Medicina de Familia. SEMERGEN 51 (2025) 102370

Medicina de Familia
SEMERGEN

www.elsevier.es/semergen

EDITORIAL

Ensuring research integrity in clinical trials

Garantizando la integridad científica en los ensayos clínicos

Clinical trials are of paramount importance for the improvement of population's health, as they provide the evidence base to determine whether an intervention benefits patients or not, or if the risk-benefit ratio is favorable. In many cases, general practitioners assume as a rule of thumb that a randomized controlled trial, per se, is sufficiently valid to decide on a given intervention, without going deeper into the methodological intrigues of the study. These details are likely to be important, because they may demonstrate that the intervention is ineffective, although the published research conclusions might suggest the opposite.

These methodological concerns may or may not be tied to research integrity-related issues in clinical trials. Research integrity is not about the methodological quality of the studies but it is about ensuring that ethical and professional practices, such as informed consent, managing conflicts of interest and transparency in funding, and role of the funding source, are upheld throughout the entire research process. However, the issue of research integrity has been hardly studied overall.

The paper by Butt et al.[1] is a relevant piece of knowledge synthesis evaluating the quality and reporting standards of recommendation documents on research integrity in clinical trials. This study reveals a worrying lack of quality in recommendation documents on research integrity that may have implications in health research. If the documents guiding responsible conduct in research are deficient, the integrity of clinical trials and the trust in evidence-based medicine are at risk. Poor-quality recommendations can lead to inconsistent practices, which may result in flawed research conclusions and even potentially harmful interventions.

Butt et al.[1] assessed the collated recommendation documents using different appraisal tools and the results indicate low quality in general, highlighting the need for an urgent call for action. The authors have observed that one of the documents they have included in the review has the best quality compared to others. This is the ''International Multistakeholder consensus statement on clinical trial integrity''.[2] This document got the highest score in all three appraisal tools used by the authors. The reason behind this scoring is that this document included all relevant aspects of the research process in clinical trials. Its comprehensive and detailed approach positions it as a model for future recommendation documents on research integrity. It has also been translated in Spanish, published in this journal.[3]

However, the results of the Butt et al.[1] paper indicate that the tools they used obtained different scores when applied to the same documents, indicating differences in performance between them. This discrepancy reflects variation in the criteria and weighting applied by the experts who developed these tools. This is surprising since, in some sense, researchers should agree on what is relevant when measuring research integrity, particularly in clinical trials. In a scientific world with the new insights of precision medicine, we seek the standardization of clinical procedures, adequate reproducibility or accuracy of tests and reduction in clinical practice variability. Butt et al.[1] raise questions about whether we pay sufficient attention to how research is conducted and communicated. The fact is that there are many stakeholders who should be vigilant in generating the best possible evidence. Researchers, academic institutions, journal editors and reviewers, the readership of scientific journals and, of course, patients' and patients' organizations all need a common language.

When it comes to researchers, we must consider if they have sufficient skills to take part in or even conduct research effectively. To do research is much more than having funds or time trying to solve a specific clinical problem. It is necessary to understand the logic of the study design, the sample size and many other issues, including how to measure variables, deciding which of them should be included and the best statistical analysis for the data. We guess that in a ''publish or perish'' world,[4] not all researchers meet these criteria. Institutions have a responsibility to train them.

Scientific journals are the gatekeepers of good science. However, it is interesting to see that many journals have endorsed certain checklists (i.e. CONSORT for clinical trials, different STROBE checklists for observational studies and many others) but have yet to endorse many of the

https://doi.org/10.1016/j.semerg.2024.102370

research integrity documents assessed by Butt et al. This is particularly concerning in light of the increasing number of publications, including clinical trials, that exhibit both methodological flaws and integrity issues.[5] Something is wrong in the scientific research arena when the number of retracted papers continues to reach higher levels year after year.[6] Though this can be seen as good news, we do not know if this is a consequence of better error/fraud detection tools, more scrutiny by authors, or just the logical consequence of the increasing number of research papers and journals published, which increase the ''denominator'' of the available papers. As new forms of research fraud are emerging constantly, such as paper mills,[7] fake reviews,[8] ghost and guest authorship, the content generated by AI and even reviews generated by AI,[9] the integrity of publications, including clinical trials, is at risk. This background highlights the urgent need for improving the standards documents and recommendations, as well as robust oversight, to ensure that the research findings we rely on are valid.

As readers of scientific evidence, we, as health professionals, must be aware that bad science can be published, including not only fraudulent research but also biased and useless research. While the first is more difficult to detect, bad quality research is easier to find. Anyhow, we have the duty to decide which research (good or bad) we introduce in our clinical practice.

To conclude, research integrity and methodological quality are critical to advancing research and ensuring evidence-based clinical practices. The findings of Butt et al.[1] highlight the urgent need for high-quality recommendation documents that increase ethical standards and professionalism in clinical trial research. In this sense, all stakeholders need to be aware of the issue at hand and use more exigent mechanisms to perform and evaluate research. This includes the need for better research training for health professionals at academic institutions but also sanctions in those cases where integrity has been eroded on purpose.[10] Integrity in clinical trials should not be seen as an ideal, but as a crucial and basic responsibility that we must uphold.

Conflicts of interest

The authors declare that there are no conflicts of interest that are relevant to this publication.

References

1. Butt F, Nunez-Nunez M, Juhasz B, Bueno-Cavanillas A, Khan K. The quality and reporting of recommendation documents to enhance the integrity of clinical trials: a systematic review and critical appraisal. Med Fam (Semergen). 2024 [in press].
2. Khan KS. Cairo Consensus Group on Research I. International multi-stakeholder consensus statement on clinical trial integrity. BJOG. 2023;130:1096–111.
3. Nunez-Nunez M. Grupo de consenso de el cairo sobre la integridad de la I [International multi-stakeholder consensus statement on clinical trial integrity]. Semergen. 2024;50:102217.
4. Rawat S, Meena S. Publish or perish: where are we heading? J Res Med Sci. 2014;19:87–9.
5. Van Noorden R. Medicine is plagued by untrustworthy clinical trials. How many studies are faked or flawed? Nature. 2023;619:454–8.
6. Van Noorden R. More than 10,000 research papers were retracted in 2023 – a new record. Nature. 2023;624:479–81.
7. Candal-Pedreira C, Ross JS, Ruano-Ravina A, Egilman DS, Fernandez E, Perez-Rios M. Retracted papers originating from paper mills: cross sectional study. BMJ. 2022;379, e071517.
8. Rivera H, Teixeira da Silva JA. Retractions, fake peer reviews, and paper mills. J Korean Med Sci. 2021;36:e165.
9. Donker T. The dangers of using large language models for peer review. Lancet Infect Dis. 2023;23:781.
10. Candal-Pedreira C, Alvarez-Dardet C, Ruano-Ravina A, Perez-Rios M. The research integrity office in Spain. A pending issue. Gac Sanit. 2022;36:557–60.

C. Candal-Pedreira[a,b,c], A. Ruano-Ravina[a,b,c,*]

[a] *Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Santiago de Compostela, Galicia, Spain*

[b] *Consortium for Biomedical Research in Epidemiology and Public Health (CIBER de Epidemiología y Salud Pública-CIBERESP), Madrid, Spain*

[c] *Health Research Institute of Santiago de Compostela (Instituto de Investigación Sanitaria de Santiago de Compostela-IDIS), Santiago de Compostela, Galicia, Spain*

* Corresponding author.
E-mail address: alberto.ruano@usc.es (A. Ruano-Ravina).