# TABLE 1. STREGA reporting recommendations, extended from STROBE Statement

| **Item** | **Item number** | **STROBE Guideline** | **Extension for Genetic Association Studies (STREGA)** | **Relevant text from manuscript** |
| --- | --- | --- | --- | --- |
| **Title and Abstract** | 1 | (a) Indicate the study’s design with a commonly used term in the title or the abstract. |  | Title: “unsupervised, phenotypic clustering analysis”Abstract: “genome-wide association study” |
| (b) Provide in the abstract an informative and balanced summary of what was done and what was found. |   | Abstract: Methods and Findings |
| **Introduction** |  |  |
| *Background rationale* | 2 | Explain the scientific background and rationale for the investigation being reported. |  | Abstract: BackgroundIntroduction |
| *Objectives*  | 3 | State specific objectives, including any pre-specified hypotheses. | ***State if the study is the first report of a genetic association, a replication effort, or both.***  | Introduction: Paragraph 4 |
| **Methods** |  |  |
| *Study design* | 4 | Present key elements of study design early in the paper. |  | Abstract: Methods and FindingsMethods |
| *Setting* | 5 | Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up, and data collection. |  | Methods: SubjectsData Availability  |
| *Participants* | 6 | 1. **Cohort study –** Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.

**Case-control study –** Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls.**Cross-sectional study –** Give the eligibility criteria, and the sources and methods of selection of participants. | ***Give information on the criteria and methods for selection of subsets of participants from a larger study, when relevant***.  | Methods: SubjectsMethods: ClusteringMethods: Association Testing |
| 1. **Cohort study –** For matched studies, give matching criteria and number of exposed and unexposed.

**Case-control study –** For matched studies, give matching criteria and the number of controls per case. |  |  |
| *Variables* | 7 | *(a)* Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. |  ***(b)*** ***Clearly define genetic exposures (genetic variants) using a widely-used nomenclature system. Identify variables likely to be associated with population stratification (confounding by ethnic origin).*** | Methods: ClusteringMethods: Association Testing |
| *Data sources measurement*  | 8**\*** | *(a)* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. |  ***(b)*** ***Describe laboratory methods, including source and storage of DNA, genotyping methods and platforms (including the allele calling algorithm used, and its version), error rates and call rates. State the laboratory/centre where genotyping was done****.* ***Describe comparability of laboratory methods if there is more than one group. Specify whether genotypes were assigned using all of the data from the study simultaneously or in smaller batches.***  | Table S1Methods: Association Testing |
| *Bias* | 9 | *(a)* Describe any efforts to address potential sources of bias.  | ***(b) For quantitative outcome variables, specify if any investigation of potential bias resulting from pharmacotherapy was undertaken. If relevant, describe the nature and magnitude of the potential bias, and explain what approach was used to deal with this.*** | Not applicable |
| *Study size* | 10 | Explain how the study size was arrived at.  |  | Methods: SubjectsMethods: Clustering |
| *Quantitative variables* | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why. | ***If applicable, describe how effects of treatment were dealt with.*** | Methods: Clustering |
| Statistical methods  | 12 | (a) Describe all statistical methods, including those used to control for confounding. | ***State software version used and options (or settings) chosen.*** | Methods: Association TestingData Availability |
| (b) Describe any methods used to examine subgroups and interactions. |  | Methods: ClusteringMethods: Identifying subtypes in PCOS families |
| (c) Explain how missing data were addressed. |  | Methods: ClusteringMethods: Association Testing  |
| 1. **Cohort study –** If applicable, explain how loss to follow-up was addressed.

**Case-control study –** If applicable, explain how matching of cases and controls was addressed.**Cross-sectional study –** If applicable, describe analytical methods taking account of sampling strategy. |  | Methods: Association Testing |
| (e) Describe any sensitivity analyses. |  | Not Applicable |
|  |  |  | ***(f) State whether Hardy-Weinberg equilibrium was considered and, if so, how****.*  | Methods: Association Testing (Paragraph 1) |
|  |  |  | ***(g) Describe any methods used for inferring genotypes or haplotypes.***  | Methods: Association Testing (Paragraph 1) |
|  |  |  | ***(h) Describe any methods used to assess or address population stratification.***  | Methods: Association Testing |
|  |  |  | ***(i) Describe any methods used to address multiple comparisons or to control risk of false positive findings.***  | Methods: Association Testing |
|  |  |  | ***(j) Describe any methods used to address and correct for relatedness among subjects*** | Methods: SubjectsMethods: Identifying subtypes in PCOS families |
| **Results** |  |  |
| *Participants* | 13**\*** | 1. Report the numbers of individuals at each stage of the study – e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed.
 | ***Report numbers of individuals in whom genotyping was attempted and numbers of individuals in whom genotyping was successful.*** | Methods |
| (b) Give reasons for non-participation at each stage. |  | Methods |
| (c) Consider use of a flow diagram. |  | Not Applicable |
| *Descriptive data*  | 14**\*** | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. | ***Consider giving information by genotype****.*  | Methods: SubjectsResults: PCOS subtypesTable 1 |
| (b) Indicate the number of participants with missing data for each variable of interest. |  | Methods: ClusteringTable 1 |
| 1. **Cohort study –** Summarize follow-up time, e.g. average and total amount.
 |  | Not Applicable |
| *Outcome data* | 15 **\*** | **Cohort study-**Report numbers of outcome events or summary measures over time. | ***Report outcomes (phenotypes) for each genotype category over time*** |  |
| **Case-control study –** Report numbers in each exposure category, or summary measures of exposure. | ***Report numbers in each genotype category*** |  |
| **Cross-sectional study –** Report numbers of outcome events or summary measures. | ***Report outcomes (phenotypes) for each genotype category*** | Results: PCOS subtypesResults: Subtype genetic associationsTables 1-3 |
| *Main results* | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence intervals). Make clear which confounders were adjusted for and why they were included. |  | MethodsResults: Subtype genetic associationsTable 3Figure 6 |
| (b) Report category boundaries when continuous variables were categorized. |  | Results: PCOS subtypes |
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. |  | Not applicable |
|  |  |  | ***(d) Report results of any adjustments for multiple comparisons.***  | Table 1Results: PCOS subtypesFigure 2Results: Subtype genetic associationsTable 3 |
| *Other analyses* | 17 | 1. Report other analyses done – e.g., analyses of subgroups and interactions, and sensitivity analyses.
 |  | Figures 10-11Results:Subtypes in PCOS families |
|  |  |  | ***(b) If numerous genetic exposures (genetic variants) were examined, summarize results from all analyses undertaken.*** | Results: Subtype genetic associationsResults:Subtypes in PCOS families |
|  |  |  | ***(c) If detailed results are available elsewhere, state how they can be accessed.*** | Data Availability |
| **Discussion** |  |  |
| *Key results* | 18 | Summarize key results with reference to study objectives. |  | Discussion: Paragraph 1 |
| *Limitations* | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. |  | Discussion: Paragraphs 10-12 |
| *Interpretation*  | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. |  | Discussion: Paragraphs 1-9 |
| *Generalizability*  | 21 | Discuss the generalizability (external validity) of the study results. |  | Discussion: Paragraphs 10-14 |
| **Other Information** |  |  |
| *Funding* | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. |  | Acknowledgements |

STREGA = STrengthening the REporting of Genetic Association studies; STROBE = STrengthening the Reporting of Observational Studies in Epidemiology.

\* Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.