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EDITORIAL

NPP's approach toward improving rigor and transparency in clinical trials research

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Neuropsychopharmacology (NPP) publishes both basic and clinical neuroscience research that advances our understanding of neuropsychiatric conditions and identifies the molecular, cellular, physiological, and psychological properties of novel and approved pharmacological treatments. NPP is committed to consistent and thorough reporting of clinical research which is essential for rigor, reproducibility, transparency, interpretation, and generalizability of published results to the broader human population. The Consolidated Standards of Reporting Trials (CONSORT) Group was established in 1996 to address the lack of standardized reporting of clinical trials worldwide and developed minimum recommendations for information that should be reported in publications describing clinical trials involving human subjects. To enhance rigor and transparency of research published in this journal, in 2017 NPP began requiring completed CONSORT documents and registration at a recognized trial registry (e.g., ClinicalTrials.gov) during submission of manuscripts involving clinical trials. However, 5 years since this implementation, there remains frequent non-compliance in providing CONSORT documentation for manuscripts involving clinical trials submitted to NPP, described in greater detail below. The failure to adequately report trial methodology increases burden on journal staff, editors, and reviewers, lengthens the peer review process, hinders efforts to critically appraise and interpret trial results, and impedes translation of results for promising treatments. In this editorial, we describe the challenges this creates and outline changes that NPP is making to improve clinical trial reporting and ease burdens at all levels of the evaluation process. We highlight how these changes will benefit the scientific community by enhancing rigor of research, improving efficiency of peer review, and increasing the reproducibility and impact of published research.

The CONSORT statement (http://www.consort-statement.org/) was first introduced in 1996 and revised in 2001 and in 2010 [1]. The CONSORT framework consists of a checklist and flow diagram (Fig. 1) that authors complete to report experimental details of clinical trials. The 25-item checklist recommends information that should be included regarding how the trial was designed, analyzed, and interpreted. Meanwhile, the flow diagram illustrates the flow of participants through a trial. Collectively, information provided in the CONSORT documents facilitates transparency in the reporting of clinical trial research and allows readers to evaluate the quality and relevance of the findings.

In 2017, NPP began requiring a completed CONSORT checklist and flow diagram during submission of manuscripts describing clinical trials. However, routine quality control checks by journal staff have revealed that authors frequently do not comply with providing these documents. For example, in 2020 NPP received 140 manuscripts that were identified as a clinical trial by the submitting author, but only 70 (50%) of these submissions included both a complete CONSORT checklist and flow diagram. When journal staff followed up with corresponding authors of the 70 submissions that did not provide both the checklist and flow diagram, 14 authors requested an exemption and 5 withdrew their submission. Even in cases where authors complied with the journal's request, follow-up correspondence significantly increased the workload of the authors, journal staff, and editors, delaying the peer review process. This remains a persistent issue, as ongoing tracking of NPP clinical trial manuscripts submitted in 2022 reveals a similar rate (~55%) of non-compliance in providing complete CONSORT documentation on the first submission.

Confusion regarding whether studies meet the definition of a clinical trial may contribute to the poor compliance in providing CONSORT documents during NPP manuscript submission. The National Institutes of Health (NIH) revised its definition of a clinical trial in 2014 to improve the design, conduct, and oversight of clinical trial research. The revised definition includes any study in which one or more human subjects are prospectively assigned to one or more interventions, to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes (https://grants.nih.gov/policy/clinical-trials/definition.htm). With this revision, a clinical trial designation could be applied to studies involving only healthy human participants, studies that do not have placebo control groups, or studies involving behavioral interventions alone without medications or other biological interventions. Importantly, this expanded definition of a clinical trial includes basic research with human subjects that involves experimental manipulations to investigate basic biological phenomena (https://grants.nih.gov/policy/clinical-trials/besh.htm). NPP adheres to the clinical trial definition set forth by the International Committee of Medical Journal Editors (https://www.nature.com/npp/authors-and-referees/editorial-policies#clinical), whose definition is aligned with NIH's: "any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome… A medical intervention is any intervention used to modify a health outcome and includes, but is not limited to, drugs, surgical procedures, devices, behavioral treatments, and process-of-care changes".

While the reason for low compliance in clinical trial reporting in NPP manuscript submissions is not clear, one possibility is that it reflects a lack of awareness of this shift toward a broader definition of a clinical trial. Nonetheless, to improve adherence to transparency and accountability in clinical trial reports published in NPP, we are implementing changes to our manuscript submission process. Text describing the definition of a clinical trial is now included directly on the submission webpage with links to more information on these definitions. Submitting authors will now be required to respond to and confirm answers to the following questions:

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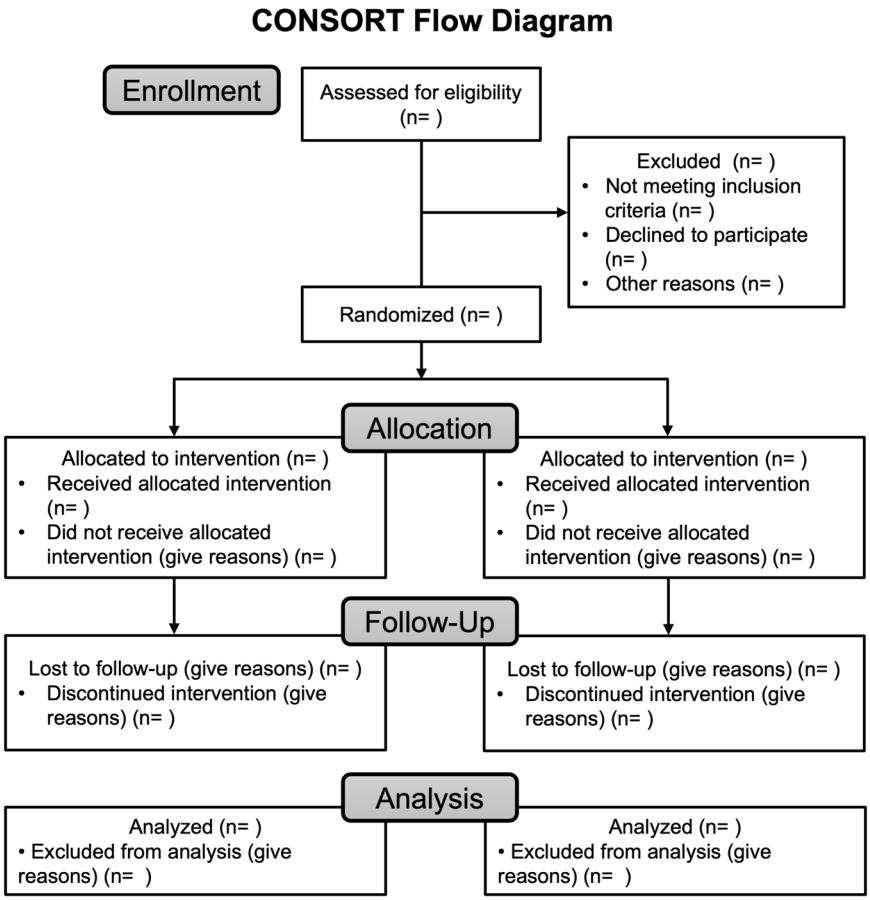

Fig. 1 CONSORT flow diagram depicting the progression of participants through a clinical trial. Reproduced from [3].

1. Did this study involve human participants?
2. Are participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention?
4. Is the effect being evaluated a health-related biomedical or behavioral outcome?

If the answers to all of these questions are yes, authors will be required to confirm that their submission includes the CONSORT checklist, flow diagram, and the clinical trial registry number. We do not anticipate granting any waivers of this requirement, even in cases where the justification is that the studies were initiated before CONSORT documents were required during manuscript submission (i.e., pre-2017). During peer review, reviewers will be encouraged to comment on CONSORT compliance when evaluating the rigor of research.

The goal of these simple changes to the manuscript submission process is to enhance transparency in the design, reporting, analysis, and interpretation of clinical trial research published in NPP. While CONSORT recommendations alone may not be sufficient to improve reporting of all aspects of trial design [2], we believe these changes will improve the speed and thoroughness of peer review while enhancing rigor and transparency in the planning, execution, reporting, and reproducibility of clinical trial research. Most importantly, these benefits will extend to the authors, who can anticipate stronger impact of their published work that is more likely to stand the test of time.

DISCLAIMER

This work was written as part of SH's official duties as a Government employee. The views expressed in this editorial are the opinions of the authors and do not necessarily represent the views of the the National Institute of Mental Health, the National Institutes of Health, the Department of Health and Human Services, or the United States Government.

Sofiya Hupalo[1], Chloe J. Jordan[2], Terri Bowen[3], Jennifer Mahar[4], Elizabeth Yepez[5], Lori Kunath[6], Sarah Timm[6], Keri Martinowich[7,8], William A. Carlezon Jr.[2], Lisa M. Monteggia[9] and Tony P. George[10,11]✉

[1]*Division of Neuroscience and Basic Behavioral Science, National Institute of Mental Health, Bethesda, MD 20892, USA.* [2]*Department of Psychiatry, McLean Hospital, Harvard Medical School, Belmont, MA 02478, USA.* [3]*Origin Editorial, Cincinnati, OH 45039, USA.* [4]*Origin Editorial and Editorial Evolution, Pembroke, MA 02359, USA.* [5]*Springer Nature, New York, NY 10004, USA.* [6]*American College of Neuropsychopharmacology, Brentwood, TN 37027, USA.* [7]*Lieber Institute for Brain Development, Baltimore, MD 21205, USA.* [8]*Department of Psychiatry and Behavioral Sciences; Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.* [9]*Department of Pharmacology and the Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN 37240, USA.* [10]*Department of Psychiatry, University of Toronto, Toronto, ON, Canada.* [11]*Addictions Division and Centre for Complex Interventions, Centre for Addiction and Mental Health, Toronto, ON M6J1H4, Canada.* ✉*email: Tony.George@camh.ca*

REFERENCES

1. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2012;10:28–55.

2. Han C, Kwak K, Marks DM, Pae C-U, Wu L-T, Bhatia KS, et al. The impact of the CONSORT statement on reporting of randomized clinical trials in psychiatry. Contemp Clin Trials. 2009;30:116–22.
3. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med. 2010;8:18. the CONSORT Group

AUTHOR CONTRIBUTIONS

TB and TPG compiled data on CONSORT document compliance. SH wrote the paper & CJJ made the figure. CJJ, TPG, KM, JM, LK, ST, LMM, TB, WAC, and EY edited the paper.

COMPETING INTERESTS

All authors have roles at NPP. SH is the Editorial Intern; CJJ is the Special Projects Manager; TB and LK are Editorial Assistants; JM is the Managing Editor; ST is the Executive Director of ACNP; KM is the Social Media Editor; WAC is the outgoing Principal Editor; TPG and LMM are the incoming Principal Editors.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Tony P. George.