Statistical Analysis Plan (SAP)

Study Identification

Study Title:

Prehospital Point-of-Care High-Sensitivity Troponin I for Rule-Out of Acute Myocardial Infarction in Suspected Non–ST-Segment Elevation Acute Coronary Syndrome: A Pilot Study

Project acronym:

Pre-POCT Troponin Pilot Study

Protocol Version:

Version 1.0 (dated 07 April 2026)

Sponsor:

Central Denmark Region, Denmark

Document Information

Document Type: Statistical Analysis Plan

SAP Version: Version 1.0

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Prepared by: Martin Faurholdt Gude, MD, PhD

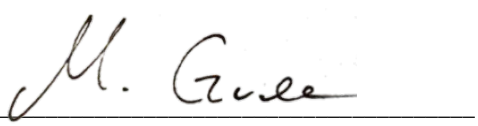
Based on Protocol: Version 1.0

Approval and Signatures

The undersigned confirm that this SAP accurately reflects the planned statistical analyses and has been finalized prior to database lock.

Principal Investigator

Name: Martin Faurholdt Gude, MD, PhD

Signature: 

Date: 2026-04-26

Purpose and scope

This Statistical Analysis Plan (SAP) specifies the prespecified statistical analyses for the primary, secondary, and other prespecified outcomes of the Pre-POCT Troponin Pilot Study.

The analyses are designed to evaluate the diagnostic performance of prehospital point-of-care high-sensitivity cardiac troponin I (hs-TnI) for identification of acute coronary syndrome (ACS) and prediction of major adverse cardiac events (MACE), as well as to describe clinical outcomes and assess feasibility and analytical performance.

Given the prospective observational design, analyses are descriptive and exploratory and will be conducted using available-case data without formal hypothesis testing. No randomization, clustering, or treatment allocation is involved, and no comparative effectiveness analyses are planned.

Exploratory analyses will further examine hs-TnI concentrations in relation to time from symptom onset and clinical outcomes, with the aim of identifying clinically relevant risk strata to inform future prehospital risk stratification strategies.

1. Objectives

The primary objective is to evaluate the diagnostic performance of prehospital point-of-care high-sensitivity cardiac troponin I (hs-TnI) for prediction of major adverse cardiac events (MACE) within 30 days and identification of ACS.

Secondary objectives are to describe clinical outcomes and evaluate feasibility and analytical performance of prehospital hs-TnI measurement.

Exploratory objectives are to assess hs-TnI concentrations in relation to time from symptom onset and to identify clinically relevant risk strata.

2. Analysis population

All included patients with available prehospital hs-TnI measurements will be included in the analyses.

Diagnostic accuracy analyses will be conducted using available-case analyses, including patients with both hs-TnI measurements and outcome data.

No per-protocol or subgroup-restricted primary analyses are planned.

3. Outcomes

Primary outcome

The primary outcome is the occurrence of major adverse cardiac events (MACE) within 30 days, defined as a composite of acute myocardial infarction, coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), or cardiovascular death.

Secondary outcomes

- Final diagnosis of acute coronary syndrome based on standard clinical evaluation
- All-cause 30-day mortality
- Coronary revascularization within 30 days
- Diagnostic performance of prehospital hs-TnI for:
    - identification of acute coronary syndrome
    - prediction of major adverse cardiac events within 30 days

Other pre-specified outcomes

- Proportion of eligible patients with successful prehospital blood sampling
- Proportion of valid hs-TnI measurements
- Time from first EMS contact to availability of hs-TnI result
- Agreement between prehospital and in-hospital hs-TnI measurements in a predefined subset

Exploratory outcomes

Exploratory analyses of hs-TnI concentrations in relation to time from symptom onset and clinical outcomes, including classification into risk strata reflecting low, intermediate, and elevated risk of acute coronary syndrome and major adverse cardiac events.

4. Reference standard

The reference standard for acute coronary syndrome is the final hospital diagnosis based on standard clinical evaluation, including serial cardiac troponin measurements, electrocardiography, and other diagnostic procedures as clinically indicated.

Patients without a diagnosis of acute coronary syndrome and without major adverse cardiac events within 30 days will be classified as not having ACS for diagnostic accuracy analyses. Patients with missing outcome data will be excluded from diagnostic accuracy analyses.

5. General statistical principles

Analyses are descriptive and exploratory.

All estimates will be reported with 95% confidence intervals. No formal hypothesis testing or adjustment for multiple comparisons will be performed.

Continuous variables will be summarized using means and standard deviations or medians and interquartile ranges, as appropriate. Categorical variables will be summarized as counts and proportions.

6. Diagnostic accuracy analyses

Diagnostic performance of prehospital hs-TnI will be evaluated for:

- identification of acute coronary syndrome
- prediction of major adverse cardiac events within 30 days

The following measures will be calculated:

- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Positive likelihood ratio (LR+)
- Negative likelihood ratio (LR−)
- Area under the receiver operating characteristic curve (AUC)

Analyses will be performed using hs-TnI both as a continuous variable and across exploratory threshold values. Exploratory threshold values will be informed by manufacturer-provided limits of detection and quantification and by previously published emergency department studies. No single predefined clinical decision threshold is specified.

Time from symptom onset to prehospital hs-TnI measurement will be described and considered in exploratory analyses, including evaluation of potential differences in diagnostic performance in early presenters. No formal time-based decision thresholds are predefined.

Receiver operating characteristic (ROC) curves will be constructed, and the AUC will be estimated with 95% confidence intervals.

For analyses based on threshold values, hs-TnI will be dichotomized according to the selected exploratory cut-offs, and corresponding diagnostic performance measures will be derived.

Diagnostic performance measures will be derived from 2×2 contingency tables comparing dichotomized hs-TnI results against the reference standard for acute coronary syndrome and major adverse cardiac events.

For each selected threshold, patients will be classified as test-positive or test-negative and cross-tabulated against outcome status (present/absent). Sensitivity, specificity, predictive values, and likelihood ratios will be calculated from these tables.

All diagnostic performance measures will be reported with corresponding 95% confidence intervals.

7. Agreement analyses

Agreement analyses will be performed on paired measurements obtained from the same blood sample.

Bland–Altman analysis will be used to estimate the mean difference (bias) and 95% limits of agreement and to assess agreement across the range of observed values.

Correlation between measurements will be assessed using Spearman's rank correlation coefficient to describe the strength of association between the two measurement methods.

Passing–Bablok regression will be used to evaluate systematic and proportional differences between measurement methods. A non-zero intercept will be interpreted as systematic bias, and a slope different from one as proportional bias.

If required, hs-TnI concentrations will be log-transformed to account for skewed distributions and to stabilize variance.

8. Feasibility analyses

Feasibility outcomes will be summarized descriptively.

Proportions (e.g., successful sampling and valid measurements) will be reported with 95% confidence intervals. Time intervals will be summarized using medians and interquartile ranges.

9. Exploratory analyses

Patients will be categorized into strata reflecting low, intermediate, and elevated hs-TnI concentrations.

The intermediate group represents a potential observation category in which repeat prehospital measurement may be considered in future studies. The elevated group includes patients with higher hs-TnI concentrations associated with increased risk, while also allowing identification of patients with elevated values but low event rates.

The distribution of acute coronary syndrome and major adverse cardiac events across these strata will be described.

No formal statistical comparisons between strata are planned.

10. Missing data

The extent and pattern of missing data will be described.

Analyses will be conducted using available-case analyses. Available-case analyses refer to inclusion of participants with non-missing data for the variables required in each specific analysis. No imputation of biomarker values will be performed.

11. Software

Statistical analyses will be performed using Stata (version 19.5 or later).

12. Appendix: Ethics Committee Determination (Central Denmark Region Committees on Health Research Ethics)

The following pages contain the formal written assessment from the Central Denmark Region Committees on Health Research Ethics confirming that the study does not require approval under Danish legislation.

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Request 91/2026

Dear Martin

Thank you for your email in which you ask whether your study "Prehospital Point-of-Care High-Sensitivity Troponin I for Rule-Out of Acute Myocardial Infarction in Suspected Acute Coronary Syndrome: A Pilot Study (the Pre-POCT Troponin Pilot Study)" has to be notified to The Central Denmark Region Committees on Health Research Ethics.

According to the Consolidation Act on Research Ethics Review of Health Research Projects, Consolidation Act number 1268 of 28 November 2024 section 14 (1) only health research studies has to be notified to the Committees. The Committees do not consider your study to be a health research study (section 2 (1)).

Therefore your study may be conducted without an approval from the Committees.

Kind regards

Anne-Marie Eybye
Secretary

The Central Denmark Region Committees on Health Research Ethics