Statistical Analysis Plan (SAP)

Study Identification

Study Title:

Prehospital Point-of-Care Testing to Support Decision-Making in Alternative and Non-Conveyance Pathways: A Matched Parallel Cluster-Randomized Trial

Project acronym:

The Pre-POCT–Non-Conveyance Trial

Protocol Version:

Version 1.1 (dated18 May 2026)

Sponsor:

Central Denmark Region, Denmark

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Document Information

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Based on Protocol: Version 1.1

This Statistical Analysis Plan (SAP) defines the prespecified statistical analyses for the primary, secondary, and selected substudy outcomes of The Pre-POCT–Non-Conveyance Trial.

The SAP was finalized prior to database lock and prior to any comparative outcome analyses between randomized groups.

Version History

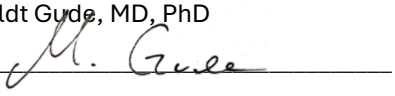
Version	Date	Description of Changes
1.1	18.05.2026	Updated SAP to align with the revised protocol, in which implementation of prehospital POCT is the primary outcome and non-conveyance is analyzed as a key secondary clinical outcome. The change was made before database lock and before any comparative outcome analyses.

Approval and Signatures

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

Principal Investigator

Name: Martin Faurholdt Gude, MD, PhD

Signature: 

Date: 2026-05-18

Trial Statistician

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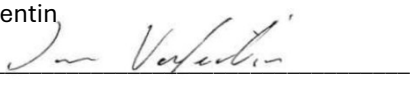
Signature: 

Date: 2026-05-18

Trial Overview

Trial: The Pre-POCT–Non-Conveyance Trial

Design: Prospective, matched, parallel, cluster-randomized trial (10 clusters; 5 intervention, 5 control), pair-matched before randomization.

Purpose and scope

This SAP specifies the prespecified analyses for the primary implementation outcome, secondary clinical outcomes, and selected prespecified substudy outcomes of The Pre-POCT–Non-Conveyance Trial. The primary analysis will evaluate implementation of prehospital POCT among intervention-cluster attended patient encounters within the study population. Clinical outcomes, including non-conveyance, will be analyzed as secondary and exploratory outcomes according to randomized cluster allocation. Statistical analyses of comparative clinical outcomes will account for the matched-pair cluster design and clustering at ambulance level where applicable.

The SAP was finalized prior to database lock and prior to any comparative outcome analyses between randomized groups.

Trial Overview — Purpose and scope / Sample size context

Sample size context

The planned sample size is determined by the trial protocol, the available POCT infrastructure, and the organizational ambulance-cluster structure. The study includes 10 ambulance clusters, with five intervention clusters and five control clusters. Each participating ambulance is anticipated to attend up to approximately 250 patients within the study population during the study period, corresponding to approximately 1,250 attended patient encounters per arm.

These figures refer to patients attended by the participating ambulances within the study population and do not imply that all patients will be eligible for POCT. Some patients may be safely non-conveyed according to existing SOP without POCT, some will require hospital conveyance irrespective of POCT, and the proportion of patients in whom POCT is clinically relevant and attempted is unknown. Estimating this proportion is a central implementation outcome of the trial.

The trial is not powered to detect a definitive difference in non-conveyance or safety outcomes. Clinical outcomes, including non-conveyance, will be reported as exploratory outcomes and used to inform the design and sample size of a future definitive effectiveness trial.

Cluster Definition, Pre-Intervention Data, and Matching Procedure

Cluster definition

The unit of randomization and clustering is the ambulance cluster (individual ambulance unit). Ten ambulance clusters participated in the trial. Five ambulance clusters were allocated to the intervention group (POCT availability) and five to the control group.

Ambulances operate either as 24-hour units (“do”) or daytime-only units (“da”), as defined by operational designation in the ambulance identifier. Only ambulances with identical operational designation were eligible for pair matching to ensure comparability of service availability and exposure time.

Contamination between clusters was considered minimal, as POCT equipment was physically installed and restricted to intervention ambulances.

Pre-intervention data source

Cluster matching was performed using pre-intervention activity data extracted from the Prehospital Patient Record (PPJ) covering the period June–November 2025. Aggregated ambulance-level data were used exclusively for matching and not for outcome comparison.

Matching strategy

A predefined hierarchical matching strategy was applied prior to randomization using aggregated pre-intervention data (June–November 2025). Matching prioritized variables directly relevant to the key secondary clinical outcome, non-conveyance.

Primary matching criterion

- Overall non-conveyance rate at the aggregated group level, defined as the proportion of attended incidents concluded on scene without hospital transport.

This criterion ensured near-identical baseline non-conveyance proportions between the aggregated intervention and control groups.

Secondary matching criteria (applied hierarchically)

1. Within-pair similarity in overall non-conveyance rate (i.e., minimization of the absolute difference between ambulances within each matched pair).
2. Non-conveyance rates within urgency strata A and B.
3. Absolute activity volumes, including:
    - Total number of attended incidents.
    - Number of incidents within urgency strata A and B.

4. Geographic proximity of ambulance base locations.
5. Operational designation (“do” vs “da”).

Each criterion was applied sequentially, with lower priority criteria used to refine matches once higher-priority balance had been achieved.

Minor residual discrepancies at individual ambulance level were considered acceptable provided that aggregated group-level proportions and activity volumes remained closely aligned.

Baseline comparability

During the pre-intervention period (June–November 2025):

- Intervention ambulances: 3,478 attended incidents; overall non-conveyance 25.27%.
- Control ambulances: 3,392 attended incidents; overall non-conveyance 24.82%

Non-conveyance within urgency A:

- Intervention: 24.7%
- Control: 23.5%

Non-conveyance within urgency B:

- Intervention: 25.8%
- Control: 25.8%

These figures demonstrate near-identical baseline non-conveyance proportions and activity distributions between groups, supporting the matched-pair analytical framework.

Matched ambulance pairs

The predefined matched pairs were:

- Her-Am-do2 ↔ Her-Am-do1
- Vib-Am-do2 ↔ Vib-Am-do3
- Aac-Am-do3 ↔ Aac-Am-do2
- Gal-Am-do1 ↔ Hot-Am-do1
- Aas-Am-do1 ↔ Aac-Am-do1

Within each matched pair, one ambulance was randomly assigned to the intervention group (POCT availability) and the other to the control group. For clarity of presentation in this document, the intervention-assigned ambulance is listed first and the control-assigned ambulance second.

These matched pairs define the cluster structure used in all subsequent analyses.

Study populations and analysis sets

Intention-to-treat (ITT) population

All patients within the study population attended by participating ambulance clusters during the inclusion period will be included and analyzed according to the randomized allocation of the attending ambulance cluster, regardless of whether POCT was performed.

Primary implementation analysis population

The primary implementation analysis will include intervention-cluster attended patient encounters within the study population. This population will be used to estimate implementation of prehospital POCT, including POCT attempt, successful measurement, documentation, and availability before the final conveyance decision.

Per-protocol population for sensitivity analysis

The per-protocol intervention group consists of patients in intervention clusters in whom POCT was performed. The comparator group consists of propensity-score–matched patients from control clusters. The per-protocol analysis will be interpreted as a sensitivity analysis to the randomized comparison of clinical outcomes and will not replace the intention-to-treat analysis.

Outcomes and Effect Measures

Primary outcome

The primary outcome is implementation of prehospital POCT, defined as the proportion of intervention-cluster attended patient encounters within the study population in which POCT was attempted, at least one valid POCT result was obtained and documented, and the result was available before the final conveyance decision.

Primary effect measure

The primary effect measure is the proportion of intervention-cluster attended patient encounters within the study population meeting the definition of implementation of prehospital POCT. The outcome will be reported as a proportion with a 95% confidence interval. No confirmatory between-group hypothesis test will be performed for the primary outcome, as POCT is only available in intervention clusters.

Each step in the implementation pathway will also be reported separately: POCT attempt, successful POCT measurement, documentation of a valid result, and availability of a valid result before the final conveyance decision.

Key secondary clinical outcome

Non-conveyance is the key secondary clinical outcome and is defined as completion of the ambulance encounter without transport to hospital after on-scene ambulance assessment.

Non-conveyance will be compared between randomized intervention and control clusters according to the intention-to-treat principle. The absolute risk difference will be estimated using a linear probability model with matched-pair fixed effects and standard errors clustered at the ambulance level. The relative risk will be estimated using Poisson regression with log link, matched-pair fixed effects, and robust standard errors clustered at the ambulance level. Estimates will be reported with 95% confidence intervals and interpreted as exploratory.

Secondary clinical outcomes (ITT)

Secondary clinical outcomes will be analyzed according to the intention-to-treat principle where applicable and interpreted as exploratory. Binary outcomes will be analyzed using linear probability models to estimate risk differences and Poisson regression models with robust variance estimation to estimate relative risks. Models will include matched-pair fixed effects, and standard errors will be clustered at the ambulance level.

Secondary clinical outcomes include:

1. **Hospital admission within 24 hours among non-conveyed patients** (binary).
2. **Short-stay hospitalization related to the index EMS encounter** (alive and discharged <6 hours and without advanced procedures, medication administration, or CT/MR imaging during the admission) (binary).
3. **Total hospital length of stay** for the index hospitalization (continuous; hours per data structure). Censored at death using tobit regression with censoring at zero for deceased patients.
4. **ICU admission** during the index hospitalization (binary).
5. **30-day all-cause mortality** (binary).

Prespecified substudy outcomes

These will be analyzed descriptively and inferentially as appropriate using the same core principles (pair fixed effects; cluster-robust variance at ambulance level) unless otherwise stated.

Safety/health services outcomes:

- **30-day hospital admission rate** (binary).

- **ED visit or hospital admission within 72 hours after non-conveyance** (binary; restricted to non-conveyed patients).
- **OOH-PC contact within 72 hours after non-conveyance** (binary; restricted to non-conveyed patients).
- **EMS recontact within 72 hours after non-conveyance** (binary; restricted to non-conveyed patients).
- **Days alive and out of hospital at 30 days (DAOH30)** (continuous, integer 0–30).

Operational/process outcomes:

- **On-scene time** (continuous; minutes).
- **Rate of unsuccessful POCT measurements** among POCT attempts in intervention clusters (binary at attempt level; summarized as proportion).

Methodological outcomes:

- ICCs for non-conveyance and selected outcomes using mixed effects analysis; observed design effects; pair-matching performance; linkage completeness (see Section 9).

General statistical principles

Statistical significance and estimation

Analyses will primarily be descriptive and estimation-based. Effect estimates will be reported with two-sided 95% confidence intervals. The primary implementation outcome will not be evaluated using a confirmatory between-group hypothesis test. Comparative analyses of clinical outcomes, including non-conveyance, will be considered exploratory.

Accounting for the matched-pair cluster design

Models will include matched pair as a fixed effect (indicator for each matched pair). Variance estimation will use cluster-robust standard errors at the ambulance cluster level.

Given the limited number of clusters, inference will rely primarily on effect estimates and confidence intervals rather than sole reliance on p-values.

Multiplicity

No formal multiplicity adjustment is planned. The primary implementation outcome will be interpreted as the main feasibility outcome. Clinical, safety, operational, and methodological outcomes will be interpreted as secondary or exploratory, with emphasis on effect sizes, precision, and clinical plausibility.

Software

All statistical analyses will be performed using Stata (StataCorp LLC, College Station, TX, USA). The specific version used for the final analyses will be documented in the statistical report. Reproducible analysis scripts will be maintained under version control.

Baseline characteristics and participant flow

Baseline characteristics will be summarized by intervention group using descriptive statistics. No significance testing of baseline differences will be performed. A CONSORT flow diagram for cluster trials will be presented with counts of eligible encounters, included participants, and outcome availability.

Primary outcome analysis

The primary implementation outcome will be analyzed among intervention-cluster attended patient encounters within the study population. The numerator will be the number of such encounters in which POCT was attempted, at least one valid POCT result was obtained and documented, and the result was available before the final conveyance decision. The denominator will be all intervention-cluster attended patient encounters within the study population.

The primary outcome will be reported as a proportion with a 95% confidence interval calculated using the Wilson score method. The outcome will also be presented descriptively by ambulance cluster. Each step in the implementation pathway will be reported separately: POCT attempt, successful POCT measurement, documentation of a valid result, and availability of a valid result before the final conveyance decision.

No between-group hypothesis test will be performed for the primary implementation outcome.

Key secondary clinical outcome analysis: non-conveyance (ITT)

A linear probability model will be used to estimate the absolute risk difference in non-conveyance between intervention and control clusters. The model will include treatment group and matched-pair fixed effects, with standard errors clustered at the ambulance level. The risk difference will be reported as a percentage-point difference with 95% confidence interval.

A Poisson regression model with log link will be used to estimate the relative risk of non-conveyance comparing intervention with control clusters. The model will include treatment group and matched-pair fixed effects, with robust standard errors clustered at the ambulance level. The relative risk will be reported with 95% confidence interval.

This analysis will be interpreted as exploratory.

Secondary outcome analyses (ITT)

Binary outcomes will be analyzed using linear probability models (risk difference) and Poisson regression with robust variance (relative risk), including matched-pair fixed effects and clustering at ambulance level. For fixed-window binary outcomes, participants who die before the outcome can occur will be classified as not having experienced that outcome, and the number of such cases will be reported descriptively. Because such events are expected to be rare in the study population, this approach is unlikely to materially influence the estimates.

Admission within 24 hours among non-conveyed patients

The analysis set will be restricted to participants with non-conveyance at the index encounter. RD and RR will compare intervention vs control.

Short-stay hospitalization related to the index EMS encounter

RD and RR will compare intervention vs control among participants conveyed and admitted as part of the index encounter, consistent with the endpoint definition. The denominator and restriction rules will be aligned to how the variable is constructed in EPJ.

Total hospital length of stay

Length of stay (LOS) is typically right-skewed. The primary LOS analysis will use **tobit regression** with matched-pair fixed effects, cluster-robust SE and censoring at death, reporting difference in mean LOS between intervention and control. If distributional skewness is extreme, a prespecified alternative presentation will be added: median (IQR) by group and a sensitivity analysis using log-transformed LOS (reporting ratio of geometric means). The inferential focus will remain the primary linear model unless transformation materially changes interpretation.

ICU admission and 30-day mortality

Both will be analyzed as binary outcomes using RD and RR models as described above.

Per-protocol sensitivity analysis of clinical outcomes

A per-protocol sensitivity analysis will be conducted among patients in intervention clusters in whom POCT was performed. These patients will be compared with propensity-score–matched controls from control clusters based on patient characteristics, vital signs, and presenting problem. The analysis will use the same modelling framework as the exploratory clinical outcome analyses, with estimation of risk differences and relative risks where appropriate. The per-protocol analysis will be interpreted as a sensitivity analysis to the randomized comparison of clinical outcomes.

This analysis evaluates the effect among those receiving POCT in intervention clusters, acknowledging that POCT is applied after EMDC physician consultation and that uptake may be selective.

Definition of PP groups

- PP intervention: intervention-cluster participants with POCT performed.
- PP controls: control-cluster participants eligible under the same clinical context, matched via propensity score.

Propensity score model (pre-specified covariates)

The propensity to receive POCT will be modeled using variables available prior to the POCT decision and plausibly associated with both POCT use and the conveyance decision. The covariate set will be restricted to routinely recorded prehospital variables available in PPJ, Logis, or REDCap and finalized prior to outcome analysis. Prespecified candidate covariates include age (categorized into 10-year age groups), sex, dispatch reference code/chief complaint category, vital signs (Glasgow Coma Scale, systolic blood pressure, pulse, oxygen saturation) categorized as clinically stable versus unstable, time factors (daytime/evening/night; weekday vs weekend), and Charlson Comorbidity Score (based on prior ICD-10 diagnosis history).

Matching procedure

Nearest-neighbor matching on the propensity score will be performed with a pre-specified caliper on the logit of the PS. Matching ratio (1:1 or 1:k) will be selected to balance precision and covariate balance; the ratio will be fixed before seeing outcome results. Balance will be assessed using standardized mean differences (SMD), targeting absolute SMD <0.10 for the prespecified covariates.

Analysis after matching

After propensity score matching, non-conveyance will be analyzed using the same risk difference (RD) and relative risk (RR) modelling frameworks as in the main key secondary clinical outcome analysis, including matched-pair fixed effects and robust standard errors clustered at ambulance level.

Because propensity score matching creates matched patient sets, a two-way clustered variance estimator will be used to account for clustering at ambulance level and within matched propensity-score sets.

Methodological analyses

ICC estimation

ICCs will be estimated for non-conveyance and selected outcomes (24-hour admission among non-conveyed, 30-day admission, 30-day mortality, short-stay hospitalization). ICC estimation will use a standard approach for binary outcomes under cluster designs (variance components from a random-intercept model).

Observed design effect

Observed design effects will be computed for non-conveyance and selected clinical outcomes to inform planning of future cluster-randomized trials.

Pair-matching performance

Pre-randomization cluster metrics used in matching will be summarized, including within-pair similarity for baseline non-conveyance and descriptive between-cluster variation. The within-pair correlation of baseline non-conveyance will be reported.

Data linkage and completeness

Linkage success rates between REDCap, PPJ/Logis, EPJ, and OOH-PC data will be summarized. Availability of primary and key secondary endpoint data will be reported overall and by group.

Missing data

Outcome missingness is expected to be low for registry-based endpoints. Analyses will use available data. The extent and patterns of missingness will be reported. No imputation is planned unless missingness is materially higher than expected and plausibly differential; any deviation will be justified and documented prior to unblinding of comparative results.

Protocol deviations and analysis integrity

Major deviations affecting eligibility or endpoint ascertainment will be summarized descriptively. No interim analyses are planned. The SAP will be finalized and made publicly available prior to database lock and before any comparative outcome analyses are conducted. Because formal permission for registry data extraction can only be sought after study completion, the SAP will be finalized before such approval is granted by the Legal Office of the Central Denmark Region.

Reporting

The primary implementation outcome will be reported as a proportion with 95% confidence interval, together with the separate steps in the implementation pathway. Comparative clinical outcomes, including non-conveyance, will be presented as risk differences and relative risks with 95% confidence intervals for binary outcomes and as mean or median differences where appropriate for continuous outcomes. Clinical outcomes will be interpreted as secondary or exploratory. Reporting will follow CONSORT guidance for cluster-randomized trials where applicable.