

H. Publication Policy

1. Goals

The goals of this publication policy are to ensure that manuscripts resulting from research conducted within HIV Prevention Trials Network (HPTN):

- Reflect accurate reporting of the design, conduct, and analysis of studies;
- Are developed in a collaborative fashion with the active participation
- Are published expeditiously and are widely disseminated (abstracts reporting the preliminary or highlighted results of a research study does not substitute for a full manuscript); and;
- Protect confidentiality of medical, personal and product information in accordance with the Privacy Act, the requirements for the protection of human subjects and any applicable clinical trials agreements.

2. Definitions

a. Manuscript Review Committee (MRC)

The MRC is a subcommittee of the Prevention Leadership Group (PLG). The major responsibility of the MRC is to ensure that any publications emanating from HPTN studies, which contain data or statistically related content, are reviewed by HPTN prior to submission for publication. This responsibility will be exercised either by having MRC members conduct the review or by identifying other appropriate professionals to assist in the process.

b. Primary Publications

Primary publications include journal articles and meeting abstracts that report the findings of study objectives (including secondary and tertiary) as described in an HPTN study protocol and are written by protocol teams.

c. Secondary Publications

Secondary publications include journal articles and meeting abstracts that address scientific questions not identified as study objectives in an HPTN study protocol, but rely on data collected or analyses performed by HPTN investigators.

d. Tertiary Publications

Tertiary publications involve research conducted in support of HPTN activities, such as literature reviews, that do not rely on HPTN data

e. Manuscript Proposal

The manuscript proposal is prepared prior to initiation of development of a primary or secondary manuscript. If the PT chair and lead statistician are not involved in the preparation of the proposal, the proposal must be submitted to them for review and approval prior to proceeding with development. The purpose of the submission is to identify and remedy any conflicting or overlapping manuscript writing projects as well as any data analysis issues. A proposal is not required for tertiary manuscripts or abstracts.

The manuscript proposal should contain the following information:

- Short (one or two paragraph) explanation of the rationale, hypothesis and objectives of the manuscript;
- Short (one paragraph or outline) summary of analysis plan, data presentation (including shell tables) and required CL support, if necessary;
- Identification and relevance to the HPTN mission; and
- Recommendation for writing team members

f. Manuscript Timeline

The manuscript timeline is prepared prior to initiation of development of a primary manuscript. If the PT chair and lead statistician are not involved in the preparation of the timeline, the timeline must be submitted to them for review and approval prior to proceeding with development. A timeline is not required for secondary or tertiary manuscripts or abstracts

The manuscript timeline should contain the following information:

- HIVNET/HPTN protocol number;
- Date of last participant follow-up;
- Date data were frozen;
- Date of proposal initiation; and
- Expected submission date to MRC

3. General Guidelines

a. Writing Team Composition

b. General guidelines for writing team compositions are:

- Any investigator is eligible to participate as a writing committee member or chair;
- For primary publications, writing committee membership should reflect the contributions of the individual investigators to the design, development, and conduct of the protocol as well as the interpretation and analysis of study/trial-related data; and
- For secondary publications, writing committee membership should reflect the contributions of the investigators in the initiation of the idea and the synthesis and interpretation of concepts or methodologies in relation to the scientific literature, and in any analysis required.

c. Authorship

The primary criteria for authorship are intellectual contributions to protocol design, conduct of the protocol, interpretation and analysis of protocol data, including relating the results to other information in the literature, and drafting substantial portions of the manuscript. In most cases, the first author will be the investigator who takes the lead in preparing the first draft of the manuscript.

Additional authors must have participated sufficiently in protocol development or implementation, in the analytic design or interpretation of the findings, or in the preparation of the manuscript to assume public responsibility for the content of the manuscript. If authorship disputes occur, the protocol team chair will mediate.

When a manuscript-writing project involves collaboration with other institutions, authorship and acknowledgment will be agreed upon by the collaborating institution and the MRC prior to release of data, provision of samples or collection of additional data from HPTN participants. Such agreement will be subject to the written approval of the NIAID Program Officer.

Although the investigator will retain custody and primary rights to the data consistent with current DHHS, PHS, and NIH policies, DAIDS will have access to all data generated by the HPTN and may periodically review it.

d. Acknowledgments

All publications and presentations will include a statement acknowledging the HPTN and NIH's support for the work and listing the applicable cooperative agreement numbers, unless the journal's policy precludes such an acknowledgment. All publications will

include the following statement: "Support for this study was provided by the National Institute of Allergy and Infectious Diseases (NIAID) through the HIV Prevention Trials Network (HPTN). The content of this publication or presentation does not necessarily reflect the views or policies of NIAID or HPTN, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government".

In addition, publications will acknowledge investigators or other personnel who made key contributions to the development of the manuscript. The MRC will review acknowledgments for completeness and recommend changes or additions for the writing committee's consideration.

e. Disputes

Disputes with respect to the manuscript development and preparation process will be resolved by the MRC. If the dispute is unresolved, it will be referred to the PLG. Disputes with respect to the manuscript review process will be resolved by the PLG

f. Third Party Agreements

Third party agreements with product sponsors will include an agreement on publications policy and authorship in accordance with the guidelines set forth above for primary/secondary publications.

g. Publicity

All press releases and scientific press briefings by HPTN investigators that present study data or results of NIAID-supported HPTN studies must be approved by the NIAID Program Officer and coordinated with the journal in which the study results are expected to be published.

4. Review Requirements

a. Manuscripts

Primary – For primary manuscripts, a manuscript proposal and manuscript timeline must be approved by the PT chair and lead statistician prior to initiation of manuscript development. Upon completion, the manuscript must be submitted to the SWG chair for review. Following approval by the SWG chair, the manuscript must be submitted to the MRC for full review. Submission to the MRC must take place within eight (8) months of last participant scheduled follow-up visit.

Secondary – The review requirements for secondary manuscripts are the same as primary manuscripts, except there is no requirement for preparation of a timeline and no deadline to submit for MRC within eight months of last participant visit.

Tertiary – Manuscript outline, writing schedule, and reviews are not required for tertiary publications. A copy should be provided to the MRC for information and tracking purposes

b. Abstracts

All abstracts must be sent for information purposes to the HPTN MRC prior to abstract submission

Using Data From Single-Site Studies – Any HPTN investigator may prepare an abstract using data from a single-site study for presentation at a scientific meeting without prior review. The abstract should be sent to the MRC Chair for an expedited review and for tracking purposes

Using Data From Multi-Site Studies – In the case of multi-center studies, the abstract will be submitted to the HPTN MRC who will in turn distribute to the SWG chair, PT Chair and the Lead Protocol Statistician for review and comment. All abstracts will be reviewed within 2-3 working days after submission.

1. Manuscript Development and Review Process

a. Primary Manuscripts

Analysis and Preparation – For primary manuscripts, the Protocol Team (PT) chair or designee and lead statistician will develop a manuscript proposal and timeline and establish the writing team. See the section on guidelines. Following approval of the proposal and timeline, the writing team begins to draft the manuscript. Within five months' of last study participant's scheduled follow-up, the SDMC will send the writing team chair a core analysis report for the manuscript. This core analysis report will be adequate for the writing team chair to prepare a manuscript draft, which will then be reviewed and refined by the writing and analysis team.

Review – Manuscripts of primary publication may not be submitted to journals until after HPTN review. This process is intended to be advisory. The review is designed to expeditiously assure and accurately report its design, conduct, and analysis. The timetable will be monitored carefully and exceptions will be made for fast tracking primary publications.

Following completion of the draft manuscript, the manuscript is submitted to the SWG chair (or designee if SWG chair is an author), who reviews it within 10 working days. The lead author will confirm that all authors have signed off on the manuscript prior to SWG Chair review. The SWG Chair suggests revisions, if necessary, and then the lead author forwards the (revised) manuscript to the chair of the Manuscript Review Committee (MRC) with a copy to the HPTN CORE.

All MRC members have the opportunity to read the manuscript. The MRC Chair designates a primary and secondary reviewer to provide comments, one of whom will be from the SDMC. Within 10 working days of manuscript receipt, the MRC Chair will convene a conference call with the MRC to discuss the manuscript. The main author will be invited to join the call. Additional comments on the manuscript will be provided to the MRC Chair. Within one week of the conference call discussion and receiving additional reviewer comments, the MRC Chair will synthesize all comments and provide written comments to the writing team. The MRC will endorse for publication, endorse with requested modifications to be reviewed by the MRC chair or, if deemed necessary by the MRC chair, require a second MRC review to obtain PTN support. Prior to submission of manuscripts for publication, a final copy will be provided to DAIDS and to the CORE for tracking purposes.

Delay in Preparation – Primary manuscripts should be ready for submission to the Manuscript Review Committee (MRC) within eight months following the last study participant's scheduled follow-up visit. This allows time for freezing and cleaning the study data set, running analyses, describing findings, and internal review of the manuscript by the relevant Science Working Group (SWG) chair. The relevant SWG chair will monitor the writing committee's progress. The writing team chair will notify the SWG if manuscript preparation is more than 30 working days behind schedule. Should the timeline completion date of a primary manuscript submission lapse by 30 days, the SWG chair in conjunction with the PT chair has the option to appoint another writing committee chair to complete the task, who would then become senior author. If another 30 days passes and the manuscript remains unfinished, a volunteer will be sought from the protocol team to complete the project.

Post-Journal Submission – If a primary manuscript is not accepted for publication and reviewer feedback indicates a need to reformulate the essential components of the study before the manuscript can be resubmitted or submitted to another journal, the

team must submit proposed revisions to the MRC for review and endorsement. If a primary manuscript is accepted provisionally with required or recommended changes/additions, if a journal invites a revised draft of the same article, or if an article is being submitted to another journal with minimal changes, the lead author in consultation with the writing team may respond to the editor without MRC review. It is the responsibility of the team to differentiate between alterations, which reflect mere editorial changes and those that essentially modify the analyses and/or conclusion of the study previously endorsed by the MRC. Communication regarding the status will be sent to the HPTN CORE.

b. Secondary Manuscripts

For secondary manuscripts, proposals may be originated by any investigator affiliated with the study. These proposals should be submitted to the PT chair and lead statistician for review and approval. Proposals for manuscripts that contain data from more than one HPTN study must be sent to each relevant PT chair and lead statistician. A lead PT chair will be selected by the group to track the progress of manuscript development. The lead PT Chair will respond to the authors of the proposal within 15 working days after receipt of the proposal.

The development and review process for secondary manuscripts is the same as that for primary manuscripts, except there is no timeline requirement or deadline for submission to the MRC.

c. Tertiary Manuscripts

Manuscript proposals and writing schedules are not required for tertiary publications.

7. Abstracts

Authorship and preparation of abstracts will follow a streamlined process of approval. Any HIVNET investigator may prepare an abstract for presentation at scientific meetings without prior approval of concept. The completed abstract corresponding to a primary publication will be submitted to the MPC Chair, the PT Chair and the Lead Protocol Statistician for review and approval. The completed abstract corresponding to a secondary publication will be submitted to the PT Chair for review and approval. Abstracts will be reviewed within 10 working days of submission.

Abstracts reporting the preliminary or highlighted results of the HIVNET will not eliminate the necessity of preparing a full manuscript for publication.

8. Timeline and Order of Papers

Baseline Data

Following standard research study protocol publication procedures, the baseline papers will be published first. All other papers using *BASELINE* data (from the Main study or Ancillary) must delay publication processes until the main papers have been published.

All Other Data

Top priority will be given to getting the primary and secondary outcomes of the study analyzed and written. The statistical center estimates this process to take approximately 8 months and during this time it is unforeseeable that other data requests can be processed. However, data analysis plans can be written and submitted.

SCHARP will release a timeline for acceptance of future data analysis plans. Following the normal processes described above, the protocol team will review and approve the order of data request analyses.

9. Data Analysis Request and Guideline

Listed below is the preferred method for requesting and writing a statistical analysis plan for a secondary publication of a HPTN protocol.

How to get the most out of your statistical colleagues at SCHARP

Author: Deborah Donnell, on behalf of the HPTN statistical team

Primary analyses for an HPTN protocol correspond to the objectives specified in the protocol, and the protocol statistician is responsible for developing the statistical analysis plan for these objectives. Secondary publications are typically analyses of data from a protocol addressing objectives that were not part of the original protocol. For these secondary analyses an analysis plan needs to be developed, as your statistical colleagues need help from you to understand what your specific objectives are, and how you were thinking of proceeding.

Writing this analysis plan is a cooperative exercise between you and the statistician. Data analysis is a technical field and you do not have to know how to do the analysis. Because the statistician has been involved with the protocol from the beginning they are very familiar with the data set and can be very helpful about all technical aspects of the analysis. However, it is critical that you are clear about why you want to do the analysis. A careful statement of the objectives of a manuscript is fundamental to the analysis.

An analysis plan is developed before the analysis begins. The sections of the

analysis plan are described below. You should draft of sections 1, 2 and 3, and the statistician will then draft section 4.

Section 1: Objectives of the Manuscript

An objective describes, in scientific terms, what underlying question the manuscript will address. Often it will be relatively easy to state, but it is very important think very carefully about your objectives. Manuscripts are likely to have a very, very long gestation period when the objective is vague. For example, compare the vague objective “Describe the cohort enrolled in the trial and look at their HIV risk,” to the more specific objectives:

- 1) Describe the observed HIV seroincidence, by population over time, by eligibility criteria, by recruitment source.
- 2) Identify and understand risk factors for incident HIV-1 infection among all women enrolled in all the domestic HIVNET observational studies.
- 3) Determine what risk factors, both sexual and drug related, are associated with HIV-1 infection, and develop estimates of attributable risk for IDU and several measures of sexual risk.

If the objectives change, typically much of the analysis will need to be redone, and much analysis already done is discarded. Time spent thinking carefully about how to focus the manuscript is time well spent. Our experience in working with authors through many manuscripts and many protocols shows that the manuscripts that get completed are those that began with a clear objective and a draft of the final manuscript in mind at the outset.

Any introductory or background work that is fundamental to your manuscript is also helpful, as it can help us understand why you are interested in the questions, as in “This is the largest cohort of women for which information on risk factors for HIV infection among women in the US has been collected.” The statistician is usually not as familiar with the subject area and literature as you are, so references to the literature and previous analytic methods used on similar data sets are useful.

Section 2: Population, Endpoints and Covariates

This section translates the objectives into specific questions that the data available can answer. For each question, important issues are:

- 1) What is the best population to use for this analysis? Oddly enough, this is often the hardest question to answer, as you have to consider sometimes subtle issues of bias, ‘representativeness’ and relevance.
- 2) What are you going to use as the endpoint or response for your questions?

Often there are issues about the measurement and coding of the response, (e.g., Yes/No, log transform, continuous), that affect the statistical methods, the sensitivity of the analysis, and the complexity of the results.

- 3) What are the covariates of interest? These are the candidate variables of interest for association with the response. Often there is a long list of these, and with each there are issues of definition, coding, grouping, transformation. Again, since the statistician is familiar with the data, it is fine to be fairly general here, e.g. “unprotected sex”, rather than “Qu6 – Qu6a + Qu6b”, or even “Any unprotected sex with an HIV+ partner”. Part of the first stage of the analysis, producing tables and plots of the covariates and response, will inform decisions about how to code the variables.

- 4) What are likely confounders (variables that are related to both the covariates and response that could be mediating an apparent association)? What are potential effect modifiers (variables or subgroups where the relationship between response and covariate are different – e.g. gender, risk group)? Many times these arise from the study design, i.e. site, risk group. Sometimes they become apparent as the analysis progresses. There is often not clear dividing line between covariates of interest and confounders/effect modifiers.

Section 3: Manuscript Tables

Write out shells of what you envision as the main tables in the final manuscript. This is a wonderful reality check for your ideas and is extremely helpful for the statistician. It will immediately reveal layers of complexity you hadn't remembered at the outset (visit schedules, changing eligibility criteria, cohort definition). Such problems will also be revealed when the statistician tries to match the data to the tables.

Section 4: Methods

For each question, the statistician describes what statistical methods will be used to model the associations and assess statistical significance.

For a secondary manuscript, it is often difficult to know which approach will be appropriate at the onset of the analysis. Depending on the specificity of the objectives, very often this section will not be written in the first draft of the analysis plan. Quite bluntly, it is not worth detailing statistical methods until it is clear there is something in the data to support a publishable manuscript. We can return to this section after the initial tables have been produced, looking at the variables and associations of interest.

The Analysis

Once you have taken the time to work out as many of these details as you can with the statistician, the first analyses we will give you are simple univariate and bivariate summaries of the variables and associations of greatest interest. Usually there will be some interaction and further refinement as unexpected findings are investigated. During this process variables of interest are identified, and variable codings are refined for the next phase.

The second phase usually entails statistical modeling and may identify the findings of greatest interest for the manuscript. Again, the phase is usually interactive, as results emerge and further refinements occur.

If at all possible, the ideal is for both parties to be very responsive while each of these phases are occurring. For both the writer and the statistician, if there are weeks of delay in responding to requests or reports, you tend to forget the details of the project and the effort to get started again creates further delays. At a minimum, it can be helpful to plan times when both parties can be responsive.

The Manuscript

Begin writing the manuscript at the earliest possible time. Our experience is that the thinking required to write the manuscript helps keep the analysis focused on the relevant and important findings. It is very easy when investigating data from studies with very complex multidimensional data to find fascinating and interesting avenues to explore. They are also extremely complex and time-consuming to code, report and document. Rather than heading off on a tangent, focus on completing the original analysis.

The statistician will usually provide a draft of the methods section for the paper. They will also help in writing or reviewing the results and conclusions sections, focusing on whether the conclusions are warranted from the results of the analysis.

10. Site Specific Data and Publications (see Section H.4.b, Single Site vs. Multi-Site)

11. Ancillary Studies

Ancillary studies will follow publication policies listed above.