**Reducing bias and improving transparency in biomedical and health research:
A critical overview of the problems, progress so far and suggested next steps**

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Introduction

It is increasingly recognised that there are significant problems in medical research. These shortcomings undermine the capacity of medical research to achieve efficient scientific discovery and ultimately our ability to improve outcomes for patients. Across different scientific disciplines, a diverse range of issues has resulted in a situation in which published research findings frequently cannot be replicated, a challenge which has been termed ‘the reproducibility crisis’. Medical research has proved to be just as vulnerable as other disciplines⁽¹⁾ even in contexts such as drug development.^(2, 3) Meanwhile, a combination of avoidable methodological failings and biases have been implicated in ‘research waste’ which it is estimated accounts for the majority of all funding invested in medical research.⁽⁴⁾

Many of these problems are rooted in incentives for medical researchers which are poorly aligned with the wider interests of medical science. Despite longstanding calls for “less research, better research, and research done for the right reasons” concerns remain that quantity is valued over quality in health research.⁽⁵⁾ Cultural problems in medical research are important in themselves, but also impede progress in tackling biases in how research is reported and improving objectivity of statistical methods.

This review provides an introduction to some of the most pervasive problems in medical research along with an overview of the efforts which have been made to address these issues. We begin by describing some of the most significant problems related to research culture, reporting biases and statistical and methodological issues. We then outline some important measures that have been instituted to address these problems. We conclude with a proposed strategy to help restore confidence in the reproducibility of medical research.

Methods

This paper was informed by literature identified using a search strategy with the following terms: open science, open research, research quality, medic*, health*. Searches were conducted on CINAHL, EMBASE, MEDLINE and PsycINFO (Supplement 1).

What are the problems in medical research?

Research culture

Academic Rewards System

Academics’ professional standing has tended to depend on demonstrating productivity through publication,⁽⁶⁾ with disproportionate rewards offered to those who attain publication in ‘luxury journals’ with high impact factors.⁽⁷⁾ Journal impact factors arguably do little to capture the quality or value of research and are too susceptible to manipulation.⁽⁸⁾ The extraordinary proliferation of research appears to reflect the pressure for academics to publish research rather than a corresponding development of genuine discovery which could lead to improved outcomes for patients.⁽⁹⁾

Conflicts of Interests

Financial conflicts of interest have been shown to affect the conclusions of studies, physician prescribing habits and guideline recommendations.(10-13) Potential competing interests have traditionally been regarded as monetary, but may also include other professional, political, or personal considerations.(14) High profile scandals have demonstrated undisclosed conflicts of interests undermine trust in the objectivity of research.(15, 16) While non-disclosure of competing interests does not necessarily affect assessments of study quality, authors' interests can have a bearing on findings.(17-18)

Interest disclosures for published research are frequently incomplete.(19, 20) Conflicts of interest recording and policies in institutions that host research are also poor and in several cases journal editors, as well as researchers, have potential conflicts of interest.(21, 22) Voluntary declarations from the pharmaceutical industry have been criticised as inadequate, due to the ability of individuals to opt out.(23) Meanwhile other voluntary registers have limited coverage since they require eligible individuals to 'opt-in'.(24) In several countries 'sunshine acts' require physicians to disclose financial interests, and calls have grown for similar requirements to be introduced to the United Kingdom.(25, 26)

Reporting biases

'Reporting bias' encompasses several types of bias caused by selective disclosure or withholding of information, either intentionally or unintentionally, related to study design, methods and/or findings.(27) While several types of reporting biases have been described, we will focus on two of the most widely studied: publication bias and spin.

Publication bias refers to the propensity of certain types of research to become published, while other types remain unpublished. This results in a distortion of the published record which disproportionately features findings that are deemed to be novel, striking, or that provide evidence in favour of a proposed intervention.(28) While publication bias is commonly understood to be driven by the perception that journals are unlikely to accept so called 'negative' or 'uninteresting' results, researchers also perpetuate this bias by failing to submit such research. Publication bias has also been demonstrated to affect regulatory decisions and ultimately clinical practice.(28) The problem appears to be culturally entrenched and in some cases conflicts of interest are implicated.(10, 29)

Spin refers to the practice of distorting or misrepresenting results to appear more 'positive', newsworthy, or interesting.(30) Whilst 'spin' falls short of outright falsification or fraud, experiments show that readers of studies with spin draw more favourable interpretations of interventions than when results are presented more objectively.(31) Of particular concern is that spin in journal abstracts influences press releases, and studies that obtain press coverage receive greater numbers of citations.(32-33) Spin manifests in a variety of ways including failure to mention study limitations, selective ordering of outcomes and drawing exaggerated inferences from study results.(34) Spin appears to be increasingly common and the process of peer review has so far proved insufficient to counter it.(35-36) Reviewers who identify spin usually do not succeed in having it removed from manuscripts and some reviewers actually suggest the addition of spin.(37)

Statistical and methodological issues

There is substantial debate throughout science about the role of P values in determining statistical significance.(38) Reporting of P values has become much more common in recent decades, with 96% of papers containing P values of 0.05 or less.(39) The ubiquity of published P values of < 0.05 can be explained by the strong incentives for researchers to publish significant results. P values are also often misinterpreted and it has been estimated that most claims based on P values are false.(38, 40) Some scientists suggest that the threshold of significance for P values should be reduced or abandoned altogether, that greater emphasis be placed on effect sizes and confidence intervals, or that Bayesian statistics should be used to provide greater discriminatory utility when appropriate.(41-42)

The availability of modern statistical software means that, in the absence of robust and independently accessible scientific protocol, it is relatively easy to generate statistically significant results through repeated analyses, a practice that has been dubbed p-hacking.(43) P-hacking in turn facilitates so called HARKing (Hypothesising After the Result is Known), whereby researchers can alight upon a result with a P value of < 0.05 and retrospectively generate a matching hypothesis.(44) Researchers may also selectively report results which are statistically significant or exploiting 'undisclosed flexibility' in how analyses are conducted, allowing researchers to provide evidence for virtually any hypothesis.(45)

Existing measures addressing problems in medical research

Several measures have been introduced in order to improve the reproducibility and transparency of medical research. Although no single measure, or set of measures, is capable of eradicating research waste and restoring confidence in research at once, many successes have been achieved. Although incomplete, these achievements demonstrate that co-ordinated action to improve the research landscape is possible and indeed necessary.

A number of important measures are considered in this article with some additional initiatives outlined in table 1. It is beyond the scope of this review to survey all of the relevant actions which have been undertaken to address problems in medical research.

Table 1: Initiatives and organisations working to reduce waste and improve the openness and quality of research.

Initiative/Organisation	Description	URL
AllTrials	Campaign to ensure all clinical trials are registered and published. Highlights problem of publication bias, e.g. through ‘unreported clinical trial of the week’	https://www.alltrials.net/
Centre for Open Science (COS)	Organisation dedicated to ‘increase the openness, integrity and reproducibility of scientific research’	https://cos.io/
Centre for Evidence Based Medicine	University of Oxford based centre which develops, promotes and disseminates better evidence for healthcare, including contributing to the EBMLive conference	https://www.cebm.net/
ClinicalStudyDataRequest.com (CSDR)	Consortium of clinical study Sponsors/Funders which facilitates access to patient-level data from clinical studies.	https://clinicalstudydatarequest.com
cOALition S (Plan S)	Formed by national research funding organisations, with the support of the European Commission and the European Research Council (ERC) to achieve greater open access publication of research	https://www.coalition-s.org/
Collaborative Approach to Meta Analysis and Review of Animal Data from Experimental Studies	Provides a supporting framework for groups involved in the systematic review and meta-analysis of data from experimental animal studies.	http://www.dcn.ed.ac.uk/camarades/
Cochrane	Charitable organisation formed to organise medical research findings to facilitate <u>evidence-based</u> choices about <u>health interventions</u> involving health professionals, patients and policy makers	https://www.cochrane.org/
Enhancing the QUALity and Transparency Of health Research (EQUATOR) Network	International initiative which aims to improve the reliability of published health research by promoting transparent and accurate reporting and wider use of robust reporting guidelines.	https://www.equator-network.org/
European Open Science Cloud (EOSC)	On-line platform which aims to facilitate curation of open science data	https://ec.europa.eu/research/openscience/index.cfm?pg=open-science-cloud

European Quality in Preclinical Data (EQIPD)	Consortium which aims to improve transition from preclinical to clinical testing and drug approval by establishing common guidelines to strengthen the robustness, rigor and validity of research data.	https://quality-preclinical-data.eu
Evidence Based Research Network (EBRNetwork)	European network established to support evidence based clinical research, particularly the need to use systematic reviews when planning new studies and when placing new results in context.	http://ebrnetwork.org/
Ensuring value in health-related research (EVIR)	Collaboration of funders which aims to increase value of health research	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30464-1/fulltext
Evidence-Based REsearch (evbres)	European Union funded project which promotes an evidence based research approach in clinical research	https://evbres.eu
FAIR Data Principles	Guiding principles to make data Findable, Accessible, Interoperable, and Reusable	https://www.force11.org/group/fairgroup/fairprinciples
German Network for Evidence Based Medicine (EBM Netzwerk)	Promoting the quality of patient care and disease prevention by applying the principles of evidence-based healthcare - in special dentistry, medicine, nursing, pharmacy, physiotherapy	https://www.ebm-netzwerk.de/
HealthWatch UK	UK charity that promotes science and integrity in healthcare and health research	https://www.healthwatch-uk.org/
The Hong Kong Principles for assessing researchers	Principles agreed at the 6 th World Conference on Research Integrity which aim to bring considerations of trustworthiness, rigour and transparency to the assessment of research	https://www.wcrif.org/guidance/hong-kong-principles
medRxiv	Server for preliminary versions of clinical research articles (preprints) so that they can be made available prior to publication	https://www.medrxiv.org/
Open Science Framework (OSF)	On-line platform which facilitates open sharing and preregistration of research.	https://osf.io/
Open Science Badges	Badges appended to publications to acknowledge and incentivise open science practices	https://cos.io/our-services/open-science-badges/
QUEST (Quality, Ethics, Open Science, Translation) Center for Transforming Biomedical Research	Based in Berlin Institute of Health, hosts three research groups and activities include meta research to identify measures for improving research practice	https://www.bihealth.org/en/research/quest-center/mission-approaches/
Preclinical Trials	International register of preclinical trial protocols	https://www.preclinicaltrials.eu/

Registered Reports	Publication format aimed at reducing reporting bias, supported by the Centre for Open Science and other institutional/individual Open Science campaigners	https://cos.io/rr/
The Reproducibility Project: Cancer Biology	Collaboration between Science Exchange & Center for Open Science, replicating experimental results from high-profile papers in cancer biology published between 2010-2012	https://osf.io/e81xl/wiki/home/
REWARD Alliance	The REWARD Alliance grew from the 2014 Lancet Series on Waste in Research, and exists to share and exchange documentation, information, and resources to help increase the value of research and reduce waste in research.	http://rewardalliance.net/
San Francisco Declaration on Research Assessment (DORA)	Initiative which calls for improvement in how research quality is evaluated	https://sfdora.org/
Sense About Science	Campaigning charity that challenges misrepresentation of science and evidence and advocates for increased openness and honesty about research findings	https://senseaboutscience.org/
Sunshine UK	Voluntary register of doctors' declared interests	http://www.whopaysthisdoctor.org/
Transparency and Openness Promotion (TOP) guidelines	Graded standards for openness and transparency of research	https://cos.io/top/
TranspariMED	Campaigning organisation which advocates for registration and full reporting of clinical trials	https://www.transparimed.org/
Trial Forge	Project which aims to collate and share ways to improve all the processes involved in clinical trials	https://trialforge.org
The Trials Tracker Project	Trackers created by EBM Datalab (University of Oxford) which monitor trial reporting performance of pharmaceutical companies, universities, funders, sponsors, and other organisations	http://trialstracker.net/
Vivli	Research data sharing platform	https://vivli.org/
Yale University Open Data Access (YODA) Project	Advocates for the responsible sharing of clinical research data and has developed a model to make data available to researchers	https://yoda.yale.edu/

Research culture

Training in medical research, like that in clinical medicine, is based largely around an apprenticeship model. Much attention has therefore been given to providing positive mentorship that promotes integrity.(46) Several initiatives such as the UK Reproducibility Network have been established to promote values and practices in research conducive to the principles of open science within academic institutions.(47)

A number of other measures have been proposed in order to improve academic promotion criteria so that these are aligned with responsible research practices. Suggestions have included appraising research quality and reproducibility, and placing limits on the volume of publications that can be periodically submitted for institutional appraisal.(48-51) The San Francisco Declaration on Research Assessment (DORA) has outlined recommendations to improve the way in which the quality of research is evaluated, and the Transparency and Openness Promotion guidelines (TOP) includes a number of standards by which to assess research and journals.

Reporting biases

Clinical trial registration

Many of the problems outlined above, such as publication bias, spin, HARKing and p-hacking occur after research has been conducted. 'Pre-registering' studies prior to conducting research can help by establishing a record of what research was scheduled to take place and the hypotheses, methods, analyses and outcomes that were planned. Researchers can then be held accountable to the methods and outcomes they prespecified and expected to justify any deviations.

Registration of clinical trials is now promoted by the World Health Organisation through a number of approved primary registries and has increasingly become an expectation of funders and publishers.(52, 53) The requirement by the International Committee of Medical Journal Editors (ICMJE) that all trials should be registered before being considered for publication and the passage of the FDA Amendments Act 2007 mandating registration in the US were major milestones in achieving widespread trial registration.(54, 55) Mandatory registration requirements have in turn facilitated mandatory reporting requirements, with the expectation that findings of all trials are disseminated in some form, be it through journal publication or in alternate dissemination routes provided by regulatory bodies or trial registries.(56) Aside from clinical trials, systematic reviews are possibly the only other type of study design for which registration is now routinely undertaken prior to study commencement.(57)

Registration should be understood as one tool to help ensure researchers share their results and to discourage unjustified deviations from research plans. However, registration alone is not a panacea. For example 'outcome switching', whereby alterations are made to outcomes between registration, trial completion and publication is common amongst registered trials.(58) Journals could routinely ensure that reported outcomes match pre-specified registered outcomes. Despite these caveats the value of registration should not be understated, since without it such deviations would not be detectable at all.(59, 60)

Registration of non-trial research

Although registration is now an expectation for clinical trials and systematic reviews it remains entirely voluntary and is employed relatively infrequently for other types of study for which registration and pre-

specification of hypotheses and methods would facilitate greater transparency. Public platforms such as the Open Science Framework are a highly accessible means for all researchers to publish detailed information about planned studies, such as protocols and analysis plans. It is the view of the authors that registration or publication of a priori protocols should become a widespread expectation. Broad adoption of study registration and publication of protocols could dissuade authors from presenting results gleaned from exploratory work as hypothesis-based research, combat p-hacking and HARKing, and create a permanent record of planned research that can be used to assess publication and other reporting biases. 'Registered Reports' are a related initiative which are discussed in the final section of this review.

Publication checklists

One means which has been employed to improve transparency and quality in study reporting has been the widespread requirement by journals for authors to submit checklists along with manuscripts, indicating whether reporting standards have been met. Checklists now exist for all major study designs of which the Consolidating Standards of Reporting Trials (CONSORT) is perhaps the best known and endorsed by hundreds of journals.(61) CONSORT has been associated with some improvement in completeness of reporting but instances of poor CONSORT compliance remain.(59, 62) Even when discrepancies are clearly identified by readers of journals, authors and journal editors make corrections infrequently.(60) While the existing self-regulation of checklist compliance has yielded imperfect results there is an opportunity for journal editors, or perhaps specially trained editorial assistants to vet publications to ensure accurate reporting before publication.(63)

Statistical and methodological issues

Education

The importance of high quality training in statistics and open science methodology are increasingly recognised.(64, 65) Several educational opportunities have been established, some of which are identified in table 1. Although provision of such training is welcome only a small proportion of medical researchers will benefit from such initiatives, with access particularly restricted in low and middle income countries.(66) Therefore it is vital that capacity to deliver such training is developed and maintained within academic institutions.

Data sharing

In order for research to be fully appraised and potentially reproduced additional information beyond a study publication is required. Registrations can provide some additional detail, but in many cases other documentation, such as study protocols, analysis plans, and individual patient data are necessary in order to understand and assess or reproduce the study. Making such data available would also allow other researchers to use the same data to answer different research questions.(57) Unfortunately research data is often not made available.(67)

The ICMJE has instituted requirements for data sharing for published clinical trials. While such policies are welcome, research suggests that even with these requirements data is available in only about one half of publications.(67) Persuasive appeals have been made to institute greater data sharing for all study types, including the proposition that research papers become one of a series of 'threaded documents' with underlying data made available as a matter of course.(68, 69)

How to improve medical research?

It has been estimated that almost all research expenditure is wasted due to some of the issues which have been described in this review. However, a large proportion of this waste can be avoided.⁽⁴⁾ Reducing research waste could increase the capacity of research budgets to improve outcomes for patients.

Significant gains in transparency have been achieved in areas like clinical trial registration through the combined efforts of researchers, journals, funders, campaigners and legislators. Meanwhile continued attention has been brought to the so called 'reproducibility crisis' through the Open Science movement, which has connected international networks of collaborators who share a determination to improve scientific practice. While it remains vital that emphasis is placed on improving statistical and ethical education for researchers and on addressing cultural issues within research, there is a need for immediate and definitive action to improve the quality of all medical research.

We propose a strategy that includes three measures to achieve further improvements in the transparency of medical research. These measures are:

- 1) mandatory registration of interests for all people and institutions who conduct and publish health research;
- 2) all journals and funders support uptake of registered reports; and
- 3) that publicly funded research is pre-registered and published on a WHO affiliated research registry.

Box 1 outlines how this strategy was developed, and Table 2 summarises some of the ways this could improve research.

Table 2: Problems in medical research and how they can be mitigated by authors' proposed strategy

Problem	Problem description	Relevant proposed solution(s)	How proposed solution(s) addresses problem
Publication bias	Tendency for results deemed 'negative' or 'uninteresting' to remain unpublished	Registered Reports Research Registry	Study accepted for publication based on methods, not results Study results and documents made available, regardless of publication status
'Spin'	Practice of presenting results of study as more striking, 'positive' or newsworthy than warranted.	Registered Reports Research Registry Mandatory Declaration of Interests	Reduced incentive to 'spin' to obtain publication Study documentation available to allow greater scrutiny of researchers' claims Information on possible conflicts of interest allows peers to judge if researchers have vested interest in applying spin to study
Scientific fraud	Deliberate falsification of evidence, for example fabrication of results	Research Registry	Availability of full study documentation allows peers to scrutinise results. Researcher compelled to demonstrate 'not just the answer but their working out'
Non adherence to checklists (e.g. CONSORT)	Inaccurate self disclosure by researchers of fulfilment of checklist statements	Research Registry	Peers can scrutinise methods from available study documentation.
HARKing	Researchers generate hypotheses to fit results and present these as if formulated prior to obtaining results	Registered Reports	Hypotheses and aims are agreed prior to undertaking research. Any further post hoc analyses are declared as such
P-Hacking	Researchers manipulate results until findings generated which satisfy statistical significance	Registered Reports Research Registry	Analyses agreed prior to generation of results Analysis plans and code available to peers for scrutiny
Outcome switching	Researchers do not report certain outcomes, or switch primary and secondary outcome, to highlight favoured results	Registered Reports	Outcomes of interest agreed prior to undertaking research

		Research Registry	Protocols and analysis plans made available to peers for scrutiny
		Mandatory Declaration of Interests	Conflicting interests which could engender bias made known to public and peers
Other Questionable Research Practices	Practices including deciding to collect more data after inspecting results, selective rounding of p-values, selective reporting of dependent variables	Registered Reports	Methods are agreed prior to publication. Incentive to generate results which favour publication removed
		Research Registry	Protocol and analysis plan made available to peers for scrutiny
Undisclosed conflicts of interest	Researchers may have, or could be perceived to have, vested interest in obtaining certain outcome in their results	Mandatory Declaration of Interests	Researchers compelled to made comprehensive statement of their pecuniary interests, gifts and hospitality received and non-pecuniary interests
Non replicable research	Results unable to be replicated, either because of insufficient information to reproduce methods or because of biases in original study (including problems in this table) mean work not reproduced when attempted	Research Registry	Adequate study documentation made available such that study can be repeated or analyses repeated.

The concept of a campaign, with specific objectives to improve health research arose from a presentation made to the EBMLive conference in Oxford in July 2019. The conference organisers facilitated a further session to discuss the concept further, chaired by Georgia Richards. An on-line survey was distributed amongst attendees of the conference session. Survey results were used to inform selection of three demands.

Drafts of a statement were prepared by Stephen Bradley, Peter Gill and Georgia Richards and distributed amongst conference attendees, who then provided feedback and became signatories. A draft statement was made available (<https://osf.io/k3w7m/>) in October 2019 and publicised via twitter (@TA_Declaration).

The feedback received informed the second major revision of the declaration, which, following consultation with signatories was made available in January 2020. As of April 2020, feedback to help further revise the statement is being accepted. Signing the statement and/or providing feedback is possible by completing this form: <https://docs.google.com/forms/d/1wHWcw77fFtvvY2tJpNrzt3HE0tF8xvFOL3U55RV4/>

Box 1- Development of the authors' strategy to achieve further improvements in medical research

Mandatory Declaration of Interests

In order to establish trust in the objectivity of research, researchers must become more open about conflicts or declarations of interests. The brief voluntary statements that currently conclude research publications are not sufficient to meet this expectation. A fully accessible database of interests should be established, with firm expectations of accurate, up to date and comprehensive disclosure from all researchers, doctors, institutions and patient advocacy groups. Such disclosures should feature both monetary payments, benefits such as travel, hospitality and conference fees, and non-monetary interests, such as memberships of committees. Researchers' declaration of interests should be required by all academic institutions, funders and journals. The Open Research and Contributor ID (ORCID) system already catalogues the identities of over 7 million researchers. Hence, ORCID identifiers could be used to index researchers' interests.(70)

Registered Reports

Registered reports are a publication format that permit authors to submit their proposed methods and analysis plan to a journal prior to conducting the research. If the journal accepts the proposal, it commits to publication as long as the research is satisfactorily conducted, regardless of the findings demonstrated.(71) This model can help limit the impacts publication bias and other reporting biases. Registered reports also curtail both the ability of authors to undertake (or peer reviewers to request) HARKing or p-hacking, and reduce the incentive to do so. Underpowered research or questionable methodological or statistical decisions can be identified and addressed through peer-review prior to study conduct. Since journals commit to publication upon review of study plans, rather than finished papers, registered reports may be an effective way to reduce the incentive for authors to 'spin' and for reviewers to request such embellishments.

Authors are not restricted from undertaking additional exploratory analyses, but registered reports help clarify that such analyses are exploratory and not based on prior hypotheses. Null findings are more likely to be published through registered reports than traditional formats and registered reports are cited just as often as conventional papers.(72, 73)

At the time of writing, registered reports were accepted by 225 journals which included only 68 (1.3%) of the 5250 journals indexed in MEDLINE (supplement 2).(71) A precursor to the registered report format was unsuccessfully introduced by the *Lancet* over 20 years ago, but was discontinued with the warning that some studies deviated substantially from pre-specified outcomes and analyses.(74) This experience suggests that consistent evaluation of registered reports and support for authors to use the format is required. Their successful adoption in other scientific disciplines suggests medical journals could adopt this format in much greater numbers than they currently do. Pressure from funders, authors, readers and editorial board members could help support journals to make this transition.

Comprehensive research registration and publication

To facilitate reproducibility of research findings and to assess the plausibility of scientific claims, it is essential that documentation including protocols and analysis plans are made available to peers. Making all study findings available is the only way to address publication bias. It is also a matter of fairness that

research which is paid for by public or charitable funding and upon which important healthcare decisions may be made, is made available for anyone to view.

For all publically funded research, not just trials, comprehensive documentation including protocols, statistical analysis plans, statistical analysis code, raw or appropriately de-identified summary data and results should be available on a WHO-affiliated open access registry. In theory, the United States already requires that protocols and statistical analysis plans for clinical trials are publically shared.⁽⁵⁵⁾ Obtaining widespread compliance with this principle for most types of study would represent a significant, but achievable advance in transparency and fairness. Funders should require that study documentation is made openly available, while governmental and national research institutions could support the development, or nomination of, an appropriate open platform where anyone can find comprehensive information about publically funded research.

Important principles such as the range of documentation that should be shared and to what level of detail would need to be established. However, we believe that establishing the expectation that sufficient information should be available for research to be adequately appraised could be an important milestone in achieving greater transparency and reproducibility.

CONCLUSIONS

The problems which beset science are the result of the cumulative failures of individuals and institutions. Concerted measures are required to improve transparency, mitigate waste, and reduce biases in research. The complexity of the problems and the difficulty in communicating these to policy makers and the public means represent significant barriers to remedying this situation.

Significant progress is required to satisfy reasonable expectations that medical research is trustworthy, reproducible and represents value for money. The proposed strategy comprising mandatory registration of potentially competing interests, increasing the uptake of registered reports and requiring all publically funded research to be pre-registered and published can be readily conveyed to policy makers and could be rapidly implemented. These ideas are not novel and we do not claim that they would solve all of the problems in medical research. But, whilst such profound problems persist in medical research we believe that it is time to implement simple measures to achieve greater transparency, reduce reporting biases and deter poor methodological practices.

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