Publication policy

The trialist's oath

Whereas

Being able to research on human beings is a privilege granted only by an accepting society,

and whereas

Research is done to advance knowledge,

and whereas

There is no advance of knowledge in the societal sense without publication.

Therefore, as a trialist, I am obliged to:

Ensure the trial I participate in is registered and that the registration is updated as the trial proceeds.

Ensure existence of a statement fashioned and approved by study investigators committing to publication when the trial is finished or stopped because of benefit or harm.

Make every effort to publish results of the trial when finished or stopped without regard to the nature or direction of results.

Be satisfied that investigators will be responsible for analysis and paper writing and for conclusions stated without interdiction of study sponsors or others.

Be satisfied that persons or agencies funding the trial will fund analysis and paper writing when the trial is finished or stopped until results are published or through the 4th rejection of the results manuscript.

Publish in peer-reviewed, indexed, medical journals.

Resist efforts by others to acquire study data until investigators have published or until they have abandoned efforts to publish after repeated rejections of the results manuscript.

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Even if individually investigators subscribe to the Trialist's Oath, those subscriptions will not translate into a publication policy. For that to happen there has to be discussions within the investigator group that translate into written policy.

So when do you start the deliberation process? Not too soon and not too late. It is "too soon" if investigators are still struggling to get the trial off the ground and it is "too late" if they have results they want to report. In a trial likely to run five years the goal should be to have a ratified policy by the end of 2nd year of funding.

The “rule of three” applies when coming to establishing publication policy. That “rule” is that key policy decisions within the investigatorship of trials should not be brought to votes until the issues underlying those decisions have been discussed on three different occasions separated in time by weeks or months.

Experience is that the first time the issue is discussed, it is greeted by silence, as if no one cares about such mundane matters. The second time the issue is discussed it is greeted with a few polite comments. The third time produces debate and meaningful discussion.

The second reality is that policies are not set in concrete. Hence, even when established the policy should be periodically reviewed and modified as needed, over the course of the trial. The reviews are beneficial in reminding investigators of the policy and in allowing opportunity for discussion and modification as circumstances change over time.

A key issue is designation of the ratifying body and how approval is indicated. The usual approach in multicenter trials is to clear policy through the steering committee with an understanding before a vote is taken as to who has voting rights and agreement on number of votes needed for approval (simple majority or 2/3rds majority). It is also a good idea to establish rules as to the number of votes needed to open discussion for changes to the policy once the policy is enacted.

Paper writing is the purview of study investigators. This means that it should be under the exclusive control of study investigators. Sponsors and DSMBs can offer comments on the policy but should not have rights of approval.

Publication policy

Issues that should be covered in statements of publication policy follows.

1. Registration
2. Publish first, present later policy
3. To whom will the policy apply?
4. Where, when, and how to publish
5. Types of publications
6. Authorship formats
7. Credits
8. Commissioning and sign-off processes
9. Presentation policy
10. Publicity policy
11. Policy on access to study documents
12. Policy on access to study data
13. Deliberations and ratification

1. Registration

Registration became a mandated part of trials with the establishment of ClinicalTrials.gov in 2000. Registration was tied to publication in 2004 when the International Committee of Medical Journal Editors (ICMJE) announced requirement for registration before initiation of enrollment for trials starting after 1 July 2005 as a condition for publication in journals subscribing to the edict.

The responsibility for registration and maintaining the registration over the course of the trial rests with study investigators. This means that the study leadership must designate someone in the study structure who does the registration prior to the start of enrollment and for updating the registration over the course of the trial and beyond.

2. Publish first, present later policy

The cornerstone of any policy is to "publish first, present later" when it comes to results of the trial. If publication is the sine qua non of medical research, than energies should go to publication, foregoing presentations until after publication. Reasons are:

Prior presentation will preclude publication in journals that regard presentations as forms of publication
Saps energy needed for publication
Analyses likely to be "preliminary"
No way of answering criticisms absent publication

A reason for favoring presentation before publication lies in the belief that presentation facilitates paper-writing. But presentation and publication are different mediums of communications. Time is better spent producing a publication straightaway than a presentation followed by publication.

When the fat is in the fire with results to publish, investigators, even if they have signed onto a "publish first, present later" policy will be tempted to want their cake and eat it too by orchestrating presentation to coincide with publication. Programs for meetings are set months in advance of the meeting dates. Journal review and acceptance processes run on their own time schedules. Gambling that the two schedules will coincide is foolhardy.

3. To whom will the policy apply?

The answer is everybody in the research group including study officers, center directors, study physicians and nurses, clinic coordinators, and personnel involved in receiving, processing, and analyzing study data. The research group may be only a few in a small single center trial but can number in the hundreds in multicenter trials.

It is pointless to try and establish publication policy without first identifying the constituent group covered by the policy.

4. Where, when, and how to publish

The "where" element of the policy relates to where results are to be published. The place is peer-reviewed, MEDLINE indexed, medical journals. Publications in "proceedings" or chapters in books are, for all intents and purposes, lost because they are not indexed in MEDLINE.

An element of "where" has to do with choice of medical journal and whether to submit to a general interest wide-circulation journal or a speciality journal. Clearly, the choice has implications as to how a paper is written. The choice is best left open until there are results to publish.

The "when" element has to do with timing of results publications and triggering events for such publications. To address this element a group must decide whether it will allow publication of interim results by treatment group, that is, results while the trial is underway. Not recommended.

The "when" portion of the policy should also include some indication of intent as to time of publication when the study is completed or stopped. The policy should be to proceed with publication in as timely and expeditious fashion as possible on completion of the trial or when a treatment is stopped. Timely and expeditious publication requires implementation of near real-time data flows to a processing site for editing and inclusion in databases suitable for analysis as the trial proceeds.

The "when" policy should be written to cover publications arising from results-based protocol changes, including those arising from decision to halt or expand use of a treatment because of evidence of harm or benefit. The need for expeditious and timely publication can be especially important in such cases if the results are of general clinical importance.

The proscriptions implied by the "when" element of the policy, means that groups must forego temptations to present interim results. Groups can be tempted to do so simply out of desire to keep the study in the "public eye". Avoid the temptation.

The proscription also means that a group is obliged to stay the course and remain quiescent when results from other trials are published, even if they are contrary to results within the trial or in some way "threaten" the continued viability of their trial.

The "when" proscriptions outlined do not extend to other kinds of publications from the study like those having to do with design and methods papers or papers characterizing baseline data. Indeed, procrastination to the end for such papers means they usually do not get written.

The "how" element of the policy is related to the "where" element. "How" can include "publication" on the internet, but only when used to supplement publication in peer-review indexed medical journals. Internet "publications" are lacking peer-review and are not easily found.

Another element of "how" is whether to publish in monograph or manuscript form. The preferred mode is as stand-alone journal articles. The monograph form of publication involving a series of related papers has appeal in that results and other relevant manuscripts appear together. The downside has to do with the time and energy required to orchestrate and produce monographs and with the fact that such

publications are largely "lost" once published to the world unless published as supplements to indexed medical journals and hence indexed.

It is useful to establish policy defining the nature and extent of review and approval rights granted sponsors in regard to study publications. In general, policy should be written to guard investigator right of primacy, that is, the right of those who conduct the trial to be first to analyze, interpret, conclude, and publish prior to being made to provide data to others for interpretation or analysis. That right is jeopardized when manuscripts are subject to approval by others prior to publication.

Policy may be written to allow sponsors (public or private) a time-limited right of review but without any assurance that their suggestions will be accepted.

5. Types of publications

A publication, herein, is a paper written by study investigators and published in a peer-reviewed, indexed, medical journal. When producing policy investigators should be cognizant of the type of publications they may produce. There are three general types as listed below.

Primary publication: Publication pertaining to primary aim of the trial; publication reporting primary outcome data by treatment group; publications detailing design, methods, and baseline results of the trial; publication pertaining to the primary aim of the trial.

Secondary publication: Publication pertaining to a secondary aim of the trial; publication reporting secondary outcome data by treatment group; publication providing added information bearing on primary outcome data.

Tertiary publication: Publication pertaining to a tertiary aim of the trial; "natural history" publication (publication of trends over time in a placebo assigned or in a no treatment control group); publication of results by treatment group for a variable or measure not related to the stated aims of the trial; publication of results of an ancillary study.

Ancillary studies are resource neutral from the perspective of the parent study. If the study involves new tests or procedures the proposing investigators are expected to cover those costs with new funding. Studies calling for the collection of additional data or the conduct of additional procedures on persons enrolled in the parent study are not likely to be approved if seen as interfering with the parent study.

Ancillary publications, by definition, are supplementary to the primary and secondary objectives of the trial. They should not be regarded as ancillary if results are relevant to the primary or secondary objectives of the trial.

6. Authorship formats

The policy should specify authorship formats for the three types of papers listed above. The masthead formats may differ depending on type of paper produced.

Conventional: Only persons listed

Modified conventional: Persons listed and name of the research group listed

Corporate: Masthead attribution to the study; no persons listed and no designation of persons responsible for writing the manuscript anywhere in the manuscript.

Modified corporate: Masthead attribution to the study; writing committee listed in credits or in a footnote to the title page.

Examples

Conventional

Results from the XYZ Trial

Ann L Jones, Fred A Brown, Ian F Smith, and Carol W Jackson

Modified conventional
Results from the XYZ Trial
Ann L Jones, Fred A Brown, Ian F Smith, Carol W Jackson
for the XYZ Trial Research Group
or
and the XYZ Trial Research Group

Corporate
Results from the XYZ Trial
The XYZ Trial Research Group
No footnote or credit listing for writing committee

Modified corporate
Results from the XYZ Trial
The XYZ Trial Research Group
Footnote or credit listing
Writing committee: Ann L Jones (chair), Fred A Brown, Carol W Jackson, and Ian F Smith

Conventional authorship
- *Advantages*
  - Identifies authors
  - Preferred by journals
  - Recognized by promotions committees
  - Compatible with National Library of Medicine indexing procedures
- *Disadvantages*
  - Difficult to devise equitable system for authorship with large investigatorships
  - Can lead to bickering and dissent in the investigatorship
  - May disenfranchise young investigators
- *Recommended use*
  - Single center trials with small investigatorships
  - Approved ancillary studies in multicenter trials
  - Special investigations or studies prompted by the trial but not directly related to it

Corporate authorship
- *Advantages*
  - Avoids association of study with specific individuals
  - Avoids bickering over authorship rights and ordering
  - Enables all personnel with role in trial to cite in C.V.
- *Disadvantages*
  - Precludes retrieval or identification by author via MEDLINE or the Science Citation Index
  - May discourage individual initiative
  - Unfair to key people
- *Recommended use*
  - Multicenter trials with large investigatorship and in large multidisciplinary trials, especially for primary publications
  - Single center trials with ten or more investigators
  - Papers reflecting a corporate activity or point of view

7. Credits

Credits listings are important parts of publications. They identify who was involved in the trial and where they are located. A necessary task for someone in the study structure is creating and maintaining the credits list over the life of the trial. Prudent policy makers will include policy pertaining to credit listings in publications. Primary publications should contain a full credit listing of all study personnel by center and composition of key study committees. The listings may be shorter for secondary publications and shorter still for ancillary publications.

8. Commissioning and sign-off processes

The policy should indicate the commissioning and sign-off authorities for manuscripts. The usual course is for primary publications to be commissioned by the study chair or the steering committee by designation of a writing committee and chair responsible for producing the paper. Usually, the study chair or full steering committee is responsible for clearing primary paper for submission for publication.

The process is generally less centralized for secondary publications and is largely investigator-driven for ancillary publications.

9. Presentation policy

Even if a group establishes policy proscribing presentation of results before publication, it is useful to outline policy where presentations are allowed. Suggested policy below.

Published results: Unrestricted; prior notification desirable; investigator approval not required

Information regarding facts of trial and details regarding design and methods: Unrestricted if information is limited to that considered to be in public domain or based on design and procedures documents publicly available; prior notification desirable; investigator approval not required

Results of ancillary studies: Review and approval of study officers required prior to presentation

Most abstracts are written within 24-hours of the deadline; that being so, recognize that policy requiring internal review prior to submission is likely to discourage would-be submitters; study reviews should be timely and produce crisp up or down decisions; if performed after submission with laissez faire policy, review must be performed within days following submission to avoid embarrassment if decision is that abstract is to be withdrawn

Presentations can be useful to the study and to presenters, therefore, practice should be liberal in encouraging presentation

Establish in conjunction with publication policy

Establish limits on what may be presented (usually limited to information on design and methods, performance and process information, and baseline results; usually written to preclude presentation of followup results, except, perhaps, for the control-treated group when that group is untreated – "natural history" results)

Write to be consistent with policy on publication (eg, if policy is "publish first, present later" in regard to treatment results, then such results must be regarded as "off-limits" for presentations prior to publication)

Establish internal procedures for review of invitations to present and for abstracts submitted for presentation at scientific meetings (typically, review in multicenter trials done by study officers); if policy on abstracts is laissez faire (ie, one where abstracts may be submitted prior to review) establish policy requiring submitter to withdraw abstract if not approved

10. Publicity policy

Establish a referral point for inquiries from the press and public concerning the study
Designated documents in the public domain such as prototype consent forms, study protocols, and data forms
Inform investigators of publicity ground rules and how to deal with queries from the press
Be forthright and honest in dealing with information requests
Do not honor requests for information on interim treatment results or that serve to compromise the integrity of the design

11. Policy on access to study documents

It is useful to enumerate study documents that are available to the public. The tendency should be toward "openness" in regard to "facts" of a trial" as reflected in funding proposals, study manuals and protocols, consent forms, and data collection forms.

There are obvious limits to openness. Investigators should not make documents or facts available to the public having the potential of violating anonymity or confidentiality protections accorded study subjects, compromising the integrity of the trial, or revealing interim results of the trial. Facts and documents routinely protected from access include:

Randomization codes and blocking procedures
Unencrypted patient data
Center specific performance characteristics or features
Minutes of study meetings
Site visit reports
Treatment effects monitoring reports
Line item budget information

12. Policy on access to study data

Limit access to study investigators during conduct of trial; use for presentation at public meetings proscribed except as approved by Study Officers; no public presentation of results of treatment until trial is completed or stopped
Datasets used in producing publications containing results placed with journal or some other public repository on publication
Preserve patient confidentiality; do not release or deposit listings or datasets where patients can be identified or identified on a probabilistic basis
Limit access to treatment results prior to publication to persons or groups responsible for treatment effects monitoring
Be kindly disposed to requests for data or analyses arising from inside or outside the study group
Deposit a composite, finished dataset just prior to cessation of all activities in the trial; deposit for unfettered use, preferably in a public archive

Usually, policy is written to give priority to requests for access from investigators in the trial over those coming from the outside. Requests from the inside will be related to paper writing activities and for use in analyzing or writing up results of an ancillary study. As a rule, requests external to the group for data to be used in meta-analyses or other analyses involving comparison of treatment groups are denied or placed on hold until the group has completed its only analyses and related paper writing activities.

The preferred approach is to deposit in relation to publications, especially in long-term trials likely to yield a series of publications produced over the time course of the trial. Under this approach, the dataset supporting a publication is deposited when the publication appears. The "deposit as you go" approach ensures timely deposits of what, most likely, amounts to the more important data of the trial. It does not, however, ensure a compete composite dataset. Variables not represented in any of the datasets will not be covered. Even if all variables are represented, the cutoff dates for the datasets will differ, therefore, piecing them together will not produce a complete composite dataset. If such is required, it must be

produced after all data have been collected, entered, edited, and checked. Policies calling for deposit of a "final" finished dataset at the "end" of the trial should include operational definitions of "final" and "end".

Requests for unfettered use of datasets by parties outside the trial prior to deposit should be denied if the investigators' right of primacy is to be protected. If datasets are provided, they should be provided as privileged transmissions, subject to use restrictions. For example, when provided to a drug company, with the restriction that the dataset may be used only in relation to the company's obligation in maintaining regulatory approvals or in obtaining a label indication from a regulatory agency.

13. Deliberations and ratification

It is the responsibility of the study leadership to produce the publication policy; typically in concert with the steering committee. The study chair can expect to preside over several meetings of the research group extending over a period of months to generate a consensus on policy. Deliberation and debate is essential for buy-in by investigators so do not rush the process. Ultimately, the policy should be voted on by the entire research group as discussed in section **3** above with clear rules before voting as to who votes, whether to be open or closed, and whether to be decided by a simple majority or 2/3rds majority.

The policy should be reduced to writing and posted on the study website. The statement should indicate procedures for amendment.