

# A call for action to improve the reproducibility of biomedical research

From the member academies of IAP for Health



**There is growing discussion within the biomedical research community about the need to improve the reproducibility of research studies so as to drive scientific progress, accelerate translation into clinical applications, and maximise returns on funding. Many improvements in national and global health are rooted in the findings of biomedical research and it is crucial that research practices are as effective as possible.**

## Introduction

The scientific endeavour relies on reproducible and reliable research studies. There has been a growing unease, evident in both the scientific and general media, about the lack of reproducibility of much biomedical research.<sup>i, ii, iii</sup>

When a study is repeated under similar conditions and comparable results are not obtained, it is considered 'irreproducible'. Scientific research involves conducting experiments to test and/or generate a hypothesis. Results of these experiments are collected, analysed and interpreted, and then shared with the wider research community through publication. Science progresses as hypotheses are refined and new ones generated and tested, building on existing findings. Such progress requires rigorous studies with reproducible findings, but this is not always the case. Irreproducibility could happen for many legitimate reasons, for example it might be due to the natural variability in the biological systems used in research. However, there are concerns that the current scale of irreproducibility is greater than might be expected. While this may result from scientific misconduct, for example where data have been fabricated or

falsified, the evidence suggests that such instances are rare. A far more common cause of irreproducible results is questionable or unsatisfactory research practices, for example:<sup>iv, v</sup>

- Incomplete reporting of research studies, particularly methodological details.
- Poor experimental design, methodologies and/or practices.
- Inappropriate statistical analysis.

Research that cannot be reproduced hinders scientific progress, delays translation into clinical applications and wastes valuable resources. It also threatens the reputation of biomedical science and the public's trust in its findings. Many improvements in global health rely on the outputs of biomedical research – it is critical that those outputs are robust, reproducible and reliable.

**Science is an international endeavour. It is clear that this issue is not specific to any single nation, but a challenge that needs to be addressed globally, through cooperation and collaboration. IAP for Health member academies are therefore ideally placed to stimulate and facilitate efforts to improve biomedical research practices at both national and international levels.**

i Van Noorden R (2011). *Science publishing: the trouble with retractions*. Nature, **478**, 26–28.

ii The Economist (2013). *Unreliable research: trouble at the lab*. <http://www.economist.com/news/briefing/21588057-scientists-think-science-self-correcting-alarming-degree-it-not-trouble>

iii The Lancet (2014). *Research: increasing value, reducing waste*. <http://www.thelancet.com/series/research>

iv Fanelli D (2009). *How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data*. PLOS ONE **4**(5). doi: 10.1371/journal.pone.0005738

v John LK, Loewenstein G & Prelec D (2012). *Measuring the prevalence of questionable research practices with incentives for truth telling*. Psychological Science. doi: 10.1177/0956797611430953

## Background

In 2005, a paper by Professor John Ioannidis argued that most study designs will lead to conclusions that are more likely to be false than true.<sup>vi</sup> However, it is difficult to actually quantify the exact level of irreproducibility in the published literature. So far, only limited data are available, but one example is the 'Reproducibility project: psychology', published in 2015, which sought to replicate selected results from 100 studies in psychology. It found that in the replication studies, the mean effect size was half the magnitude of the mean effect size of the original studies. It also reported that only 36% of the replications had significant results, whereas 97% of the original studies had claimed to have significant results.<sup>vii</sup> Other examples of studies that reflect similar findings have come from industry, which highlight the impact on the drug discovery pipeline if results published in the literature, which form the basis of drug discovery programmes, are not reproducible.<sup>viii, ix</sup>



## Previous work by academies

IAP for Health member academies have started to highlight this issue. The US National Academies of Sciences, Engineering, and Medicine hosted a workshop in 2014 that considered 'Reproducibility Issues in Research with Animals and Animal Models'.<sup>x</sup> Researchers from around the world explored the many facets of animal-based research that could contribute to irreproducible results and provided perspectives on improving experimental planning, design and execution; emphasized the importance of reporting all methodological details; and recommended the establishment of harmonization principles of reporting on the care and use of animals in research studies.

In April 2015, the UK Academy of Medical Sciences organised a joint symposium with the UK Biotechnology and Biological Sciences Research Council (BBSRC), the UK Medical Research Council (MRC) and the Wellcome Trust. A report of this meeting concluded that there is no single cause of irreproducibility and that a 'one size fits all' approach is unlikely to be effective.<sup>xi</sup> They identified that a number of measures may help to improve reproducibility, including:

- Greater openness and transparency of methods and data.
- Better use of advice from other experts, e.g. through collaboration.
- Reporting guidelines to ensure the right sort of information is included in publications.
- New approaches to publishing, such as pre-registering research protocols so that published studies can be compared to the original plans; and post-publication peer review to encourage continued appraisal of previous research. It is important that studies are reported in a rigorous manner that enables researchers to reproduce others' experiments.
- Better use of standards and quality control measures, perhaps even through automation in some cases.

A number of overarching factors will drive the implementation of specific measures and ultimately enhance reproducibility, including:

- Education and training for individuals at all career levels to improve research methods, design and statistical expertise.
- The need to raise awareness among researchers about the importance of reproducibility and how to achieve it.
- The environment and culture of biomedical research, in which robust science and the validity of research findings must be prioritised.
- Active efforts on the part of researchers to discuss this issue openly within and outside the community.

vi Ioannidis JP (2005). *Why most published research findings are false*. PLOS Medicine **2**(8), e124.

vii Open Science Collaboration (2015). *Estimating the reproducibility of psychological science*. Science **349**(6251).

viii Prinz F, et al. (2011). *Believe it or not: how much can we rely on published data on potential drug targets?* Nature Reviews Drug Discovery **10**, 712.

ix Begley CG & Ellis LM (2012). *Drug development: raise standards for pre-clinical cancer research*. Nature **483**, 531–533.

x <http://www.nap.edu/catalog/21835/reproducibility-issues-in-research-with-animals-and-animal-models-workshop>

xi Academy of Medical Sciences et al. (2015). *Reproducibility and reliability of biomedical research: improving research practice*. <http://www.acmedsci.ac.uk/researchreproducibility>

## Recommendations

IAP for Health strongly supports the conclusions derived from previous work by academies and others to draw attention to this important issue and identify ways to improve the reproducibility of biomedical studies. IAP for Health member academies consist of national and international leaders of the academic and scientific communities with important access to key stakeholders, policy makers and the public. They must use their unique position to actively promote better research practices.

In signing this statement, IAP for Health member academies recognise that:

- It is critically important for the progress of science that the reproducibility of research is optimal. Where policies to improve national and global health are concerned, they must be based on the best available evidence – the value of research and the efficient use of resources can only be maximised through the most robust science.
- There is no single cause of irreproducibility and a number of measures are required to address it. These measures will rely on multiple actions from many stakeholders. For example:
  - Universities and research institutions should embrace a culture change that rewards robust methods as much as novel findings, particularly when making decisions about career progression. Institutions should encourage the use of quality-enhancing infrastructures (e.g. electronic laboratory notebooks, quality assessment systems), as well as expert advice (e.g. in biostatistics).
  - Funders should use their position at the start of the research process to set the tone for reproducible research, for example by rigorously assessing experimental design to minimise bias and improve statistical power.
  - Publishers and journal editors should enable greater openness and transparency in methods, results and data; and be willing to publish replications and neutral or negative ('null') results from adequately powered studies. They should take steps to ensure that peer review focuses on the quality of the science rather than the excitement generated by the results. This may include measures to reduce the potential for bias, for example by implementing blinded peer review in which reviewers do not know the names or affiliations of authors.
  - Researchers should take responsibility for portraying their results accurately, alongside science communicators where relevant, and engage in open communication and dialogue around replication attempts.

At country level, IAP for Health member academies should consider this issue within their own leaderships to establish the most effective role they can play in efforts to improve reproducibility, including by:

- Raising awareness about the challenge of irreproducibility and the possible causes – initially among their elected Fellows, who have an important leadership role to play; but then extending to the broader biomedical research community, including early career researchers, and wider society.
- Meeting national stakeholders to raise awareness and discuss measures that should be taken to improve research practice. These will include leaders within research funding agencies, publishers, institutions and professional bodies. Where possible, IAP for Health member academies will look to coordinate discussions *among* these stakeholders as well.
- Promoting the importance of an environment and culture for research that values the robustness of studies as much as their originality.
- Working to ensure that the biomedical research community is engaged in discussions as solutions are developed and implemented.
- Supporting education and training around optimal standards of research design and integrity.

Science is a global endeavour and reproducibility presents a global challenge, which must be addressed through collaboration and cooperation. Therefore, at a regional and global level:

- IAP for Health member academies, including regional networks of academies, should work together to draw attention to this issue and promote measures to improve research practices, and share experiences of their own efforts in these endeavours.
- IAP for Health, working with its member academies at a national level, should join the efforts of the international science community to encourage discussions among partners, including international research funders and publishers/editors, about how to address this issue – seeking opportunities to facilitate these discussions, where appropriate.





## Working group

- Professor **Dorothy Bishop**, United Kingdom (Chair)
- Professor **Alejandro Federico de Nicola**, Argentina
- Professor **David L Vaux**, Australia
- Professor **Hajera Mahtab**, Bangladesh
- Professor **Umberto D'Alessandro**, The Gambia
- Professor **Gerd Heusch**, Germany
- Professor **Gita Ramjee**, South Africa
- Professor **Nadira Karunaweera**, Sri Lanka
- Dr **Story Landis**, USA

## The InterAcademy Partnership for Health

IAP for Health is a component network of the InterAcademy Partnership.

Its membership comprises 78 academies of medicine or academies of science and engineering with medical sections.

IAP for Health is committed to improving health world-wide, including through the release of consensus statements on matters of importance to global health. IAP for Health Statements such as this one are prepared by a working group comprising experts nominated by member academies, and are released once they have been endorsed by more than half the member academies of the network.

Additional copies of this statement can be downloaded from:  
<http://tinyurl.com/IAP-Reproducibility-Statement>



the interacademy partnership

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## A call for action to improve the reproducibility of biomedical research

Academies that have endorsed the statement by 31 August 2016

1. National Academy of Medicine (Buenos Aires)
2. Australian Academy of Science
3. Bangladesh Academy of Sciences
4. Federation of European Academies of Medicine
5. *Académie Royale de Médecine de Belgique*
6. *Academia Nacional de Medicina*, Brazil
7. Brazilian Academy of Sciences
8. Cameroon Academy of Sciences
9. Canadian Academy of Health Sciences
10. *Academia Chilena de Medicina*
11. Chinese Academy of Engineering
12. Croatian Academy of Medical Sciences
13. Academy of Sciences of the Czech Republic
14. Academy of Sciences of the Dominican Republic
15. Council of Finnish Academies
16. *Académie Nationale de Médecine*, France
17. *Académie des Sciences*, France
18. Georgian Academy of medical sciences
19. Union of German Academies of Sciences and Humanities
20. German National Academy of Sciences, Leopoldina
21. *Academia de Ciencias Medicas, Fisicas y Naturales de Guatemala*
22. Hungarian Academy of Sciences
23. Academy of Medical Sciences of Iran
24. *Accademia Nazionale dei Lincei*, Italy
25. Science Council of Japan
26. Kenya National Academy of Sciences
27. Academy of Sciences Malaysia
28. Hassan II Academy of Science and Technology
29. Royal Netherlands Academy of Arts and Sciences
30. Nigerian Academy of Science
31. National Academy of Science and Technology, Philippines
32. Academy of Medical Sciences of Romania
33. Slovak Academy of Science
34. Academy of Science of South Africa
35. National Academy of Sciences of Sri Lanka
36. Sudanese National Academy of Sciences
37. Royal Swedish Academy of Sciences
38. Swiss Academy of Medical Sciences
39. Tanzania Academy of Sciences
40. Turkish Academy of Sciences
41. Academy of Medical Sciences, UK
42. African Academy of Sciences
43. Caribbean Academy of Sciences
44. Islamic World Academy of Sciences
45. TWAS - The World Academy of Sciences
46. World Academy of Art and Science