CoroPrevention
PERSONALISED PREVENTION FOR CORONARY HEART DISEASE

CoroPrevention-
A prospective clinical trial to evaluate the clinical value and cost effectiveness of a personalised prevention programme in subjects with high-risk stable Coronary Heart Disease

www.coroprevention.eu

Clinical Protocol Training, date of training 19.03.2026

Based on protocol v3.0 13 Aug 2025

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 848056

Content

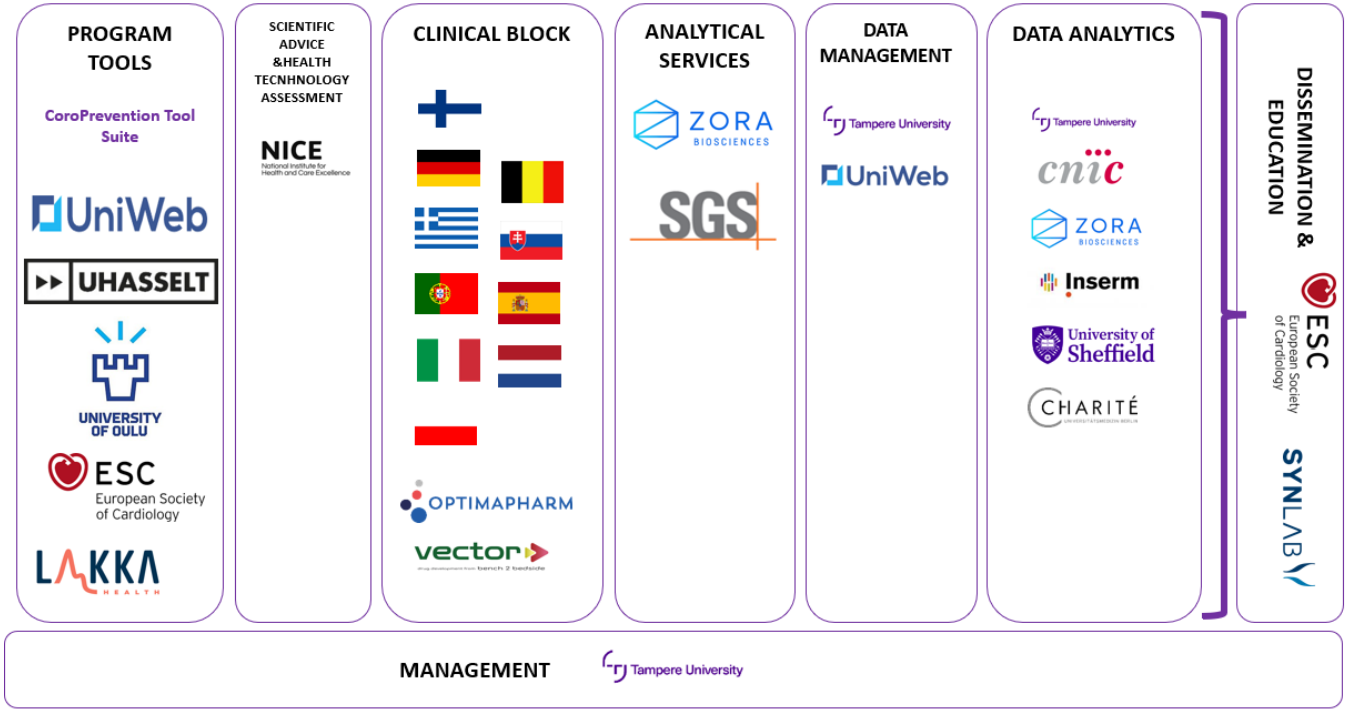
Summary of changes protocol V2.0 to V3.0

- Addition of new countries (Belgium, Netherlands, Slovakia and Spain) to enhance recruitment
- Enrolment target has been reduced from 12.000 to 10.000 subjects.
- Current biomarker-based high-risk definition, as previously communicated in the protocol clarification letters dated 22 May 2023 and 03 November 2023 was included in the protocol.
- Endpoint data collection procedures have been revised to reflect the process followed in most countries. One additional telephone contact has been added for the high-risk usual care subjects to enable more efficient and reliable collection of endpoint data.
- Clarification added regarding the exact names of the questionnaires to be completed at each study visit.
- Current cardiac medications in common use that collected in the study database.
- Updates to reflect the final version of the CoroPrevention Tool Suite, and references to initially planned functions that are not available have been deleted.
- List of National Coordinating Investigators and study administrative parties updated

General Information

- Sponsor and Manufacturer: Tampere University (Finland)
  - Scientific Director: Dr. Reijo Laaksonen
  - Clinical trial Manager: Mia Mäkinen
- CoroPrevention Tool suite Design:
  - Hasselt University (Belgium)
  - University of Oulu (Finland)
- EDC and CoroPrevention Tool suite development:
  - UniWeb BVBA (Belgium)
- Up to 10 European countries:
  - Finland, Poland, Greece, Portugal, Italy, Germany, Belgium, Spain, Netherlands, Slovakia
  - Approximately 40 sites

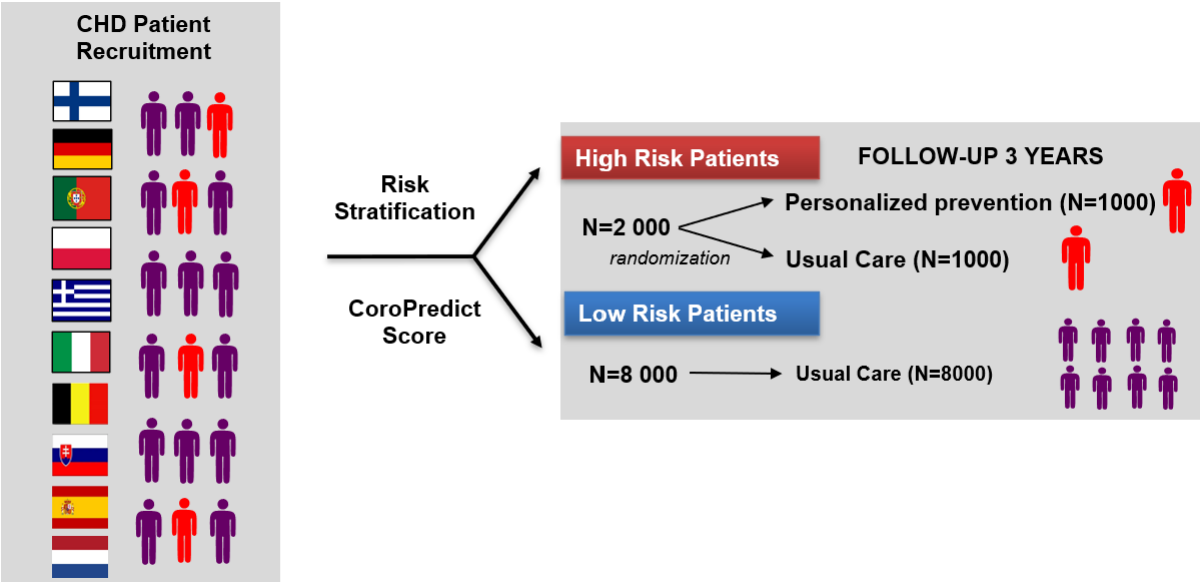
CONSORTIUM PARTNERS



Background

- AIM: Evaluate the **effectiveness and cost-effectiveness** of a **personalised prevention programme** for high-risk coronary heart disease patients using the **CoroPrevention Tool Suite** (investigational device, Class IIa).
- **Duration per subject:** ~3 years
- The study will check that the CoroPrevention Tool Suite is safe and works as intended. It will also confirm that the device meets the EU Medical Device Regulation (MDR 2017/745) safety and performance standards (Annex I).

Study design



PART A: a prospective biomarker-based risk screening in coronary heart-disease subjects

Part B: a nested randomized clinical study up-to 3 years in an enriched subpopulation of high-risk stable CHD subjects.

Primary objectives and endpoints

PART A

- To prospectively validate biomarkers in risk stratification among stable CHD subjects, i.e. evaluation of the biomarker performance in accurately predicting CV events including CV death, nonfatal MI, HF events
- To identify high-risk CHD subjects for the subsequent RCT, i.e. approximately 15-20% of the screened patient population at the highest risk

PART B

- To demonstrate whether a PPP strategy in high-risk CHD subjects results in a decreased risk of CV events (CV death, nonfatal MI or HF events) compared to the UC

Primary endpoint:

- The time from randomisation to the occurrence of the first CV event included in the composite endpoint of the trial (CV death, nonfatal MI, HF events) over 3 years follow-up.

Secondary objectives and endpoints

- To evaluate the difference between the PPP arm to the UC arm in the following:
  - The times from randomisation to the occurrence of the specific items included in the composite endpoint over 3 years of follow-up
  - The times from randomisation to the occurrence of secondary CV events
  - Treatment adherence
  - All-cause mortality
  - Incidence of additional clinical endpoints
- To evaluate the health economic value of the PPP
  - A cost-effectiveness analysis of PPP versus UC, based on evidence from the RCT portion of the trial, using within-trial analysis and long-term cost-effectiveness modelling for the participating countries
- To prospectively study associations between separate risk biomarkers or their score and the following:
  - Primary composite CV event
  - Specific CV events separately
  - Specific secondary CV events
  - Incidence of new onset DM2, CKD, PAD, and hypertension
- To evaluate the value of the CoroPrevention Tool Suite to support the PPP.
  - Evaluated with analysis of the characteristics and components of shared decision making, decision support systems and general user experience

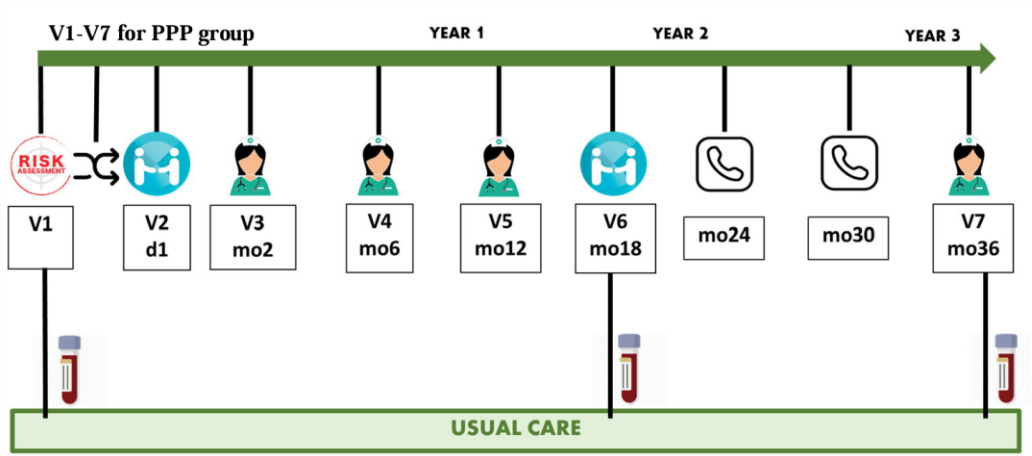
Study inclusion criteria

- Inclusion criteria
  1. IC form signed by the trial subject.
  2. Male or female aged 30 to 80 years on the day of enrolment.
  3. ≥ 50% stenosis in one or more major coronary arteries on angiography or CT performed within the preceding year (from enrolment visit)
     or Myocardial infarction (type I, II) during the preceding year.
  4. For sites in Belgium only: Subject understands Dutch well enough to use the trial application in that language.

Study exclusion criteria

- Exclusion criteria
  1. Hospitalisation for acute coronary syndrome, MI, stroke, coronary revascularisation or acute HF within the preceding month (30 days). These subjects can be enrolled after a one-month stabilisation period, which begins from the time of the event.
  2. Subjects with New York Heart Association class III-IV HF, i.e. marked limitation in activity due to symptoms, comfortable only at rest.
  3. Uncontrolled arrhythmias such as ventricular tachycardias.
  4. Subjects undergoing dialysis due to severe renal disease.
  5. Diseases that severely disable exercising (per investigator's judgement), such as rheumatoid arthritis, neurological or orthopaedic diseases.
  6. Known aplastic or haemolytic anaemia, or other severe anaemia.
  7. Concomitant non-coronary disease, such as malignancy that limits life expectancy to less than three years.
  8. Concurrent participation in another interventional study.
  9. Subjects not able and/or willing to attend all scheduled visits and comply with all trial procedures and use a smartphone application.

Timeline

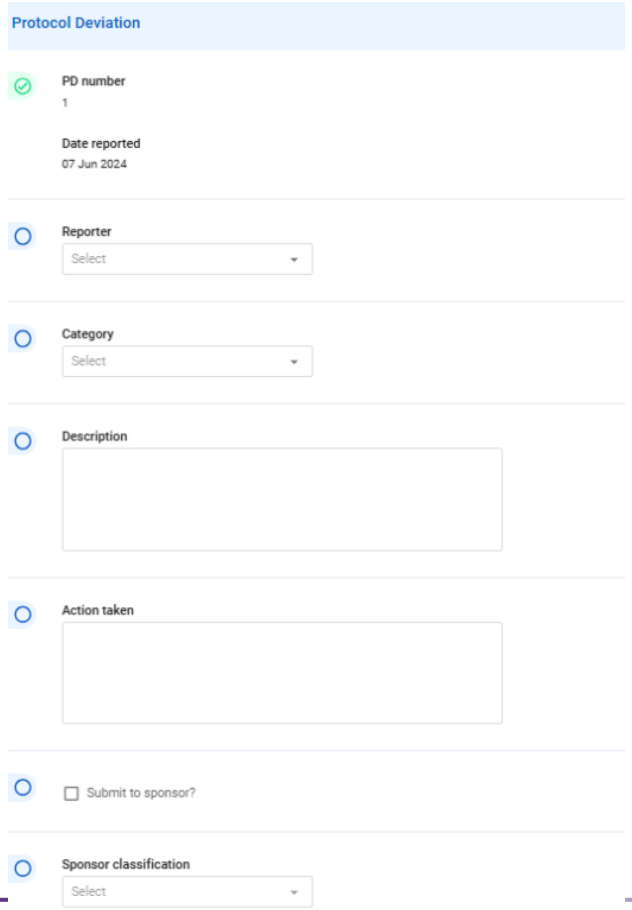


The visits V3-V7 are calculated from the date of treatment assignment (randomisation)

- Procedures for PPP group (V2-V7) includes clinical assessment (interview), vital signs, Blood sampling (V6 and V7), concomitant medication review, ePROs, PPP counselling, reporting device deficiencies and adverse events, collection of subject reported endpoints and 6 min walk test (V2, V6 and V7)
    - An investigator reviews the medication for PPP group at V2 and V6, with help of Tool Suite (Medication decision support system algorithm)
- Procedures for high-risk UC V6 and V7 includes clinical assessment (interview), vital signs, blood sampling (V6 and V7), ePROs, concomitant medication review and collection of subject reported endpoints

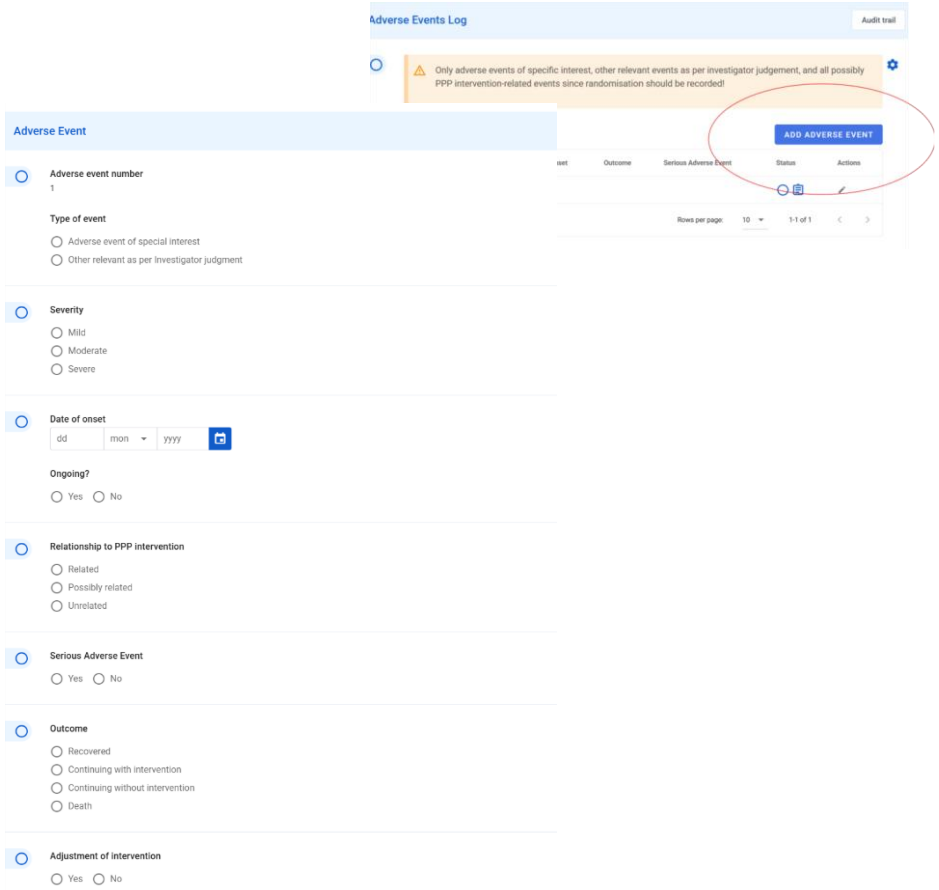
Protocol deviations (PD)

- Protocol deviation is any instance of failure to follow, intentionally or unintentionally, the requirements of the Ethics Committee/ Competent Authority approved CoroPrevention study protocol.
- All Protocol deviations are collected in eDC system
- Some deviations are automatically recorded by the system, such as out-of-window visit deviations. Please check the PD log entries to avoid duplicate manual reporting.
- Reporter of the protocol deviations can be: CRA,PI, sub-investigator, study nurse, data manager etc. (who has access to the eDC)



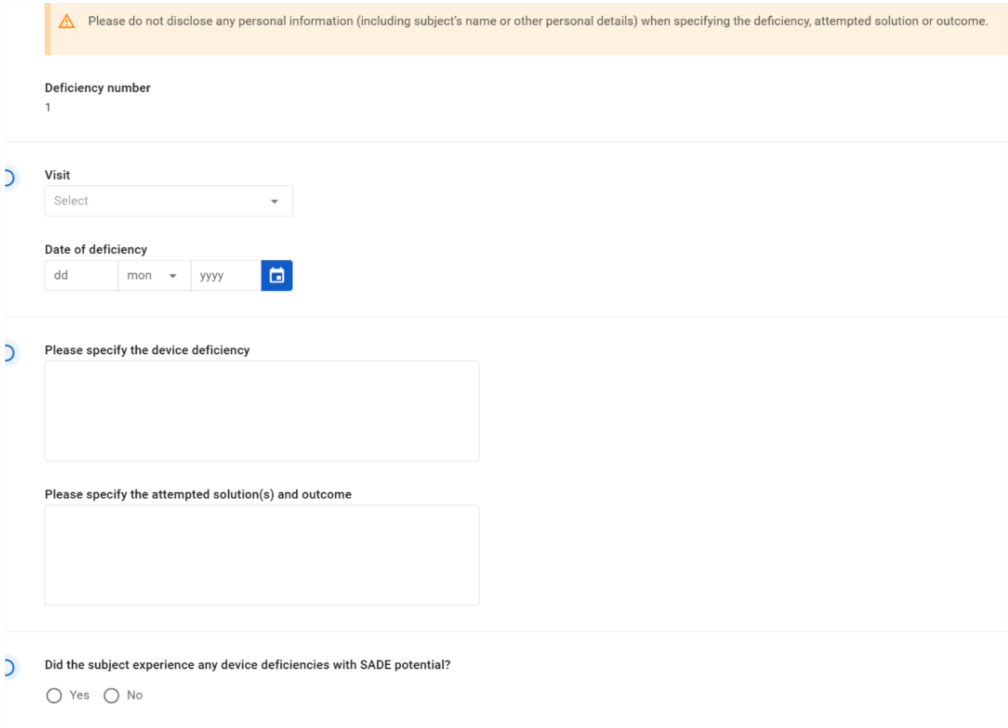
Safety management

- AE reporting applies only to randomized (high-risk) subjects. Adverse events will not be collected from low-risk subjects.
- Adverse event (AE), serious adverse event (SAE), adverse device effect (ADE), and serious adverse device effect (SADE) must be reported in the EDC system by the Principal Investigator or a qualified member of the site staff (e.g., Study Nurse, Sub-Investigator).
- Adverse Events of Specific Interest must be reported. All other events should be reported based on the investigator's clinical judgement. For PPP arm, also all potentially PPP-intervention–related events must be reported.
- All relevant events must be documented in the EDC system and, where applicable, submitted using the appropriate event-specific forms.
- Events that form the clinical endpoints for the trial are excluded from SAE reporting



Device Deficiency

- Device deficiency is an inadequacy of an investigational device with respect to its identity, quality, durability, reliability usability or performance.
  - This includes malfunctions, use error and inadequacy in information supplied by manufacturer.
- Record any device deficiencies in the eDC system when such is noted. The manufacturer will review these logs and take corrective actions as appropriate.
- Investigational medical device (CoroPrevention Tool Suite) deficiencies that could have led to a serious adverse device effect, if appropriate action had not been taken must be recorded and reported as a device deficiency with SADE potential using the SAE/SADE form.



Endpoint data collection (high-risk arms)

- PPP arm: Primary and secondary endpoint data will be collected at every visit (V2-V7) and during the phone calls (mandatory or per-needed)
- High-risk Usual Care arm: Subjects will be reminded (phone, email, letter) to report possible clinical end-points at 6, 12 and 24 months from randomization.
  - Subjects are asked about primary and secondary endpoint events also at V6 and V7
- Primary and secondary endpoints will be adjudicated by a separate committee; related data and evidence of the events need to be entered in the EDC and requested evidence for the event uploaded.
- Following endpoints will be adjudicated:
  - CV Death
  - Myocardial infarction
  - Heart Failure event
  - Stroke
  - Unstable angina
  - Coronary revascularizations
- Extended end point collection 5 and 10 years will be also carried out to evaluate maintenance of the potential effect of PPP (at selected sites)

Endpoint data collection (low-risk arm)

- The low-risk UC subjects will be reminded (phone, email, letter) to report possible primary and secondary end-points at 12, 24 and 36 months after randomization.
  - Subjects report possible endpoints to the nurse through an e-mail/phone call as a follow-up to the reminder that is sent to them.
- Endpoint data for this group will not be adjudicated.