|  |
| --- |
| **Statistical Analysis Plan (SAP)****This document is modified from the guidelines. If you are interested in publishing your SAP or submitting the SAP as supplementary material to your research article, you must follow the structure from the guidelines cited below and revise the administrative information. You can find an explanation for each item in the document “SAP\_explanation (e.Apendix2).”** |
| Table of content | 1. Objectives
2. Trial design
3. Randomization
4. Sample size
5. Framework
6. Statistical interim analysis and stopping guidance
7. Timing of final analysis
8. Timing of outcome assessments
9. Confidence intervals and P values
10. Adherence and Protocol deviations
11. Analysis of the population
12. Screening data
13. Eligibility
14. Recruitment
15. Withdrawal/ Follow-up
16. Baseline patient characteristics
17. Outcome definitions
18. Analysis methods
19. Missing data
20. Additional analyses
21. Harms
22. Statistical software
23. Additional items to the statistical analysis plan
 |
| **OBJECTIVES** |
| 1. Objectives  | Description of specific objectives or hypotheses, e.g. *“To develop and evaluate a diagnostic model identifying patients with kidney disease… “* OR *“The null hypothesis is that there is no difference in time to first bloodstream infection between the standard and impregnated (antibiotic and heparin combined) groups. The alternative hypothesis is that there is a difference between the two groups.”* |
| **STUDY METHODS** |
| 2. Study design | Description of study design. **[Only required for RCT]:** Brief description of trial design, including the type of trial (e.g., parallel-group, multi-arm, crossover, factorial), and may include a short description of interventions |
| 3. Randomization | **[Only required for RCT]**: Randomization details, e.g., whether any minimization or stratification occurred (including stratifying factors used or the location of that information if it is not held within the SAP) |
| 4. Sample size | **[Refer to protocol if necessary]** Complete sample size calculation or reference to sample size calculation in protocol |
| 5. Framework | **[Only required for RCT]:** Superiority, equivalence, or noninferiority hypothesis testing framework, including which comparisons will be presented on this basis |
| 6. Timing of outcome assessments | **[Only required for RCT and prospective clinical studies]**: Time points at which the outcomes are measured, including time frames for visits |
| 7. Statistical interim analysis and stopping guidance | **[Only required for RCT and prospective clinical studies]:**Information on interim analyses specifying what interim analyses will be carried out and listing of time pointsAny planned adjustment of the significance level due to interim analysisDetails of guidelines for stopping the trial early |
| 8. Timing of final analysis | **[Refer to time plan in protocol if necessary]**Timing of final analysis, e.g., all outcomes analyzed collectively or timing stratifiedby the planned length of follow-up e.g. anticipated to be November 2010 |
| **STATISTICAL PRINCIPALS** |
| 9. Confidence intervals and P values | Level of statistical significance (P values) and whether one‐ or two‐sided and confidence intervals to be reportedDescription and rationale for any adjustment for multiplicity and, if so, detailing how the type 1 error is to be controlled |
| 10. Adherence and Protocol deviations | **[Only required for RCT and prospective clinical studies]**: Definition of adherence to the intervention and how this is assessed, including the extent of exposureExplanation of protocol deviations for the trial Description of which protocol deviations will be summarized |
| 11. Analysis of populations | **[Only required for RCT]:**Definition of analysis populations, e.g., intention to treat, per protocol, complete case, safety |
| **STUDY POPULATION** |
| 12. Screening data | **[Refer to protocol if necessary]**Reporting of screening data (if collected) to describe the representativeness of the trial sample  |
| 13. Eligibility | **[Refer to protocol if necessary]**Summary of eligibility criteria, inclusion, and exclusion criteria |
| 14. Recruitment | **[Only required for RCT and prospective studies]:** Recruitment strategy. Information to be included in the CONSORT flow diagram |
| 15. Withdrawal/ Follow-up | **[Only required for RCT and prospective studies]:** Level of withdrawal, e.g., from intervention and/or from follow-upTiming of withdrawal/loss to follow-up dataReasons and details of how withdrawal/loss to follow-up data will be presented |
| 16. Baseline patient characteristics | List of baseline characteristics to be summarized (Typically Table1)Details of how baseline characteristics will be descriptively summarized |
| **ANALYSIS** |
| 17. Outcome definitions | **[Refer to Data Management Plan if necessary]**List and describe each primary and secondary outcome, including details of:Specification of outcomes and timings. If applicable, include the order of importance of primary or key secondary endpoints (e.g., the order in which they will be tested)Specific measurement and units (e.g., glucose control, hbA1c [mmol/mol or %]) Any calculation or transformation used to derive the outcome (e.g., change from baseline, QoL score,Time to event, logarithm, etc.)  |
| 18. Analysis methods | **[For guiding you can check the statistical decisiontree]**For each objective:What analysis method will be used, and how the treatment effects will be presented Any adjustment for covariatesAny planned sensitivity analyses for each outcome, where applicableAny planned subgroup analyses for each outcome, including how subgroups are defined |
| 18a. Model diagnostics | Methods used for assumptions to be checked for statistical methodsDetails of alternative methods to be used if distributional assumptions do not hold, e.g., normality,proportional hazards, etc. |
| 19. Missing data | Reporting and assumptions/statistical methods to handle missing data (e.g., multiple imputation) |
| 20. Additional analyses | Details of any additional statistical analyses required, e.g., complier-average causal effect10 analysis |
| 21. Harms | **[Only required for RCT and prospective studies]:** Sufficient detail on summarizing safety data, e.g., information on severity, expectedness, and causality;details of how adverse events are coded or categorized; how adverse event data will be analyzed,i.e., grade 3/4 only, incidence case analysis, intervention emergent analysis |
| 22. Statistical software | Details of statistical packages to be used to carry out analyses. |
| 23. Aditional items to the statistical analysis plan | The following items are required if you are planning to publish your SAP |
| **ADMINISTRATIVE INFORMATION** |
| Title | A descriptive title that matches the protocol, with SAP either as a forerunner or subtitle,and trial acronym (if applicable) |
| Trial and Trial registration | [**Only required for RCT]**Trial registration number |
| SAP Version | SAP version number with dates |
|  Protocol Version | Reference to the version of the protocol being used |
| SAP revisions | SAP revision historyJustification for each SAP revisionTiming of SAP revisions in relation to interim analyses, etc. |
| Roles and responsibility | Names, affiliations, and roles of SAP contributors |
| Signatures of: | The person writing the SAPSenior statistician responsibleChief investigator/clinical lead |
| **INTRODUCTION** |
| Background and rationale | [**Refer to protocol if necessary]**Synopsis of trial background and rationale including a brief description of the research question and brief justification for undertaking the trial |
| **REFERENCES** |
| References | References to be provided for nonstandard statistical methodsReference to Data Management PlanReference to the Trial Master File and Statistical Master FileReference to other standard operating procedures or documents to be adhered to |
| **Taken from the paper:** Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Doré C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337-43.**Detail explanation list of each item in the SAP**: Microsoft Word - JSC170004supp1\_edited (jamanetwork.com) **Abbreviations:** CONSORT, Consolidated Standards of Reporting Trials; hbA1c, haemoglobin A1c; QoL, quality of life; SAP, statistical analysis plan. |

**t**