# Statistical analysis plan for the third International Stroke Trial (IST-3); part of a 'thread' of reports of the trial

Peter Sandercock[1]*, Richard Lindley[2], Joanna Wardlaw[1], Will Whiteley[1], and Gordon Murray[3] on behalf of the IST-3 collaborative group

The way randomized clinical trials (RCTs) report their results is changing rapidly. Most high-impact journals now expect reports of RCTs to meet several requirements: to have been registered at inception with a recognized trial registry, for the trial protocol to be publicly available (or at least available to peer reviewers), and for the report to conform to the standards set out in the Consolidated Standards of Reporting Trials (CONSORT) statement (1). Whilst the trial protocol may set out an outline of the statistical analysis plan (SAP), a detailed SAP may only be specified and date-stamped shortly before the data are locked and the trial investigators (and authors) are unblinded to the results.

It is critical that a SAP is published prior to unblinding of the investigators to treatment allocation. If investigators design the SAP in the knowledge of data by allocated treatment group, there is risk they will take several methodologically inappropriate actions: place undue data-dependent emphasis on particular analyses, selectively report only those outcomes showing a favorable effect, make a data-dependent selection of subgroups and apply other analytic strategies to 'massage the data' into giving results that are most favorable (2). However, it is not common practice for an investigator to publish the SAP for their trial in peer reviewed journals, though the recent SHARP trial may have set a trend (3).

SAPs are rather 'dry' reading, full of methodological detail that is of little interest to the general reader. Nonetheless, a critical reader will want to find out as much as possible about a trial and its methods, in order accurately to judge the validity of the trial results. Transparency in reporting trial results is therefore vital, but space constraints in journals in the past have made it hard to publish fine methodological detail. Fortunately, online publishing has enabled journals to react positively to the requirement for more extensive reporting of trial methods and results. The idea of a 'thread of publications' (4) associated with a trial is now developing, which stretches throughout the life of a trial. It begins with publication of the protocol, goes on to updates on the progress of the trial, the main report of the trial results, and ends when the full trial data set is made publicly available for analysis. Both the NINDS trial of thrombolysis for stroke and the first International Stroke Trial have published their full data sets online as the final step in the thread (5,6). In that spirit, we are grateful to the International Journal of Stroke for enabling us to add a publication to the IST-3 'thread' by publishing our SAP as a web-appendix to this article (Appendix S1), supplementing the IJS paper describing the rationale for the trial (7), the IJS podcast reporting progress and our update paper recently published in *Trials* (8). The IST3 data will be added to the Cochrane Database of Systematic Reviews review of thrombolysis for acute ischemic stroke (9) and in due course, the IST3 data set will be incorporated in an individual patient data meta-analysis of all the trials of thrombolysis with rt-PA, and at some further point in the future, a subset of the data will be available for even wider data sharing.

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Correspondence: Peter Sandercock*, FRCPE, FMedSci, Department of Clinical Neurosciences, Western General Hospital, Edinburgh, EH4 2XU, UK.
E-mail: peter.sandercock@ed.ac.uk
Twitter: @IST_3
[1]University of Edinburgh, Department of Clinical Neurosciences, Western General Hospital, Edinburgh, UK
[2]Discipline of Medicine, Sydney Medical School – Westmead and The George Institute for Global Health, University of Sydney, NSW, Australia
[3]University of Edinburgh Centre for Population Health Sciences, Medical School, Teviot Place, Edinburgh, UK

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## Supporting information

Additional Supporting Information may be found in the online version of this article:

**Appendix S1** Statistical Analysis Plan (IST-3)

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