Reporting and authorship

Clinical trial reporting

"If physicians are to base treatment decisions on the evidence in the medical literature, all the relevant results of trials must be available easily and consistently." (CONSORT revised, *JAMA*, 2001).

Reporting the results of a clinical trial is one of the most important aspects of clinical research. In fact, failure to publish is a type of scientific misconduct.

Reporting requirements are context specific and reflect the necessities of the study. I am listing some examples for the major study categories considered in this course.

Authorship on the other hand is a difficult and frequently tense exercise. I deal with this at the end of this lecture.

Clinical trial reports
Dose finding studies

Although there have not been many reviews of the adequacy of reporting for dose-finding studies, deficiencies arise in every review of the literature.

Recalling that the focus of dose-finding studies is to assess the PK properties of a new compound, find a good therapeutic dose, evaluate toxicity, and look for efficacy.

Features of Phase-I study reports

A good Phase I study report should have the following characteristics:

- Study design features
- Characteristics of the study population
- Estimates of clinically important PK parameters
- Recommendations for proper dosage
- Nature, severity and reversibility of toxicity or adverse events
- Evidence of treatment efficacy

Clinical trial reports
Dose finding studies

- *Study design features*
  With rapidly evolving designs for dose-finding studies, it is it si important to describe the exact nature of the study design, including selection criteria, the biological rational for the starting dose, definition of the best biological dose and route and schedule of administration.
- *Characteristics of the study population*
  Points to report is the primary disease sites, extent of disease, extent of previous treatment, demographic characteristics and the proportion of patients with poor prognosis based on objective criteria.

Clinical trial reports
Dose finding studies

- *Estimates of clinically important PK parameters*
  Of clinical importance are estimates of drug excretion rate, half-life, peak concentration and area under the time-concentration curve (AUC). These parameters, as well as the model that generated them, should be reported along with any association between them and observed toxicities.
- *Recommendations for proper dosage*
  Dose recommendation is a critical issue of early phase studies. The basis of the recommendation should be reported as well as whether this dose should be modified based on baseline criteria (e.g., age).
- *Evidence of treatment efficacy*
  Although evidence of efficacy is uncommon in early phase studies, when it occurs, efficacy should be properly reported along with the response criteria used, number of responders and duration of benefit.

Clinical trial reports
SA study reports

SA studies are supposed to demonstrate feasibility, estimate efficacy and adverse event rates and inform the decision of further study of the new intervention. SA trials also provide additional information about dose and scheduling of therapy.

- *Feasibility*
  The SA report should report any problems that prevent the administration of the intervention or side effects that require its modification. Patients that present problems of non-feasibility must be accounted for and not excluded. In addition, eligible patients that did not get accrued should be accounted for in case the therapy is unacceptable to some patients.
- *Efficacy and toxicities*
  Response criteria should be defined *a priori* as responses defined in retrospect are always suspect. Minor and major side effects should be defined and presented.

Reporting CTE Trials
Early developments

Structured reports for randomized controlled trials (RCT) emanated from a meeting, in Ottawa Canada in 1993, by about 30 medical journal editors, clinical trialists and epidemiologists with the aim of developing a set of standards to assess the quality RCT reports because of the realizations that the quality of reporting was less than optimal (Pocock et al., *NEJM*, 1987, Altman and Doré, *Lancet*, 1990).

The result was a the Standardized Reporting of Trials (SORT) statement, a 32-item checklist and flow diagram for reporting randomized controlled trials.

Jointly with another group of experts, this resulted in the Consolidated Standards of Reporting Trials (CONSORT) statement (Begg et al., *JAMA*, 1996), which has been revised in 2001 and is under another revision currently.

The CONSORT checklist

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomized", or "randomly assigned").	
INTRODUCTION Background	2	Scientific background and explanation of rationale.	

The CONSORT checklist (cont'd)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	

The CONSORT checklist (cont'd)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
Randomization Sequence generation	8	Method used to generate random allocation sequence, including details of restrictions (e.g., blocking, stratification)	
Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	

The CONSORT checklist (cont'd)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
RESULTS			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	

The CONSORT checklist (cont'd)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	

The CONSORT checklist (cont'd)

PAPER SECTION and topic	Item	Descriptor	Reported on Page #
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

Other standards

A number of other standards have been put forward regarding specific types of studies. Some of these are:

- The MOOSE statement for meta-analysis of observational studies in epidemiology (*JAMA*, 2000)
- The QUOROM statement of reporting for meta-analyses of randomized controlled trials (*The Lancet*,1999)
- The STARD initiative for accurate reporting of trials of diagnostic accuracy (*AJR*, 2003)
- The REMARK recommendations for tumor marker prognostic studies (*JCO*, 2005)

Other standards (continued)

- The STROBE statement for observational studies in epidemiology (*BMJ*, 2008)
  - STROBE checklist for case-control studies
  - STROBE checklist for cohort studies
  - STROBE checklist for cross-sectional studies

Authorship

The current principal of authorship inclusion is based on the standard that separates the conduct of the clinical trial and the intellectual contributions to the writing of the manuscript and taking responsibility for the report.

This is an imperfect standard and creates tension given the limited opportunities for authorship for clinical researchers and the time required to complete a study. This is because seemingly disproportionate credit may be given to someone coming late in the collaboration but making a contribution to the manuscript. On the other hand, it does not appear to be fair to grant authorship to someone performing routine clinical work.

Standard for authorship are expressed in the International Committee of Medical Journal Editors (ICMJE)(*NEJM*, 1997).

The uniform requirements of the ICMJE
Authorship criteria

The requirements for receiving authorship credit and conducting and reporting research articulated by the ICMJE include the following major categories: According to the ICMJE standard, "[a]n 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study". Authors should fulfill all three following conditions:

- Substantial contribution to the conception and design, acquisition of data, or analysis and interpretation of data
- Drafting the article or revising it critically for important intellectual content
- Final approval of the published version.

Some journals require someone among the authors to be identified as a "guarantor" of the entire work.

The uniform requirements of the ICMJE
Other contributors listed in Acknowledgments

All other contributors, who do not meet the criteria for authorship should be listed in an acknowledgments section. These contributors include those providing routine technical help, assist with the writing or provided only general support.

Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under such headings as clinical or participating investigators. Their contribution should be described such as “scientific advisors or having “critically reviewed manuscript, or having “collected data or “cared for study patients.

The uniform requirements of the ICMJE
Other criteria

The ICMJE has developed criteria for other categories of contributors or other contexts. Some of these include:

- Editorship, which articulates the role of journal editors and issues such as editorial freedom
- Peer review of submitted manuscripts, as the cornerstone of the scientific process
- Conflicts of interest in writing, peer-review and editorial decision making to safeguard the scientific integrity of published work
- Privacy and confidentiality pertaining to study participants as well as authors and reviewers
- Procedures for the protection of human subjects and animals in research must be reported