STATISTICS IN YOUR APPLICATION
August, 2021

Background: The Committee for Scientific Evaluation (SEC) reviews LOIs and invites a limited number of applicants to submit a full proposal. One key consideration is on strength of statistical methods, applicable to most proposed projects. APSF would like studies to stand up to rigorous scientific review. The SEC is supported by two experienced, well-published Biostatisticians, who provided the following suggestions for good statistical practices for applications to APSF. These suggestions may seem challenging to meet in an LOI or a proposal, but many investigators have succeeded even for complex projects. The SEC adds a section below on those safety studies that are qualitative.

1. Team's statistical support. Include a person with strong statistical credentials and include adequate funding for the proposed statistical work. The statistical expertise should be demonstrated by correct and clear statistical writing in the LOI and proposal, along with a strong biosketch. For qualitative studies, there should be expertise in the types of the data that will be collected and in the analysis methods that will be used.

2. Study design. Clearly state the primary study goals. Use an appropriate study design and appropriate statistical methods that match your goal. For example, you may hypothesize that a new treatment T will be superior to, non-inferior to, or equivalent to an established treatment R. Even though all three are two-group comparisons, statistical approach is different. For any study, including comparative, descriptive, exploratory, pilot or qualitative studies, describe how you will recruit subjects who are representative of the population to which the findings will be applied in the future.

If there will be multiple groups with different treatments, describe how randomization or other methods will be used to make the groups similar or equivalent except for the treatment assignment. State whether there will be parallel treatment groups vs. cross-over (each subject rotates through all treatments) vs. another design. Describe how subjects will be enrolled or sampled into each group so that the groups will be comparable in terms of characteristics and timing.

If the study is qualitative or exploratory (sometimes with a small sample size), explain how the results of this study will be used to design a larger, more definitive study.

3. Statistical analysis. Describe the analysis that will be used to determine if the proposed treatment, procedure or device is a success. What comparisons will be made and what statistical methods will be used? What is the main outcome variable and the primary analysis of that variable for determination of success? What are the secondary outcome variables and their analyses?

Describe potential confounding variables and show how you will test and control for them in the analysis.

State how much missingness (missing data) is expected among the relevant variables. If missingness may be an issue, describe approaches used to limit missingness prior to statistical analysis. If present, how will missingness be addressed in the analysis?

If there are repeated measurements of individuals, describe the methods that will control for the statistical dependence (correlation) among the measurements from each individual.

If there are many outcome variables being assessed or many statistical tests (often called "multiple testing" or "multiple comparisons"), describe methods that will be used to minimize false positive statistical significance among the many tests.

While statistical significance may play a role, confidence intervals (CI) are strongly recommended for means, differences and other key numeric results. For example, CIs can show a plausible range for a treatment effect. Don't use p-values alone for evaluation. Statistical non-significance does not always mean "no difference," and a clinically non-significant difference may be statistically significant.

If multivariate analysis is planned, describe how the multivariate models will be constructed. What variables will be candidates for inclusion in the model? Describe how your multivariate model will be developed so that it is not overfitted to the specific sample (and then, potentially, perform poorly on a new sample).

If development of a predictive model is the goal, such as prediction of a good or a poor outcome, describe methods for estimating performance of the prediction model, either using the same sample (e.g., using "cross-validation") or an independent test sample.

Some statistical tests require data that are approximately normally (bell-curve) distributed. Describe how transformations or nonparametric or other methods will be used if data are not normal.

4. Sample size and power analysis. Use and justify a sample size such that the study has sufficient power to detect a clinically meaningful change or difference. Specify all parameters used in carrying out the power analysis (so that the calculations may be checked); describe the source for the parameters and justify the parameter values as relevant for your study; justify any assumptions used.

The statistical method used for analysis of the primary outcome variable should be the paradigm for the power analysis. However, a complex, planned primary analysis can often be adequately approximated by a simpler analysis—just for the purposes of estimating power. For example, while the planned analysis may involve linear regression to assess associations between individual predictors and a continuous-variable outcome, the power analysis may be easier to express using correlation.

5. Additional notes on safety studies with qualitative and engineering methods. Include experts with track records of chosen methods, such as interviews and observations to identify key themes or perspectives. Define clearly how you aggregate different data sources such as transcriptions, photos, videos, and documentations. For interviews, provide key interview questions or thematic probes, clarify if audio recording will be used and detail the analytical approach or framework. Specify any software that will be utilized in this process. For systems analysis, include specific details about the types of analytical frameworks and approaches to be used, and about sources of data to be analyzed. Examples of systems-analytic frameworks include Systems Engineering Initiative in Patient Safety and Functional Resonance Analayis Method. Data collection methods include process mapping, cause-effect "fishbone" diagrams, task analysis, and flow disruption analysis.

For projects with interventions, consider measures outlined in implementation science frameworks (e.g., REAIM or CFIR), and include details of corresponding data collection methods (e.g., post-meeting notes). Include sufficient details on sampling strategies and analytical approaches to allow a reasonable chance of replication, a prerequisite for publishing in most peer-reviewed journals.

Provide explanations on concepts and methods that may be unfamiliar to those in anesthesia patient safety fields. Highlight the value of these concepts and methods.