Pre-registration: not a daunting practice

Pre-registration is the practice of publishing information about research studies before data analysis to demonstrate transparency for what is being done and how data will be interrogated and interpreted. It is becoming a key indicator of scientific rigor and quality.

In decisions about submitted research reports, Addiction aims to avoid prejudice against study findings that do not support the authors’ hypotheses or expected results. If the questions being asked are valid and important, the data adequate to address them and the reporting competent and transparent, then the results should be given credence regardless of their direction.

However, there appears to be an entrenched anxious belief among some researchers that if study findings do not turn out as anticipated, then a mistake must have been made in either the conduct of the research or the analysis, which will reflect badly on them if reported. Beliefs like this can engender publication bias toward false-positive findings [1], with hindsight bias taking future research in the wrong direction or down false paths. This problem also contributes to the so-called ‘crisis of reproducibility’ in contemporary science [2].

Pre-registration— the increasingly common practice of publicly sharing information about a research study’s questions, hypotheses, methods and analyses in advance [3]— is one way of preventing the tendency for results to be reported that provide evidence for a certain hypothesis. Essentially, it is a demonstration of transparency for what is being done and how data will be interrogated and interpreted. Registration of an intended study in advance of the data being accessed should promote publication of the study regardless of the results. There are benefits for the researcher too: pre-registration oils the wheels of the peer review process; reviewers can see that the findings manuscript aligns with what was planned, securing a smoother and faster path toward publication.

If we take the example of a clinical trial, pre-registration is reflected in a three-step sequence, as follows:

1. the study is registered on a standard registry database (e.g. clinicaltrials.gov; ISRCTN; https://www.isrctn.com) before the first participant is enrolled;
2. the protocol is published on a freely accessible repository or published in a peer-reviewed journal (or at the very least submitted) no later than the last day of participant recruitment; and
3. the final version of the analysis plan is published (e.g. on the Open Science Framework; https://osf.io) before the dataset is locked in for the analysis, with this implemented as soon as possible. (NB: The third stage is not formally required at the moment, but is rapidly becoming best practice).

Pre-registration has long been expected for the conduct of systematic reviews, but if done at all, it appears that key information for observational cohort/longitudinal studies is usually published after the study has commenced and with limited description of outcome measures and statistical procedures [4]. To our knowledge, pre-registration is rarely done for qualitative studies. High-quality qualitative studies analysed thematically apply a theoretical or conceptual framework, so this should be specified in advance, alongside plans for the synthesis of the findings. For a detailed description and guideline for qualitative analysis methods see Neale [5,6]. We recommend that researchers planning observational quantitative and qualitative (and mixed-methods) studies should commit to publishing their protocols and specific analysis plans.

The methods section of the manuscript submitted for peer review should contain a concise description of the pre-registration process. Researchers should imagine that reviewers will hold up the protocol and analysis plan in one hand and the manuscript in the other to see if they match. In an ideal scenario, the study is implemented and analysed as planned. However, things do not always go to plan and good science requires some level of flexibility. Study protocols are very often amended to address things that were not clearly described or unforeseen—including additional interventions (e.g. specifying concomitant medications), participant responses (e.g. how adverse events are defined and classified) and new rules for data collection (e.g. telephone follow-ups included in addition to face-to-face interviews at the clinic).

In our experience, reviewers may lose faith in a manuscript if there are apparent and unjustified differences in the description of the participant inclusion and exclusion criteria, as well as deviations in how participants were exposed to interventions, and—most seriously—changes in the way outcome measures are defined, analysed and reported. However, all major differences should be accounted for. But what if independent experts and editors determine that a mistake has been made in the analysis plan? This can be corrected through a revised approach. Missing observations in the dataset is a good example where the pattern of missingness and often the factors associated with it are unknown at the outset. Standard operational procedures during data collection and validation, and decision rules for the analysis, can prepare for this. Explorative analyses can also lead to important new hypotheses. Pre-registration does not
exclude these, so long as they are clearly identified as such in the manuscript.

So what makes good pre-registration practice?

1. Make sure the main aims and outcomes of the study match as closely as possible to the description of the analysis foreseen in the protocol.
2. Try to refrain from publishing the analysis plan until any and all amendments to data collection have been done, to ensure that the analysis plan is the one that is implemented.
3. Build flexibility into determining the final methods, especially in the situation where there is likely to be uncertainty.
4. Consider making the statistical command code available for others to see and use.
5. Include in the submitted and revised manuscript a description or reference to all changes to the planned study and its analysis and, as appropriate, ensure a clear distinction is made between planned and explorative analysis.

Last year, approximately two-thirds of reports, clinical trials and systematic reviews and one-tenth of manuscripts of cohort/longitudinal studies were pre-registered. We hope to see a further upward trend this year. To recognise good practice, Addiction now enables researchers to select a pre-registration badge to be displayed in the published article (https://authorservices.wiley.com/open-research/open-recognition-and-reward/open-research-badges.html).

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Bias, open science, pre-registration, protocols, reproducibility, statistical analysis plans

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**AUTHOR CONTRIBUTIONS**

John Marsden¹ Janna Cousijn² John Stapleton¹

¹Institute of Psychiatry, Psychology and Neuroscience, King’s College London, UK
²Erasmus University, Rotterdam, Netherlands

**ORCID**
John Marsden https://orcid.org/0000-0002-1307-2498
Janna Cousijn https://orcid.org/0000-0002-7699-2582

**REFERENCES**