Gender comparisons in non-acute cardiac symptom recognition and subsequent help-seeking decisions: a mixed methods study protocol

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ABSTRACT
Introduction: Coronary heart disease (CHD) is one of the leading causes of death in both men and women worldwide. Despite the common misconception that CHD is a ‘man’s disease’, it is now well accepted that women endure worse clinical outcomes than men following CHD-related events. A number of studies have explored whether or not gender differences exist in patients presenting with CHD, and specifically whether women delay seeking help for cardiac conditions. UK and overseas studies on help-seeking for emergency cardiac events are contradictory, yet suggest that women often delay help-seeking. In addition, no studies have looked at presumed cardiac symptoms outside an emergency situation. Given the lack of understanding in this area, an explorative qualitative study on the gender differences in help-seeking for a non-emergency cardiac events is needed.

Methods and analysis: A purposive sample of 20–30 participants of different ethnic backgrounds and ages attending a rapid access chest pain clinic will be recruited to achieve saturation. Semistructured interviews focusing on help-seeking decision-making for apparent cardiac symptoms will be undertaken. Interview data will be analysed thematically using qualitative software (NVivo) to understand any similarities and differences between the way men and women construct help-seeking. Findings will also be used to inform the preliminary development of a cardiac help-seeking intentions questionnaire.

Ethics and dissemination: Ethical approvals were sought and granted. Namely, the University of Westminster (sponsor) and St Georges NHS Trust REC, and the Trust Research and Development Office granted approval to host the study on the Queen Mary’s Roehampton site. The study is low risk, with interviews being conducted on hospital premises during working hours. Investigators will disseminate findings via presentations and publications. Participants will receive a written summary of the key findings.

BACKGROUND
Coronary heart disease (CHD) is often thought of as a ‘man’s disease’, but it has been shown to have worse clinical outcomes in women1 2 in terms of bleeding (post-treatment), stroke and reoccurrence of cardiovascular events.3-5 In fact, EU and US research has shown that more women die of CHD than men.6-8

Despite advances in technology, CHD remains a leading cause of death worldwide ranking highly in the UK and EU mortality rate indicators, accounting for 46% of all deaths.9 In view of this high mortality, there has been a significant public health focus on improving access to prompt cardiac diagnosis and treatment (for both men and women), through the establishment of revascularisation therapy targets (90 min) for acute myocardial infarction (heart attack) and rapid access clinics for stable cardiac symptoms.10 11

Revascularisation is a process of restoring blood flow to an ischaemic area. In the context of cardiology, it relates either to the opening of a blocked or narrowed coronary artery by balloon inflation (widening the artery) or bypassing the blocked arterial area using a vein graft. It is known that early presentation and subsequent rapid interventional revascularisation following the onset of a
CHD event is associated with improved clinical outcomes. These public health strategies have begun to show benefit—a recent epidemiological review reported a significant fall in CHD mortality rates in the EU, but it was argued that further improvement was being hampered by the nature of help-seeking decisions of patients. Health professionals can only act once a patient has sought help for these symptoms, and evidence suggests that many patients, particularly women, delay help-seeking, which in turn results in poor outcomes.

Biological sex and gender

The term gender is often used interchangeably with biological sex but they are different. The WHO distinguishes between the two, defining gender as “the socially constructed roles, behaviours, activities and attributes that a given society considers appropriate for men and women”; and sex as “the biological and physiological characteristics that define men and women.” Different contexts including cultural, political, religious, national, social norms and personal choice all influence gender. Our study will focus on sex and gender, as both being a biological man or woman (women experience chest pain differently to men) and gender constructions (eg, women may believe heart disease is a male problem and underestimate their own risk) are known to impact on help-seeking decisions in a cardiovascular context. However, for simplicity sake, this study protocol will refer to sex differences throughout, while assuming that gender constructions influence both men and women, thus also requiring investigation.

Help-seeking and sex differences

Rickwood et al have defined help seeking as “the behaviour of actively seeking help from others. It is about communicating with other people to obtain help in terms of understanding, advice, information, treatment and general support in response to a problem or distressing experience” (p.4). Health-related help-seeking is the conscious decision to seek assistance to change one’s health status (illness). Help or assistance might be sought from a health professional or friends and family. One paper analysed the term help-seeking and supported Rickwood’s definition by concluding that help-seeking is an intentional action to resolve health issues. The paper also added that in order for a help-seeking intentional action to occur, there must be an acknowledgement of the existence of a health issue and ultimately acceptance that external help is needed.

Help-seeking decision-making for both men and women is a complex and multifaceted process and concept. Literature in general suggests a higher tendency for women to report symptoms to friends and family than men. Yet when it comes to consulting a health professional, there is some divergence of opinion in the literature with the balance of evidence supporting higher general practitioner/health professional consultation rates in women, although the evidence for gender difference is weaker for particular conditions (eg, headache and back pain).

Sex differences in cardiovascular disease and help-seeking

The literature on sex differences in help-seeking for cardiac disease in emergency situations is conflicting. However, on balance, the evidence suggests that women delay help-seeking longer than men—the opposite behavioural pattern assumed of general help-seeking for most other conditions. However, most studies reporting that women delay longer than men cited challenges in symptoms presentation as the result of biological sex differences in anatomy, rather than focusing on gender constructions, as possible explanations.

A typical presentation of cardiac chest pain often involves central crushing chest pain, radiating down the left arm and into the jaw, a pattern widely experienced by men. However, it is well documented that this ‘classical’ presentation is not so often experienced by women, who experience more varied symptoms of lower intensity. For instance, one recent study noted that women are more likely to experience a spreading pain as opposed to a more focused crushing pain. Although the reasons for atypical symptoms experienced by women remain open for debate, the literature suggests physiological, anatomical and psychosocial differences could all play a role. Women are more likely to experience plaque erosion (as opposed to the plaque eruption found in men) and microvascular coronary disease (MVD); they also have smaller coronary arteries.

Plaque refers to the different types of cholesterol-rich lipid deposits within the coronary artery walls, each with a variable risk of thrombosis. The highest risk is linked to plaque deposits covered by a thin fibrous cap, which is vulnerable to cracking (plaque rupture), exposing lipid plaque to the luminal blood flow, initiating a clotting cascade which ultimately occludes or severely restricts arterial blood flow potentially resulting in myocardial infarction (heart attack). Plaque erosion has a different pathological process—an area of the endothelial cellular covering of the tunica intima layer of an artery wall is absent, exposing blood flow to inner layers of artery wall, initiating the clotting cascade and thrombosis. The clotting process in plaque erosion is less aggressive than rupture and is associated with less luminal stenosis (smaller artery blockage).

MVD is the result of diffuse plaque in coronary arterioles (smaller arteries), as opposed to the wider coronary artery tree. The arterioles are too small to be visualised by angiography. The plaque build-up in these arterioles does not lead to obstruction but causes endothelial damage, resulting in a thickening of the smooth muscle of the arteriole wall. This arterial remodelling results in wall stiffness and consequent loss of ability to dilate in response to emotional and physical stress.
stimuli, reducing myocardial blood flow (even though the arteriole lumen remains patent).

It is thought that such differences in the disease pathway may account, at least in part, for how women experience atypical cardiac symptoms. MVD (which is more common in women as stated above) is not amenable to percutaneous coronary intervention to provide symptom relief for chest pain.33 Additionally, MVD was once thought to be clinically insignificant,34,35 but recent studies have shown links to increased morbidity and mortality.36,37 Smaller coronary arteries in women, which are independent of body size,38 are notoriously difficult to revascularise (reopen) and are considered to be a significant contributor to worse clinical outcomes in women.3–5

It is also possible that psychosocial factors mediate symptom perception. For instance, in one study of a condition linked to cardiovascular disease (CVD; heart failure), it was found that women generally perceive their health to be better than men, and seem to adjust better to living with heart failure, viewing it as second chance.39 This may partly account for the increased longevity in females compared with male heart failure patients—men viewed the illness as loss of control and deprivation of a normal life.39 In another review, women and men were shown to have different ways of relating to pain. Women experience pain throughout life as a result of non-pathological processes including menstruation and childbirth.40 As a result of differing relationships between pain, gender and pathology, women relate pain to the monitoring of health as well as of injury. Men on the other hand do not experience the specific types of non-pathological pain as women do, and therefore view pain more as diagnostic symptom of injury.40

Over 400 publications examine help-seeking and cardiovascular disease.18 They are predominately quantitative studies and are exclusively based on emergency cardiac events (heart attacks). A few studies have undertaken comparative analysis between men and women. In the studies that look at the differences between men and women (sex differences), there is no consensus on whether women delayed longer than men or the reasons behind any delayed help-seeking.16,17,19,41–43

The wider body of evidence in the area of gender and CVD—like the comparative studies—is weak and conflicting. Most of the studies used ‘response to symptoms’ instruments. The validity of these instruments to accurately measure cardiac symptoms is questioned because they are based on men and male symptoms rather than being developed and tested with women.27

The qualitative literature appears to be more decisive and suggests women experience cardiac symptoms differently to men, making symptoms difficult to interpret, which in turn affects help-seeking decisions.1,27,44 Symptom recognition in women is also a challenge for health professionals. Professionals may fail to diagnose cardiac symptoms correctly, resulting in women being undertreated.2,19 A review of 60 qualitative studies concluded that the perception that heart disease is a male problem was likely to account for a delay in help-seeking in women. It also noted the lack of comparative analysis between men and women, and called for further research in the area.2

This overall weak evidence, together with limited qualitative gender comparative research,2 and no enquiry into the help-seeking decisions of patients with stable angina accessing chest pain clinics, demonstrates a clear gap in the literature and therefore justifies further exploration. A recent review of the literature in 2013 called for further exploration of gender and help-seeking for cardiac symptoms.45 Understanding what influences these help-seeking decisions—enablers or barriers—could have a significant public health and health promotion benefit, as it is known that early presentation and treatment of cardiac symptoms is associated with better clinical outcomes.3,45

METHODS AND STUDY DESIGN

The study design has two phases and is a mixed methods project. The first phase will be qualitative with semistructured interviews analysed using a thematic approach. In the second phase, the findings from the analysis of interview data will inform the construction of a help-seeking questionnaire in the area of CAD.

Theoretical framework

The study will take a social constructionist approach to understand patients’ meaning-making in relation to non-emergency cardiac symptoms.46 This approach starts from the view that individuals and groups construct or create their realities, influenced by multiple factors including sex, culture, ethnicity and expected social behaviours. It also considers the consequences of these social constructions, for example, a belief that women do not get heart disease is likely to impact on help-seeking. Semistructured interviews using an interview guide will be used to ensure we uncover the meaning patients attribute to their circumstances, and cover topics considered important to the project.

Sampling

Maximum variation sampling will be used in order to capture a wide range of perspectives within the phenomena being studied.27 The sampling dimensions are sex, age and ethnicity to ensure the recruitment of a heterogeneous sample and will include at least:

▸ Four male patients >50 years of age and include a mixture of white and ethnic minority participants.
▸ Four female patients >60 years of age and include a mixture of ethnic minority and white participants.
▸ Four male patients <50 years of age and will include a mixture of ethnic minority and white participants.
▸ Four female patients <60 years of age and include a mixture of ethnic minority and white participants.
The sample will be drawn from referrals to the rapid access chest pain clinic (RACPC), which specialises in the assessment of non-emergency cardiac symptoms (stable angina), at Queen Mary’s Hospital, Roehampton. The RACPC operates on Mondays and Thursdays and sees over 80 patients a month. The service covers a large and highly diverse catchment area, making it the ideal centre to capture the maximum variation required.

Recruitment
Recruitment will last approximately 12 months, starting February 2014 and continue until data saturation, that is, no new themes important to the project are being elaborated on. It is envisaged a sample of 20–30 participants will be recruited. Although this sample might be considered too small for quantitative research, in qualitative research it is considered that this sample is large enough to reach saturation of concepts. Indeed, Baker and Edwards expert discussion paper suggests saturation can be achieved with as low as 12 participants with the average being 30 participants.48 Similar studies in gender comparison work have shown concept density (saturation) at around 20 participants.19 43 Referrals, medical records and the Patient Administration System (PAS) system will be used to identify candidates who meet the inclusion/exclusion criteria, as detailed in table 1.

It is necessary to use multiple sources to extract these data as all the information required may not be available for all patients from a single source, for example, missing data on the referral or PAS system may be found in the medical notes. Suitable candidates identified by the researcher will be sent a patient information sheet with their chest pain clinic appointment letter inviting them to participate. Potential participants will receive a follow-up telephone call approximately 1 week later by one of the clinical triage cardiology staff, confirming they have received information sheet and asking if they would like to participate. If they agree by phone, understanding of the participant information sheet and written consent will be confirmed on the day of the chest pain appointment. An opportunity to ask further questions will be provided before consent is taken by the researcher or designated assistant. This modus operandi allows sufficient time away from the hospital between receipt of the patient information sheet and giving consent.49 Patients who consent will be assigned a unique study number to identify them throughout the study.

DATA COLLECTION
Semistructured interviews with key topics and probes will be used for two reasons. First, they enable a focused interview while allowing for rich data collection, including areas not covered by the key topics.46 This design is optimal when balancing rich data collection against the operational and time limitations of an NHS-based academic study. Second, one-to-one interviews are recognised as the best form of data collection for sensitive topics including potentially serious health matters where little is currently known.46

The interviews will be conducted face-to-face in the researcher’s private office based in the cardiology department. The length of each interview will be dependent on individual participant responses. However, consideration will be given to the fact that very long interviews will be operationally difficult to accommodate in the NHS clinic, and introduce fatigue for both researcher and participant, potentially reducing the usefulness of participant responses.50 In view of this, a maximum of 1 hour per interview will be set aside.

All interviews will be transcribed verbatim using a professional transcription agency. Although the agency will not receive patient identifiable information other than the circumstances where a patient identifies themselves in the digital recording, they will be asked to sign a confidentiality agreement in line with usual practice. The investigator will, on receipt of transcripts, check and anonymise them by removing all identifying information. Interviews will be undertaken by the same researcher to increase consistency.51

An in-depth semistructured interview process adopting the Berg style of questioning50 will be used to elicit the participant’s meaning-making in terms of cardiac symptoms and the decision to seek help. Berg’s style of questioning is useful when trying to draw out people’s

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Males and females over the age of 18 years</td>
<td>Patients presenting with an acute cardiac event</td>
</tr>
<tr>
<td></td>
<td>Have been referred to the RACPC for assessment of non-emergency cardiac symptoms</td>
<td>Patients not accessing the RACPC. For example, patients referred directly by a cardiologist for the evaluation of chest pain. These patients do not meet the requirements for a RACPC referral because they are comorbid (heart failure or other unstable cardiac problems)</td>
</tr>
<tr>
<td></td>
<td>Fall within the maximum variation dimensions in terms of gender, age and ethnicity</td>
<td>Unable to give consent for whatever reason (eg, mental illness), or are deemed unable to give consent</td>
</tr>
<tr>
<td></td>
<td>Able to communicate sufficiently in English</td>
<td>Unable to communicate in English</td>
</tr>
<tr>
<td></td>
<td>Able and willing to consent to the study</td>
<td>RACPC, rapid access chest pain clinic.</td>
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</tbody>
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opinions and experiences. This style of questioning includes essential questions which focus on the central issue, questions to recheck reliability by rewording, throw-away questions which are mostly demographic or designed to build rapport and pace the interview, and probing questions to draw out details and encourage participants to elaborate. The interview will close with a few general questions, constructed to elicit participants’ background, non-cardiac and cardiac medical history.

The interview questions were originally informed by the current literature and were assessed by all investigators to ensure that topics were clear and likely to be comprehensible to participants. The guide was piloted with two patients who had previously attended the chest pain clinic for non-emergency cardiac symptoms. The interview schedule was then revised, and prewritten, probes were reduced to enable participants to better tell their own story in their own words. Specific probes seemed to inhibit patient storytelling, perhaps also giving the message to patients that a clinical history was being taken. After a set of initial interviews, the interview guide was revised further in order to encourage the patient’s story and include additional topics, for example, the level of explanation that professionals provided and how patients managed information they gave to professionals. The interview topics are detailed in table 2. On average, initial interviews lasted about 30–40 min, and 1 h was deemed sufficient for scheduling interviews.

DATA ANALYSIS
An inductive thematic approach will be used to analyse the data. Transcribed interviews (verbatim) will be entered into a qualitative data management software program—Nvivo. The programme allows easy manipulation of data under areas of interest. In the first stage of the analysis, the researchers will use a line-by-line analysis of transcripts to search for areas of interest and compare them with each other. The emerging common themes (phenomena) will be labelled as open codes (first level coding). The researchers will undertake further analysis to group together the open codes to form a number of smaller themes (second level coding), as well as linking codes together. The second level codes will be organised by the researchers into final themes which will be tabulated and the tables populated with supporting quotes from the raw data. The final themes will demonstrate patterns of help-seeking decisions, within the different social contexts for men and women with non-emergency cardiac symptoms. The data and quotations contained in these tables will form the basis of the written up results.

To date, 16 interviews have been conducted. From these interviews, an initial list of 60 codes (first level coding) has been constructed through debate between investigators. This list will continue to be revised as further interviews are conducted.

Table 2 Interview guide

<table>
<thead>
<tr>
<th>Theme</th>
<th>Sample question</th>
</tr>
</thead>
<tbody>
<tr>
<td>What was happening before the symptoms?</td>
<td>Tell about what you were doing before your symptoms started?</td>
</tr>
<tr>
<td>The symptom experience</td>
<td>What was it like having those symptoms?</td>
</tr>
<tr>
<td>Describing symptoms</td>
<td>Can you describe your symptoms to me?</td>
</tr>
<tr>
<td>Decision to seek help from doctor/health professional</td>
<td>Tell me what made you decide to see a doctor?</td>
</tr>
<tr>
<td>Influences of others</td>
<td>Did you seek advice from friends and family?</td>
</tr>
<tr>
<td>Barriers/enablers to help-seeking</td>
<td>How do day-to-day pressures affect your ability to see a doctor?</td>
</tr>
<tr>
<td>Patient clinic experience</td>
<td>What was the chest pain clinic pathway (nurse consult/tests/diagnosis) like?</td>
</tr>
<tr>
<td>Subsequent experiences</td>
<td>What kinds of things did you leave out telling the doctor?</td>
</tr>
<tr>
<td>Understanding of risk of heart disease</td>
<td>How do feel now that you have completed the pathway and have a diagnosis?</td>
</tr>
<tr>
<td>Perceptions of risk and genders</td>
<td>What is your understanding about heart disease and its risk?</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Tell me about what understand about differences in risk (of heart disease)</td>
</tr>
<tr>
<td>Background/general health</td>
<td>between men and women?</td>
</tr>
</tbody>
</table>

Diagnosis                              | How do you feel about your diagnosis today?                                   |
|                                       | Tell me about your background/health in general?                             |

Questionnaire development
Data analysed from the interviews and insights from the literature will inform the development of a draft questionnaire to measure help-seeking intentions and practices for cardiac symptoms in non-emergency situations. It is intended that such a draft questionnaire, once further developed, could be used to further our understanding about help-seeking and patients in the general population, as well as those presenting with cardiac symptoms. Studies in the literature have raised concerns over the validity of existing generic help-seeking instruments, especially for women.

The full development and testing of this questionnaire (comprehensive reliability and validity testing) is beyond the scope of this study. However, the initial stages of development and preliminary testing will be undertaken by the researchers including item generation and selection, establishing content validity, and testing comprehensibility to patients.
Questionnaire items will each have five participant response options: ‘strongly agree’, ‘agree’, ‘neither agree or disagree’, ‘disagree’ and ‘strongly disagree’ for each item.53 Items will be scored ranging from a value of five at the positive end, to a value of one at the negative end. It is envisaged that the questionnaire will comprise 10–16 questions, providing for a maximum score of 50–80. A high score will denote highly proactive help-seeking intentions and practices, a midrange score moderately proactive help-seeking and a low score suggesting the likelihood of delayed help-seeking help for critical symptoms which could negatively affect long-term outcomes.

Establishing content validity
To ensure all help-seeking practices for non-emergency cardiac symptoms are identified by the questionnaire, its content validity will be measured. This determines the extent to which the questionnaire represents all aspects of the given social construct it aims to measure.54 The study will use Lawshe’s (1975) methods for confirming content validity. The advice of a panel of experts—including cardiology experts, behaviour experts and a questionnaire construction expert—will be sought. The panellists will grade the relevance of each item (question) and the Lawshe (1975) formula (Content Validity Ratio) will be applied to the grading to determine the overall relevance of each item. Items with weak relevance can then be reworded or excluded from the questionnaire.54 In addition, a review by supervisors and professional colleagues will be undertaken to ensure questions are grammatically correct, make sense and thus have good face validity.54

Testing comprehensibility to patients
The draft instrument will then be piloted on a sample of the interview patients (10–15 patients) to assess the comprehensibility. The participants will be invited to participate in this second phase of the research when consent is taken initially. The questionnaire will be emailed or posted to participants (with stamped addressed envelopes for return to the researcher) as per patient preference. Patients will be asked to complete the questionnaire and will then be encouraged to comment (open text boxes) on what it was like to complete the questionnaire. For example: Were the questions clear? Did the wording make sense? Were they confused by anything? What did they think the questionnaire was trying to get at? They will also be asked if they think anything should be covered on the instrument that is not currently addressed.

ETHICS
Application for ethical approval had three phases. First, we sought approval from the University of Westminster research office to obtain a letter of sponsorship. The application was then submitted to the NHS Research Ethics (Fulham Committee) for proportionate review, where favourable opinion subject to minor amendments was issued (reference no 14/LO/0169). Finally, we obtained NHS management approval from the St Georges Healthcare NHS Trust’s Research and Development Office to allow the study to be conducted on the Queen Mary’s site (approval was granted in January 2014, reference no.14.0007).

DISCUSSION
This mixed methods study provides an opportunity to undertake a comparative analysis of the gender similarities and differences in help-seeking decision-making for non-acute cardiac symptoms, while taking into account the wider factors (eg, emotions, personal relations, perceptions of cardiac risk, culture) that are thought to affect both gender constructs and help-seeking decisions. While there have been many studies within this field, none have sought to evaluate the non-acute context, and no such studies compare men and women.

Uncovering the barriers and enablers to men and women seeking help for the early signs of cardiac symptoms is of considerable public health importance, as there is a potential to reduce the risk of acute cardiac syndrome (ACS). ACS events are known to increase mortality and morbidity. They are associated with heart muscle damage which can lead to heart failure; myocardial scarring is associated with arrhythmic events and, in some cases, sudden cardiac death events. Some types of ACS treatments are linked to severe bleeding complications. The prevention of an ACS is a better option (in terms of patient well-being and financial cost) than treatment and management after an ACS event. Being able to capture patients in the early stages of heart disease by improving awareness and promoting behavioural change (eg, early presentation enabling ‘non-emergency’ treatments) could significantly improve the long-term clinical outlook.

In order to examine the participant’s help-seeking decision process, the study will use qualitative semistructured interviews interpreted with a social construction viewpoint. This is considered the best method for extracting rich data from participants and understanding the meaning participants attach to their cardiovascular experience when little is understood. The literature suggests that decision-making is affected by differences in the way men and women experience cardiac symptoms, societal misconceptions around the fallacy that heart disease is a ‘man’s disease’ and the suggestion that women prioritise their role as a primary care giver above their own health needs. In order to facilitate deeper exploration of the known key themes and assumed barriers/facilitators to help-seeking, the interviews use probes designed to ensure rich data are collected. However, the overarching interview topics are general to encourage the participant to tell their story and share their experience to ensure new themes are not missed.

Investigating gender, help-seeking decisions and cardiac symptoms is complex, and few larger quantitative
studies have produced convincing statistical results. Many studies have criticised the lack of inclusion of a specific valid instrument for gender, help-seeking and cardiac symptoms. Studies used generalised non-specific response-to-symptoms. In order to facilitate further study—a large quantitative trial with generalisable results—the qualitative data elicited in this study will be used to construct and undertake preliminary validation testing for a gender and help-seeking questionnaire with a specific focus on cardiac symptoms.

FEEDBACK AND DISSEMINATION

The investigators will send a written summary to participants at the end of the study to thank them for their involvement, let them know the study is concluded and provide key study findings. In addition, investigators will disseminate findings to the scientific community via publication in peer journals, presentations and the creation of patient advice leaflet for chest pain clinics.

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Contributors NS designed the study protocol with guidance from DR and AC. NS drafted the manuscript. DR and AC edited and gave feedback on multiple drafts of the manuscript. All authors read and approved the final manuscript.

Competing interests None.

Ethics approval IRAS.

Provenance and peer review Not commissioned; externally peer reviewed.

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