Analytical Plan for Association between four risk scores and myocardial infarction: case-control stratified analysis

DOCUMENT: SAP-2023-023-HY-v01

From: Felipe Figueiredo **To:** hsyed5 (fiverr.com)

2023-07-11

TABLE OF CONTENTS

Analytical Plan for Association between four risk scores and myocardial infarction: case-control stratified analysis

Document version

Version	Alterations
01	Initial version

1 ABBREVIATIONS

- ACS: Acute coronary syndrome
- CI: confidence interval
- GRACE: The Global Registry of Acute Coronary Events
- HEART: History, Electrocardiogram, Age, Risk factors, and initial Troponin
- MI: myocardial infarction
- OR: odds ratio
- SD: standard deviation
- TIMI: Thrombolysis in myocardial infarction
- VCS: Vancouver chest pain score

2 CONTEXT

2.1 Objectives

1. To determine the effect of the association between the four risk instruments (GRACE, TIMI, HEART and VCS) and the occurrence of MI, stratifying by sex and race;
2. To rank the four risk instruments according to the estimated effect.

2.2 Hypotheses

1. Cases have a higher GRACE score compared to controls, after controlling for sex;
2. Cases have a higher GRACE score compared to controls, after controlling for race;
3. Cases have a higher TIMI score compared to controls, after controlling for sex;
4. Cases have a higher TIMI score compared to controls, after controlling for race;
5. Cases have a higher HEART score compared to controls, after controlling for sex;
6. Cases have a higher HEART score compared to controls, after controlling for race;
7. Cases have a higher VCS score compared to controls, after controlling for sex;
8. Cases have a higher VCS score compared to controls, after controlling for race.

3 DATA

3.1 Raw data

Upon study start the raw data will be collected in a raw table, that will be processed before analysis. The raw dataset to be collected will have 9 variables collected.

Table 1 shows the structure of the raw dataset.

Table 1 *Raw dataset structure.*

id	outcome	sex	age	race	grace	timi	heart	vcs
1								
2								
3								
…								
N								

Each row represents all information collected from each study participant, and each participant included will require a unique study ID. The outcome should be recorded as a binary variable: either the study participant reached the endpoint (MI diagnosis at admission) or reached the end of study period without experiencing the event. This information can be recorded in either text form (eg, yes/no), or an indicator (MI diagnosis at admission = 1, non-MI at admission = 0).

Sex will be recorded as a binary variable. Self-reported race will be recorded as a categorical variable. It is recommended that the number of classes (races) be as small as possible, to avoid loss of precision in the analysis estimates, without the need to increase the sample size. Broader categories of ethnicity should be preferred, whenever possible.

3.2 Analytical dataset

The four risk scores (GRACE, TIMI, HEART and VCS) will be dichotomized into “high-risk” and “others” groups prior to analysis.

After the cleaning process 9 variables will be included in the analysis. The total number of observations excluded due to incompleteness and exclusion criteria will be reported in the analysis.

All variables in the analytical set will be labeled according to the raw data provided and values will be labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Study design

This is a case-control retrospective study, based on hospital records.

4.2 Inclusion and exclusion criteria

The study period will be defined in the study protocol. All participants who were admitted to the medical medical floor, step down unit or medical ICU at the North Central Bronx hospital during the study period are eligible for inclusion.

4.3 Exposures

- GRACE score group
- TIMI score group
- HEART score group
- VCS score group

4.4 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) ACS
2. (Specific measurement) MI
3. (Specific metric) End-value
4. (Method of aggregation) Odds

Primary outcome

Odds of MI in participants.

4.5 Covariates

- Sex
- Self-reported race

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described. Demographic and clinical variables will be described as mean (SD) or as counts and proportions (%), as

appropriate. The distributions of participants' characteristics will be summarized in tables and visualized in exploratory plots.

5.1.2 Inferential analyses

Differences in distribution of categorical variables will be assessed with the chi-square test without Yates correction. The OR will be used as a measure of effect of the independent variable on the dependent variable.

The stratification by sex and race will be used to assess if the effect changes across male and female strata, and by race strata. As a rule of thumb, a minimum change of 20% in the OR will be considered before concluding that there is an interaction between the stratification variable and the independent variable. The homogeneity of the OR across strata will be assessed with the Cochran-Mantel-Haenszel test.

After calculations are made the OR for all instruments will be ranked, across both stratifying variables.

5.1.3 Statistical modeling

N/A

5.1.4 Missing data

No missing data imputation will be performed. All evaluations will be performed as complete case analyses. Missing data counts and proportions will be reported in tables.

5.2 Significance and Confidence Intervals

All analyses will be performed using the significance level of 5%. All significance hypothesis tests and confidence intervals computed will be two-tailed.

5.3 Study size and Power

It is intended that data from 2,300 participants will be included in the study.

5.4 Statistical packages

This analysis will be performed using statistical software R version 4.3.0.

6 OBSERVATIONS AND LIMITATIONS

Recommended reporting guideline

The adoption of the EQUATOR network (http://www.equator-network.org/) reporting guidelines have seen increasing adoption by scientific journals. All observational studies are recommended to be reported following the STROBE guideline (von Elm et al, 2014).

In particular when a retrospective study is conducted using hospital records, it is recommended that the RECORD extension of the STROBE guideline is considered (Benchimol et al, 2015).

7 REFERENCES

- **SAR-2023-023-HY-v01** – Association between four risk scores and myocardial infarction: case-control stratified analysis
- Zarin DA, et al. The ClinicalTrials.gov results database – update and key issues. N Engl J Med 2011;364:852-60 (https://doi.org/10.1056/NEJMsa1012065).
- Gamble C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337–2343 (https://doi.org/10.1001/jama.2017.18556).
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014 Dec;12(12):1495-9 (https://doi.org/10.1016/j.ijsu.2014.07.013).
- Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM; RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015 Oct 6;12(10):e1001885 (https://doi.org/10.1371/journal.pmed.1001885).

8 APPENDIX

This document was elaborated following recommendations on the structure for Statistical Analysis Plans (Gamble, 2017) for better transparency and clarity.

8.1 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

https://philsf-biostat.github.io/SAR-2023-023-HY/