Grant Advice for Trial Statisticians

Version 2.0: 10 November 2023

Requesting funding for statistical support for a clinical trial

Statisticians have an important role throughout the life of a clinical trial. In the planning and design stage, statistical input is essential to ensure that the research question is answerable, the study design and plan for data collection are appropriate to address the research question, the outcomes are well defined, and the sample size calculation and planned analysis methods are appropriate for the study design. Before the start of the trial, an independent statistician generates a randomisation schedule and a statistician contributes to statistical aspects of the trial protocol. During the conduct of the trial, issues regularly arise where statistical input is essential to maintain the integrity of the trial, for example regarding data collection and cleaning, participant withdrawal, and protocol violations, making it important for a statistician to attend regular meetings with the study team. Also, where applicable, statisticians are involved in Data and Safety Monitoring Boards/Committees (DSMB/C) as the independent DSMB/C statistician[1], the (ideally independent) unblinded statistician preparing statistical reports for the DSMB/C[2], and the (ideally blinded) trial statistician overseeing the DSMB/C processes[3]. Finally, statisticians play a crucial role in the analysis of trial data and the interpretation and reporting of the trial results. These various tasks are ideally covered by more than one statistician, both for quality control and so the primary trial statistician can remain blinded to the treatment group allocations, although this is not always possible.

[1] DSMB/C Statistician: A statistician who is a member of the DSMB/C and is independent from the trial.
[2] Reporting Statistician (also sometimes referred to as the independent statistician): A statistician who prepares the DSMB/C reports, including the closed report which involves unblinded information, and may attend closed session meetings to answer queries.
[3] Trial Statistician: A statistician who is part of the study team and involved in the day-to-day activities of the trial, blinded to the treatment allocation.

Given the integral role of statisticians in the trial team, **we recommend that an experienced trial statistician be included as a Chief Investigator (CI) on grant applications** (or if not as a CI then as an Associate Investigator). This role is usually an oversight role that may be unfunded (e.g. for a statistician whose salary is already covered by an academic appointment or a fellowship) or require a small budget for salary support (e.g. for a senior statistician who is funded by multiple grants). In the latter case, a salary request in the range of 0.05-0.1 full time equivalent (FTE) per year (approximately 2-4 hours per week) at Personnel Support Package (PSP) level 4 or 5 to provide statistical leadership at the trial steering committee level and supervision of the trial statistician (see below) would be suitable for most conventional trials. However, this FTE would be considerably higher for trials with an adaptive design and/or that require regular interim monitoring.

In addition to the statistician CI role, **we advocate for the inclusion of a PSP for a more junior "trial statistician" to provide hands on statistical support for the duration of the trial**, which would be overseen by the statistician CI (or a more senior statistician could potentially fulfil both the trial statistician and CI roles). For a reasonably small, single centre trial with a simple design, we suggest requesting fractions in the order of 0.2 FTE for the first year during the planning stage of the trial, 0.1 FTE for the middle years during trial conduct period, and then 0.4 FTE during the final year for analysis at PSP level 3 as part of the trial budget. For large, multicentre and/or complex trials, we suggest requesting fractions in the order of 0.3-0.4 FTE for the first year, 0.2 FTE for the middle years (which could be split across the trial statistician and an independent statistician producing the DSMB reports) and 0.6 FTE for the final year at a minimum PSP level 4. Adaptive trials typically require considerably more statistical time and expertise, and this should be reflected in both the FTE and PSP level requested. For example, adaptive platform trials which require extensive simulations to establish the trial design that often need updating during the trial, as well as regular data analyses, may require 1.0 FTE or more for statistical support throughout the trial. It is important to calculate the total amount being requested in dollars to make sure this amount will adequately cover the cost of providing statistical support for the trial.

The amount of statistical time required for any trial will depend on the specifics of the trial and the exact tasks to be assigned to the trial statistician (for example, data cleaning is a time consuming task that may be partly or wholly performed by the trial statistician). **It is therefore important for trialists to consult with a statistician early in the grant application process to determine a suitable budget for statistical support for their trial.** In the case of adaptive trials, early engagement with a statistician is especially important to assess the suitability of an adaptive design for the specific trial, advise on which adaptive aspects are worth the additional complexity, and run extensive pre-trial simulations.

Example text for the justification for statistical support (trial statistician, PSP3) in a small, single centre, 4-year trial is:

In year 1 the requested PSP position will be needed to generate the randomisation list, help design the case report forms, oversee the development of the study database, help set up procedures for data management including data checking and cleaning, and provide input into the trial protocol and trial registration. In years 2 and 3, the PSP will be required to attend regular study group meetings, write a detailed statistical analysis plan, monitor the data collection and assist with data checking. Finally in year 4, the PSP position will be required to conduct a full evaluation of the data including data checking, summarising the available data and the statistical analysis of the final trial results. This person will also be involved in the presentation of results both at conferences and in scientific papers on which they will be named as an author. These tasks require considerable time and specialist training in statistics to ensure the quality of the output from this research. The PSP3 level is the minimum for someone with the necessary high-level statistical skills (preferably at Masters level in biostatistics or applied statistics or similar) and depth of experience in trials.

Example text for the justification for statistical support provided by two separate statisticians (a statistician CI and a PSP4 trial statistician) for a more complex, 5-year trial with a DSMB/C is:

CIX is a biostatistician with over X years of experience providing statistical leadership on large, multicentre clinical trials. They will serve on the trial steering committee, supervise the trial statistician and provide oversight of all statistical aspects of the trial (trial design, data collection and quality checks, statistical analysis plan, analysis and reporting). A small component of their salary is requested to ensure their ongoing involvement for the duration of the trial.

A statistician with postgraduate qualifications and clinical trials experience (PSP4 level) is required to provide high quality, day-to-day statistical support for a trial of this size and complexity, under the supervision of CIX. In year 1 they will contribute to the trial protocol, data collection tools and DSMB/C charter, and prepare the test randomisation schedule (final schedule to be generated by an independent statistician to maintain blinding). In years 2-4 they will attend regular project meetings, develop a detailed statistical analysis plan, work with the data manager to ensure ongoing data quality, and program reports required for annual DSMB/C meetings (to be run by an independent statistician to maintain blinding). In year 5 they will undertake the final analyses involving complex statistical methods and contribute to the interpretation and dissemination of the trial results.

Budget requests for statistical support are sometimes included in grant applications under other research costs, rather than salary requests for a CI and/or PSP statistician, which may be appropriate

in some cases (for example, when engaging a trial statistician at an hourly/daily rate through a private consulting arrangement rather than paying a portion of their salary to an academic institution, or when seeking an independent statistician to produce unblinded reports for the DSMB/C).

It should be noted that, in general, a statistician does not set up nor manage the trial database, and hence the FTE estimates above exclude those activities. Therefore, in addition to requesting funding for statistical support, it is important to request additional funding for database creation and data management. The amount of funding required for this will vary depending on the scope and complexity of the study. Advice should be sought from an experienced database programmer and/or data manager regarding a suitable budget for this work.

Applying for funding for methodological research

It can be difficult to obtain funding for methodological research. In particular, it is challenging to sell the clinical relevance and the translational impact of such research. In our experience, when applying for funding for methodological research it is important to hinge the research on applied examples where the research can make a difference. It is also important to include details on how the findings from the research will be disseminated. This needs to be more than simply journal articles and conference presentations. For example, think about how you can use the findings from your research to directly change practice in the teams that you work in, and more widely. Can tools be developed to encourage uptake of new methods (e.g. R Shiny apps)?

In terms of what funding to apply for, it is important to consider the different categories of funding. To date, members of ACTA STInG have received funding for methodological research in the form of project/ideas grants, fellowships/investigator grants, and centres of research excellence. In all of these funding streams, we have emphasised the clinical impact of the research, and have stressed the importance of conducting biostatistical research in order to remain on the forefront of medical research and to make the most of the vast amounts of data that are collected from applied research projects.

Selling a statistical track record

Working as a biostatistician often means collaborating with many different applied researchers across a variety of clinical areas. This mean that biostatisticians often do not have a large number of first author publications and have very few, if any, grants as lead investigator (CIA), because both papers and grants are generally led by the applied researchers. This can make it very difficult to have a

competitive track record when applying for future grants, either as a CI on an applied project or as the CIA on a methodological project or fellowship.

When writing a track record as a CI on an applied grant, it is important to explain that as a biostatistician you are responsible for leading the statistical aspects of the studies that you are/have been involved with. For example:

> *My role in my previous successful grants was to assist in the development of the research question and study design, and to lead the statistical aspects of the proposal. All of these grants included a fraction of salary for statistical support which I am now managing.*

It can also be useful to explain why you have a limited number or no first author publications. For example:

> *As a research biostatistician there is a trade-off between developing a personal portfolio of methodological research and providing statistical leadership in collaborative projects, which results in co-authored publications. This means that a large number of my publications are co-authored papers as opposed to first authored papers. Of note, on X of my co-authored publications I am 2nd or 3rd author reflecting the critical input I have provided as an analytic expert in empirical research.*