The Fundamentals of International Clinical Research Workshop
February 2004

DEVELOPING AN ANALYTICAL PLAN
Mario Chen, PhD.
Family Health International
The Analysis Plan for a Study

✦ Summary Analysis Plan:
  – Principal Features of Statistical Methodology
  – Purposes:
    • Assuring objectives can be achieved.
    • Justifying design and data collection.

✦ Detailed Analysis Plan:
  – Detailed description of Statistical Methodology.
Before Starting an Analytical Plan

✿ Objectives and Endpoints:
  – Estimation of parameters.
  – Group comparisons.
  – Associations of interest.

✿ Design issues:
  – Type of study (cross-sectional, retrospective, prospective, RCT).
  – Sample selection or recruitment.
  – Matching.
Analysis Plan: Analysis Populations

- **Intent-to-treat**: No one is excluded. Analyses are performed by treatment assigned.
- **Treated**: Participants who never received treatment or never provided follow-up data are excluded.
- **Per protocol**: Participants who had major protocol violations are excluded.
Missing Data Considerations

- Data collection problems.
- Informative missing.
- Imputation methods.
- Sensitivity analysis.

BIAS
Analysis Plan: Statistical Methodology (Crude Analysis)

For an objective designed to estimate parameters:
- Key parameter(s) to be estimated.
- Sub-populations.
- Method of calculating variance and confidence intervals.
Analysis Plan: Statistical Methodology (Crude Analysis)

For an objective designed to test hypothesis:
- Research hypotheses to be tested (Statistical Hypotheses).
- Statistical tests to be employed.
- Alternative tests if assumptions are violated.
- Level of significance.
- Direction of the tests (one vs. two-sided).
Analysis Plan: Statistical Methodology (Adjusted Analyses)

**Adjusted Analyses (Modeling techniques):**

- Model to be fitted (e.g., Linear, Logistic, Poisson Regression, Mixed Models or GEE, Cox proportional hazards Model).

- **Model specification:** Main variables (exposure, treatment variable); Confounding variables (age, baseline severity); Interactions.

- Variable selection procedures.

- Model checks.
Analysis Plan: Statistical Methodology (Other Aspects)

- Accounting for design features:
  - Matching.
  - Repeated measures.
  - Clustering.

- Adjustment of significance and confidence levels due to multiplicity:
  - Multiple primary endpoints.
  - Multiple comparison groups.
  - Repeated evaluation over time (interim analysis).
Analysis Plan: Interim Analyses

🌟 Early termination:
  – Serious adverse events in the intervention group.
  – Greater than expected beneficial effects.
  – Evidence of improbable significant result at the end of study.

🌟 Needs for collection of additional data.

🌟 Independent and blind review of the data.
Analysis Plan: Interim Analyses (cont-d)

✦ Timing, methodology and frequency of analyses.
✦ What will be done with the results of the analyses.
✦ Early stopping rules.
✦ Data and Safety Monitoring Board.
Analysis Plan: Template Example

I. Objectives.

II. Analysis Populations.

III. Analysis of Baseline Data.

IV. Analysis of Participant Follow-up:
   a) Participant flow.
   b) Discontinuations.
   c) Protocol violations.
Analysis Plan: Template example, cont.

V. Analysis of Primary objectives:
   a) Descriptive Analysis.
   b) Crude Analysis.
   c) Adjusted Analysis.

VI. Analysis of Secondary objectives.

VII. Analysis of Interim Data.

VIII. Other Planned analyses:
   a) Sensitivity analyses.
   b) Subgroup analyses.
Summary Analysis Plan

✦ Describe statistical methods to be employed for each of the objectives of the study.
✦ Provide sufficient details regarding the analysis of the primary objective(s) and important secondary objectives. More general statements can be used for other secondary objectives.
✦ Clearly linked to objectives, endpoints and sample size.
✦ Timing, methodology, and frequency of Interim analyses.
Final Remarks

- A summary analysis plan needs to be included in the protocol.
- A more detailed analysis plan should be written before starting data analysis:
  - Helps you prepare for report and manuscript writing.
  - Helps in the validity and credibility of the results.