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HEART-GP: developing a quick way to check for heart issues in primary care

Submission date 18/10/2023	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol
Registration date 20/10/2023	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 20/10/2023	**Condition category** Signs and Symptoms	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
General practitioners (GPs) frequently assess patients with chest pain. The challenge in primary care is to make the distinction between acute cardiac conditions versus far more common, non-urgent diagnoses in an unselected case-mix of patients, with limited resources and time constraints. All while being fully aware that symptom characteristics and signs are at best a mediocre indicator in both male and female patients. Currently, both misdiagnosis and over-testing are key concerns, and standardized diagnostic strategies may help GPs balance these risks. A recently developed fingerstick test for high-sensitivity(hs) troponin is proposed and may present a breakthrough in this regard for the safe rule out of acute cardiac conditions, particularly when integrated with a pretest probability assessment, using clinical risk scores. This study aims to evaluate whether acute chest pain can be improved when GPs are provided with modern decision-support tools

Who can participate?
Patients aged 18 years and over with new-onset, non-traumatic chest pain in which a cardiac etiology is considered possible, and who present to an out-of-hours primary care facility for a face-to-face consultation with a GP

What does the study involve?
This is a comparative diagnostic accuracy study incorporating a qualitative study using interviews and focus group meetings.

The goals of our study are to evaluate:
1. The performance of a single fingerstick-obtained hs-troponin measurement using universal and sex-specific cut-off values in out-of-hours primary care
2. Whether embedding hs-troponin in a clinical risk score (HEART, INTERCHEST, Marburg Heart Score) will further improve performance, in terms of increased efficiency without compromising safety
3. The experiences and preferences of GPs, triage nurses and patient participants in regard to the evaluated risk stratification tools
4. A chest pain decision rule that is safe, efficient, fit for use and implementable in out-of-hours primary care

Intervention:
GPs will be asked to fill out a digital questionnaire containing the elements of the 3 clinical risk scores. A finger stick hs-troponin POCT will be assessed for each patient.

Main study parameters/endpoints:
Diagnostic test characteristics (sensitivity, specificity, accuracy, negative predictive value (NPV) and positive predictive value (PPV)) for the occurrence of major adverse cardiovascular events (MACE) within 6 weeks of the index consultation.

What are the possible benefits and risks of participating?
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The benefit for participants is that the study reduces the risk of missing a heart attack. The collection of relevant patient information will take additional time during the consultation, estimated at 10 minutes. The measurement of hs-troponin requires a finger stick blood sample, which brings little to no additional risk to the patient. The patient will experience a short sting when a few droplets are collected. The clinical course (i.e. referral and/or treatment) will be decided by the clinical judgement of the GP.

Where is the study run from?
Amsterdam University Medical Centers (The Netherlands)

When is the study starting and how long is it expected to run for?
January 2023 to January 2027

Who is funding the study?
Dutch Heart Foundation (Hartstichting) (The Netherlands)

Who is the main contact?
Dr Ralf Harskamp, heartgp@amsterdamumc.nl (The Netherlands)

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Ralf Harskamp

ORCID ID
https://orcid.org/0000-0001-9041-0350

Contact details
Meibergdreef 9
Amsterdam
Netherlands
1105AZ
+31-20-5669111
heartgp@amsterdamumc.nl

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
NL82428.018.22

Study information

Scientific Title
HEART-GP: developing a rapid rule-out strategy for acute cardiac conditions in patients with acute-onset chest pain in out-of-hours primary care

Acronym
HEART-GP

Study objectives
Evaluation of acute chest pain can be improved when GPs are provided with modern decision support tools

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/02/2023, METC Office Amsterdam UMC (Meibergdreef 9, Amsterdam, 1105 AZ, Netherlands; +31-20-4445585; metc@amsterdamumc.nl), ref: NL82428.000.22

Study design
Comparative diagnostic accuracy study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Acute chest pain

Interventions
This is a diagnostic accuracy study with a qualitative element that will gather data using interviews and focus group meetings with GPs. GPs will be asked to fill out a digital questionnaire containing the elements of the 3 clinical risk scores. A finger stick point-of-care testing with high-sensitivity cardiac troponin assays will be assessed for each patient.

Part A: Diagnostic accuracy
The study will be coordinated by the Department of General Practice of the Amsterdam UMC. Prospective participants will be approached for enrolment at one of four out-of-hours primary

care (OOH-PC) facilities in Alkmaar, Amersfoort, Leiden and Venlo regions. Patients, in whom ACS is considered in the differential diagnosis by the treating physician, will be asked for study participation by the treating physician during face-to-face consultation at the primary care facility. This will take place during operating hours, which means during weekends, holidays and during weekdays between 5 pm and 8 am. Given that this study takes place in an acute care setting (in which delays should be kept to an absolute minimum), verbal initial consent will be asked initially, followed by a formal written consent procedure at a later stage, in which the latter will be done by research physicians and nurses from the Amsterdam UMC. This two-step approach is felt necessary due to safety (harm due to time delay) and acceptability concerns, and is also used in the POB-HELP trial, a troponin POCT strategy in daytime general practices (NL: 9525).

The diagnostic properties of a finger stick hs-troponin measurement will be investigated alone or in combination with pretest probability assessment tools, consisting of the clinical risk scores: HEART, INTERCHEST, or Marburg Heart Score. For troponin and risk scores, sex differences (i.e. specific cut-offs and stratified analyses) will be taken into consideration. There are 900 patients anticipated at 4 OOH-PC facilities, which is expected to require 24 months for inclusion, accounting for the non-inclusion of 50% of consultations and a roll-in/start-up period.

Study flow
Once the patient reaches the facility, the GP will evaluate the patient, ask for initial verbal consent and enter the data required for the risk scores. After obtaining verbal consent, the GP asks the nurse to obtain a resting 12-lead electrocardiogram (ECG), and a hs-troponin measurement via a capillary sample. At the end of the consultation, the physician provides the patient with an information leaflet regarding the study, including contact information of the study investigators. The study personnel will
obtain the formal informed consent procedure at the earliest convenience, depending on the clinical condition of the patient, and after providing ample time after receiving the patient information folder. All management decisions will be left to the discretion of the treating physician.

From a scientific perspective, ideally, the physician and the patient will be blinded from the troponin test results. However, the study team decided against blinding the treating physician for the ECG or troponin test findings, as this is not ethical nor easy to enforce. Instead, information on what findings should be considered normal versus abnormal will be provided. It is important to stretch the safety aspect here. To be specific, it is strongly recommended to immediately refer each patient with chest pain and an elevated troponin level, irrespective of clinical gestalt, for safety reasons. In addition, GPs will be strongly advised to immediately refer a patient with chest pain when there is a high clinical level of suspicion, even for those with a negative troponin test result. The fact that providing this information will likely affect decision-making in the setting of chest pain is acknowledged. To semi-circumvent this, GPs will also be asked what their level of suspicion was prior to the results (i.e. clinical gestalt), and whether they acted based on clinical presentation alone or also based on the findings of the ECG and/or troponin test, and compare referral patterns using historic controls. To maximize feasibility it is aimed to minimally disrupt routine care, as the treating GPs will only be required to verbally ask patients for interest in study participation and minimal data
collection. All research-related activities, such as the informed consent procedure, data collection (i.e. ECG, troponin) and follow-up will be performed by the research team.

Structured telephone follow-up will be conducted for all subjects by a study nurse, at 6 weeks after the index consultation. Patients will be asked whether they have consulted another physician had experienced ACS or had undergone any cardiac testing, including coronary

angiography with or without invasive intervention. If the patient answers in the affirmative or is unsure of the answer to any of these questions, or when the patient cannot be reached by telephone, the patient's own GP will be contacted to verify vital status and obtain a copy of relevant documentation. Finally, the final diagnosis of each case with elevated troponin will also be documented to study whether it was due to myocardial infarction or another acute condition that warrants immediate evaluation (e.g. pulmonary embolism or myocarditis) or was due to a less urgent, chronic condition (such as renal failure).

Part B: End-user involvement and study evaluation
The study aims to develop a chest pain decision rule applicable for use in OOH-PC and starts out with consulting with our GPs and triage nurses from the four participating sites as well as patient representatives from Harteraad. Context mapping will be used to ensure clarity in what context the study is conducted, for instance by identifying local stakeholders (cardiologists, paramedics) and to check their needs and expectations as well as how they may affect the study. Once the diagnostic accuracy study is (near) completion, in-depth interviews with GPs and triage nurses who participated in the study will be performed to evaluate their experiences with the troponin and risk stratification tools. The study will also explore whether they hold a preference for a specific decision rule and why, and what is most important for them to make it work, in terms of practical use. Based on the output, there will be subsequent focus group discussions held on the most important topics. There will also be interviews held with enrolled patients (50% female, 25% with an ethnic minority background) to ask them to reflect on the point-of-care test and the risk scores and how the physician discussed these with them, as well as on the flow-of-care and satisfaction.

Part C: Chest pain decision rule
In part C, which of the studied options (hstroponin, HEART, or hs-troponin + INTERCHEST or MHS) would be the best chest pain decision rule is determined based on the lessons on diagnostic properties as well as the practical input from GPs, triage nurses and patients, in terms of diagnostic properties and implementation. Besides end-users, other stakeholders (i.e. cardiologists, paramedics, professional societies) will also be consulted to obtain their input. The end product is a concept version of a chest pain decision rule.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Diagnostic test characteristics (sensitivity, specificity, accuracy, LR+, LR-, NPV and PPV) for the occurrence of major adverse cardiovascular events (MACE) measured using medical record data (primary care and/or hospital records) within 6 weeks of the index consultation

Key secondary outcome(s))
1. Test characteristics measured using sensitivity, specificity, accuracy, LR+, LR-, NPV and PPV using a more restricted definition of acute coronary syndrome within 6 weeks of the index consultation
2. End-user involvement will be measured using interviews with GPs and triage nurses who participated in the study to evaluate their experiences with the troponin and risk stratification tools, and enrolled patients who will be asked to reflect on the point-of-care-test and the risk scores and how the physician discussed these with them, as well as on the flow-of-care and satisfaction by the end of recruitment
3. Study evaluation measured using interviews with GPs and triage nurses who participated in the study to evaluate their experiences with the troponin and risk stratification tools, and

enrolled patients who will be asked to reflect on the point-of-care-test and the risk scores and how the physician discussed these with them, as well as on the flow-of-care and satisfaction by the end of the overall study

Completion date
01/01/2027

Eligibility

Key inclusion criteria
All participants must meet all of the following criteria:
Age 18 years or older

Patients:
Presence of chest pain at the time of consultation (with a duration of at least 15 minutes) where a cardiac etiology is considered possible

Participant type(s)
Patient, Health professional

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Patients:
1. Hemodynamic instability
2. Chest trauma preceding chest pain
3. Not able to provide informed consent
4. Not registered with a GP in the Netherlands

Date of first enrolment
17/03/2023

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
Netherlands

Study participating centre
Amsterdam UMC
Amsterdam
Netherlands
1105AZ

Study participating centre
Huisartsenpost Eemland
Amersfoort
Netherlands
3813 TZ

Study participating centre
Huisartsenpost Noord-Limburg/Cohesie
Venlo
Netherlands
5912 JX

Study participating centre
Huisartsenpost De Limes
Leiden/Leiderdorp
Netherlands
2353 GA

Study participating centre
Huisartsenpost Noord-Kennemerland (HONK)
Alkmaar
Netherlands
1823 DL

Sponsor information

Organisation
Amsterdam University Medical Centers

ROR
https://ror.org/05grdyy37

Funder(s)

Funder type
Research organisation

Funder Name
Hartstichting

Alternative Name(s)
Heart Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
Extracted data will be recorded in an electronic cloud-based, data capturing platform (CastorEDC, Amsterdam). This platform allows for secure data management, including the monitoring of patient inclusion, and missing data elements, and importantly includes an audit trail. Each enrolled patient will be assigned a Castor identification code. This identification code cannot be linked to an individual in Castor. Instead, this information is kept in a separate, password-protected Access database, on a secure server of the Amsterdam UMC (G:\divjk\Huisartsgeneeskunde Onderzoek\). Access to this Access database will be restricted to members of the research team (e.g. principal investigator, research nurses), the monitor and IGJ (inspectie gezondheidszorg en jeugd).

Audio recordings of focus group meetings as well as verbatim transcriptions of interviews will be digitally stored on a secure server of the Amsterdam UMC. Hard copy data will be stored in the trial master file (TMF) in a locked cabinet and will only be accessible to the research group. Hard-copy data will also be scanned and saved as digital data. Digital data will be stored in the Amsterdam UMC network storage, with access restricted to the research team. The network storage is backed up automatically.

Future data analyses will be performed by exporting the final and locked Castor data file to our institutional secure data drives. From here we will use statistical software packages (including SPSS, R, MedCalc) to analyze our data.

All data will be handled according to the rules of the Amsterdam UMC, the General Data Protection Regulation and the Dutch Act on Implementation of the General Data Protection

Regulation. (in Dutch: Uitvoeringswet AVG, UAVG). Data will be kept until 20 years after finishing the study. When data will be used for publication, they will never relate to individual traceable patients.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2.4	28/11/2022	20/10/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes