FULL/LONG TITLE OF THE STUDY

Prehospital Point of Care Testing to Enable Decision-making (PrePoCTED)

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Contents

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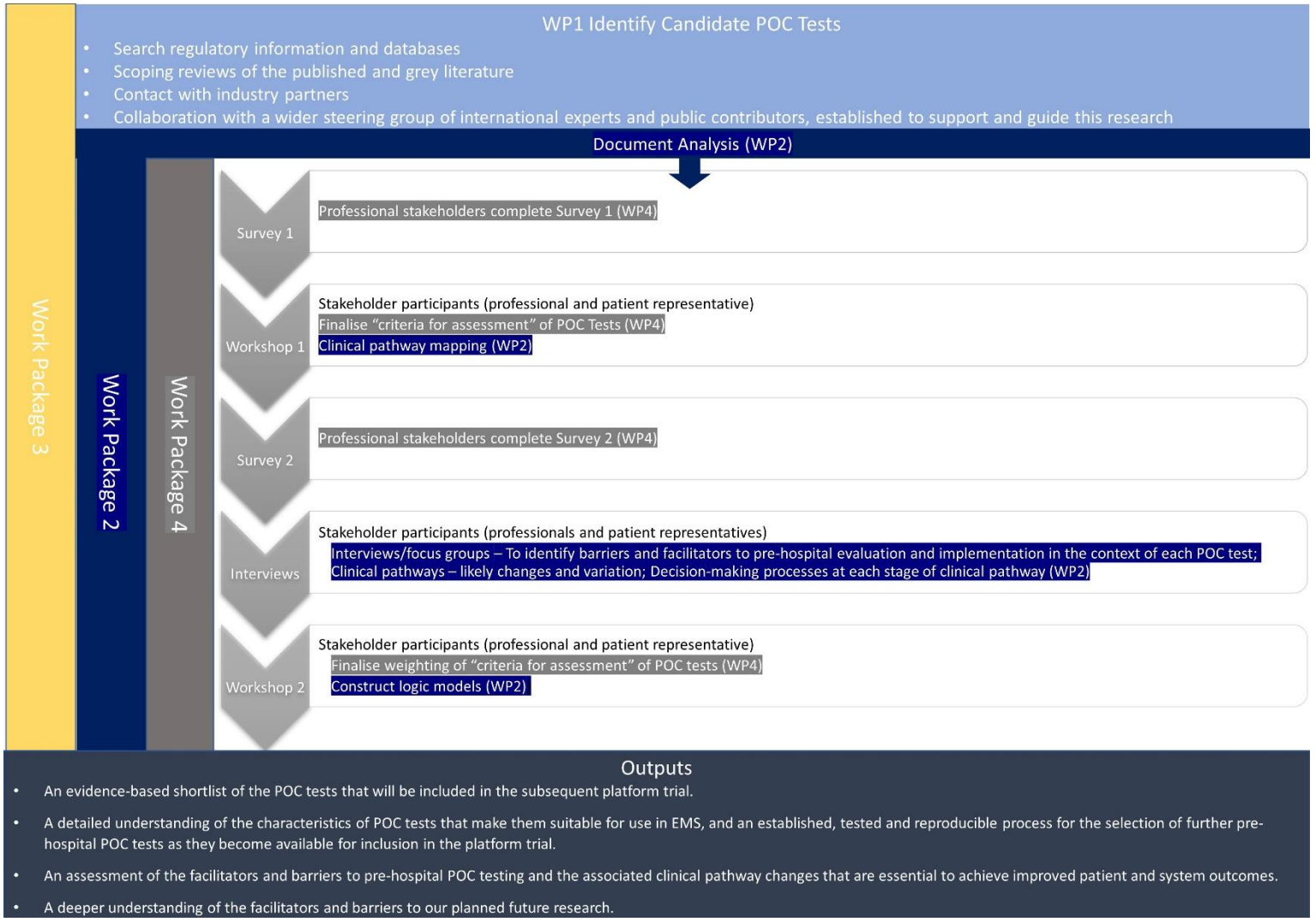
Funder(s)	NIHR

Study flow chart



Study Protocol

Background

United Kingdom (UK) Emergency Medical (Ambulance) Services (EMS) are experiencing a sustained growth in demand.[1] This is combined with lengthy delays in handing over patients to crowded Emergency Departments (ED), which in turn compromises their ability to respond to further emergency calls and leads to extended ambulance response times.[2,3] Consequently, there is substantial pressure to ensure that ambulance staff avoid patient conveyance to hospital whenever it safe and appropriate to do so.[4] At the same time, it is important to ensure that those patients who are conveyed reach the facility best suited to their needs in a timely way.[5]

Point of Care (POC) testing is becoming increasingly available and utilised across the National Health Service (NHS), and the adoption of this technology has been further accelerated by the Covid-19 pandemic.[6,7] It is estimated that the POC testing market will continue to grow rapidly, and may rival the pharmaceutical industry globally within two decades.[8]

At present, about half of those contacting EMS in the UK are not conveyed to hospital, and this proportion has the potential to increase.[9,10] However, paramedics currently have very limited access to diagnostic tests, especially in vitro diagnostics. Effective POC tests delivered by ambulance staff have substantial potential to facilitate effective decision-making at scene that will:

- Support alternatives to ambulance conveyance;[11]
- Allow the initiation of correct treatments at an earlier stage, improving clinical outcomes;[12]
- Ensure patients are conveyed or directed to the facility or service best suited to their needs;
- Accelerate patient pathways, promote safety and enhance patient and carer experience.

Electrocardiograms (ECGs) and blood glucose testing have been successfully used at the point of care by EMS in the UK for many years. Systems to rapidly transfer patients with evidence of a heart attack on their ECG to interventional cardiology centres are well established, and the prompt detection and correction of low blood sugar levels is regularly lifesaving. However, other POC tests (for example lactate and procalcitonin, both important markers of serious infection) have been trialled without progression to adoption, and the reasons for this are unclear.[13] There is also a risk that POC tests completed by ambulance clinicians are not trusted or appropriately documented by other elements of the health system, leading to these being repeated with a wasteful duplication of resources,[14] or no significant change in the patient pathway and clinical outcomes that follow POC testing.

As the availability of POC tests in EMS expands, there is an urgent need to build a reliable evidence base that will identify which of these tests should be adopted into routine practice. Candidate POC tests must demonstrate technical feasibility, acceptable diagnostic accuracy and have the appropriate regulatory approvals.[15] They must also be practical in EMS, where there is a need for portability, robust construction and the ability to withstand extremes of temperature. Of particular importance is the clinical impact of POC tests, and their capacity to modify and enhance existing patient pathways in ways that are clinically safe, effective and cost effective, which improve patient outcome and experience and support greater efficiency of resource use. Examples include the ability to safely exclude a serious diagnosis, thereby facilitating discharge from scene, rather than an unnecessary hospital attendance, or diagnosing serious bacterial infection so antibiotics can be administered at an earlier stage. We have therefore assembled a multidisciplinary research

partnership to establish a platform trial of POC testing in UK EMS. This platform will generate evidence in an efficient way that is flexible and responsive to the rapidly expanding POC market.

However, before proceeding to a platform trial it is necessary to develop a reliable and reproducible process to screen and select the POC tests that will be included in the platform, and understand the facilitators and barriers to POC testing in EMS and their acceptance across the wider healthcare system, including patients and carers. This will inform the clinical pathway changes that are required to create demonstrable benefit and underpin the subsequent platform trial. We also seek to strengthen our team with enhanced stakeholder engagement and meaningful input from diverse patient and public partners.

To further enhance this work, we have engaged with the NIHR Applied Research Collaboration (ARC) West who are supporting the completion of a series of rapid evidence reviews both before and during the proposed accelerator award, and with additional input from the Test Evaluation Research Group (TERG) and Birmingham Clinical Trials Unit (BCTU) at the University of Birmingham. This process is underway currently, and to date we have carried out several targeted searches and reviewed the full text of 250 potentially relevant publications and reports on the use and diagnostic accuracy of POC tests in EMS.

We identified four systematic reviews on the use of POC tests in EMS,[16-19] and three on EMS plus other settings such as General practices or Emergency Departments.[20-22] There appear to be few primary studies that directly address the effects of implementing POC tests in EMS, indicating a need for further research. Two randomised trials in Canada looking at POC troponin tests for identifying non-ST segment elevation myocardial infarction in patients with chest pain reported conflicting results.[23,24] None of the systematic reviews on troponin assessed changes to patient care pathways or outcomes.[16,17,20]

Less information is available for POC lactate tests in detecting severe infection and critical illness. We found five observational studies and one systematic review of POC lactate.[18,25-29] Most examine the feasibility and practicality of testing, alongside the diagnostic test accuracy for critically ill patients. None assessed whether POC lactate testing could change the patient pathway or improve patient outcomes. In the UK, Heaney et al reported the pilot implementation of a backpack-sized portable laboratory with >10 POC tests for blood and urine biomarkers deployed in rapid response vehicles within a single ambulance service. The POC tests changed conveyancing decisions in 31% patients in which they were used.[30]

We found only one study that assessed costs for the use of POC tests in EMS. McPherson et al looked at a range of POC tests for frail and elderly patients to reduce transport to the ED with redirection to community based care. They identified a net cost saving of £75 per person and a return on investment of 4.6.[31]

We identified 80 potentially relevant studies describing assessments of diagnostic test accuracy (DTA) for POC tests in EMS. Only a minority of these have been formally assessed in rigorous systematic reviews; we therefore propose to conduct such DTA reviews for the most promising tests selected as part of WP1.

For some tests there were no systematic reviews; for example coagulation testing in suspected stroke patients to guide treatment decisions, or they were reviewed but no studies of diagnostic test accuracy were found, for example use of arterial blood gas analysis in seriously ill patients.[19]

This accelerator award will generate a unified body of evidence and clear selection criteria to determine which POC tests should be evaluated further in a platform trial of POC testing in EMS, the associated facilitators and barriers and an established team capable of delivering a successful platform trial that fully engages patient and public partners in an inclusive way, whilst building on existing collaborative links with the diagnostic testing industry.

Objectives

1. To identify candidate POC tests with the greatest "promise and plausibility"[32] to improve EMS patient care pathways through a multimodal scoping phase.

2. To complete targeted literature reviews to establish the level of evidence for the diagnostic accuracy, clinical and cost effectiveness and associated safety profile of the main candidate test groups. This objective, whilst fully integrated into the accelerator, will be supported by additional resource provided by the NIHR Applied Research Collaboration (ARC) West.

3. To map in detail the current pre-hospital care pathways that are associated with each of the main clinical conditions to which POC testing can be applied.

4. To engage a full range of stakeholders, including patient and public partners, to understand the potential for clinical pathway modification, the implications and value of such modifications, associated measures of consequence and outcome and potential facilitators and barriers to both the proposed platform trial and the successful implementation of POC testing in UK EMS.

5. To scope an approach to articulating the potential value propositions for EMS POC testing, the overall impact of specific POC tests and economic modelling that will support the subsequent platform trial.

6. To combine the above information in a process of multi-criteria decision analysis (MCDA) involving a full range of stakeholders to select the tests that will be included in subsequent research.

7. To establish an effective and inclusive multidisciplinary team and full stakeholder engagement that will support a successful application to the linked HTA call. 1.

Study design and methods of data collection and data analysis

WP1: Scoping and review.

We will identify candidate POC tests suitable for use in EMS through a multi-modal approach combining:

• Search of regulatory information and databases to identify all potential POC tests that have relevant CE marking and are approved for use in the UK;

• Scoping reviews of the published and grey literature;

• Contact with industry partners in the UK and overseas;

• Collaboration with a wider steering group of international experts and public contributors, established to support and guide this research (this group is described in more detail below).

This initial exploration will create a "long list" of candidate tests that will be assessed using a matrix approach to demonstrate their characteristics. At this stage, and to ensure the scope remains clear and manageable, we will confine our work to the evaluation of in vitro diagnostic tests in adults.

Imaging technologies (e.g. ultrasound) and POC testing in children will be out of scope, but will be considered for addition at a later stage in the research trajectory.

For the most promising tests and test groups we will then complete supporting reviews of the relevant literature relating particularly to diagnostic accuracy, usability, clinical impact, cost effectiveness and safety, paying particular attention to information describing the challenges associated with the use of these tests in an EMS setting. During this phase we will work with expert colleagues from the NIHR Applied Research Collaboration (ARC) West, who are providing dedicated resources to support the work, and the Test Evaluation Research Group (TERG) at the University of Birmingham. The team will undertake a set of reviews designed to address specific research questions relating to the diagnostic accuracy of selected tests and the clinical effectiveness of their introduction. Searches will be developed by an experienced information scientist at NIHR ARC West. We will follow accepted standards for conduct and reporting appropriate to the types of reviews being carried out (e.g., diagnostic, intervention, scoping etc.) [33-37]

A review of the clinical effects of POC tests in EMS will include study designs likely to allow causal inference. We will assess clinical outcomes relevant to the selected POC test(s) and the condition being studied and service outcomes relating to the feasibility of the test in EMS (e.g., hospital admissions or discharge from service, change in patient pathway, proportion of successfully taken tests, as appropriate). Assessments of cost effectiveness and safety will be based on the studies included in the review of clinical effects. Where necessary, additional safety information will be sought from further observational studies.

Summarising diagnostic accuracy in a review requires specification of the index test, reference test and patient population. Strict criteria for these will be established, and we anticipate that several reviews will be required to accommodate the variation in tests available, reference standards, comparator tests, biomarkers, thresholds for ruling in or ruling out disease and the populations of interest. Assessment of acceptability for patients and EMS and hospital staff will be assessed by scoping of qualitative evidence.

WP2: Mapping clinical pathways, building logic models and identifying facilitators and barriers.

We will assemble a diverse group of approximately 20 stakeholders to assess the most promising EMS POC tests using a multimodal approach. We will encourage wide and representative input to the stakeholder group to recognise the range of local variation in service provision and clinical circumstances. The stakeholder group will include the following representation as a minimum:

• Clinicians with expertise in EMS care and pre-hospital diagnostic testing.

• Researchers with a track record in POC evaluation. This will include individuals with specific expertise in diagnostic testing, statistics and cost effectiveness analysis.

• Patient and public representatives, with a particular emphasis on inclusion and ensuring effective input from seldom-heard groups.

• EMS service provider organisations.

• Commissioners of EMS services.

• Individuals with expertise in healthcare policy, service delivery and workforce.

• International experts in EMS and POC testing to provide a wider perspective.

We will work with this stakeholder group using a range of modalities including workshops, interviews and documentary analysis to map the clinical pathways associated with the most promising tests identified in WP1, assess any potential variation, identify the likely changes in these pathways that will result from POC testing, and determine the facilitators and barriers to pre-hospital evaluation and implementation in the context of each POC test. Detailed understanding of the decision-making process at all stages of the pathway will help to identify the facilitators and barriers to pre-hospital evaluation, and clarify essential prerequisites for the effective implementation of each POC test. This will allow us to construct detailed logic models that move from inputs to activities and then to outcomes,[38] thereby informing the outcome measures (both generic and specific to each POC test) that will be used in the subsequent platform trial.

WP3: Initial health economic modelling.

We recognise the central role that health economic analysis will occupy in our plans to determine the added value and cost effectiveness of each POC test selected for the platform trial. WP3 will therefore integrate a health economic framework into WP1 and WP2. Working with the stakeholder group described in WP2 and the long list of POC tests in WP1, the mechanisms by which testing will add value will be articulated clearly in WP3 defining the primary and secondary value propositions for these technologies. The size of patient populations, the disease burden and the best-case potential for improvement in outcomes, costs and capacity will be quantified to assist in the process of identifying the most promising and plausible POC tests.[32] Once the most promising POC tests have been selected, the detailed POC-specific logic models created during WP2 will be overlaid with health economic inputs to provide value-models demonstrating likely impact. Value will be conceptualised broadly, beyond just outcomes and costs, and will also include the ability of tests to improve policy-making objectives such as increasing capacity within EMS, reducing waiting times, the ability to triage patients and improving the experience of care.

WP 4: Multiple criteria decision analysis (MCDA)

In the final stage we will use MCDA to triage the candidate POC tests for potential inclusion in the platform trial. The POC test 'options' will be identified in WP1. Stakeholder engagement during WP4 will be conducted in conjunction with the stakeholder engagement in WP2. Firstly, we will conduct a survey of the stakeholder group to determine the longlist of 'criteria' for assessment and this will be finalised during Workshop 1. We will then conduct a second survey of the stakeholder group to weight the criteria finalised in Workshop 1. During workshop 2, the stakeholders will continue to score the candidate tests and generate a shortlist of candidate POC tests in order of priority for entry into the platform trial.

Outputs

• An evidence-based shortlist of the POC tests that will be included in the subsequent platform trial.

• A detailed understanding of the characteristics of POC tests that make them suitable for use in EMS, and an established, tested and reproducible process for the selection of further pre-hospital POC tests as they become available for inclusion in the platform trial.

• An assessment of the facilitators and barriers to pre-hospital POC testing and the associated clinical pathway changes that are essential to achieve improved patient and system outcomes.

• A deeper understanding of the facilitators and barriers to our planned future research.

As a component of this work we will, in Autumn 2023, submit an application to the Health Technology Assessment (HTA) Programme of the National Institute for Health and Care Research

(NIHR) to establish a platform trial of POC testing in UK EMS, commencing with an initial feasibility stage. The aims of this application are envisaged to be as follows:

1. To explore and understand the factors that govern successful adoption of POC testing into routine EMS practice in the UK.

2. To establish the feasibility of a platform trial that will test and compare multiple POC tests in Emergency Medical (Ambulance) Systems in the UK.

3. To estimate the diagnostic and clinical utility of the POC tests selected during the accelerator.

Study setting

WP2 is the only work package which will recruit participants as a stakeholder group. The stakeholders are:

• Clinicians with expertise in EMS care and pre-hospital diagnostic testing.

• Researchers with a track record in POC evaluation. This will include individuals with specific expertise in diagnostic testing, statistics and cost effectiveness analysis.

• Patient and public representatives, with a particular emphasis on inclusion and ensuring effective input from seldom-heard groups.

• EMS service provider organisations.

• Commissioners of EMS services.

• Individuals with expertise in healthcare policy, service delivery and workforce.

• International experts in EMS and POC testing to provide a wider perspective.

Stakeholders will be identified and recruited through existing professional networks. All data collection via workshops and interview will be conducted online via MS Teams.

Sample and recruitment

Eligibility Criteria

The WP2 stakeholder participants are:

• Clinicians with expertise in EMS care and pre-hospital diagnostic testing.

• Researchers with a track record in POC evaluation. This will include individuals with specific expertise in diagnostic testing, statistics and cost effectiveness analysis.

• Patient and public representatives, with a particular emphasis on inclusion and ensuring effective input from seldom-heard groups.

• EMS service provider organisations.

• Commissioners of EMS services.

• Individuals with expertise in healthcare policy, service delivery and workforce.

• International experts in EMS and POC testing to provide a wider perspective.

Sampling

Sampling will be conducted via professional networks. We aim to recruit approximately 20 participants to the stakeholder group in WP2.

Recruitment

Potential participants in WP2 will be identified via the research teams' professional networks and contacted by email with a participant information sheet and consent form and asked to return the consent form, if they would like to consent to participate in the study. Potential participants will be followed up weekly for two weeks, if there is no contact then it will be assumed that the person does not wish to participate.

Public participants will be offered renumeration for their time, paid in lieu and via vouchers to the value of £25 per hour. Professional participants will be renumerated in lieu for their time to their employing organisation.

Ethical and regulatory procedures

As this research will not directly recruit NHS staff or patients there is no requirement for HRA approval or NHS REC approval. An application will be made to the University of the West of England Research Ethics Committee.

Patient & Public Involvement

Our team benefits from a PPI co-applicant who supported the NIHR-funded pre-hospital evaluation of sensitive troponin (PRESTO) study, and therefore has prior experience of relevant high-quality point of care testing research. The PPI co-applicant and wider group of PAG members will be involved in each Work Package (WP) in the following ways:

WP1: Scoping and review Patient and public contributors (PCs) will be involved in selecting the candidate tests for inclusion in systematic reviews. PCs will also be involved in developing the protocols for evidence synthesis including assisting with devising the scope of the search and interpretation of the findings.

WP2: Mapping clinical pathways, building logic models and identifying facilitators and barriers PCs will be involved in helping us to understand the range of variation in service provision and patient circumstances. This will include looking at the potential alternative care pathways that can be accessed by testing and describing the facilitators and barriers to pre-hospital testing from a patient/carer perspective. They will also advise on the pre-requisites that make pre-hospital testing and alternative care pathways acceptable from a patient and carer perspective.

WP3: Initial health economic modelling PCs will contribute to the development of the value-models demonstrating the likely impact of POC testing. Value will be conceptualised broadly to include what patients and carers consider to be valuable and cost effective as both service users and tax-payers. PCs will also help clarify the patient and NHS benefit in terms of variables that are important from their perspective, e.g., reduced waiting times, the ability to access appropriate care and improving the experience of healthcare.

WP 4: Multiple criteria decision analysis (MCDA) PCs will be involved in the development of the stakeholder survey to create the longlist of 'criteria' for assessment and the post-workshop survey to define the weighting of criteria. PCs will also participate fully in both stakeholder workshops.

Dissemination All PCs will work with members of the project team to develop a dissemination plan for non-academic audiences with a particular focus on explaining the research and its findings to patients and carers. We will utilise the PHWE ambassador network to explore dissemination and communication with specific underserved communities.

Governance

The PPI co-applicant will attend all TMG meetings. Two PCs from the PAG will be full members of the Study Steering Committee (SSC).

Evaluation

Public involvement impact logs developed by PHWE will be kept by both PCs and researchers to ensure that a clear record of involvement is maintained, along with outcomes and reflections on how involvement practice can be improved. These logs are easy and quick to use but ensure that appropriate and meaningful feedback is given to PCs and is reported back to the funder.

This will be supplemented by the organisation and delivery of two evaluation workshops; one halfway through the project and one at the end, which will use the Cube Evaluation Framework developed by Gibson to gain a greater understanding and provide feedback on the quality of our partnership working with all PCs.

Training and support will be provided by the co-applicant Gibson in collaboration with members of the wider team to enable meaningful involvement. PCs will be paid £25.00 per hour plus reasonable expenses in keeping with NIHR guidance.

Data protection and patient confidentiality

UWE Bristol will use information from participants in order to undertake this study and will act as the data controller for this study. This means that UWE Bristol is responsible for looking after participants' information and using it properly. UWE Bristol will securely erase identifiable information at the conclusion of the study.

Any notes, documents, video-recordings, audio-recordings and personal information will be kept in the strictest of confidence and managed in accordance with the General Data Protection Regulation (GDPR) (2018). Only members of the study team will have access to the data. Participants' contact details will be stored separately from any notes, documents, transcripts and audio recordings.

Participants will not be personally identifiable from any reports or outputs from the research. Identifiable information will be securely erased on completion of the study. De-identified study data will be stored for 5 years after the end of the study.

Virtual interviews and workshops will be recorded using Microsoft Teams, anonymised and transcribed verbatim by a University approved supplier with a data processing agreement in place. Any face to face workshops or interviews will be video or audio recorded on a portable device before being transferred to a UWE Onedrive secure file . All research data will be stored on password protected, encrypted university computers. Hard-copy data will be stored at the University of the West of England in a fireproof, lockable filing cabinet which will only be accessible to the research team members. Hard copies of identifiable information will be destroyed when no longer required by the research team.

All electronic participant data will be stored on password protected, encrypted university computers. Participant contact information will only be stored as long as is necessary, on password protected, encrypted laptops and USBs.

Dissemination

We will take advantage of all opportunities to present our findings and outputs to stakeholder groups. Dissemination to non-academic audiences including patients and public, clinicians, service providers, commissioners and the POC testing industry will be facilitated using existing networks such as email lists and social media. These networks will be utilised to drive traffic to a study website that will act as a repository of materials designed to increase accessibility. Academic outputs will include a minimum of three papers, submitted to peer-reviewed journals, and at least three conference presentations or workshops. This will begin to generate impact, which will then be developed further during subsequent research. All outputs will be made publicly available via the study website. Summaries of the key findings will be produced for a wide range of audiences. We will use email lists and social media to publicise and encourage commentary and generate debate. We will seek opportunities for press releases and media interviews and explore the use of digital stories and blog posts. Other ways of presenting our findings will be investigated such as animations and infographics. We will evaluate impact using alternative metric tools.

Gantt Chart

Month	1 Mar-23	2 Apr-23	3 May-23	4 Jun-23	5 Jul-23	6 Aug-23	7 Sep-23	8 Oct-23	9 Nov-23	10 Dec-23	11 Jan-24	12 Feb-24
Study Set Up												
Research Governance												
WP1 Scoping and review												
Search regulatory information and databases												
Scoping reviews												
Contact industry partners												
Collaboration with steering group												
Finalise list candidate tests												
Matrix approach to candidate test characteristics												
Literature reviews for most promising tests												
WP2 Clinical Pathways, logic models, F&Bs												
Identify stakeholder group												
Document analysis												
Workshop 1												
Stakeholder interviews												
Interview analysis												
Workshop 2												
Construct detailed logic models												
WP3 Health economic modelling												
Health economic modelling candidate tests												
Health economic modelling during WP2												
WP4 Multiple criteria decision analysis												
Stakeholder survey 1												
Workshop 1 (in conjunction with WP2)												
Post workshop survey 2												
Workshop 2 (in conjunction with WP2)												
Finalise shortlist of candidate tests												
Finalise reproduceable process for test inclusion												
Finalise facilitators and barriers to PH POC testing												
Finalise facilitators and barriers to further research												
HTA grant writing												
Grant writing												
Submit grant application												
Reporting												
Final report writing												
Disemmination												
PPI												
WP1 - interpretation of findings												
WP2 - Stakeholder engagement												
WP3 - Development value models												
WP4 - Survey development and workshops												
Trial Management Group Meetings												
Core Team Meetings												
Operational Team Meetings (weekly)												