CoroPrevention

PERSONALISED PREVENTION FOR CORONARY HEART DISEASE

# Clinical Protocol Training


## Tampere University

## Version 2.0 4.11.2022

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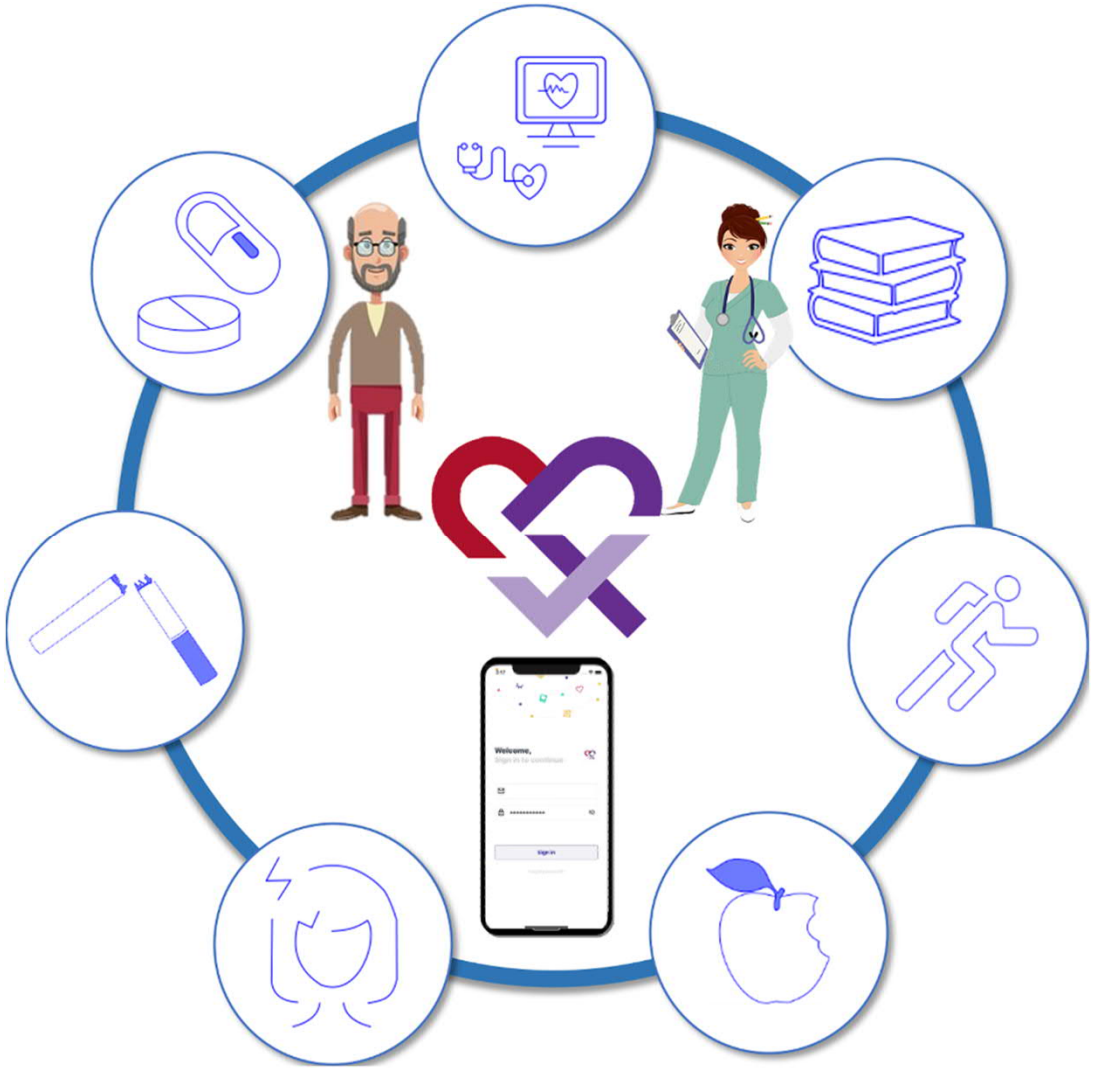
# Content

- General information
- Background
- Trail Design
- Protocol objectives and endpoints
- Protocol inclusion/exclusion criteria
- Timeline
- Protocol deviations
- Safety Management
- Endpoint data collection



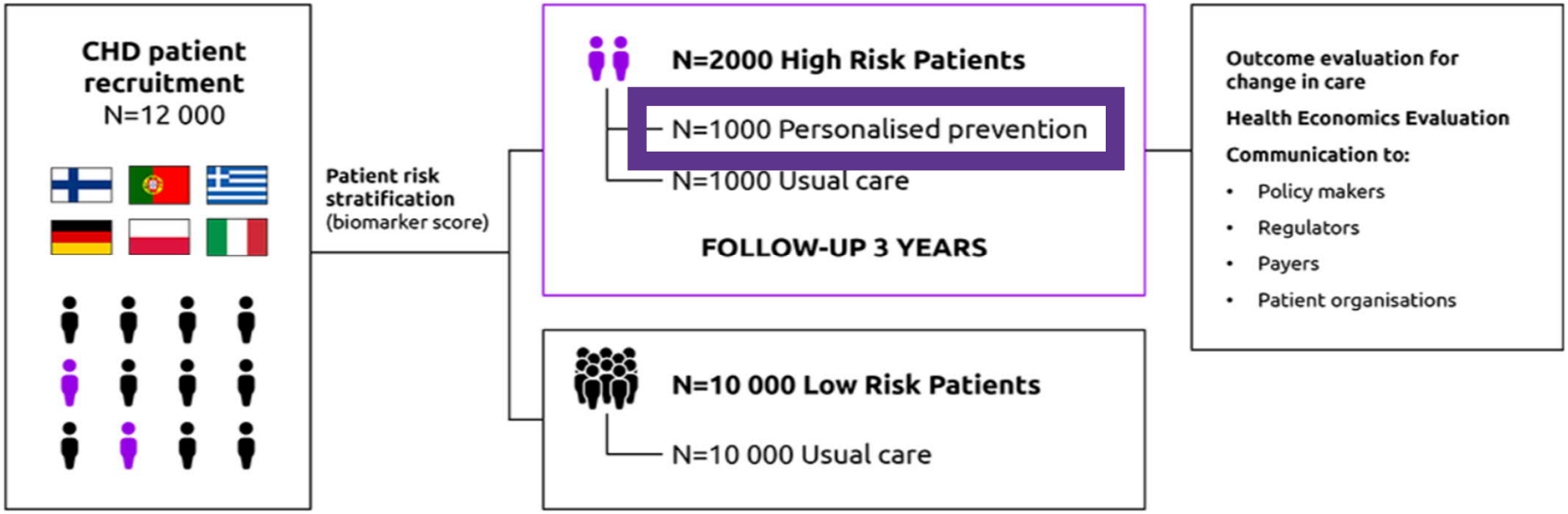
# General Information

- Sponsor and Manufacturer: Tampere University (Finland)
    - Scientific Directior: Dr. Reijo Laaksonen
    - Clinical trial Manager: Dr. Sippy Kaur
    - Data Manager: Dr. Markus Vattulainen
- Coroprevention Tool suite Design:
    - Hasselt University (Belgium)
    - University of Oulu (Finland)
- EDC and Coroprevention Tool suite development:
    - UniWeb BVBA (Belgium)
- 6 European countries:
    - Finland, Poland, Greece, Portugal,  Italy, and Germany
    - 25 sites

# Background

- **AIM:** The purpose of the clinical trial is to is to evaluate the effectiveness and cost-effectiveness of the personal treatment program and cost-effectiveness in the treatment of high-risk coronary heart disease patients, using the investigational device CoroPrevention Tool suite medical device (class IIa).
- The overall trial duration for each individual subject is approximately 3 years.
- In this trial the clinical safety and performance of CoroPrevention Tool Suite, will be evaluated to confirm that the clinical safety and performance of the product is in compliance with the General Safety and Performance Requirements (Annex I) of the Medical Device Regulation (EU) 2017/745.

# Trial design




**Clinical trial consists of two parts:**

- ***PART A:*** a prospective biomarker-based risk screening trial in CHD subjects
- ***PART B:*** a nested randomised clinical trial upto 3 years in an enriched subpopulation of 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. 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

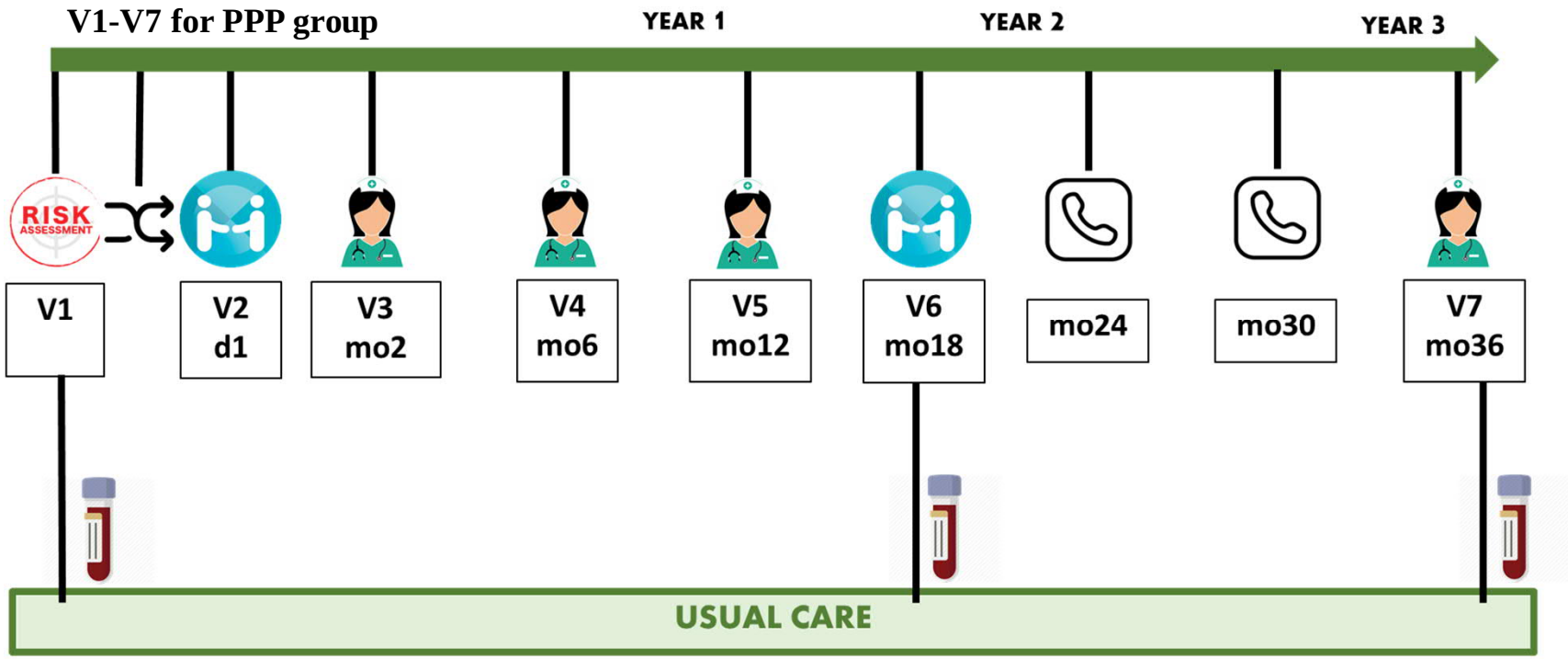
# Protocol inclusion criteria

| Inclusion Criteria | Yes | No |
| --- | --- | --- |
| Informed consent form signed by the study subject. | ○ | ○ |
| Male or female aged 30 to 80 years on the day of enrolment. | ○ | ○ |
| ≥ 50% stenosis in one or more major coronary arteries on angiography or computerised tomography (CT) performed within the preceding year (from enrolment visit) or myocardial infarction (type I, II) during the preceding year. | ○ | ○ |

# Protocol exclusion criteria

| Exclusion Criteria | Yes | No |
|---|---|---|
| Hospitalisation for acute coronary syndrome, myocardial infarction, stroke, coronary revascularisation or acute heart failure 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. | ○ | ○ |
| Subjects with NYHA class III-IV heart failure i.e. marked limitation in activity due to symptoms, comfortable only at rest. | ○ | ○ |
| Uncontrolled arrhythmias such as ventricular tachycardias. | ○ | ○ |
| Subjects undergoing dialysis due to severe renal disease. | ○ | ○ |
| Diseases that severely disable exercising (per investigator's judgement), such as rheumatoid arthritis, neurological or orthopaedic diseases. | ○ | ○ |
| Known aplastic or haemolytic anaemia or other severe anaemia. | ○ | ○ |
| Concomitant non-coronary disease, such as malignancy that limits life expectancy to less than three years. | ○ | ○ |
| Concurrent participation in another interventional study. | ○ | ○ |
| Subjects not able and/or willing to attend all scheduled visits and comply with all study procedures and use a smartphone application. | ○ | ○ |

# Timeline



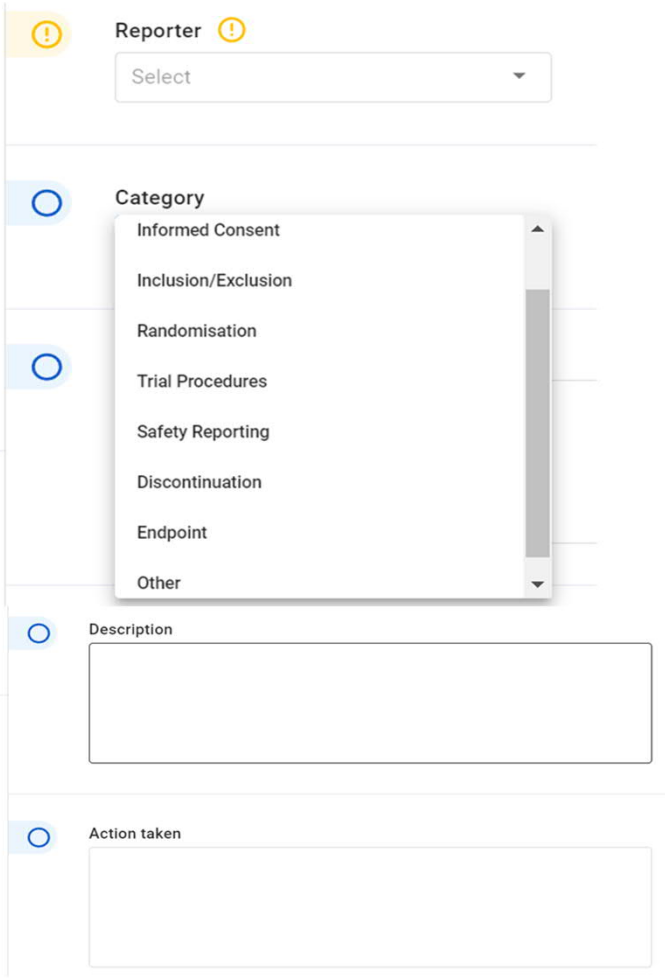

- The visit window for V3-V7 is calculated from the date of randamization
- Procedure for PPP group (V2-V7) includes: Clinical assesment, Vitals, Blood sampling (V6 and V7), concomitant medication, ePRO, counselling, reporting device deficiencies and adverse events, smoking behavior, subject reported endpoints and 6 min walk test (V2, V6 and V7)
- Investigator reviews the medication for PPP group at V2 and V6

# Protocol deviations

- Protocol deviation is any instance of failure to follow, intentionally or unintentionally, the requirements of the Ethics Committee/ Competent Authority approved CoroPrevention trial protocol.

- All Protocol deviations are collected and submitted to sponsor by EDC system.

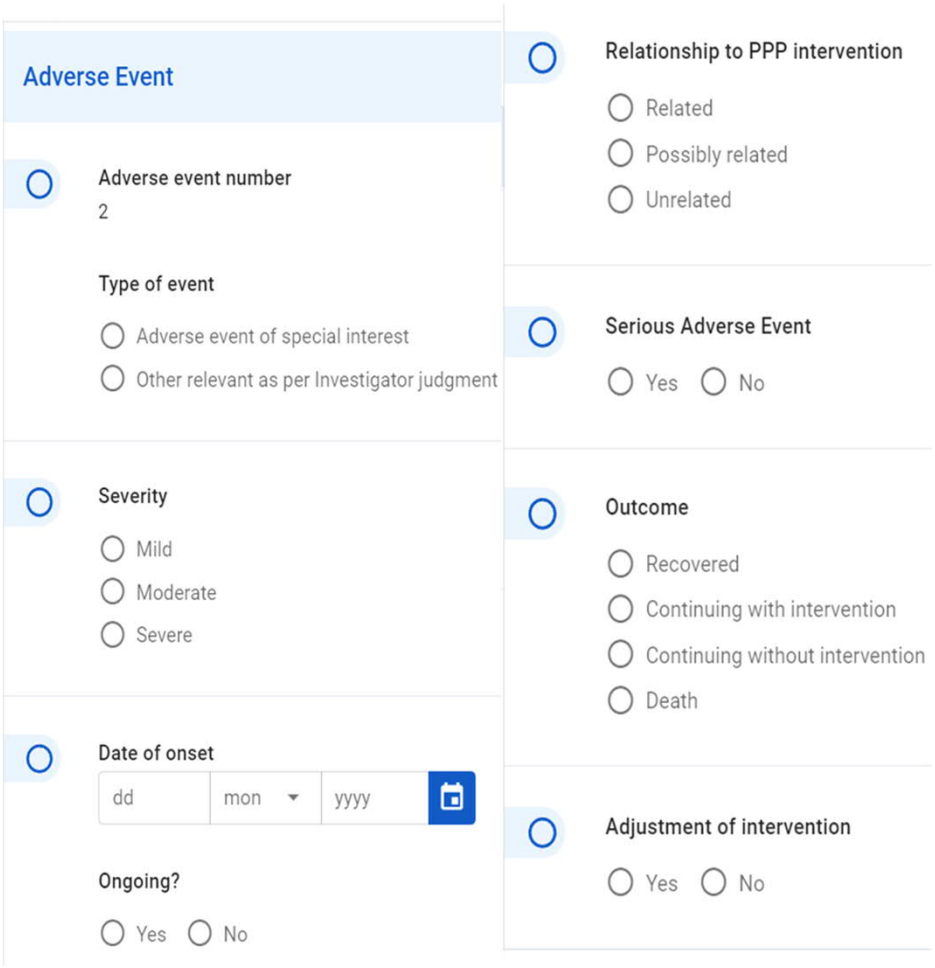
- Reporter of the protocol deviations can be: CRA,PI, sub-investigator, study nurse, data manager etc.



# Safety management

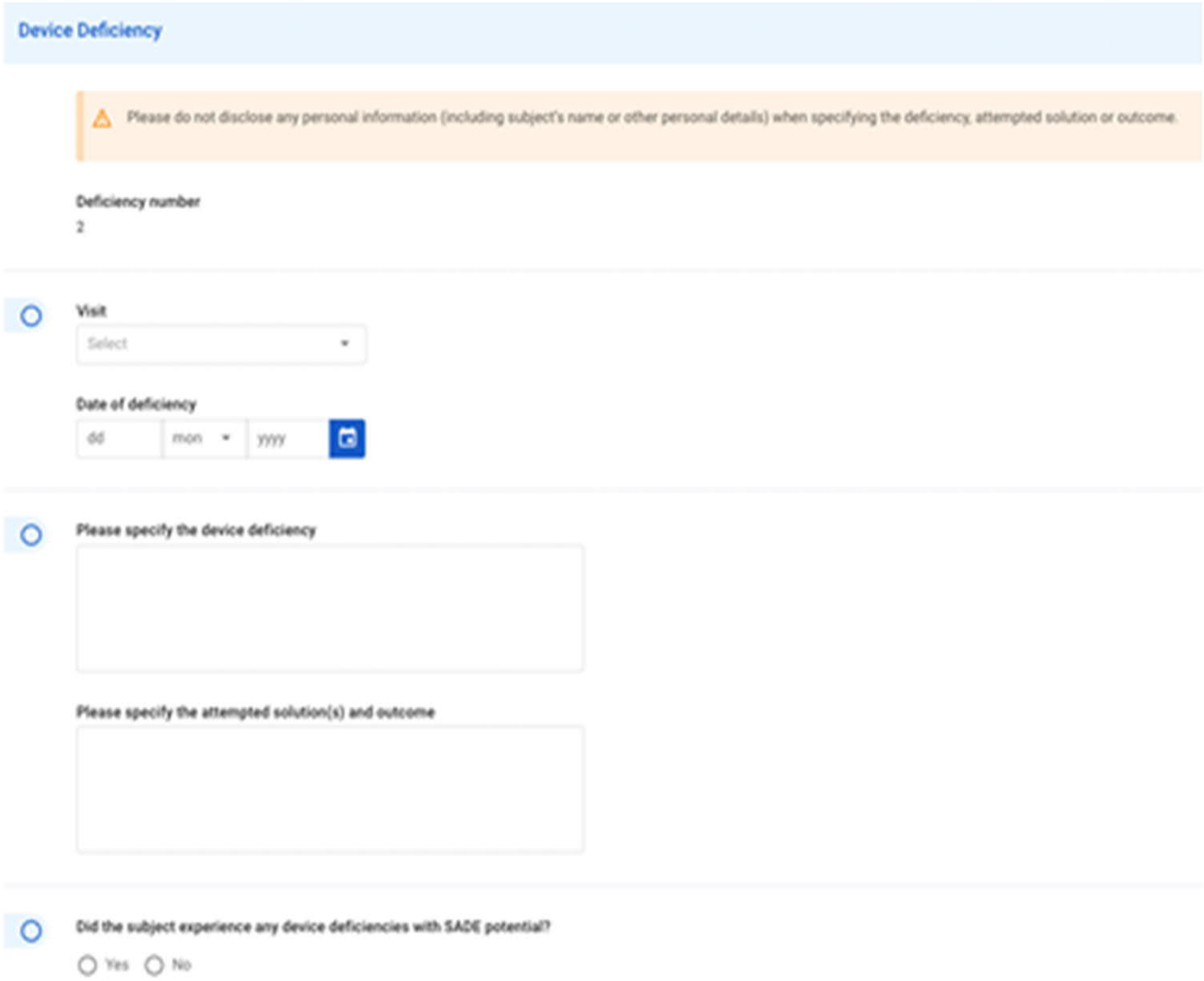
- Any adverse event/serious adverse event /adverse device effect/serious adverse device effect /device deficiencies (all as listed in protocol) should be reported through EDC system by the Principal Investigator, or qualified personal (study Nurse, Sub-Investigator etc.)

- serious adverse events/ serious adverse device effects and reportable device deficiencies must be reported to sponsor within 24 hours of the investigator becoming aware of the event.



# Device Deficiency

- 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.
- Device deficiency log should be filled when required and Manufacturer  will review the device deficincy logs and take appropiate actions.



# Endpoint data collection

- In the PPP arm, subject reported primary and secondary endpoint data will be collected at every visit (V2-V7).
- Prior to their next clinic visit at M18, Randomized Usual Care high risk subjects will be reminded (phone, email, letter) to report possible clinical end-points at 6 months and 12 months from 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.
- In randomized Usual Care arm subject reported primary and secondary endpoint data will be at V6 and V7
- Primary endpoints will be adjudicated by a separate committee, related data need to be entered in the EDC.
- Following endpoints will be adjudicated, only the ones from these categories and reported on the Primary and Secondary Endpoints form will be adjudicated:
    - - CV Death
    - - Myocardial infarction
    - - Heart Failure event
    - - Stroke
    - - Unstable angina
    - - Coronary revascularizations

# Endpoint data collection

- An interim analysis will be performed using non-adjudicated primary endpoint data at 18 months in randomized high risk subject arms
- Non-randomized low risk UC subjects will be reminded (phone, email, letter) to report possible primary and secondary end-points at 12 and 24 months after randomization. End point data for this group will not be adjudicated.
- 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.
- Extended end point collection 5 and 10 years will be also carried out to evaluate maintenance of the potential effect of PPP.

- Please attend endpoint collection webinar for detailed information.

# CONSORTIUM PARTNERS