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OPINION

Standards in semen examination: publishing reproducible and reliable data based on high-quality methodology

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ABSTRACT: Biomedical science is rapidly developing in terms of more transparency, openness and reproducibility of scientific publications. This is even more important for all studies that are based on results from basic semen examination. Recently two concordant documents have been published: the 6th edition of the *WHO Laboratory Manual for the Examination and Processing of Human Semen*, and the International Standard ISO 23162:2021. With these tools, we propose that authors should be instructed to follow these laboratory methods in order to publish studies in peer-reviewed journals, preferable by using a checklist as suggested in an Appendix to this article.

Key words: reproducibility / basic semen examination / standardized laboratory procedures / andrology / reproductive medicine / laboratory training / quality control / patient security / science development / journal requirements

Appeal to the scientific society involved in Andrology and Reproductive Medicine

As scientists are aware, there has been much discussion about the transparency, openness and reproducibility of science. This is not a new issue. Ten years ago, Begley and Ellis proposed a series of recommendations to improve the reliability of studies in preclinical cancer research (Begley and Ellis, 2012) that helped to initiate a series of developments to address and improve reproducibility. These have included more detailed reporting and transparency of methods such as the STAR Methods for *Cell Press* journals https://www.cell.com/star-authors-guide. Concomitant with these developments, national programmes, such as The MDAR (Materials Design Analysis Reporting) Framework, for transparent reporting in the life sciences have been launched (Macleod *et al.*, 2021) and specific consortia have been developed to repeat key published experiments, e.g. Reproducibility Project: Cancer Biology (RP: CB) (https://elifesciences.org/collections/9b1e83d1/reproducibility-project-cancer-biology) (Rodgers and Collings, 2021). Furthermore, there are significant resources available such as EQUATOR guidelines (https://www.equator-network.org/). The clear direction of travel is to improve standards and have transparent reporting of research (Amara, 2022). There are challenges, however. For example, in the RP:CB project, insufficient information was available to repeat selected experiments published in high impact journals. Furthermore, in the experiments that could be repeated (50/193), fewer than half yielded similar results. As such, the final report of the RP: CB consortia suggested that 'it is hard to assess whether reported findings are credible' (Errington *et al.*, 2021).

In our own discipline of Andrology and Reproductive Medicine, there is a plethora of evidence to show that using non-standardized methods produces unreliable data including, for example, for human sperm concentration and sperm motility assessments. This has created significant problems for the field, making it difficult to determine the scientific accuracy of many studies and ultimately establish their real clinical and public health impact. A recent example of this is the study of Campbell *et al.* where they updated the World Health Organization (WHO) semen analysis distribution values (Campbell *et al.*, 2021). The authors reported several challenges in obtaining key information of the quality of the semen examination methods used across the studies being considered for inclusion. Standardization of semen examination has been a long-standing issue that the profession has collectively failed to address, despite the availability of proven accurate methods and robust training approaches (Björndahl *et al.*, 2002, 2016; Barratt *et al.*, 2011; Carrell and De Jonge, 2016; Cairo Consensus Workshop, 2020). Too many studies depending on semen analysis derived data continue to demonstrate poor robustness and rigour in semen analysis methodology (Serrano *et al.*, 2014). When methods with a high degree of uncertainty are used, differences between normal and pathological conditions are likely to be impossible to discover since each observation, burdened by large variability due to measurement uncertainty, will have a more-or-less random result. This will cause considerable overlap in results from the different populations, making them practically inseparable.

The question for all of us working in Andrology, including Editors of journals publishing research in this field, is: What can be done to improve the situation? We believe there is currently a window of opportunity for action. The recent publication of ISO Standard 23162 for the basic examination of human semen (International Organization for Standardization, 2021) finally means that the field has *de facto* reference methods. These methods form the basis of those recommended in the new 6th edition of the WHO andrology laboratory manual (World Health Organization, 2021), which contains simple to follow and proven high-quality methods for semen examination. We propose that authors should be instructed to follow these laboratory methods in order to publish studies in peer-reviewed journals. To facilitate this, we present in the Appendix an author checklist, modified from Björndahl *et al.* (2016), which authors can complete and submit with their manuscript, making it simple for the journals, reviewers and readers alike to assess the quality of the semen assessment methods used,

and hence of the data being reported. We suggest that any deviation from the checklist, for purposes of testing a new reagent, different method or procedure for improving on the performance of a current recommendation, should be specified and measured against those in the checklist. If authors did not follow these methods, a separate section of the Materials and Methods should specify what differed and why, and how the variations might have impacted the accuracy of results. In other disciplines, checklists have assisted with improving the reporting of results (Nature, 2018; NPQIP Collaborative Group, 2019). This approach is consistent with the TOP Guidelines (Transparency and Openness Promotion; Centre for Open Science, https://www.cos.io/initiatives/top-guidelines; Nosek *et al.*, 2015).

This is an important initiative. We suggest it be implemented by all journals in our discipline to help improve the transparency, openness and reproducibility of science.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

No new data were generated or included in the manuscript.

Authors' roles

L.B., C.B. and D.M. outlined the first manuscript and contacted all other authors for comments. L.B., C.B. and D.M. summarized all suggestions and finalized the manuscript that all authors have received and confirmed their participation in.

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Conflict of interest

This is an Opinion article based on the necessity for improvement of standards in the field of Andrology and Reproductive Medicine, based on the two non-profit publications, by the World Health Organization and the International Organization for Standardization. No conflicts of interest are declared. CB, as an employee of the University of Dundee, serves on the Scientific Advisory board of ExSeed Health (from October 2021, financial compensation to the University of Dundee) and is a scientific consultant for Exscientia (from September 2021, financial compensation to the University of Dundee). CB has previously received a fee from Cooper Surgical for lectures on scientific research methods outside the submitted work (2020) and Ferring for a lecture on male reproductive health (2021). CB is Editor for *Reproductive Bio Medicine Online*. DL, as an employee Weill Cornell Medicine, declares: American Board of Bioanalysis (Secretary-Treasurer: Honorarium); Fellow Health (Equity); Roman Health (Consultant and Advisory Board) (Equity and compensation).

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