members mostly view their general practitioners as supportive and understanding but faced with a complex illness and lacking a toolkit to help.

Far from patients' organisations wishing to politicise the consulting room, we simply ask for a little more understanding, mixed with a little humility and matched with an eagerness to obtain training and information about diagnosis and treatment.

We do not seek a special status, just that people who are ill with chronic fatigue syndrome or myalgic encephalomyelitis should be treated with the standard of care

and professionalism that the severity and impact of their illness merits. Is this politics?

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1 Raine R, Carter S, Sensky T, Black N. General practitioners' perceptions of chronic fatigue syndrome and beliefs about its management, compared with irritable bowel syndrome: qualitative study. *BMJ* 2004;328:1354-7. (5 June.)
2 CFS/ME Working Group. *Report to the chief medical officer of an independent working group.* www.dh.gov.uk/assetRoot/04/06/49/45/04064945.pdf (accessed 19 Jun 2004).

Should reviewers of papers have their names published?

Reviewing is not vicarious authorship

Editor—Dimoliatis raises some important points in his personal view asking whether reviewers of papers should have their names published.[1] There are two aspects of the debate on open access reviewing that strike me as interesting points from a qualitative perspective. The first is whether the authors think that the paper has been genuinely improved and the second whether readers preferred the first or second version.

Firstly, speaking as an author, I know many hurt feelings may result from seeing a beloved creation "grow up" in a completely unexpected way. Although there can be the benefits of a more coherent and rigorous paper that is more scientifically readable, there can be the risk of "watering down" the message with rather soulless, lifeless papers as the end result.

Secondly, from a reviewer perspective, there is no way I could condone "hijacking" authorship, no matter how much work has gone into reviewing. We are privileged to be exposed to new ideas and different ways of viewing things; we are simply there to clarify, simplify, and amplify points—and not as vicarious authors. This is a fine line—but remember, who came up with the idea for the paper in the first place?

Reviewers should also be reviewed on the quality of what they do and this should be open—what have we got to hide? Perhaps reviewers should also be asked to explain their decisions more and why they think the paper grew and flourished as a result of their intervention.

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1 Dimoliatis I. Should reviewers of papers have their names published? *BMJ* 2004;328:1267. (22 May.)

Let reviewers own responsibility for the papers they pass

Editor—The article by Dimoliatis on whether reviewers should have their names published and the electronic responses to it discussed an interesting issue.[1 2] We worked as student editors for our college magazine, which is but a small thing when considering the context of the current discussion. But we know how tiring the work seemed sometimes as we had to read every single article, understand the logic, and go to the depths before we could reject any article. It seemed as if sometimes we worked harder than the authors themselves.

As most of the journals follow a double blinded policy for review, we do not see any reason why a reviewer's name should not be included at the end. We agree that being a reviewer of a journal is an achievement in itself, but we could give more credit to reviewers for doing, what they sometimes might perceive as, a thankless job. To the question that more substandard articles would get published—well, we cannot police everything and everyone. Reviewers are persons of repute and holding high positions themselves. We are sure most would still be honest about their job and not just pass a paper because their name is published with it. On the contrary, their name is at stake if a substandard article passes through. This might actually make them work harder towards the standard and the value of the article they pass, and that they in a way guarantee.

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1 Dimoliatis I. Should reviewers of papers have their names published? *BMJ* 2004;328:1267. (22 May.)
2 Electronic responses. Should reviewers of papers have their names published? bmj.bmjjournals.com 2004. bmj.bmjjournals.com/cgi/eletters/328/7450/1267 (accessed 28 May 2004).

Practical example gives encouraging insights

Editor—*The Journal of Medical Internet Research* (www.jmir.org), an open access journal that I edit, has for five years practised routinely what Dimoliatis proposes[1]: reviewers are acknowledged at the end of each published article.

In our experience, concerns over reviewers becoming too uncritical only to see their name published are unfounded. Moreover, editors never follow blindly the recommendation of the reviewer(s). It is comparatively easy to identify review reports that are too uncritical or superficial. Reviewers' comments are intended mainly as an opportunity for authors to improve their manuscript. Few editors will admit this, but if editors really want to see something published, they will overrule the overly critical reviewers, and vice versa.

Herein lays the real (and only) problem of publishing reviewers' names, which we encounter from time to time. If one reviewer strongly thinks that a paper should not be published, but the second reviewer or editor overrules the recommendation of one reviewer, the reviewer may not be happy to see his or her name published at the end of a paper. We did have reviewers objecting to publish their name at the end of an article if we accepted it.

The appropriate solution to this is to educate readers that publishing reviewers' names is a mere acknowledgment of their work and the input they gave, and that it is not necessarily an endorsement of a manuscript. If this can be accepted, acknowledging reviewers at the end of articles will and should become common practice in other journals.

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1 Dimoliatis I. Should reviewers of papers have their names published? *BMJ* 2004;328:1267. (22 May.)

Go one step further

Editor—Dimoliatis's cri de coeur for better recognition of reviewers of papers has much merit.[1] Some of your respondents,[2] however, are concerned that the quality of peer review could suffer as reviewers succumb to the temptation of seeing their names in print; the counter argument so cogently put forth by Yeluri et al (letter in this cluster) is a forceful one: reviewers' reputations are at stake if a substandard article passes through.

Although most journals do not publicly acknowledge the efforts of their reviewers, which are so essential to the credibility (and quality) of the published work, some appease their reviewers by publishing their names periodically. Several open access publishers, as other respondents have pointed out, publish full details of the review process alongside the published paper.[2]

I dare publishers to go one step further: publish a list of all papers received and rejected at peer review, with the names of the reviewers. This would ensure the highest quality of peer-review, greater transparency, and a sense of justice for authors of rejected papers. I would then be interested to see if such papers eventually find a home, and in what form.

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Competing interests: AAS may live to regret his dare.

1 Dimoliatis I. Should reviewers of papers have their names published? *BMJ* 2004;328:1267. (22 May.)
2 Electronic responses. Should reviewers of papers have their names published? bmj.bmjjournals.com 2004. bmj.bmjjournals.com/cgi/eletters/328/7450/1267 (accessed 28 May 2004).