Hi Reddit, we're Malcolm MacLeod and David Howells, and we published a paper in PLOS Biology that found an elevated average risk of bias in work from leading institutions or work published in high-impact factor journals – Ask Us Anything!

PLOSScienceWednesday [1] and r/Science AMAs[1]

[1]Affiliation not available

April 17, 2023

Abstract

Hi Reddit, My name is Malcolm Macleod and I am Professor of Neurology and Translational Neuroscience at the University of Edinburgh. I'm interested in risks of bias in animal research, and how these might get in the way of the development of new drugs. And my name is David Howells and I am Professor of Neuroscience and Brain Plasticity at the University of Tasmania. My research on stroke focuses on how we translate good ideas into solid bench science that might then survive the rigor of clinical trialing to provide treatments for brain diseases. We recently published a study titled "Risks of bias in reports of in vivo research: A focus for improvement" in PLOS Biology. This study extends work across multiple neuroscience domains which highlights the risk of overestimation of the potential for translational success when studies fail to take measures to reduce the impact of bias. This study investigated whether this held true across a broader range of science and whether where the work was conducted or published influenced the risk of bias. We already know that publications which do not describe certain design features which reduce the risk of bias (e.g. randomization, blinding) tend to exaggerate observed effects, at least in the neurosciences. We were interested to see whether this was the case more generally, and if this was different in journals with a high impact factor or in work from leading institutions. We found that nobody is doing particularly well but also that work from leading institutions or published in high impact factor journals was at greater than average risk of bias. We hope that scientists, institutions, journals, and funders will use these findings to help improve the process of drug discovery and development. We will be answering your questions at 1pm EST (10am PST and 5am on 1/14/16 in Melbourne). Ask Us Anything! You can follow Malcolm on Twitter @maclomaclee, and @CAMARADES_

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PLOSSCIENCEWEDNESDAY R/SCIENCE

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WRITE A REVIEW

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DOI:
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Are there common 'warning signs' one should look for when self-determining legitimacy of a published article?

blpsoup

Well, there's really nothing to beat a detailed critical appraisal, but if a study is testing an hypothesis, comparing two groups, and has neither randomisation or blinding; then I'd be really concerned about the risk of bias

Are there common 'warning signs' one should look for when self-determining legitimacy of a published article?

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David: I agree with Malcolm. The disturbing issue in basic science is that so few authors bother to report whether they attempted to reduce these risks or not. Pragmatically in our analyses we are forced to take a "worst case" approach in making that assessment. The authors may indeed have done the right thing, but if they don't report it as a reader you just can't tell.

Through the course of your research, did you face any ethical quandaries that surfaced regarding specific practitioners? If so, how did you address them?

Clsjajll

David: The occasional author did have somewhat dubious publication ethics allowing them to publish the same data in a number of journals.

Through the course of your research, did you face any ethical quandaries that surfaced regarding specific practitioners? If so, how did you address them?

Clsjajll

No, because the overall performance (68% of the studies from leading UK institutions met none of the 4 criteria we looked for), so singling out any that were particularly worse than average was not possible!

Do you believe this risk of bias has increased in the past 20 years with the internet giving more attention to journals and scientific findings?

nallen

David: Objectively authors are (very) slowly getting better at reporting whether they take measures to avoid bias and reputable publishers are increasingly asking to see the evidence for this when they accept articles for publication. However we still have a long way to go. I suspect, but don't know how to prove, that pressure to "publish or perish" does lead to more bias but this is not caused by the internet.

Hi there! I'm working for some neuroscientists on the imaging side. What concerns me most of the research we make and other groups that I read also do, is the too big reliance on "big-data"/"omics" techniques. Where everything is just spun in huge algorithms that are biased towards "finding" results. I see this in neuroimaging but, as an example, the technique that I like the least, glasso inverse covariance analysis, is very big also in genetics/genomics and biology.

What's your take on this?

lucaxx85

Malcolm: John Ioannidis and others talk about "vibration of effects" and "flexibility in data analysis" ... and the larger the dataset, and the more complex the analysis, the greater are the opportunities for these. One approach is to have a (published) study protocol which outlines the primary outcome measure and statistical analysis plan - so you can understand what they intended to do, and what they actually did - and if these are different

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research we make and other groups that I read also do, is the too big reliance on "big-data"/"omics" techniques. Where everything is just spun in huge algorithms that are biased towards "finding" results. I see this in neuroimaging but, as an example, the technique that I like the least, glasso inverse covariance analysis, is very big also in genetics/genomics and biology.

What's your take on this?

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David: I'm not familiar with the specific algorithm you mention but false positive discovery is always likely to be a problem, and not just for "big data" techniques, since our brains have probably evolved to allow our senses to detect patterns. As in survival (the occasional imagined lion), a false positive is probably less expensive overall than a false negative because it also focuses attention on technical advance.

Do you think the bias is there by design to get those publications into the high impact factor journals? We all know the pressure of bit universities to publish in high impact factor, especially for young scientists. Did you analyzed the data based on age of the senior author or tenure status?

DRHdez

Malcolm: great suggestion, and we didn't look at seniority: but I suspect that behaviors learned on the journey to tenure will persist. And to answer the first question, I dont think they are deliberate any more than the way I shift my centre of gravity on a bike to avoid a pot-hole - they are likely to be learned but unconscious behaviours

You say in your article:

Finally, the relationship between institutional esteem and risk-of-bias reporting may be a consequence of the editorial practices of the journals in which high-quality research is reported; that is, they may be more likely to accept manuscripts from institutions of repute. Alternatively, the relationship between journal impact factor and risk of bias may be a consequence of such journals making publishing decisions based on institutional esteem rather than the quality of submitted manuscripts. However, the most parsimonious explanation of our findings is that journal editorial policies and those charged with assessing the quality of published work, including peer reviewers, have given insufficient attention to experimental design and the risk of bias, and that this has led investigators to believe that these factors are not as important as the novelty of their findings.

First off I'm not sure what the difference between your first two points is (more likely to accept from institutions of repute vs publishing decisions based on institutional esteem). But then you state that "the most parsimonious explanation" is just that investigators prefer novelty to experimental design because publishers don't care about experimental design (if I'm reading it right?). If that were the case though then there would be no reason that high impact factor journals report more poorly designed studies since the editorial policies would presumably apply to everyone, and in my experience most people start by submitting their manuscripts to higher impact factor journals then work their way down if they get rejected. On the other hand I can definitely believe that your first examples happen all the time, where reviewers look at the researchers and when they know who they are they go much more lightly on the criticism. Do you disagree?

afreet1506

Malcolm: good catch on our tautology - my apologies. I think the difference is that high impact journals look for exciting stories .... which are more likely to be wrong, and more likely to have been fuelled by

bias. So by selecting on the basis of newsworthyness, they are enriched by studies at high risk of bias - which is what, usually, makes them newsworthy

Given that Ioannidis has claimed that as much as 75% of biomedical research is false, this seems to point to at least one cause. Are there automated ways to identify such bias deficits, which would allow us to weight less data from that source, say in a meta-analysis? Is that even possible, or should the study be redone?

And as corrolary, shouldn't we demand that all raw data be deposited with an open access website?

milagr05o5

Malcolm: His argument is based solely on the interpretation of statistical tests. Say in a field 20% of hypotheses are correct, and studies are powered at 50%. So of 1000 studies 200 will be correct, of which 100 will be called but the experiment (true positive) and 100 will be missed (false negative). With p of 0.05, and 800 negative studies, 5% of these (40) will falsely be called as positive. So of your 140 positive studies, 40 - or 28% - will be falsely positive. Bias is a problem additional to this.

And yes, all data should be made available on a recognised, sustainable open access repository

Good Morning Prof. McCleod,

Thank you so much for doing this AMA.

Do you think there is anything inherent about the review process for high-impact journals that leads to bias?

ClaireAtMeta

Malcolm: There's an old russian joke which says that Pravda means truth and Izvestia means news - and that means there's no news in Pravda and no truth in Izvestia. I think in the past the same might have been applied to some papers in some high impact journals

This sub is also hosting an AMA today with Dr David Mellor who is pushing for pre-registration for human subject studies. Do you think this would help reduce biased reporting of findings? Why or why not?

firedrops

Malcolm: absolutely, but in vivo studies tend to have a shorter life cycle than a full on clinical trial - so we need a new form of registration of protocols that is easy but robust: I have proposed a web repository for Population; Hypothesis; Intervention: Sample Size Calculation; Primary Outcome Meaure; and Statistical Analysis Plan. The idea is that it is restricted access, but you get a link to your PHISPS protocols to submit with your article; and on publication of your article the PHISPS protocols become visible to the world, linked from the article

So basically you guys are saying that there are many poorly designed studies that yield unreliable results because of unseen built-in biases?

goldenspear

Malcolm: Yes, but biases that would be apparent on detailed critical appraisal of the paper

So basically you guys are saying that there are many poorly designed studies that yield unreliable results because of unseen built-in biases?

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David: Essentially yes. But the biases are not built-in in the sense of being deliberately constructed, rather we hope they are due to the naivety of the science work force.

This is how I imagine the system works: someone wants a study done on the viability of a substance. So they offer a sum of money to various institutions to conduct research. Only one institution will get the grant, but numerous groups write up a proposal. The grantor institution looks at the proposals and choose the one that appears most closely aligned with their desired conclusion. Confirmation bias does the rest and they get a result that coincides with their preferred solution. How does this align with your conclusions?

Allez_

Malcolm: Or they could commission all the research, and junk, or find reasons to distrust, the rest. But I suspect that some people have a highly preferred result (to get a drug to the next base, or to fuel their grant applications), and this is the major driver

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David: My direct experience of the pharmaceutical industry has been quite the opposite. I worked on a compound that CSL viewed as a candidate treatment for stroke. When my data cast doubt on this potential they were happy to kill further development.

Do you have any short term and/or long term solutions to combat this?

Masterbader666

Malcolm: Lots - see the Lancet Waste in Research Series - but at base it is I think about current incentive systems for scientists (grants in, papers out, never mind the quality feel the width), and for institutions. See also the Leiden Manifesto for better approaches to appointment and promotion decisions

If you (both) were empowered to implement a few changes aimed at reducing risk of biases such as those desire in your paper, what would those be? And why do you think such methods have not already been implemented - is this a broader cultural issue in science (i.e., publish and perish) or something that should be implemented at the review or journal level?

explodingbarrels

Malcolm: I think that one problem is that the commanding heights of our ecosystem is largely populated by those who have prospered under the status quo ante - who almost by definition dont see this as a major problem. But journal publication policies, schemes for continuing professional development for scientists, and institutional improvement activities all have a role

If you (both) were empowered to implement a few changes aimed at reducing risk of biases such as those desire in your paper, what would those be? And why do you think such methods have not already been implemented - is this a broader cultural issue in science (i.e., publish and perish) or something that should be implemented at the review or journal level?

explodingbarrels

David: A multi-pronged approach is needed, all centered around education. Yes the funding bodies and journals have a part to play ensuring that pressure is applied in experimental design and reporting but I think we also need to teach undergrads about these issues and how to deal with them before they even enter the research work force and have our research institutions reinforce this by not allowing communications in their name without adherence to these basic elements of good science.

Do you think if journals required authors to publicly archive data/code it would help reduce bias or at least increase author's focus on measures to control potential bias?

mrandish

Malcolm: It's always a slightly frightening experience when you let your raw data out into the world, lest someone spots a basic error and you look stupid - so it does increase the motivation to get it right first time

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mrandish

David: Transparency and being able to share raw data are highly desirable. Since the money for the enterprise of science comes mainly from the public purse it is not just the journals responsibility to push this issue.

Do Malcolm and/or David have any thoughts on how (open source) text & data mining services like ContentMine might help their work ?

steelgraham

Malcolm: Hi Graham - short answer, an awful lot. In ENKI (European Network for Knowledge Impact) we are trying to develop ML/TM tools to (1) identify in vivo papers from pubmed feeds; (2) attribute the papers to institutions; (3) categorise papers according to their risk of bias; and then (4) create a report, by institution, of the risks of bias of the research they published in the last year. Once set up this system could run with very little human input, and would certainly be a lot cheaper than the REF!

How can we trust that this study wasn't biased?

BrofessorBroDown

Malcolm: see above

How can we be sure that your study itself is not biased?

redditorriot

Malcolm: good question: we tried to avoid bias by (1) having every article that we included being screened by two independent reviewers, with disagreements resolved by a third; (2) publishing our study protocol on line prior to data analysis; (3) explaining in our paper where we had to deviate from that protocol; and (4) making our entire datasets available on Figshare to allow independent replication. But you're right, this is observational research, and susceptible to bias. We're involved in an RCT just now where the outcome assessment is truly blinded. If anything, however, we tried to give the authors the benefit of the doubt at every stage, so I suspect we are more likely to have understated rather than overstated the risks of bias

How can we be sure that your study itself is not biased?

redditorriot

David: Indeed a very good question. It is probably best answered in two steps. Firstly with regards to our intentions, when we first started this process we were looking for evidence to support selection of drugs that we could take to the clinic to treat stroke. As such if we had a bias it was towards finding something that would work, rather evidence of failure. Secondly we try very hard to let the data do the talking. Therefore we either go to great lengths to find all of the available data for our systematic reviews, or as is the case with this publication, we randomly sample from within that data. The place where we are at greatest risk of bias is in the application of our inclusion and exclusion criteria, but we are transparent about reporting these and are happy to get suggestions for improvement.

Serious question: How can you be sure there's no bias in your research?

slimej

Malcolm: see above ;-)

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Malcolm: Sometimes people see things which aren't there, things that look like patterns that are just random noise. When your career depends on seeing patterns, you can fool yourself. So best to do everything you can to stop yourself being misled.