# This is a template SAP example for a primary endpoint of a randomized clinical trial.

## 1. STUDY SUMMARY AND AIMS

**Study Purpose**: *Brief statement of purpose.*

**Study Design**: *Describe design (e.g. non-blinded multisite two-arm randomized non-inferiority clinical trial). Briefly describe arms.*

**Study Population and Sites**: *Brief statement of who will be included (e.g. HIV-infected adults on ART for at least for >18 months) and study sites.*

**Study Size**: *Total and per arm*

**Study Duration**: *Approximate total duration, accrual period, and follow-up period.*

**Treatment Regimen**: *Specific treatment information for each arm (e.g dosage, frequency for drug studies.)*

**Primary Aims:** *List of aims that can be easily translated into well-defined outcomes and statistical hypotheses, for example:*

## 2. STUDY ENDPOINTS

*Specify definitions for study endpoints.*

## 3. SAMPLE SIZE CONSIDERATIONS

*Specify which aim(s) drive the sample size calculations.*

*Specify and define your statistical measure of effect, for example: mean difference between intervention and control arms, hazard ratio comparing intervention to control arm, etc.*

*State the null and alternative hypotheses in terms of your statistical measure.*

*Referencing your statistical measure of effect, specify the difference between treatment arms that you would like to be able to detect. This should be the minimum difference that you judge to be clinically or scientifically meaningful.*

*Make explicit any assumptions about the control group (or in certain cases, the intervention group) that you make in your sample size calculations, for example estimates of incidence rates, means, or variances. Provide references to prior studies if applicable.*

*Specify alpha (usually 0.05), power (usually 80% or 90%), and whether you're conducting a one-sided or two-sided test (usually two-sided).*

*State the sample size you will need, based on the values you've selected for alpha, power, and difference between treatment arms. Give details on total sample size and size per arm.*

## 4. ANALYSIS SETS

*For a randomized clinical trial, clarify what data will be used in intent-to-treat (ITT) versus per-protocol analyses. In particular, specify how you will handle data for "crossovers", i.e. participants who are assigned to control regimen but follow the intervention regimen or vice versa.*

## 5. STATISTICAL ANALYSES AND DESCRIPTION OF MAIN TABLES

*Describe the main tables and statistical analyses that will be prepared at the end of the trial and for DSMB meetings if applicable. Include references to shell tables and figures.*

*This section should include a sub-section for each study aim describing the statistical analyses that you will conduct for that aim. Include information on:*

- *The statistical technique: be as specific as possible.*
- *Other* a priori *analysis-related decisions, e.g. method for handling tied survival times, method for handling correlated data, what variables (and in what form) will be included in the model*
- *Provide references for non-standard statistical methods.*

*This section may also describe other analyses you will conduct to assess:*

- *Study accrual*
- *Baseline characteristics*
- *Retention*
- *Treatment crossover/non-compliance rates*
- *Safety endpoints such as adverse events*

*Throughout this section, you can include references to shell tables and figures (these can be placed in an Appendix).*

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**Randomization scheme text for a randomized, unblinded study**

[Adapted from Dr Barbra Richardson]

Participants will be randomized to either arm X or Y at enrollment. A block randomization scheme with variable block sizes will be generated using STATA 8.0 (ralloc.ado v2.2.1). Treatments will be allocated in 1:1 ratio. Study investigators and staff will be blinded to the block number, block size and sequence in the block. Arms will be assigned via pre-prepared sealed, opaque envelopes and the envelopes will be ordered in the sequence of arm assignments generated by the STATA code. Once a participant's eligibility for enrollment has been determined, the first available allocation envelope will be assigned to the participant. The participant will be randomized to the treatment arm indicated inside the envelope.

The randomization code will be maintained by the Study Coordinator at the study site. The treatment allocation will be un-blinded once it is assigned.

## 6. INTERIM ANALYSIS PLAN

*Provide details on any planned interim analyses, including boundaries used for benefit and harm, as well as details on the alpha spending function as applicable.*

## 7. REFERENCES

## 8. PROPOSED TIMELINE

| Activity | Jan to Jun '12 | July to Dec '12 | Jan to Jun '13 | July to Dec '13 | Jan to Jun '14 |
|---|---|---|---|---|---|
| **Proposal writing** | | | | | |
| **Data abstraction** | | | | | |
| **Data cleaning and analysis** | | | | | |
| **Thesis writing** | | | | | |
| **Defending thesis** | | | | | |
| **Manuscript writing** | | | | | |

## 9. APPENDIX: SHELL TABLES AND FIGURES

*Provide shells of all the tables and figures described in section 4. They will be empty but should otherwise look like tables/figures for manuscripts or DSMB reports with respect to general format, captions, table structure, row and column labels, figure legends, etc.*

*NOTE: Tables stratified by randomization arm will be included in the DSMB Closed Report.*

Figure 1: Trial Profile

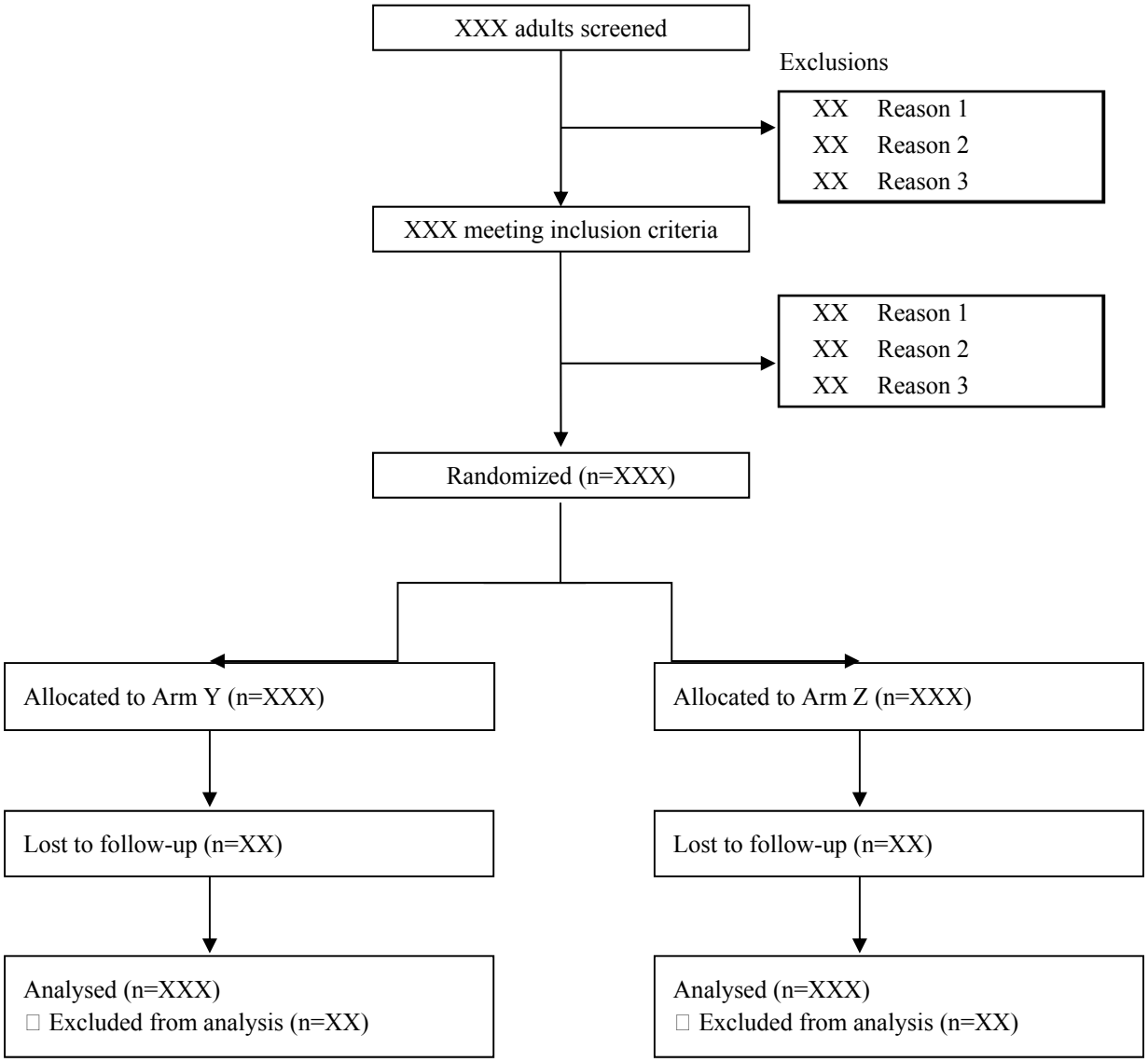

Table 1a. Characteristics of the study participants at baseline.

| **Characteristic** | **N (%) or Median (IQR)**<br>**N= XXX** |
|---|---|
| Female gender | |
| Age, years | |
| Marital status | |
| Married | |
| Divorced/separated/widowed | |
| Single | |
| Education (highest completed) | |
| Less than primary | |
| Primary school | |
| Secondary school | |
| Vocational school | |
| University | |
| Estimated monthly income (Kenyan Shillings) | |
| <5,000 | |
| ≥ 5,000 | |
| Number of household residents | |
| Number of rooms in residence | |
| Water source | |
| Piped or well water | |
| Environmental water source | |
| Toilet type | |
| Flush toilet | |
| Pit latrine | |
| Bush | |
| Bed net use | |
| Boil or purify drinking water | |
| Hospitalized in past three months | |
| Screening CD4, cells/$mm^3$ | |
| Enrollment CD4, cells/$mm^3$ | |

Table 1b: Characteristics of the study participants at baseline, by study arm.

| Characteristic | Arm Y<br>N (%) or Median (IQR)<br>N= XXX | Arm Z<br>N (%) or Median (IQR)<br>N= XXX |
|---|---|---|
| Female gender | | |
| Age, years | | |
| Marital status | | |
| Married | | |
| Divorced/separated/widowed | | |
| Single | | |
| Education (highest completed) | | |
| Less than primary | | |
| Primary school | | |
| Secondary school | | |
| Vocational school | | |
| University | | |
| Estimated monthly income (Kenyan Shillings) | | |
| <5,000 | | |
| ≥ 5,000 | | |
| Number of household residents | | |
| Number of rooms in residence | | |
| Water source | | |
| Piped or well water | | |
| Environmental water source | | |
| Toilet type | | |
| Flush toilet | | |
| Pit latrine | | |
| Bush | | |
| Bed net use | | |
| Boil or purify drinking water | | |
| Hospitalized in past three months | | |
| Screening CD4, cells/$mm^3$ | | |
| Enrollment CD4, cells/$mm^3$ | | |

## Table 2a. Study retention

| | **N (%)<br>N=XXX** |
|---|---|
| Attendance at study visit: ***** | |
| Month 0 (enrollment visit) | |
| Month 3 | |
| Month 6 | |
| Month 9 | |
| Month 12 | |
| Lost to follow up: | |
| Deaths: | |
| Withdrawals: | |

* Denominator for percentage is the number of participants expected to attend visit

## Table 2b. Study retention, by study arm.

| | **Arm Y<br>N(%)<br>N=XXX** | **Arm Z<br>N(%)<br>N=XXX** |
|---|---|---|
| Attendance at study visit:* | | |
| Month 0 (enrollment visit) | | |
| Month 3 | | |
| Month 6 | | |
| Month 9 | | |
| Month 12 | | |
| Lost to follow up: | | |
| Deaths: | | |
| Withdrawals: | | |

* Denominator for percentage is the number of participants expected to attend visit

Table 3a. List of Study Withdrawals

| Participant ID | Time of Withdrawal (Study Day) | Reason for Withdrawal |
|---|---|---|
| | | |
| | | |
| | | |
| | | |

Table 3b. List of Study Withdrawals by Arm

| Participant ID | Time of Withdrawal (Study Day) | Reason for Withdrawal |
|---|---|---|
| ARM Y | | |
| | | |
| | | |
| ARM Z | | |
| | | |
| | | |
| | | |

Table 4. Compliance to randomization arm assignment

| | Discontinuation Arm N=XXX | Continuation Arm N=XXX |
|---|---|---|
| N(%) taking TMP/SMZ at follow-up visit: | | |
| Month 3 | | |
| Month 6 | | |
| Month 9 | | |
| Month 12 | | |

Table 5. Details of TMP/SMZ re-start in those randomized to discontinue TMP/SMZ.

| Participant ID | Time of TMP/SMZ Re-start (Study Day) | Reason for TMP/SMZ Re-start |
|---|---|---|
| | | |
| | | |
| | | |

Table 6. Morbidity incidence rates by randomization arm.

| | **Arm Y**<br>**Incidence per 100 person years**<br>**(number of cases)**<br>**XX.X py total** | **Arm Z**<br>**Incidence per 100 person years**<br>**(number of cases)**<br>**XX.X py total** |
|---|---|---|
| Combined outcome of malaria, pneumonia, diarrhea, and mortality | | |
| HR (90% CI) & p value ;<br>Arm Y / Arm Z | | |

Table 7: Mean change in CD4 count per year controlling for baseline values

| | **Arm Y** | **Arm Z** | **p-value of the interaction** |
|---|---|---|---|
| Mean change in CD4 (cells/$mm^3$/year) | | | |

Table 8: Mean CD4 count by arm

| | **Arm Y** | **Arm Z** |
|---|---|---|
| CD4, cells/$mm^3$/year; mean(SD) | | |
| Month 0 | | |
| Month 6 | | |
| Month 12 | | |

Figure 2. CD4 Counts for Randomized Subjects by Arm

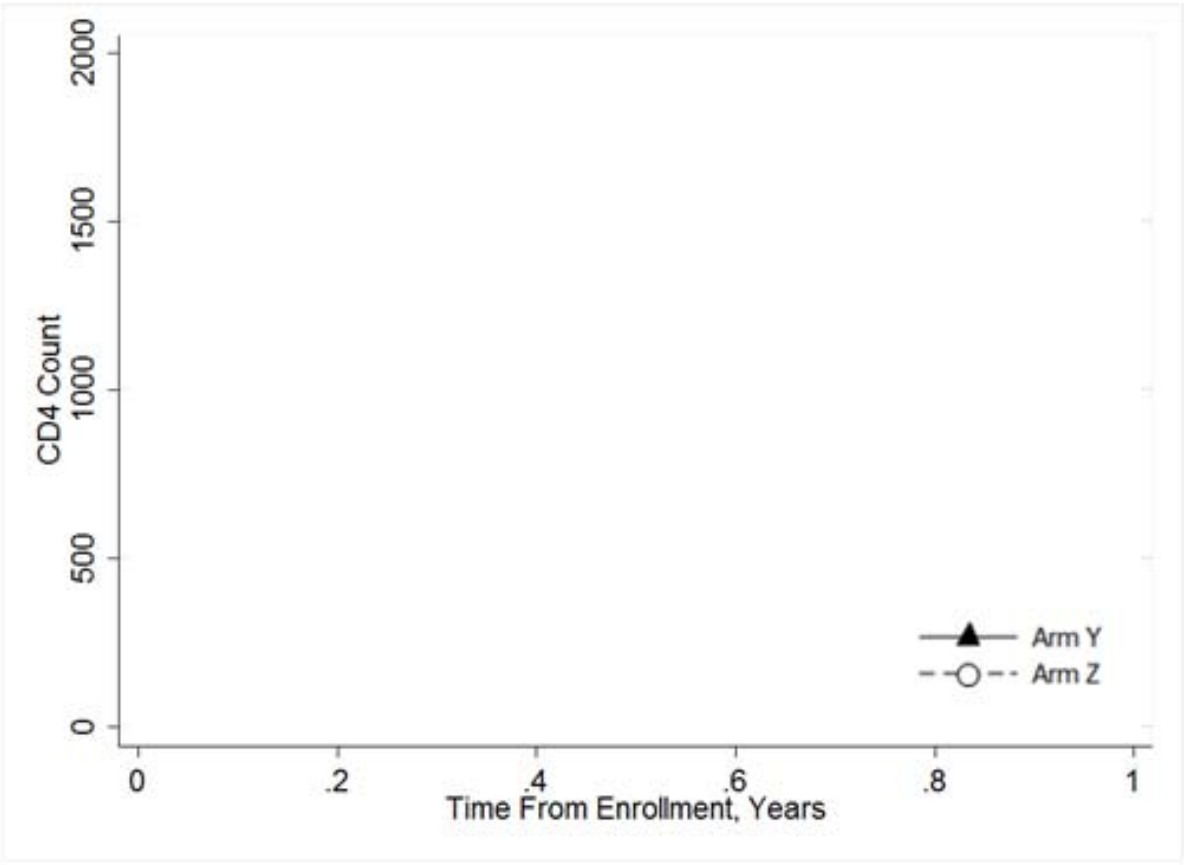


Table 9. ART treatment failure rates by randomization arm.

| | **Arm Y**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Arm Z**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** |
|---|---|---|
| ART treatment failure (clinical, immunologic, or virologic)) | | |

Figure 3. Kaplan-Meier plot of time to ART treatment failure by randomization arm

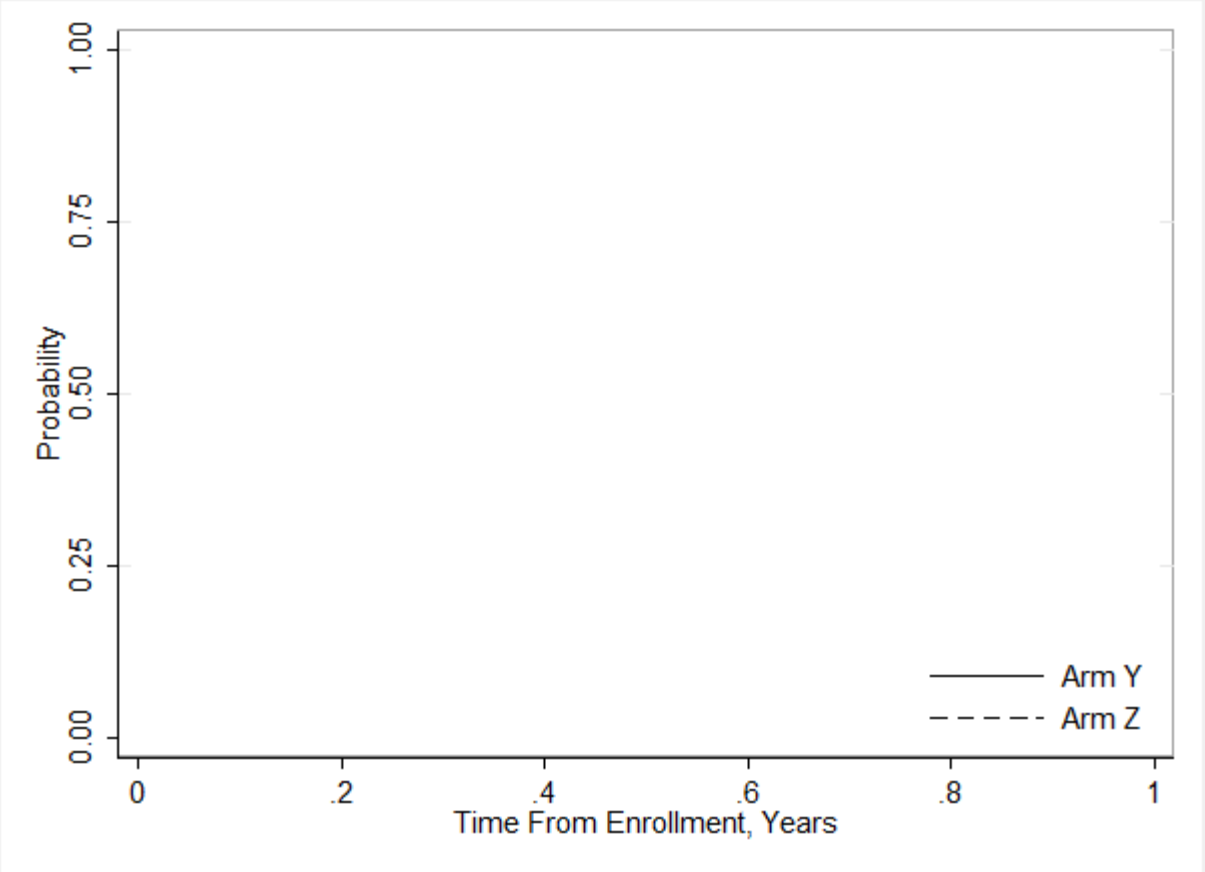


Table 10. Rates of 1) any Grade 2 or higher and 2) any Grade 3 or higher adverse events (AEs), by randomization arm.

| | **Arm Y**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Arm Z**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** |
|---|---|---|
| Any grade 2 or higher AEs | | |
| Any grade 3 or higher AEs | | |

Table 11. Incidence rates for common Adverse Events by randomization arm.

| **Condition** | **Arm Y**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Arm Z**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Hazard ratio (95% CI)**<br>**Arm Y**<br>**Arm Z** | **p-value** |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |

Table 12. Summary of Serious Adverse Events by randomization arm.

| | **Arm Y**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Arm Z**<br>**Incidence per 100 person years (number of cases)**<br>**XX.X py total** | **Hazard ratio (95% CI)**<br>**Arm Y**<br>**Arm Z** | **p-value** |
|---|---|---|---|---|
| Any serious adverse event | | | | |

Table 13. List of adverse events by randomization arm.

| **AE Number** | **Subject's AE Number** | **Subject ID** | **Condition** | **Category** | **Grade** | **Duration (Days)** |
|---|---|---|---|---|---|---|
| **ARM Y** | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| **ARM Z** | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

## 10. APPENDIX: CFAR ACKNOWLEDGEMENT.

https://depts.washington.edu/cfar/discover-cfar/acknowledge-cfar

We would kindly request that you acknowledge the CFAR and assistance by its Cores and Programs in your publications, abstracts, grants, and presentations. You can also click on the above link to download the CFAR logo.

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