SBRI Study Report

Cardisio UK Limited

SBRI Reference: SBRIH21P3013

The Cardisio Test

August 2024

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INTRODUCTION

This report provides a formal record of the SBRI Study (ref: SBRIH21P3013) to introduce the Cardisio test into the NHS, providing real-world evidence of its use in Primary Care to improve Secondary Care referrals. It provides a management summary of the study delivery and outcomes, and covers the key aspects of the study setup, mobilisation, management and conduct throughout the study period with summaries of the methods used, objectives and outcomes achieved

This was an SBRI funded study to understand and demonstrate how the Cardisio test can be implemented within a UK health environment. The study was granted approval in September 2022, mobilised in October 2022, with implementation from July 2023 to March 2024.

The Study was designed to demonstrate how, in different primary care settings, administrators can perform the Cardisio test accurately and supply test result data reliably to the central secondary care team in Sandwell Hospital.

The West Midlands was chosen as the test area due to its appropriate healthcare infrastructure, patient density, health profile and demographic, significant elements of deprivation and health inequality. The Study specifically selected participants that were asymptomatic and were considered as having a high CVD risk based on their medical profile, QRisk score and family history, amongst other selection criteria.

Test administration was undertaken in three different Primary Care Settings with a Secondary Care team included the Chief Investigator and team from the Cardiac Department in Sandwell Hospital. The Principal Investigators and their teams, selected from the primary care settings, were mobilised and trained for the Study, and played key roles in delivering the Cardisio tests into the care pathways as defined in the Study Protocol.

The Test Administrators were based in the primary care settings of a GP Surgery, a local Pharmacy linked to a health centre, and a Community Pharmacy who travel to various centres of the local community to reach out to patients.

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The Study Report Structure

This Study report has been structured with a Management Summary and four parts:

Management Summary

Part (A) Study report, which focuses on the study design, process, results, how the study met its' scope and objectives, the overall results from the testing, how the study was managed, the assessments of the study's environmental, social and governance (ESG), and lessons learned and opportunities identified.

Part (B) Care Pathways, this outlines the specific care pathway that was developed for the study, and based upon the study experience and outcomes the likely care pathways that could be considered for implementation at an ICB level.

Part (C) Market Access Plan, this summarises the Study and implementation considerations for ICBs and Trusts undertaken by HIN Eastern.

Part (D) Budget Impact Model, this summarises the budget and financial modelling undertaken, post the study test administration, where the Cardisio test can be used on symptomatic patients. It is important to note that the SBRI Study was designed and conducted on asymptomatic participants.

There is a tabularised view of how this Study Report is aligned to the key study deliverables in the next sub-section.

Study Report alignment with Key Study Deliverables

The study scope detailed key study deliverables to be produced. They are separate documents that provide details on patient outcomes achieved, overall test results, what the data collected demonstrates about patients versus the communities they come from, and their socio-economic groupings, what patients think about the test, an ESG Assessment and NHS budget impact, as well as the key lessons learned for future use of the Cardisio test within NHS England. This Study Report summarises these deliverables, and is aligned to the full suite of reports as follows:

Study Deliverable	Study Report section	Details
The Study Protocol	**Part A**	This deliverable provided the rational, approach, required outcomes and key processes that the Study needed to follow. Driven by the Medical professionals involved with the study, and compliant with NHS guidelines and practices this document was the basis of the study project plan, its timeline and governance. It is an integral document of the Study itself.
Study Overview and Key Results Document	**Part A**	This deliverable is the report that captures and summarises the quantitative and qualitative data results of the study. It shows the key results of the study, analysis and insights. It is an integral document of the Study itself.
Study ESG Report	**Part A**	This deliverable summarises the environmental (carbon) impact of the study delivery as well as the potential impact of the Cardisio test within the NHS in terms of the social impact achieved for the community in the study area. It also reviews how the study was delivered and managed from a governance perspective. It is an integral document of the Study itself, though its approach has relevance for subsequent studies.
Market Access Plan	**Part B**	This deliverable outlines the Cardisio Test in terms of its benefit to the NHS and alignment to various policy objectives and drivers that are necessary for implementing the test at a Trust and practice level. It considers the feedback from study participants, effectiveness of the test in Secondary and Primary Care settings as well as the potential cost benefit with a summary of the budget impact model. It is intended as a stand-alone document to be used beyond the study.
Cardisio Care Pathways Report	**Part C**	This deliverable outlines the care pathway used in the Study, and how current NHS care pathways could be modified to utilise the Cardisio test. It is intended as a stand-alone document to be used beyond the study.
Budget Impact Model (BIM)	**Part D**	This deliverable is a summary from a budget impact modelling (BIM) system that forecasts how the implementation of the Cardisio device as a symptomatic test will lead to savings in the NHS over a period of 5 years. The BIM highlights considerable monthly reductions in various secondary care diagnostic tests and procedures, along with waiting times for these services.

MANAGEMENT SUMMARY

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Purpose of the study

The use of the Cardisio test provides an opportunity to improve patient outcomes by testing heart health, detecting issues and facilitating effective triage before issues become debilitating, or unnecessary referrals are made. Cardisio enables Primary Care clinicians to confidently refer to secondary care, or to exclude cardiac concerns.

The study purpose was to demonstrate and collect real-world evidence of how, in three different settings, the Cardisio Test can be implemented, administrators can be trained, patients engaged and how test outcomes can then be used by GPs and other clinical experts in secondary care. The Study sought to demonstrate how a test can be administered and the results interpreted more effectively than the current standard of care (12-lead ECG). The study was able to demonstrate that the results collected were consistent, and not dependant on the setting or clinical expertise of the administrator of the Cardisio test.

The method of deployment into the Primary Care setting provides Secondary Care teams with more data and insights, and over time Primary Care practitioners, specifically General Practitioners, can improve the confidence of a referral into Secondary Care pathways. In turn, Secondary Care teams will be able to more rapidly assess, prioritise and then prescribe the appropriate care pathway for a referred patient.

Purpose of the Cardisio Test

Cardisio was developed with the purpose of providing GPs and other primary care practitioners an improved tool that allows them to determine if a patient has, or is developing heart disease, and so improve patient care and outcomes. By providing more informative results for Primary care professionals, use of the Cardisio test creates better referral confidence to Secondary Care potentially saving time and resources. By being able to detect early stages of heart disease alternative issues can be explored or advice given on lifestyle modifications and/or medication to manage disease progression.

The test has been designed to be cost effective, and scalable within Primary Care and, through the study, it has been proven that non-clinical staff from pharmacies (in Pharmacy and in Community Settings) are able to reliably perform the test. Secondary Care professionals were able to successfully access reports online from which they have been able to make decisions to see patients or rule out heart disease for many participants.

Study Protocol

The Study Protocol design was overseen by Dr. Nisar Shah (Cardiologist, Sandwell and West Birmingham NHS Trust and Chief Investigator) supported by Kelly Hard (Head of Research and Development, Sandwell and West Birmingham NHS Trust) and Prof. C. Schmidt-Lucke (Cardiologist, MD, PhD Assistant Professor Charité, Managing Partner, MEDIACC GmbH). Guidance on requirements for statistical validity was provided by Alexander Passow with further support from John Fitzpatrick (CFO Cardisio GmbH and Project Sponsor).

Funding was provided by the Nottingham University Hospitals Hospital NHS Trust and Cardisio UK.

Protocol development was supported by Health Innovations East and IX Associates Ltd, in consultation with the wider study team, in particular:

- The Study Steering Committee
- The Study Management Group and
- The Public Patient Involvement and Engagement (PPIE) Advisory Board.

The Study Protocol provided an in-depth guide to the study team and how the study was to be undertaken.

In summary, the Study Protocol includes the following key aspects:

- A summary of the study scope,
- the challenges the study was addressing,
- a definition of what the Cardisio test is and how it could be used,
- the objectives of the study,
- the roles and responsibilities of study management,
- the expected outcomes of the study,
- the study design,
- how feedback was to be obtained,
- how participants were to be selected,
- an in-depth plan of the procedures to be put in place for the study at each stage,
- and how study data was to be managed.

The Study Protocol was submitted for ethical approval to progress with the testing.

Study Teams

The Study was designed to be delivered by three teams:

(i) the Central Study management team that worked remotely and comprised independent Project Management and ESG team members, Cardisio management specialists, SteerCo members and Management committee members (from various health groups).

(ii) The Secondary Care team lead by the Chief investigator based at Sandwell Hospital

(iii) The Primary Care teams, comprising three teams of Principal Investigators based in locations throughout the West Midlands:

- A GP Practice: Church Road, Aston
- A pharmacy connected to a GP Practice/Health Centre: Ridgeacre in Quinton
- A community pharmacy: based in the Brierley Hall Health Centre in Dudley, with outreach services in community centres, mosques and temples in Dudley, Tipton, Walsall, Halesowen and Brierley Hill.

The three testing teams, across the three distinct test settings, were trained and mobilised independently using the same methods. There was no day-to-day interaction between the test administrators in the three teams, though the Principal Investigator from each setting was involved in weekly Study Management Team calls for study governance, co-ordination and sharing of lessons learned.

Study Governance

In addition to many individual, ad hoc meetings between those delivering the study, the project manager co-ordinated a formal weekly Operational Committee and a Monthly Steering Committee as well as regular communication with the study funder, SBRI. All formal meetings we documented and progress against deliverables and timelines tracked.

When governance processes highlighted that tasks were falling behind schedule on two occasions, project extensions were requested and granted to allow for the testing of a statistically valid sample of participants to be completed. The delays in testing administration were due to the lack of availability of staff and resources caused by the autumn Flu Vaccine roll out, which started midway through the testing cycle and impacted the Pharmacy team in Quinton.

Study Performance

The SBRI Cardisio Study formally commenced on 12th December 2022 after a two month mobilisation period, with the Study Protocol development from February to May 2023, and Study Protocol approval on 16th June 2023. Testing Commenced on 31st July 2023, and after an extension due to resourcing challenges, testing concluded on 24th February 2024. The Study analysis and reporting was undertaken from March 2024 to July 2024. In delivering the study 25 Management Group meetings, and 9 Steering Group meetings were held between July 2023 and March 2024.

During the study the three separate Primary Care teams, totalling 25 Test administrators, were trained and mobilised independently. By the end of the Study these teams had tested a total of 628 candidates in the primary care setting context, working with Chief Investigator and the central Secondary Care team at Sandwell Hospital. It is important to note that the Community Pharmacy setting provided an Outreach service to 6 communities spread across 6 further locations in the study area, primarily west of the M5, many of which are regarded as being deprived areas with potential for health inequality.

The Study performance showed that the use of the Study Protocol was broadly consistent and effective with low variances in study participant selection, inclusion and exclusion, and the method of participant and test administrator communication, engagement and provision of documentation. This combined with positive feedback from participants, administrators and Investigators collected throughout the study indicates that the deployment of the Cardisio test on a wider scale carries a low implementation risk.

Overall, 628 tests were completed, with 570 participants providing feedback via the questionnaires pre-test and 558 post-testing. Feedback from participants was positive (88% would probably or definitely recommend the test to friends and family), giving a **Net Promoter Score of 88**. In addition, over 90% saw benefit in the test being available through Primary Care (P16 of data report). While not all participants received all the Study documentation, typically because they were “walk in” Community Pharmacy candidates, of those who did over 90% felt it provided the information they needed.

The Principle Investigators and teams across the test settings reported that they were confident in administering the tests and were able to manage the reporting and data collection processes required of them. The Chief Investigator was able to use the Cardisio Platform to review test results online and manage the right participants on to the right pathways. Part way through the study the Chief Investigator was also able to work with the Cardisio Technical team to fine tune the test algorithms in terms of amber results, to ensure that the right participants were identified for referral, minimising clinical effort.

Key Data points summarising the Study performance

628	Tests completed
25	Administrators tested
8	Communities engaged (1x GP, 1x Local Pharmacy & 6x Outreach Pharmacy
570	Participants provided feedback
90%	Participants who saw value in the test being delivered in primary care
88%	Net promoter score

Study ESG assessment

Innovative healthcare technologies, such as the Cardisio test, introduce options for future alternative, pathways which can have beneficial to patients and have a positive impact on Environmental, Social and Governance (ESG) dimensions. Decision makers need to be well informed about the sustainability, social impact and management load that an innovation brings.

Quantitative and qualitative data was captured from the questionnaires completed by the 90.2% of participants who completed them. This, for example enabled the collection of participant post code which combined with methods of travel allowed the carbon footprints of test delivery to be calculated. Such calculations provide strong indicators of the carbon profile for a wider scale implementation of the Cardisio test into the ICBs across England.

The ESG assessment was able to show:

- The Environmental impact of the Study and testing performed as part of the Study was lower than current care pathways in terms of carbon emissions, and showed the benefits of primary care based testing.

- The Social profile of the Study in terms of the Study Area, the socio-demographics covered, the diversity in terms of gender and economic status met the study requirements for addressing health inequality. The ability to support out-reach healthcare will inform future roll-outs of the Cardisio test and service.

- The Governance profile of the Study in terms of how the Study was managed, decisions made, compliance and ethics achieved was strong. Lessons were learned that will inform future roll-outs.

Key Data points from the Study ESG assessment

60.7%	Potential CO_2e savings through testing locally of patients
49:51	Gender balance achieved (Women : Men)
67.8%	Participants from diverse ethnic minorities
68	Study Management meetings held

Overall Study Summary

As summarised in the Study Protocol:

> "The study objective is to show that the Cardisio Test can be easily integrated into an existing NHS care pathway (NHS Right Care CVD Prevention) in a variety of community & primary care settings.
>
> The secondary outcome is to gain real world evidence of its performance as a tool to aid clinicians with the early detection of heart disease in community-based settings. Findings from this study will be incorporated into a proposed ICS-based national roll-out plan."

The study has achieved this overarching objective and the full range of primary and secondary Objective Outcomes (Section A6 of this report).

The introduction of technological innovations with the potential to change standard processes and impact care pathways, provides its own set of challenges. To tackle these challenges the study team adopted a fully inclusive, consultative approach throughout and was able to overcome obstacles with the help of wider support whilst maintaining a focus on ethical conduct of the study in terms of diversity, gender, medical practice and participant engagement.

It has been demonstrated that testing in Primary Care can play a larger role in early identification of cardiovascular disease, while also highlighting many of the obstacles that exist. These obstacles are addressed within the proposed Care Pathways, summarised in Part B of this report, and the suggested stages within the implementation plans, summarised in Part C, the Market Access Report. Many of these considerations are not thought to be unique to the Cardisio test, but are common to changes expanding the role of Primary Care providers, and when introducing new AI, web enabled technology into the NHS.

From a Cardisio perspective, some of the processes required for a new technology to become available within the NHS assume that the providers are long established large organisations, these can act as barriers for new and smaller innovations, such as Cardisio and many others. This needs to be factored into considerations for future roll-outs and studies.

Overall, the use of the Cardisio test provides an opportunity to improve patient outcomes for people at risk of cardiovascular disease (CVD) in primary care settings, eg. GP Surgeries, Pharmacies or Diagnostic Centres. Potentially this could reduce the burden on Secondary Care referrals and resources, whilst increasing the quality of front-line assessments and subsequently improving the quality of primary care to secondary care referrals.

Furthermore, the study has demonstrated that by reliably testing "at risk" people in Primary Care settings close to their homes, reduces the carbon footprint by removing the need for patients to have to travel to Hospital for an initial test. In addition, by reaching into the community with the Cardisio Test, it has been demonstrated that the harder to reach parts of the community can be engaged better.

Follow on areas of study have also been identified which would see the Cardisio test being used in the diagnostic pathway as an alternative to more expensive tests, helping to reduce long waiting lists.

Key Data Points for further implementation consideration

£9.7M	Saved across the NHS over 5 years
27,789	Reduction in referrals to secondary care
91%	Proportion of "good" referrals leading to further treatment, testing or necessary action, versus current typical level of 50%.

PART A - STUDY REPORT

A1. Introduction to the Cardisio Test

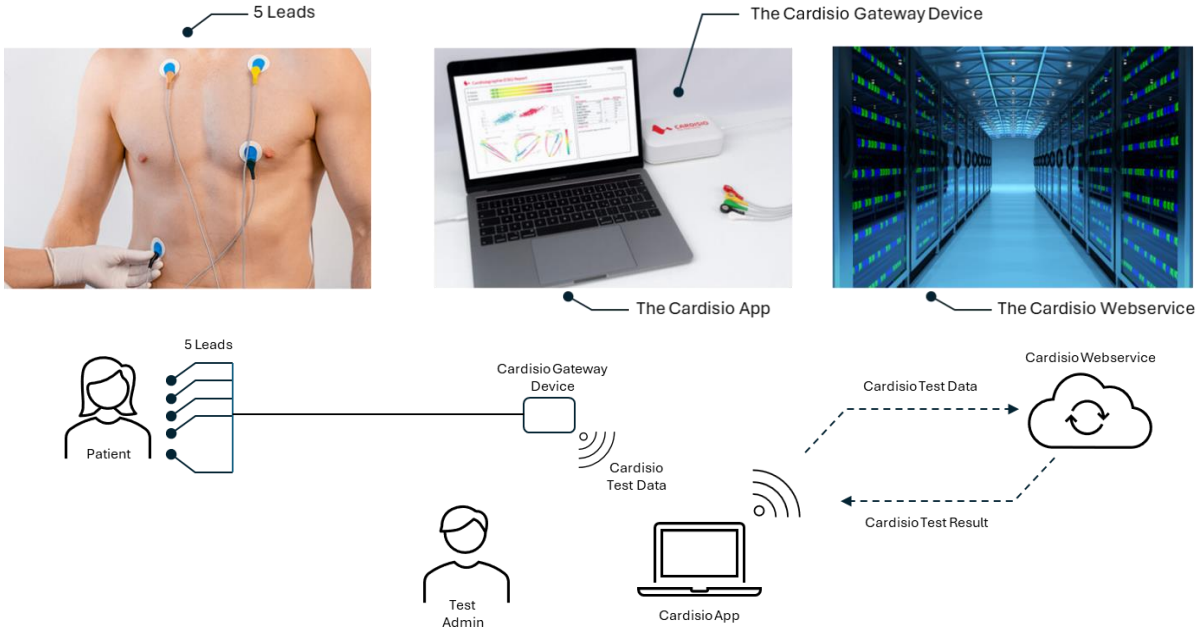
A1.1 The Cardisio Test

The Cardisio test is a diagnostic tool offer by Cardisio, a German medical technology company focused on the early detection of cardiovascular diseases. Cardisio uses vectorcardiography, which is a method of recording the magnitude and direction of the electromotive forces that are generated during the beating of a heart.

The test is similar to administering to a traditional ECG test but with the data collected, over a 4 minute period, a 3D model of the electrical activity in the patient's heart is built up. Data are compared to standard reference values, highlighting out-of-range parameters that suggest the presence of a range of potential conditions requiring further attention.

The Cardisio system comprises the following components:

- The Cardisio Gateway Device
- The Cardisio App
- The Cardisio Webservice



The electrical activity in the heart is captured by electrodes placed on the patient's chest and back, these are connected to the Gateway Device. After approximately 4 minutes sufficient data is collected and the data is sent to the Cardisio Cloud based application via the Cardisio App.

Then a 3D-Vectorcardiogram is produced as part of the Artificial Intelligence-driven analysis process to assess heart health risks for three CVD conditions: perfusion (P), structural (S) changes in the heart and arrythmias (A).

The use of AI in this way enables the analysis of data for many parameters within each heartbeat and reduces the reliance on the ability of the primary care administrator to interpret the outputs of this enriched ECG, as a triage mechanism before deciding to refer a patient to secondary care.

The P, S and A factors are presented as red, amber or green for the clinician to aid diagnosis. Within 5 minutes after the data capture, or test, being completed the test result is available for use in diagnosis on the Cardisio portal.

To keep participants safe during the study, any test showing amber or red, P, S or A indicators were reviewed by Secondary Care in Sandwell Hospital, further guidelines will need to be developed and provided during roll out. A sample of fully green P, S and A results were also reviewed in Secondary Care to identify if false negative results were being recorded.

It is also important to note that the results are pseudonymised to protect patient confidentiality and privacy in support of information security protocols. Measurement data is also anonymised to allow it to be used to further improve the algorithm.

A1.2 Alignment of the Cardisio test to the NHS

The Cardisio Test is a response to the challenges in the NHS of determining the heart health of individuals in a consistent way using non-invasive, advanced digital technologies. The Cardisio Test adds value in several ways including:

A. **Addressing NHS Pressures:** The NHS is currently grappling with unprecedented healthcare pressures, including increased patient demand, long wait times, and economic constraints. Integrated Care Boards (ICBs) are looking to innovation to help improve efficiency and patient outcomes.

B. **Exploitation of Innovative Technology:** Cardisio leverages advanced artificial intelligence and 3D vectorcardiography to accurately detect heart diseases such as coronary artery disease (CAD), arrhythmias, and structural heart disease. This non-invasive technology facilitates early detection, enabling timely intervention and better management of cardiovascular conditions.

C. **Improved and Proven Efficacy:** Clinical studies have demonstrated Cardisio's high sensitivity and specificity in diagnosing coronary artery disease, with significant reductions in misdiagnosis compared to traditional methods. For example, Cardisio has shown a sensitivity of 95.4% and specificity of 90% in detecting CAD, outperforming conventional electrocardiography.

D. **Comparative Advantage over other diagnostic tools:** Compared to other diagnostic tools like EKG, Holter monitors, CT-Calcium scores, and MRIs, Cardisio stands out as a non-invasive, cost-effective, and highly accurate solution. It combines the benefits of multiple diagnostic methods into a single, streamlined process that is patient-friendly, cost effective and efficient.

E. **Cost-Effectiveness:** Implementing Cardisio can lead to significant cost savings for the NHS. The technology reduces unnecessary referrals to secondary care and decreases the need for expensive diagnostic procedures. Over a five-year period, Cardisio is projected to save the NHS approximately £9.7 million and reduce GP referrals to cardiology by 27,789, while also shortening wait times for secondary care diagnostics.

F. **Enhanced Patient Outcomes:** By facilitating early and accurate diagnosis, Cardisio improves patient outcomes and quality of life (QoL). It supports the NHS's strategic goals of enhancing patient care, reducing health inequalities, and optimising resource utilisation.

G. **Alignment with NHS Policies:** Cardisio supports the NHS Long Term Plan's emphasis on early detection and treatment of cardiovascular diseases. It aligns with key NHS guidelines and initiatives, such as the CORE20PLUS5 framework and the NHS Outcomes Framework, ensuring that the technology is well integrated into existing care pathways.

H. Sustainability and Future Growth: Cardisio is committed to ongoing innovation and regulatory compliance, ensuring continuous improvement and adaptation to evolving healthcare needs. The company also emphasises sustainability, aligning with NHS goals for reducing carbon emissions and promoting environmental responsibility.

A2. Study Protocol

A2.1 Protocol development

To explore the wide range of outcomes defined for the study it was important that the study protocol was developed carefully, through extensive consultation and that every opportunity was taken to gain data, opinion and comments from those helping to deliver the study as well as from participants. The protocol that emerged set the parameters for the project plan, its structure, timeline and governance.

The most important facets of the protocol, that required significant consideration in designing the protocol, were the methodology for recruitment of participants to the study, the participant experience of being involved in the study and the engagement with existing prevention pathways into secondary care as required. The complexity of demonstrating the potential economic benefits to the NHS emerged through the delivery of the study and was modelled in the Budget Impact Model after the testing phase concluded.

A2.1.1 Desired Outcomes

The project protocol was designed to achieve the following Study Objective Outcomes, which guided the planning and were frequently referred to during delivery of the study:

Primary Study Objective Outcomes:

1. Cardisio can be used in community settings without extensive training or specialist knowledge by the tester.
2. Secondary Care teams can review the Cardisio Test results remotely resulting in fewer patient journeys to busy hospitals for tests. This should also contribute to the NHS Net Carbon Zero targets.
3. The Cardisio Test delivers a superior and richer test result when compared to a traditional 2D ECG. More data about disease conditions will make the cardiologists ability to diagnose easier or clarify next steps.
4. To demonstrate that a revised care pathway could be considered by the NHS for future adoption, based on a central cardiology team reviewing test results and selecting patients for further diagnostic test procedures, a so-called “pull model”.
    a. Better availability of community testing should offer a better patient experience.
    b. Through the use of Allied Healthcare Professionals to undertake routine testing, a reduction in GP appointments should be possible.
    c. Secondary care teams will be able to triage and prioritise patients, making better use of scarce resources.

Secondary Study Objective Outcomes

Feedback and observations generated by all the study participants will provide a richer view on key metrics around user experience, from allied healthcare professionals, patients and cardiologist. For example:

1. How the test environment is integrated into a Primary Care Setting.
2. Ease of training in person and online training materials.
3. Ease of test procedure and administration.
4. Patient experience and preference for community-based testing.
5. The view of the cardiology team in the process and impact on the quality of their patient lists.

A2.2 Key Aspects of the Protocol Development

A2.2.1 Engagement and consultation

The methodology for development of the study protocol required the Cardisio team carry out the widest possible consultation with those involved in the delivery of the study, protection of patients and with clinical staff. The many stakeholders engaged included:

- GP surgery managers and nurses
- GPs
- Pharmacists and their frontline team members
- Community groups and leaders, for those study settings in the community such as mosques, community halls, gurdwaras for example
- Patient panel
- Ethics panel
- Cardiologists
- Secondary care managers who made available resources for those patients identified with conditions that need urgent follow-up
- Medical data management departments, as patient data needed to be protected from being identifiable outside of the NHS firewall

Given the wide range of stakeholders, clinicians, ancillary and administrative staff involved, the protocol development needed extensive consultation, and several rounds of review to deliver a protocol that would be produce the required outcomes of the study.

Stakeholders were engaged in Groups and as individuals, face to face, and over video-conferencing during the protocol development. This approach ensured the requirements of each stakeholder were understood and they had the information needed to fulfil their role in the study.

The wider team came together in weekly meetings to review progress in each specific area during the test administration phase, while a steering group met to ensure overall direction, that deadlines were being met and the objective outcomes were being achieved. These meetings carried on throughout the study and after the testing phase concluded.

A2.2.2 Settings

The West Midlands area was selected for the study because of its diverse community, strong evidence of health inequality, as well as a high CVD prevalence in certain communities such as those of Afro-Caribbean and South Asian heritage. These communities also provide the possibility of identifying participants from different socio-economic groups, and those who have not registered with a GP.

Three settings were selected within reach of Sandwell Hospital:

- GP surgery – Church Road, Aston
- Community Pharmacy – Ridgeacre, Quinton
- Out-Reach Pharmacy - Brierley Hall Health Centre in Dudley

Each setting was engaged to help understand their requirements and to provide context for how the test could be administered. This informed the protocol design, and were visited by Study team members to assess suitability and facilities and to understand the Test Setting and participant requirements. Targets were then finalised, administrators trained, reviewed progress and gathered feedback.

The Principal Investigators in the different settings were extremely helpful in defining what was required to make the Test Administrators effective, and participants experience as comfortable as possible. Meetings in the specific settings were also helpful in advising on what would be possible in terms of recruitment of participants and marketing to attract participants.

The Cardisio test requires a computer with access to the internet to upload data for analysis. While each setting had sufficient computers a reliable connection to the internet proved problematic in the GP setting, as it required a separate login to the NHS VPN, and in the community settings Wi-Fi was not always available. To be able to establish a reliable internet connection Wi-Fi "dongles" were provided where needed.

A2.2.3 Participant recruitment and selection

The study required asymptomatic candidates who scored highly in a series of standard risk factors such as cholesterol levels and family history or scored highly on the QRisk2/3 assessment. To adopt a systematic approach, candidate selection criteria were developed in the form of a list of medical risk factors, to meet the needs of the GP surgery. These were translated for the pharmacies into a list of medication likely to be prescribed for risk factor conditions (as shown in Section A2.4).

Using the recruitment criteria, all settings were able to identify people who were thought to be asymptomatic and with the risk factors. This activity proved relatively easy for the GP Setting with their online access to patient records and QRisk2/3 experience. It was more difficult for the community pharmacy to filter potential participants from their records in advance, but they did manage to identify participants. The outreach pharmacy, who set up pharmacy support in community and religious centres where members of the community drop in, found it impossible to identify participants in advance, given the nature of their work in non-healthcare settings. Participants were identified by the outreach Pharmacy in "real-time" with people coming along to be tested as word spread through the community.

A2.2.4 Test Administrator Training

For many of the staff nominated to become the test administrators by the setting Principal Investigators, especially in the pharmacies, this was the first time they had administered tests similar to ECG tests.

The study team trained all the administrators in person as required. The training was carried out by an experienced doctor who was able to explain the whole patient impact and answer any questions that arose. During the training administrators each had the opportunity to practice on each other both in terms of performing the test, but also accommodating privacy requirements of the various groups of participants.

A2.2.5 Informing Participants

To assist the study participant selection process a series of posters and pamphlets were developed. These enabled participants to make informed decisions about whether to participate in the study, and be aware of the inclusion and exclusion criteria. This required the following to be created:

- Posters to make potential candidates aware of the study
- A pamphlet to explain who is eligible for the test
- A more detailed explanation of the test and its benefits

The posters made potential candidates aware of the study and were displayed at the Test Settings as part of the Participant selection process, the pamphlets were handed out to potential participants.

A2.2.6 Gaining Participant feedback

Anecdotal feedback from participants was received from administrators and Principal Investigators, however, the main method for gathering feedback from study participants was from questionnaires.

These questionnaires were designed to collect defined responses where possible, offering respondents scores between 1 and 5 for example. There were also sections where freeform text was collected. They were presented to participants on arrival at the test setting once they had provided their written consent to participate before being tested, and immediately afterwards.

As well as exploring participant views on the test itself, questions were posed to participants to support the Environmental, Social and Governance (ESG) aspects of the study. For example, distance from home to the test setting to support CO^2 calculations and Environmental impact assessment; demographic information to assess Social impact; participant views on being able to receive the test in a primary rather than secondary care setting for evidence of good Governance.

A2.2.7 Gaining Study Team feedback

The Study required the support and feedback from those administering the test and those helping to select participants, and from the Secondary Care team who assessed the quality of the test result and decided upon whether the further actions were needed, primarily a follow-up Outpatient appointment (Secondary Care).

Feedback was obtained through dialogue with these team members throughout the study on an ad hoc basis, regular Study Management group meetings, and Steering Committee meetings, to which the CI and all PI's were invited. The Study Team also carried out a post study structured interview with representatives of the settings and the Secondary Care team.

A2.3 Use of the Cardisio test in Primary Care

The study was primarily focussed on demonstrating that the Cardisio test can be effectively and reliably administered in a Primary care setting to the satisfaction of patients, as well as primary and secondary care clinicians. The protocol outlined a study specific care pathway to allow the Cardisio test to be delivered in the Primary care setting.

A2.3.1 Provision of diagnostic assistance

Diagnostic assistance was incorporated into the study protocol at two levels, the test itself and Secondary Care, as Cardiovascular Diseases are complex in nature and present a wide range of symptoms making it hard for GPs to distinguish and diagnose. The aim of the test is to be beneficial in the following ways:

- More reliable initial assessment means that fewer patients are unnecessarily referred to secondary care, potentially reducing the size of waiting lists

- Patients will naturally be concerned by a referral for CVD and with the improved accuracy of a CVD assessment fewer will need to suffer the anxiety of waiting for a secondary care appointment.

As outlined the Test provides a simplified status for the three CVD conditions of perfusion (P), Structural changes (S) and Arrythmia (A). This provided greater specificity of potential condition. For the Study the Chief Investigator was then able to review both the test result and the medical records of the study participant to make a determination of further steps, which was the next level of diagnostic assistance. This was detailed as the core part of the study specific care pathway.

A2.3.2 New interactions between Primary and Secondary Care

In establishing the Study Protocol it was clear that the Cardisio test has a potential, significant impact on the interactions between Primary and Secondary Care. Typically only tests carried out by GPs lead to GP referrals to Secondary Care, with the possible exception of those services included in the “Pharmacy First” programme.

For the Study, administering the Cardisio Test in a Pharmacy setting required a referral effectively originating from a Pharmacist, and particularly in the case of the Outreach Pharmacy where a participant/patient may not have a GP, this presents a novel challenge for the current CVD care pathway.

This was managed through the limited scope of the Study and the planned “hand-off” between the PI in the Primary Care Test Settings, and the CI and their team in Secondary Care was much smoother than expected, as the mechanism deployed was via the Test results reports which were made visible to the CI via the Cardisio Portal.

A2.3.3 Patient/Participant acceptance of CVD testing in Primary Care

A further key aspect of the Study was the informed acceptance and consent by participants. In order to ensure knowledge of the test, the process and the potential benefits, a series of pamphlets and brochures were provided by the study team. These were very well received as evidenced in the study questionnaires completed by 90% of participants before and after the test administration.

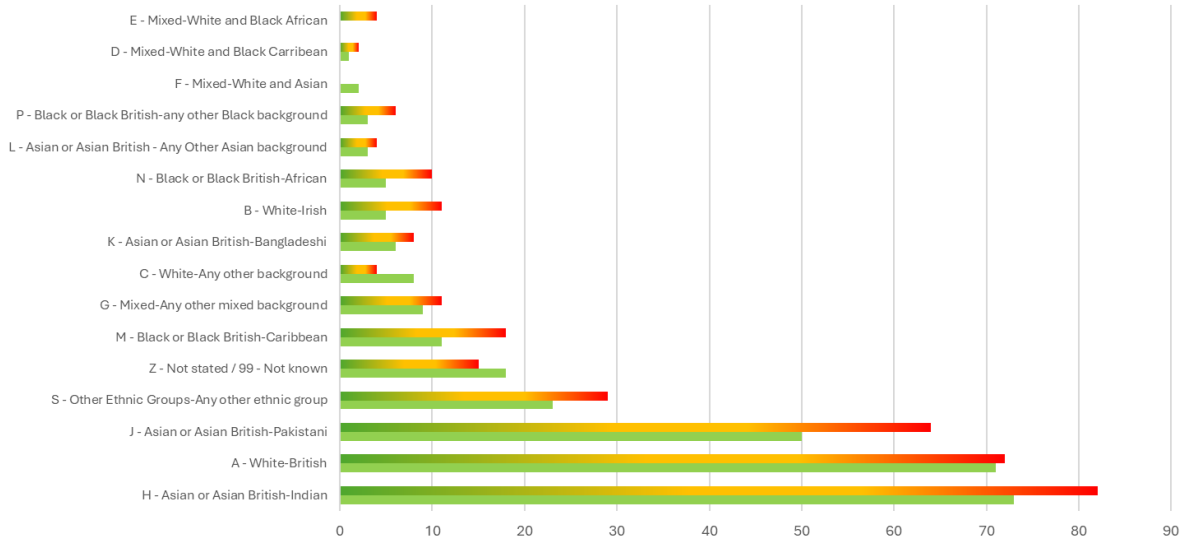
Therefore, prior to the test administration itself, each Study Participant was required to provide their written consent. These were recorded in a pre-agreed template, and the physical copy was kept at the Test Setting, and then scanned and uploaded to the NHS Secondary Care team at Sandwell. These consents were not available to the Study Team other than as confirmations of consent in the master study record.

A2.4 Participant Inclusion and Exclusion

Patients presenting with symptoms for a condition as serious as CVD were deemed to be outside of the scope given that they were either already in the standard CVD care pathway or required urgent and direct attention with secondary care.

Participants for the study were therefore required to be asymptomatic and selected based on their CVD risk factors and their gender to ensure as near as possible 50% of participants were female; 49% was actually achieved. The area selected, in the West Midlands, provided a rich diversity of ethnicities and above average medical/health inequality, as detailed in the Study ESG Report.

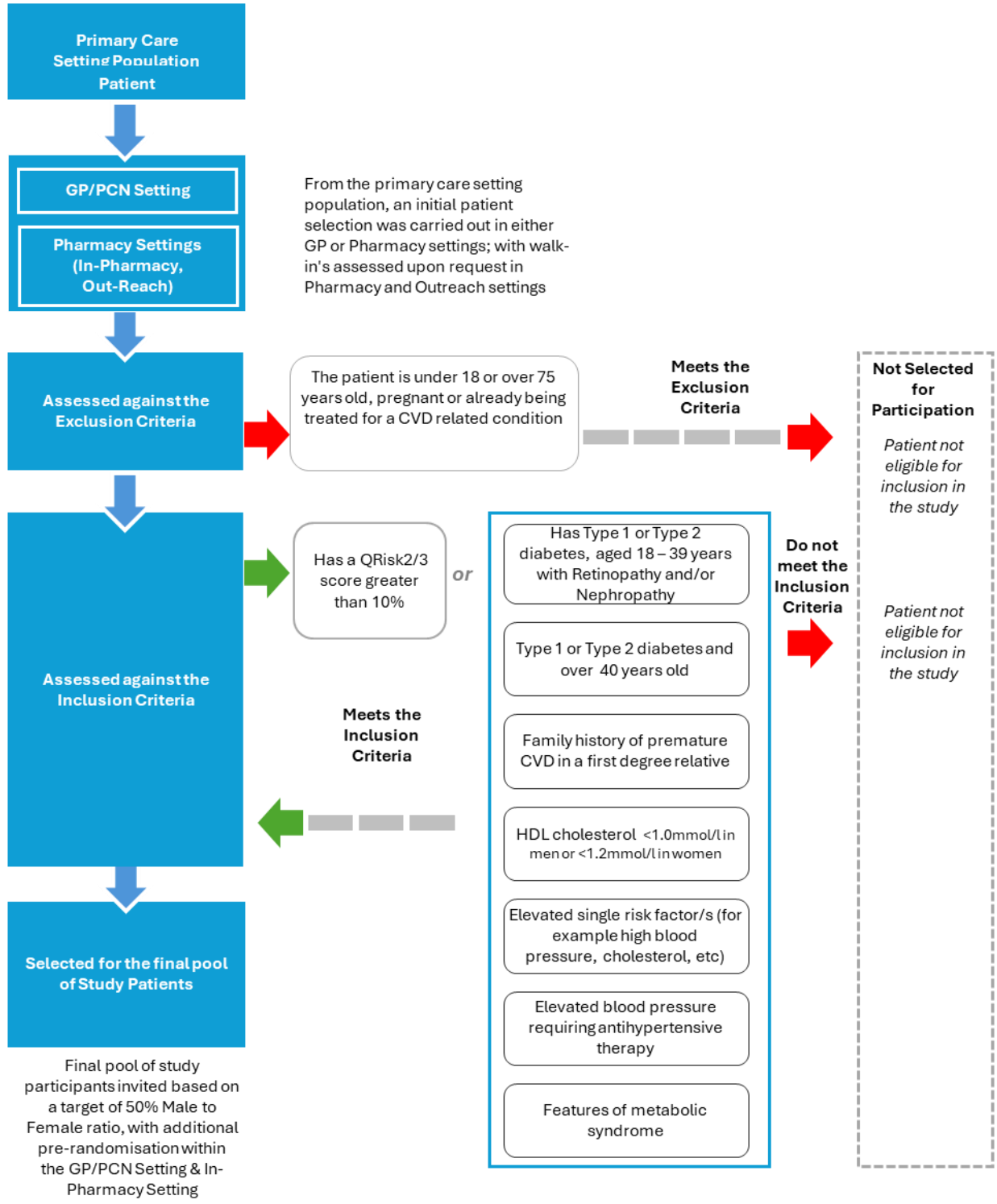
Figure: Distribution of Study Participants by Ethnicity and overall result profile.



Diversity was achieved primarily through the selection of the areas chosen to run the test, with ongoing monitoring throughout the delivery phase to ensure a good gender balance.

The methodology for participant identification and selection is shown below, and this was undertaken by each Test Setting, independently of the central study team.

Overview of exclusion and inclusion methodology as per the Study Protocol



The selection assessment used exclusion and inclusion criteria that were agreed to provide the consistency needed in recruiting and selecting the study participants across the primary care settings. The table below summarises the eligibility criteria used by the GP setting and for the Pharmacy settings an equivalent medication profile view:

EXCLUSION FACTORS	
Participant Medical Profile Age, condition, indicative CVD risk	**Participant Medication Profile** Examples of typical medications indicating a medical risk or condition
1. Already being treated for a CVD related condition or are symptomatic	Combination of Anticoagulants, Blood Thinners, Antiplatelets, ACE Inhibitors, Angiotensin II Receptor Blockers, Beta Blockers, Calcium Channel Blockers, Diuretics, Vasodilators, Nitroglycerin and Statins
2. Age is under 18 and over 75	
3. Pregnant	
4. Study conflict (participating in other studies) or unable to provide consent	
INCLUSION FACTORS	
Participant Medical Profile **Age, condition, indicative CVD risk**	**Participant Medication Profile** Examples of typical medications indicating a medical risk or condition
1. Type 1 or Type 2 diabetes and aged > 40 years	Insulin, Metformin, Sulphonylureas, alpha-glucosidase inhibitors, prandial glucose regulators, thiazolidinediones or glitazones, GLP-1 analogues (incretin mimetics), DPP-4 and SGLT2 inhibitors, Statins
2. Type 1 or Type 2 diabetes aged 18 – 39 years but who have been diagnosed with one or more of the following:	
2.1 Retinopathy	Ranibizumab (Lucentis) and aflibercept (Eylea), steroid medications
2.2 Nephropathy, including persistent microalbuminuria, persistent poor glycaemic control (HbA1c >9%)	ACE inhibitors, dapagliflozin, statins, furosemide
3. Elevated blood pressure requiring antihypertensive therapy	ACE inhibitor or an angiotensin-2 receptor blocker (ARB), calcium channel blockers such as amlodipine, felodipine, nifedipine, diltiazem and verapamil. Diuretics such as indapamide and bendroflumethiazide. Beta blockers such as atenolol and bisoprolol.
4. Elevated single risk factor/s, e.g. total cholesterol >6.0mmol/l	Statins
5. Features of metabolic syndrome (central obesity and fasting triglycerides) >1.7mmol/l (non-fasting >2.0mmol/l)	As per medication for blood pressure, blood sugar and cholesterol
6. HDL cholesterol <1.0mmol/l in men or <1.2mmol/l in women	Statins, and ezetimibe, fibrates, bile acid sequestrants and bempedoic acid. Also, injections – such as alirocumab, evolocumab and inclisiran
7. Family history of premature CVD in a first degree relative	Known medication profile of a close family member taking appropriate CVD medication.
OR	
8. QRISK2 ≥ 10% or QRISK3 ≥ 10%	

A3. Study Planning and Management

A3.1 Overview of the Study Plan and Management

The approach and definition of the study plan was extensively discussed with the study Steering Group from the very start of the study and documented within the Study Protocol. The resulting study plan was broken down into the following stages:

STUDY STAGES	STAGE ACTIVITIES
[A] PREPARE	Focused on preparing the arrangements with participating parties and teams
[B] MOBILISE	Focused on mobilising the Study Group team including primary and secondary care teams, independent specialist support
[C] SETUP	Focused on setup of the study including formulating the Study Protocol, the development of the consistent methodologies to recruit and select study participants, provision of training for both primary and secondary care setting professionals, the arrangements for testing to be conducted, hardware and software provision, patient documentation, survey questionnaires, control documents
[D] TESTING	Focused on testing by the Primary Investigators from pre-testing which entails recruiting and selecting study participants consistently, testing which includes the rate of tests to be conducted, test shadowing, the interactions between primary and secondary care teams and subsequent case management. Post Testing activities including patient, PI and Secondary Care surveys.
[E] OUTCOME ANALYSIS	Focused on the analysis of post testing data at an aggregate level, for both quantitative and qualitative data.
[F] POST STUDY	Focused on the development, finalisation of the Study reports
[G] STUDY CLOSE	Focused on closing out any final activities from the Study

These stages were adhered to strictly throughout the study, with frequent reference back to the Study Protocol document, signed off by the project Sponsor, Chief Investigator and Project Statistician.

A3.2 Ease of deployment of the Cardisio Test

In order to enable administration of the Cardisio test reliably in Primary Care, the level of clinical expertise required cannot be prohibitive. In fact a number of the 25 Administrators trained during the study had little or no clinical experience, and they all found the training to be effective, accessible and were quickly confident proceed with administering the tests in the different settings. The Study Team were able to understand the level of training required in future and that it can be delivered online, leading to a measurable CO_2e saving as described in the Study ESG Report.

Each Cardisio test provided a report a vectorcardiogram and a PSA result which enabled the PI's and the CI to use the test findings with minimal additional training. In terms of a wider roll out of the test, the training and materials will aim to provide more information on interpreting the reports to enable clinicians to rapidly become confident in using the test.

A3.3 Study Governance

The success of the study was attributable to a considerable extent to the governance model used by the teams working with their resources to deliver the study. This governance model consisted of:

- The Steering Committee, which met monthly and included the Study Sponsor and acted as the advisory body for the study.

- The Study Management Group, who met monthly as a full group, and weekly as smaller teams dependent on the requirements and stage of the study, and responded to the operational needs of the study at that time. This Group included:

    - The CI and Secondary Care Team who managed the review of all Red and Amber results, engaged with participants, organised Out Patient Appointments for those requiring further tests as part of existing CVD Pathways and engaged with the Cardisio clinical team to fine tune the test reporting in their local context.

    - The PI, Testing Administration teams in each of the 3 Primary Care settings (GP Practice, Pharmacy and Outreach Pharmacy) who engaged participants, administered the test, reported back the results and collected qualitative data from participants.

The makeup of these teams is shown in the next tables, with further details on how they interacted and communicated to manage the study in the Governance Section of the Study ESG Report (also summarised in Section A7 of this report).

Details of the main governance bodies

Steering Committee

Role	Member
Chairperson	Dr Simon Rudland
Sponsor	John Fitzpatrick – CFO, Cardisio GmbH
Chief Investigator	Dr Nisar Shah
Project Manager	Gary Herbert
Expert members	Kelly Hard – Head of R&D, Sandwell Hospital Prof Alan Nevill – Emeritus Research Professor in the Faculty of Education Health and Wellbeing, Wolverhampton University, Study Statistician Meik Baumeister – CEO, Cardisio GmbH Sebastian Deiss – Chief Medical Officer, Cardisio GmbH
Principle Investigators	Dr Sajjid Sawar GP/PCN Junaid Duberia (Pharmacy) Jaspal Johal (Out-reach Pharmacy)
PPIE representative	Lindsay Cooke
AHSN Representative	Joanne Dempsey / Lamprini Kaftantzi
ESG & Study Support	Rav Bains / Terry Watts

Study Management Group

Role	Responsibility	Meeting Member
Chairperson	Responsible chairing the Study Management group meetings	Gary Herbert
Sponsor	Responsible for the Cardisio involvement and support of the Study, and the conduct and alignment to SBRI requirements	John Fitzpatrick
Project Manager	Responsible for the overall coordination and management of the study, including recruitment, data collection, and study logistics.	Gary Herbert
Chief Investigator	Responsible for the overall secondary care conduct of the study	Dr Nisar Shah
Principle Investigators	Responsible for each testing site, participant recruitment, obtaining informed consent, and monitoring of participant well-being during the recruitment and test stages of the study.	Dr Sajjid Sawar GP/PCN Junaid Duberia (Pharmacy) Jaspal Johal (Out-reach Pharmacy)
Sponsor	Responsible for the Cardisio involvement and support of the Study, and the conduct and alignment to SBRI requirements	John Fitzpatrick
Data Management	Responsible for data collection, storage, management, and quality control oversight and support.	Sati Bains / Angie Williams
Test Training	Responsible for training of test administrators	Dr Murat Celebi
Statistician	Responsible expert in statistical analysis who provides guidance on study design, sample size determination, and data analysis	Prof Alan Neville
Health Innovation East (HIE)	Responsible for HIE oversight of the study	Joanna Dempsey / Lamprini Kaftantzi
ESG & Study Support	Responsible for assessing ESG and for providing Study Support	Terry Watts

A3.4 Study Patient and Public Involvement and Engagement

A3.4.1 Aim of the PPIE Role

The aim of PPIE in this study was to ensure that the Cardisio heart testing technology aligned with patient needs and healthcare professional expectations. This involved integrating patient and public voices throughout the development and deployment phases to ensure the tool is user-friendly, accessible, and meets the clinical and practical needs of diverse patient populations. The specific goals included validating the technology's efficacy in a community setting, refining patient-facing materials based on direct feedback, and ensuring the study's processes were transparent and comprehensible to potential participants.

A3.4.2 PPIE activities planned and undertaken

Several key activities were planned and executed to involve patients and the public meaningfully:

1. **Document Review and Feedback Sessions:** 1:1 interviews were conducted with patients to gather detailed feedback on patient-facing documents. This included materials such as the invitation to participate, consent forms, and test day instructions.

2. **Virtual Meetings:** Regular virtual meetings via Teams were scheduled to discuss revisions to patient documents, review pre-test and post-test questionnaires, and gather patient input on study protocols.

3. **Patient Feedback:** Organised feedback sessions where patients could discuss their experiences, provide feedback on the testing process, and suggest improvements.

4. **Involvement Payments (PPIE):** Patients were offered involvement payments as per NHS guidelines to recognise their contributions and time commitment.

5. **Ongoing Engagement:** Continuous engagement with patients to ensure ongoing feedback and adjustments throughout the project lifecycle.

A3.4.3 PPIE alignment to Study outcomes and delivery

The PPIE activities resulted in several critical outcomes:

1. **Document Improvements:** Feedback led to substantial improvements in patient-facing documents. Suggestions included simplifying language, ensuring clarity on procedures, and improving the readability of materials for older adults or those with visual impairments.

2. **Enhanced Test Understanding:** The pre- and post-test questionnaires were refined to be more user-friendly and relevant, ensuring patients fully understood the test and its implications.

3. **Inclusivity and Accessibility:** Efforts were made to ensure that the test was accessible to a broad demographic, including those from hard-to-reach communities. This included placing testing stations in accessible community locations and employing outreach strategies.

4. **High Satisfaction Rates:** The study reported an 87.5% recommendation rate among participants, indicating high levels of satisfaction with the Cardisio test process and the clarity of information provided.

5. **Patient-Centred Adjustments:** Specific changes were made to address patient concerns, such as explaining technical terms (e.g., “non-invasive”) in more relatable language and ensuring that the test's non-invasiveness and ease were communicated effectively.

A3.4.4 Conclusion on the extent to which the PPIE influenced the Study

The involvement of patients and the public was integral to the study's success, profoundly influencing several aspects:

1. **Document Revisions:** Patient feedback led to numerous revisions of study documents, making them clearer and more patient-friendly. This ensured that participants were well-informed and comfortable with the study procedures.

2. **Protocol Adjustments:** Discussions during patient workshops and virtual meetings provided insights that helped refine study protocols to better suit patient needs and expectations.

3. **Enhanced Trust and Transparency:** Continuous engagement and transparent communication helped build trust between the research team and participants, which is crucial for the success of such community-based studies.

4. **Implementation Feasibility:** The feedback ensured that the Cardisio test could be feasibly implemented in community settings, with considerations for ease of use and patient comfort.

5. **Broad Acceptance:** The high recommendation rate and positive feedback from participants underscored the acceptance and perceived value of the Cardisio test, supporting its potential for wider adoption within the NHS.

Overall, the PPIE activities were fundamental in shaping the project, ensuring it was patient-centred, accessible, and effective in meeting its goals.

A3.5 Study Plan Amendments

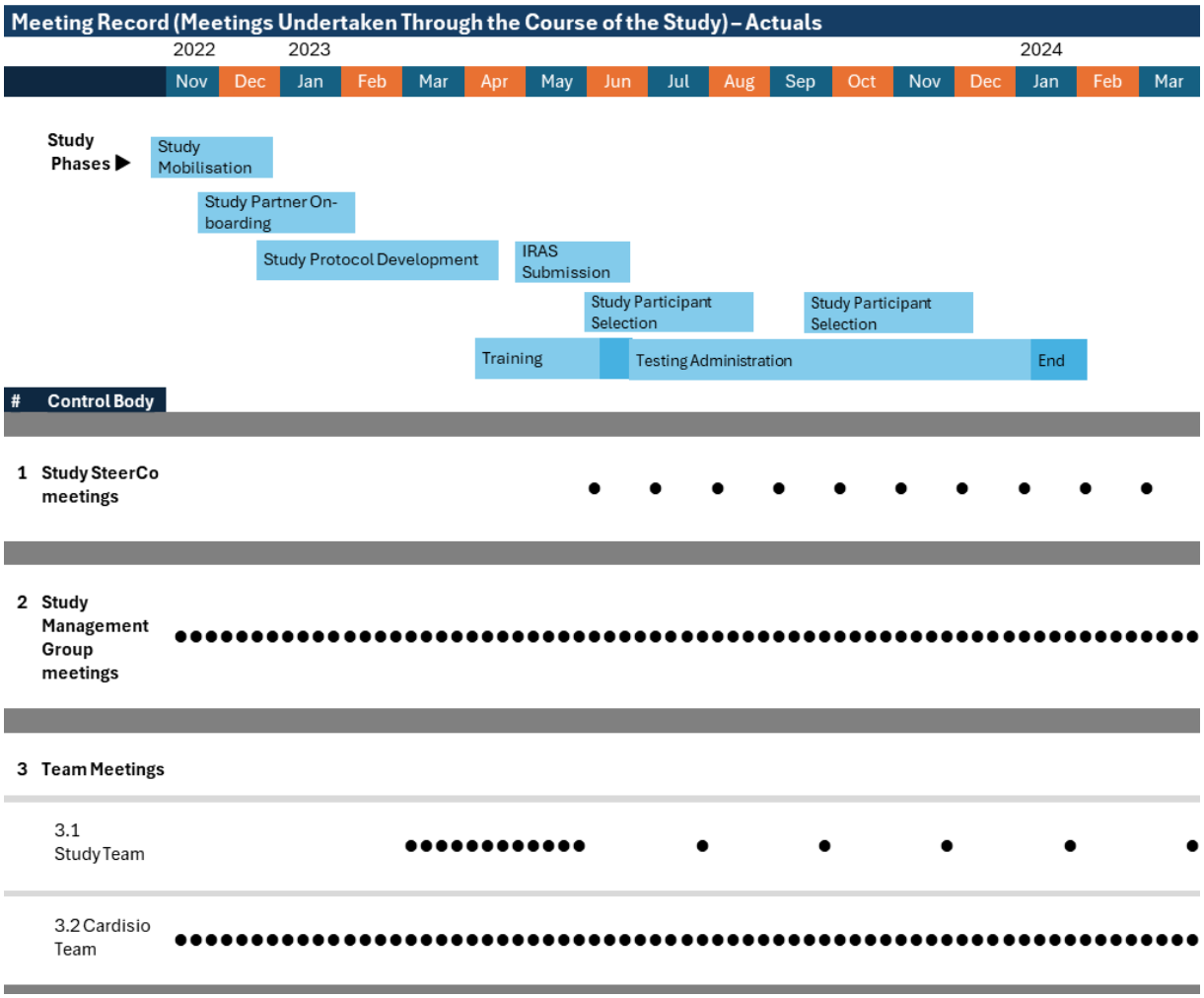
The Study plan was in the main consistent, with two change requests made to the SBRI to seek project schedule extensions, both of which were granted.

The first extension was required in order to complete the documentation and sign off of the Study Protocol with the Steering Committee which over ran due to the extended time needed for full consultation to be completed, and the second extension was required to enable more testing to be undertaken in one test setting that had faced resource constraints (the assigned people and space was temporarily diverted to support the 2023 Flu Vaccine roll out schedule.

A3.6 Study Plan Meetings and Decision Making

The Study was managed through a series of regular, scheduled and documented meetings between of the Steering Committee, Operations Management Group, Study Team and the Cardisio team. The following schedule diagram shows how the Study Phases/Stages were delivered by the various "Control Bodies"/Teams over the lifetime of the study.

Figure: Study Management Schedule



A3.7 Summary Report on plan delivery

In order to deliver the study a number of key approaches on the day to day management were required:

- **All partners in the study were aligned in understanding the potential benefits of the study.** Time and effort was taken by the Study Team and the Cardisio Team to make sure that all partners in the study were aligned in their purpose for effective deployment of the Cardisio test, and how it would benefit patient outcomes and the accessibility of heart health care, demonstrate an enhanced role for Primary Care and provide more cost effective early diagnosis. This was of particular importance with the Principle Investigators (PI) and their teams who were asked to learn about a new test, undertake a novel test and use a comprehensive reporting method.

- **The Study Team frequently engaged with the three settings beyond the initial setup, training and guidance.** The result was motivated teams of test administrators who worked hard to engage participants and complete all the stages required of them from the Protocol.

- **The Secondary Care the team**, led by the Chief Investigator (CI), took on the extra work to review all tests indicating any sign of a heart issue (all tests with one or more red or amber indicator) and a significant sample of clear (all green) tests. Furthermore, many of these tests originated directly from Pharmacy settings to the Secondary Care team, which was not a standard care pathway.

- **Calibration of the Cardisio algorithm** was arranged through the collaboration of the Study and Cardisio Teams with the Chief Investigator. This shows a potential benefit in the ability to deploy the test more widely within NHS England.

- **Data security** was a strict requirement of the study so that participant results could be analysed by the study team, and Cardisio, without tests being attributed to identifiable individuals. This was achieved using the Microsoft Teams environment within the NHS Firewall to capture results onto a series of spreadsheets. Partial copies of these spreadsheets with personal information removed were shared with the Study Team and Cardisio who had no access to the original spreadsheets and data.

Consequently, 638 tests were administered, only 10 of which failed to give a valid result due to the length of time taken to capture and process the test results. Of the 628 valid tests 340 were reviewed by secondary care because of a red or amber indicator and 35 all green (clear) tests were reviewed to check for false negatives, of which there were none. Further details of the results are provided in Section A4 of this report.

A4. Study Results

A total of 811 tests were originally planned to be performed by all test settings, with the following initial targets of:

1. GP setting for 300 tests,
2. In-Pharmacy setting for 300 tests and
3. the Community Pharmacy setting for 211 tests.

The Study Participants were selected as per the Inclusion and Exclusion Criteria, and this was a material driver for the number of study participants actually tested that limited the potential participant population available.

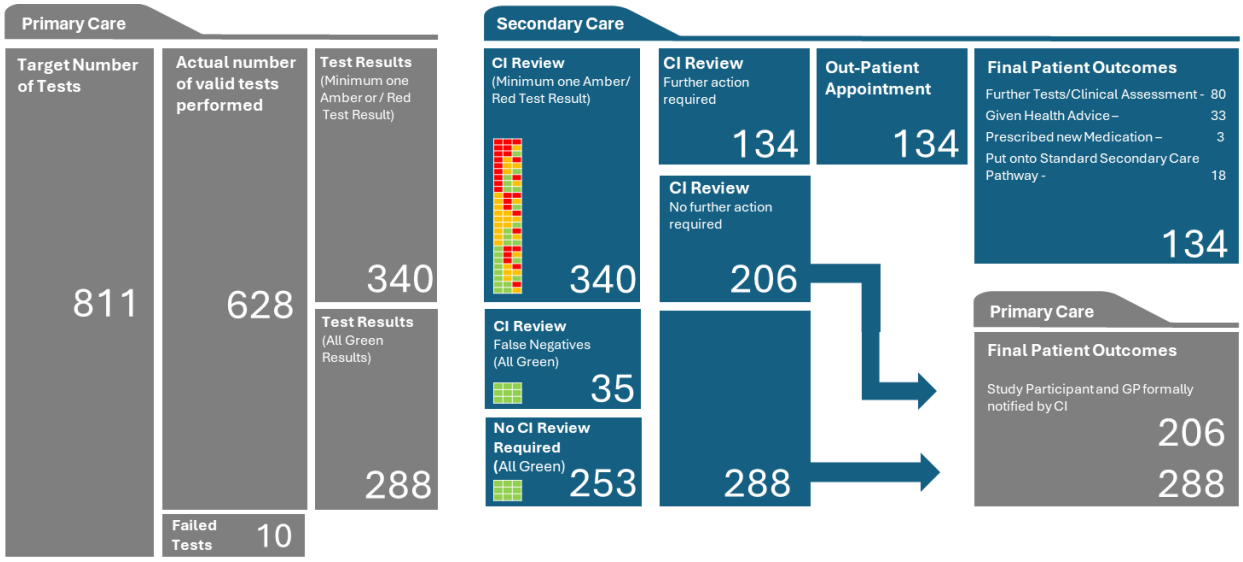
By the end of the Study period, 628 tests were eventually performed, due to this lack of availability and a small number of "on the day" no shows, and for the In-Pharmacy setting several other factors limited the tests performed there including a delay due to the seasonal focus on flu and COVID vaccines.

A4.1 Tests Results

A4.1.1 Quantitative Results

A summary of all tests results are shown in the Figure below.

Figure: Test Dashboard



Within Secondary Care, the Chief Investigator reviewed all of the results that had a minimum one amber or red result, and additionally reviewed a sample of those testing with "All Green" results. This enabled the CI to become familiar with the look and feel of reports in different scenarios and, in the case of the 35 all green results reviewed as a false negative control, the confidence that there were no false negative results.

Further qualitative insights were available via study participant feedback collected by the Study questionnaires. Post the testing period some final verifications were made by the Secondary Care and the NHS Teams as minor data updates. In the accepted final count 10 test failures were recognised, so ultimately there were 628 valid tests during the 9 month test period.

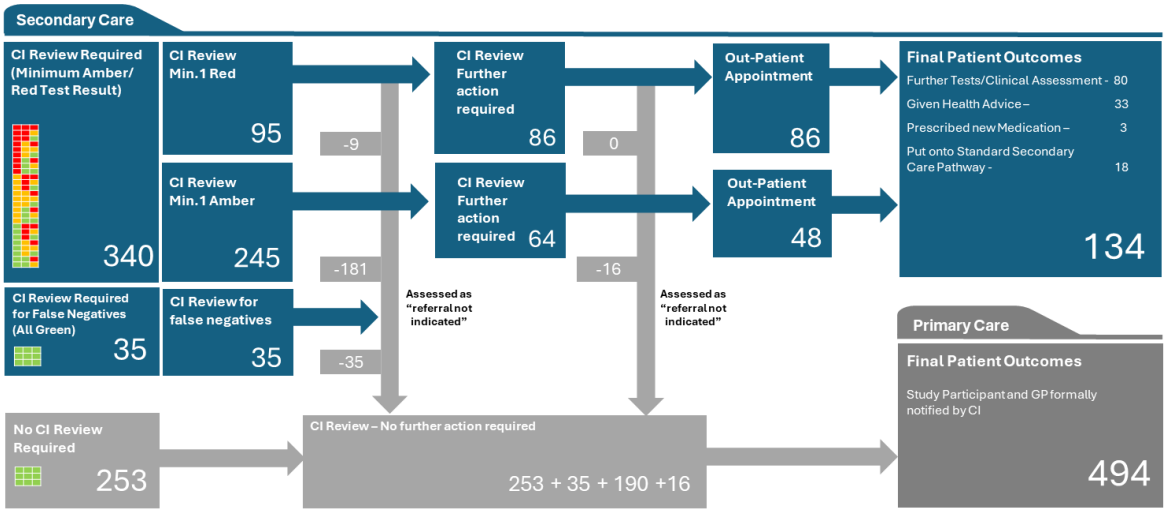
From a Secondary Care perspective, 340 Study Participants were recognised by the Cardisio test results as requiring a review. Additionally, a sample of 35 Study Participants that showed all Green results were reviewed to check for false negative results.

The review process of each case (the 340 tests) with a minimum of the amber or red result across P, S or A used three classifications to determine whether further action was required. This was developed by the CI and was based on three questions or conditions to be considered for :

1. **Referral indicated** – could the Cardisio result correspond with the need to refer the Study Participant for Secondary Care attention?
2. **Referral may be indicated** – could the Cardisio result correspond with a <u>potential</u> need to refer the Study Participant for Secondary Care attention?
3. **Referral not indicated** - does the Cardisio result correspond to a case where a referral to Secondary Care is not needed?

The Figure below shows that the Study yielded a smaller number of in-person referrals, i.e. Out Patient Appointments (OPAs) than anticipated.

Figure: Secondary Care Test Dashboard



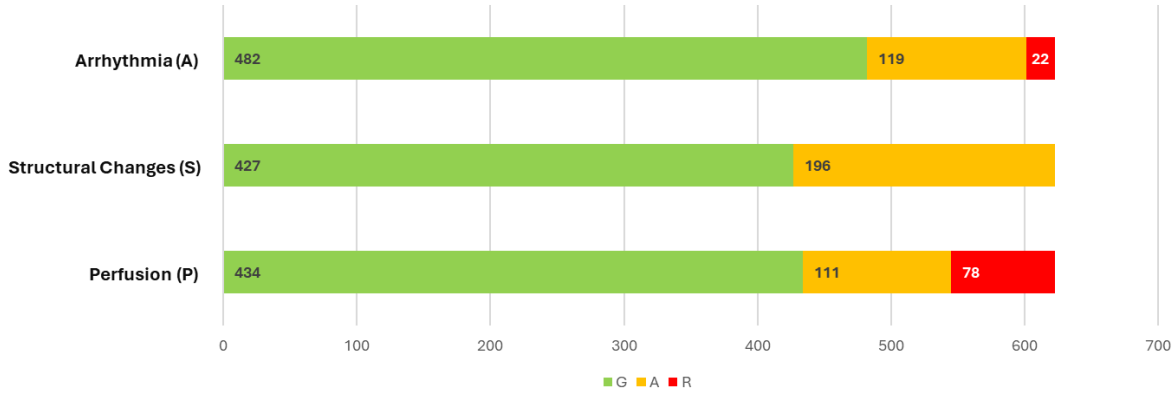
Application of the CI process outlined above led to a very effective and efficient review of potential referral requests, using the Cardisio Portal, that saw only 9% of the final referrals being considered to not be required. This compares to a current state where up to 50% of those referred to Secondary Care with CVD do not have Cardiovascular problems, but yet have had to wait the average 213 days to be told so in their face to phase appointment with a Cardiovascular specialist.

The breakdown of medical outcomes, or next steps for those referred on the basis of the Cardisio Test are as follows:

Referral indicated category The test results meet the threshold for a Secondary Care referral.	Referral indicated 76 At least one red status for P, S or A.	**80%** of Study Participants with one or more Red indicator for P, S, or A required a referral into the Secondary Care Pathway
Referral may be indicated category Further investigation is required to see whether the test results meet the threshold for a Secondary Care referral.	Referral may be indicated 10 At least one red status for P, S or A.	**11%** of Study Participants with one or more Red indicator for P, S, or A may have required a referral into the Secondary Care Pathway
Referral not indicated category The test results did not meet the threshold for a Secondary Care referral.	Referral not indicated 9 At least one red status for P, S or A.	**9%** of Study Participants with one or more Red indicator for P, S, or A did not require a referral into the Secondary Care Pathway

During the study the three most common causes of CVD were identified; Arrythmia, Structural Changes and Perfusion as can be seen in Figure below. While no examples of Structural Changes were identified among the participants, 78 results indicating Perfusion was identified. This is of particular significance as Perfusion is a difficult condition to diagnose using other simple tests. Moreover, its identification early will enable patients to be treated appropriately more quickly than currently. Equally budget savings will be possible as other expensive tests may no longer be necessary.

Figure: Result Distribution by Condition



A4.1.2 Statistical Analysis

There was a strong association between the Cardisio test result of one or more red result and the CI assessment that referral to a secondary care cardiology clinic was or maybe indicated (p= <0.001). The presence of a negative Cardisio test was strong association with the CI decision that no further cardiovascular intervention was required (P= <0.001). 74% (n=181) of the amber test were judged not to require a referral to secondary care cardiology clinic. The Cardisio test had a positive predictive value (PPV) of 80% and negative predictive value (NPV) of 90.4% (prevalence of 5%, Z= 1.96, precision 1.7% n = 628).

Figure: CHI Squared Calculation

3 by 3 CHI			Cardiologist Opinion		
			Referral Indicated	Referral Maybe indicated	Referral Not Indicated
Cardisio Result	Red	95	76	10	9
	Amber	245	27	37	181
	Green	35	0	0	35

2 by 2 CHI			Referral Indicated	Referral Not Indicated
Cardisio Result	Red	95	76	9
	Green	35	0	35

The (3 by 3) Chi-squared test of independence (c2=192.8 with 4 degrees of freedom) and chi-squared test of linear trend (c2= 159.1 with 1 degree of freedom) revealed a strong relationship between the CI opinion and the Cardisio results (both P<0.001). Focusing on just the red and green Cardisio results and their association with the CI opinion (referral indicated vs not indicated), we observed an even stronger association, as seen in the 2 by 2 CHI table.

The reduced (2 by 2) Chi-square test of independence (c2=85.3 with 1 degrees of freedom) and chi-square test of linear trend (c2= 81.5 with 1 degree of freedom) reveals an even stronger relationship between the CI opinion and the Cardisio results (both P<0.001).

The corresponding Kappa statistic for the above (2 by 2) table is 0.831, confirming an excellent measure of agreement between the CI opinion and the Cardisio results. 35 all green test results were selected at random and subjected to desktop evaluation by the CI. These negative results were identified as reflecting true negatives. If we assume those 35 selections to be representative the Cardisio test has a sensitivity of 73.8% and specificity of 94.4%. All the test settings revealed a broadly similar age profile with the predominance of at least one amber and one red result been found between the ages of 61 and 70 years, figure 6. Less than 2% of the conducted tests (n=10) failed due to technical problems.

A4.1.3 Qualitative results

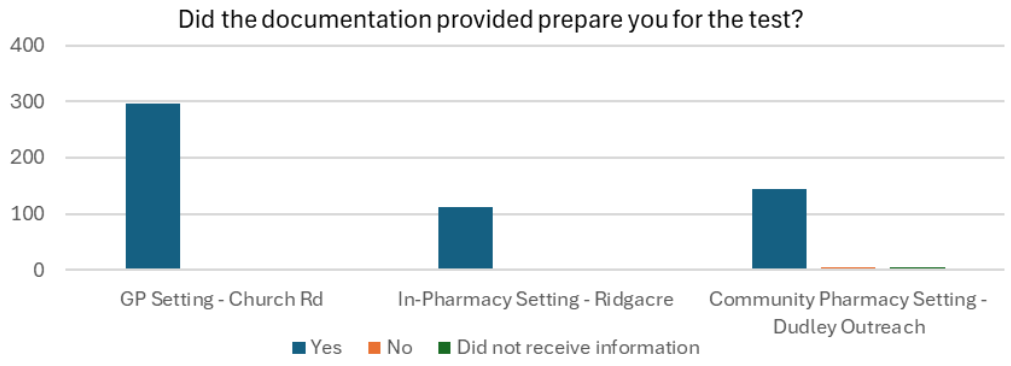
In addition to the quantitative results, it was a key aspect of the study to check with participants, administrators, PIs and the CI to ensure their experience of all aspects from introduction, selection, training, communication delivery and reporting were of a high standard. These qualitative results were compiled from the questionnaires competed by participants before and after the test administration and through structured interviews with Administrators, PIs and the CI. These are analysed in detail in the Study Overview and Key Results Document

Study Participant feedback

With the support of the Patient and Public Involvement (PPIE) team the suite of documents developed (as outlined in A2.2.5) were provided to participants. In addition, the questionnaires developed to capture study participant feedback pre- and post-test administration were used. This provided a qualitative dataset for analysis of the patient engagement and acceptance of this testing approach. For pre-test 91% and post-test 88% of participants, respectively responded, giving a strong basis for assessing participant views on the Cardisio test.

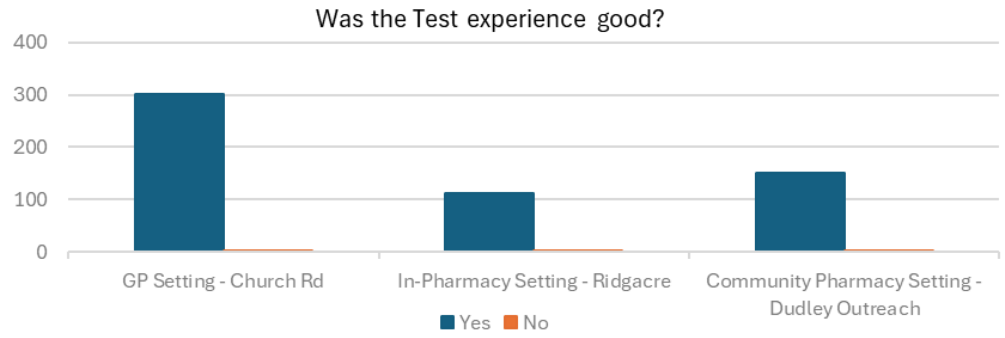
Engagement with Study Participants

Most of the study participants reported that the study documentation used to engage with them was very effective and welcome, with over 97% of those who received the documentation agreeing that they received the information they needed. There is therefore confidence that the materials produced will form a strong basis for use in future implementation plans.



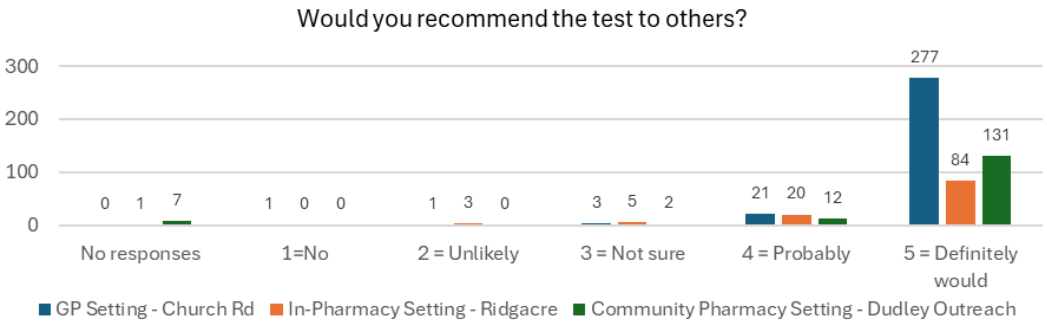
Test Experience

Participants gave feedback on their test experience, approaching 100% positive response for (i) the experience overall, (ii) for the preparedness of the test administrators and (iii) the quality of the pre-test documentation.



Participant views on benefits of this novel CVD test

The Study Participants fed back they would recommend the Cardisio Test. Anecdotally, there were several instances where there is evidence of them already recommending it to friends and family. 97% of participants responded that they were satisfied or very satisfied with the experience of taking the test and 97% said that they felt there was a benefit to providing this type of heart health testing in the community. A Net Promoter Score of 88% was demonstrated when participants responded that they probably, or definitely would recommend the Cardisio Test to others as shown below.



A4.1.4 Structured Interviews Chief Investigator, Principal Investigators and Administrators

Members of the Study Team were interviewed to obtain their perspectives on the Cardisio test and the study.

Chief Investigator – Sandwell Hospital - Nissar Shah, Cardiovascular Consultant

"Having tested non-symptomatic, at risk patients the test would be helpful for use with symptomatic patients, which would be helpful in Secondary Care. The test may have a role as part of the CVD Right Care Programme."

Dr Shah had initial concerns that the number of people identified with CVD could overwhelm the service, and that the additional funds provided for extra Out Patient Appointments would not be sufficient. When results started coming through to secondary care however, while the number with of amber results was higher than expected, the number needing follow up appointments was not as high as had been feared.

The test was shown to have been set to be too sensitive, leading to unnecessary amber results. Cardisio worked to adjust sensitivity and results were then manageable.

The process of reviewing all red and amber results in Secondary Care worked well and those needing further appointments were invited in to Sandwell Hospital.

The testing in Primary Care did help in reaching hard to reach parts of the local a multicultural community, many of whom do not like going to hospital. However, even though problems are identified some are still reluctant with one participant, for example, who failed to arrive for a 3 consultation appointments and phone support to encourage attendance. It was felt that providing taxis and more support in the community might be helpful.

Principal Investigator - Church Road GP Surgery - Dr Sajjad Sarwar (GP)

"Pleased to be involved in the study and consider the opportunity to introduce a mechanism to identify heart disease early, through testing in the community we serve, very welcome."

The community suffers with CVD along with Diabetes, Blood Pressure, High Cholesterol for example. Tests like this are helping to close the medical care inequality gap. Dr Sarwar would like to see more widespread use of the test within Primary Care with potential screening of an risk patients and "pop up" testing centres.

The online, remote review of deferred results by secondary care was a welcome way to improve responsiveness for patients with only an estimated 20 patients needing referral.

There were a number of challenges in getting testing started with poor internet connectivity, requiring some tests to be re-run, and the high level of paperwork alongside the practices paperless processes.

Principal Investigator & Test Administrator- Ridgacre Pharmacy, Aneil Nath (Practice Manager)

"At the beginning, the test was seen as too new (by potential participants). However, as time has gone on we have been inundated with people who want to do it."

As a result of the testing 12 patients were identified with heart conditions and were accepted for Outpatient appointments in Secondary Care, some of these were in fact quite young and should have been fit and healthy. For these people the study was very important in reaching people who would not otherwise have been reached.

Against expectations it was found that men were harder to recruit than women. A walk-in service would work for Pharmacy, but a planned workflow would be better and it was requested that the test be added to the Pharmacy First funding model.

A paperless, digital process would have made the study easier to deliver as the paperwork was time consuming. Digital consent forms would have been much quicker and simple and sending out letters to those with green test results added to the workload.

Staff who had no clinical background found that they could do the test effectively and grew in confidence but were very careful to not tell patients what their exact results to manage their expectations.

Test Administrator - Church Road GP Surgery – Fatima (Healthcare Assistant)

"The test was well received by participants some of whom expressed concerns about how quickly they would hear back from hospitals."

Fatima's role was to administer the tests to the participants. Although Fatima had not done tests of this nature before she found the tests simple to administer.

From a Test Administrators perspective the study was well designed, although there were some initial issues with connectivity of the devices, but once that was sorted out things worked well.

There was a lot of data to collect and forms to fill out, which also needed scanning. Some participants were excited about the opportunity to be being tested and needed to be reassured that if there were any concerns as a result of testing that follow up reviews would be done promptly.

Practice Administrator - Tracey Wellin, Practice Manager, GP Surgery Practice Manager

“The study was a useful exercise, and well received here in the Practice and by the participants, however the testing documentation required to be completed* was over burdensome and involved too much paper work”.

*This is in reference to the consent forms and feedback questionnaires.

With 9 years’ experience as a Practice Manager, and 18 months in post, Tracey’s role was to manage the overall delivery for Church Road Surgery. The main concern was the level of paperwork expected in the study, all of which required scanning, when the practice has embraced the national drive from NHS England for Paperless care. There was some confusion within the team who were managing the paperwork as this was contrary to their standard practice and remedial work was needed to be done to align the right records with the right participants.

It took a while for communication to establish with the study team at mobilisation, but once up and running the communication was good and the study was well designed.

Access to WiFi for the devices was a concern initially, as they are outside of the NHS VPN, but a simple fix was identified with a 4G dongle which worked well.

There was not a problem in searching datasets to identify “at risk” participants and communicating with patients was simple and there were no complaints from participants who were pleased to be engaged.

A4.1.5 Structured Interviews with Study Participants by PPIE

The PPIE Team interviewed a sample of Study Participants, and the following was typical of the feedback:

Diagnosis and Outcome: "Dr. Shah called me in after the scan. He said, 'You had two ambers and a red, but you don't have any significant problems; it's just in line with your age. You've got nothing to worry about.' I felt truly blessed to hear that. I was relieved to get the right medication quickly and felt less pressure knowing I didn't need an urgent hospital cardiology appointment."

Experience with the Test: "The test itself was comfortable. The person administering the test made sure I was relaxed to get an accurate reading. They showed me the screen and explained what they were looking for. She also gave me some information to read, which helped me understand the process better."

Reflection. "Participating in this research allowed me to address my concerns. I felt listened to, and my worries weren't ignored. This process was similar to an ECG but aimed at alleviating concerns more quickly."

Gratitude Expressed "I’m especially grateful because when people tell you that you're at risk of a heart attack, it's terrifying. Seeing the amber indicators was alarming but knowing that it got escalated and addressed was a relief.”

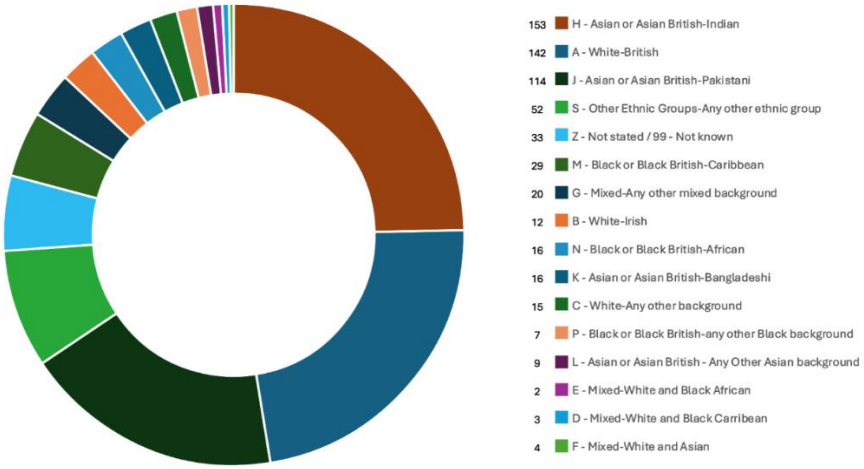
A5. Study Participants involved

A5.1 Diversity

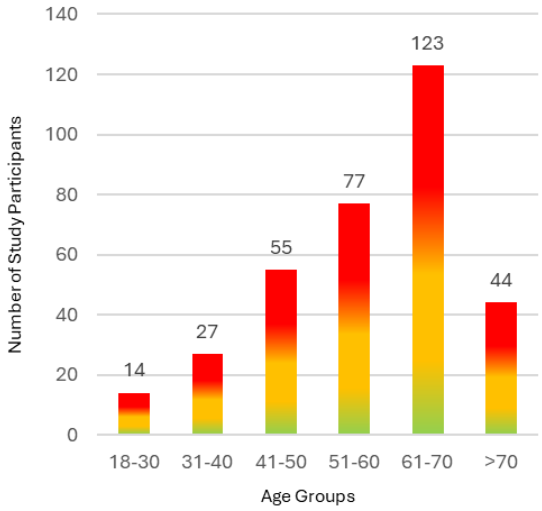
The area around Sandwell Hospital in the West Midlands is a demographically varied area, by any measure. In this study care was taken to include an ethnically diverse community, ensure as far as possible an equal male/female gender balance and to demonstrate that by working through Primary care partners a people from disadvantaged communities, those hardest for the NHS to reach, can be reached and in doing so health inequalities can start to be addressed.

The detail of the demographics of the participants who were tested is found in the "Study Overview and Key Results" and the analysis of the dimensions of social inequality is contained in the "Study ESG Report".

The Figure below shows a breakdown of the number of study participants per their ethnicity.



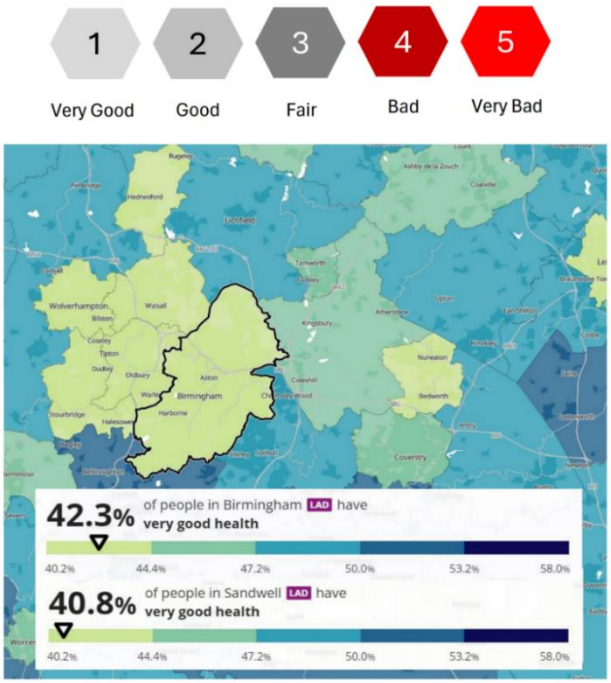
Age is a CVD risk factor, so inevitably the asymptomatic participants selected were generally older members of their community, however a range of ages were involved. The following Figure shows the age profile of Study Participants who were tested with a minimum of Amber or Red across all three test settings.



ALL THREE SETTINGS		
Age	#	%
18-30	14	4%
31-40	27	8%
41-50	55	16%
51-60	77	23%
61-70	123	36%
>70	44	13%

A5.2 Health Inequality

It was important for the study to demonstrate the effectiveness of reaching those suffering from health inequality through Primary Care. This was achieved by basing the study in the area chosen. In the ONS report of 2021, derived from census data, five standard classifications are used to measure general health, which for Local Authority Districts in England and Wales gives an average "Very Good Health" of 47.8%. People in Birmingham provide an average assessment of "Very Good Health" of 42.3% as shown in the diagram below; much lower than national average. In the Sandwell area the score is lower still at 40.8%.



Source: Office for National Statistics (ONS), 2021, General Health, England and Wales, Census 2021

A6. Key Objective outcomes of the Study

The following tables describe how the key outcomes, defined in the Study Protocol have been achieved.

A6.1 Primary Study Outcomes

1. Cardisio can be used in community settings without extensive training or specialist knowledge by the tester.	25 Test Administrators were trained. These tested 628 participants. Only 10 Tests were incomplete of invalid and Administrators reported that they felt confident in using the test.
2. Secondary Care teams can review the Cardisio Test results remotely resulting in fewer patient journeys to busy hospitals for tests. This should also contribute to the NHS Net Carbon Zero targets.	Secondary Care Teams were able to review and provide confident plans for patients remotely, using the Cardisio Portal. Significant Carbon savings were identified with a notional saving of 60.7% for a participant receiving the Cardisio test in Primary Care rather than having to travel to Sandwell Hospital.
3. The Cardisio Test delivers a superior and richer test result when compared to a traditional 2D ECG. More data about disease conditions will make the cardiologists ability to diagnose easier or clarify next steps.	The information provided to Secondary Care from the Cardisio test enabled those requiring further diagnosis to be identified, with only 9% of those given a follow-up Out Patient appointment not requiring further tests or treatment.
4. To demonstrate that a revised care pathway could be considered by the NHS for future adoption, based on a central cardiology team reviewing test results and selecting patients for further diagnostic test procedures, a so-called “pull model”.	The ”pull model” with Secondary Care reviewing the Cardisio test results through the Portal was very successful in reducing referrals for those who do not required further tests or treatment. The Kappa statistic for the study is 0.831, confirming an excellent measure of agreement between the CI opinion and the Cardisio results, see Section A4.1.2.
a. Better availability of community testing should offer a better patient experience.	Approximately 90% of participants responded to study questionnaires. Of those, 97% responded that they were satisfied/very satisfied with the experience of taking the test and 97% felt there was a benefit to providing this type of heart health testing in the community. A Net Promoter Score of 89% was demonstrated.

b. Through the use of Allied Healthcare Professionals to undertake routine testing, a reduction in GP appointments should be possible.	The demonstrated ability to administer the test in Pharmacies of different types will reduce the load on GP Surgeries, and could, if the "pull model" is adopted reduce the need for GPs to meet patients before referral .
c. Secondary care teams will be able to triage and prioritise patients, making better use of scarce resources.	The Secondary Care team was able to review test results online and did prioritise patients effectively. This reduced the number of unnecessary referrals from up to 50% (reported anecdotally) to 9% measured in the study. The ability of the test to narrow down the CVD issue and allow clinicians to make better informed decisions on the most appropriate next step will be seen as the test is used in subsequent roll out programmes.

A6.2 Secondary Study Outcomes

Feedback and observations generated by all the study participants provide a richer view on the key metrics around user experience, from allied healthcare professionals, patients and cardiologist. For example:

1. How the test environment is integrated into a Primary Care Setting.	Qualitative feedback was collected from Primary care patients, Test Administrators and PIs which confirmed that there were no issues in integrating the test within primary care. Furthermore both participants and clinical staff welcomed the opportunity to improve the effectiveness of initial investigation of CVD in a local Primary Care setting.
2. Ease of training in person and online training materials.	25 Administrators were trained all of whom quickly became comfortable and confident in administering the test. Online training has been refined from the lessons learned that will enable training to be completed online in future.
3. Ease of test procedure and administration.	Administrators expressed their confidence and 97% of participants confirmed that the test administration was of a good quality. Only 10 of over 600 tests failed.
4. Patient experience and preference for community-based testing.	97% of participants welcomed the provision of the Cardisio Test in a local Primary Care setting with an overall Net Promoter Score of 89%.
5. The view of the cardiology team in the process and impact on the quality of their patient lists.	The Secondary Care Cardiology team were pleased that a very high proportion of the people identified by the test for referral were in need of further testing or treatment, and that the type of CVD was indicated by the test. This has the potential to make more efficient use of Secondary Care expertise, and enable more targeted further testing to be carried out with consequent budget savings.

A7. Study ESG Assessment

The Cardisio Study has assessed impact across the three dimensions of ESG. The assessment sought to understand how the Study achieved environmental, social and governance goals for "at risk" Study Participants that met the inclusion criteria agreed and defined in the Study Protocol. The summary findings from an ESG perspective are as follows:

Environmental

- The Study created a much lower level of carbon compared to the standard care pathways, as highlighted in Scenario C comparisons in the Environmental section of this report. This is a significant outcome.

- The Study's low carbon footprint shows that the deployment into Primary Care can yield significant benefits for NHS England's carbon reduction plan. This does require consideration of the current care pathways to optimise the use of the test for carbon reduction. The supply of Cardisio devices and accessories will need to be managed to continue supporting the lower carbon profile of the test. As part of the carbon reduction plan, the ability to train, set-up and deliver the environment remotely using carbon neutral 3PL and remote working and media is a significant advantage of the Cardisio proposition.

Social

- The accessibility of the tests at a community level was very well received by the Study Participants, however it was noted that cost of travel to attend Secondary Care appointments could be an issue. This could be solved by holding future Secondary Care clinics closer to patients who are referred by future Primary Care based testing.

Governance

- The Study was well managed throughout though the Project had to be extended twice due to slower than expected testing rates. The decision making and reporting was effective and timely throughout.

- The market entry (or large-scale roll-out) of the Cardisio test into NHS England can be achieved through careful co-ordination of the medical teams in both Primary and Secondary Care settings. The ability to train diverse cohorts of test administrators that can consistently and independently perform tests at the required level of quality is a significant benefit for heart care.

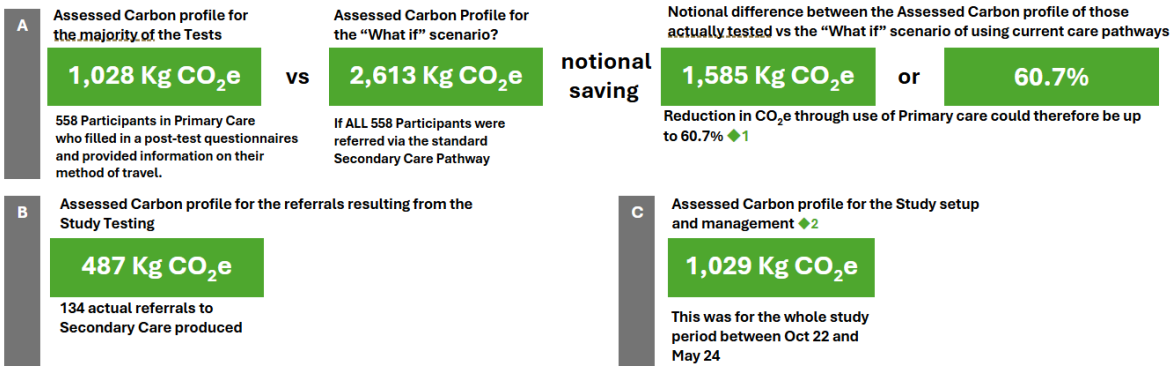
The following sections expand on these high level findings. More detailed analysis can be found in the accompanying Study ESG Report.

A7.1 Environmental

As awareness of the Cardisio test expands and more tests are done the overall environmental impact attributed to its use will inevitably increase. However, the study demonstrates that the environmental cost of delivering the test in a primary care setting, local to the patient, versus the current scenario of having all participants referred to secondary care setting as outpatients even for their very first assessment which would likely entail re-appointment to undertake formal testing, the Study showed an achieved 60.7% reduction of the carbon footprint for the included Study Participants; demonstrating clear alignment to the NHS Carbon Reduction imperative.

In terms of the delivery of the SBRI study itself (Study Management), the carbon footprint of training and supporting test administrators, and secondary care users of the Cardisio device and portal, was calculated. Having established the requirements in different settings, the Cardisio team has been able to establish remote, online delivery formats for future roll out. Consequently, much of the travel required to deliver the study will not be required in future.

The following summarises the key sustainability outcomes of the Study itself:



It should be noted that the carbon savings, driven primarily by the mode of travel, were achieved in densely populated urban areas where secondary care was still relatively local. In the future, there is likely to be different environmental benefits depending on the locations of patients, primary care and secondary care.

The result of this analysis is that if, in the most impactful scenario, all initial testing for potential CVD patients were carried out using the Cardisio Test, in a Primary Care setting versus that testing being carried out in Secondary Care, a Carbon saving of almost 61% can be achieved. Making a significant contribution the NHS environmental objectives.

A7.2 Social

The area in which the Study was completed (spread across the West Midlands) experiences higher than UK average health and inequality issues. The Study Area had the following socio-demographic characteristics:

- A greater proportion of minority groups, particularly Asian, and fewer white people
- A lower proportion of single parent families
- Greater health issues (40.8% of people in the Sandwell area are regarded as having very good health, versus 42.3% in Birmingham and 48.5% across England)
- The area scores unfavourably in all 4 ONS deprivation factors (Education, Employment, Housing and Health)
- According to a separate Aston University study "Health Inequalities in Birmingham" 2023, there are multiple barriers facing people from this community wishing to engage with the NHS, including access to GPs and a lack of understanding of the system.

As well as engaging with a GP surgery, Church Road in Aston, the SBRI study team worked with Ridgeacre Pharmacy, based adjacent to a health centre in Quinton, and a community pharmacy based in the Brierley Hall Health Centre in Dudley, who provide an outreach service at community meeting points such as mosques and temples in Dudley, Tipton, Walsall, Halesowen and Brierley Hill. The Community pharmacy attracted the majority of “walk-in” participants, who still were assessed using the inclusion criteria; data review showed that these criteria were applied consistently as demonstrated in the ESG Report.

This variety of settings and flexible outreach model led to a better understanding of how to reach under-served communities and the benefit of primary care-based testing. For example, it was expected that women would be reluctant to engage with testing in Primary Care and so settings were given a target to achieve gender balance. In fact, Ridgeacre reported that women proactively engaged with the opportunity to undertake Cardisio test, and they in turn proactively encouraged their husbands, fathers and sons to also participate.

As shown below, the planned gender split was achieved within these areas, which are considered to have greater health inequality that England and Wales.

Gender Split Achieved 51% (M) : 49% (F)	**Health Inequality Addressed Study Area 3.8% vs England & Wales Average of 2.63% (Bad to Very Bad Health ratings)**

A7.3 Governance

The SBRI study was designed, from inception, to engage with and to support the use of the Cardisio's test in Primary Care settings, and additionally in areas of higher-than-average deprivation in the West Midlands.

In accordance with the SBRI and NHS requirements, this included the design of a study protocol that was to be approved by patient groups, those responsible for data privacy, ethics, technology and clinicians from primary and secondary care. The work of the study was directed by the Steering Group and carried out by the teams of the people who made up the Management Committee, who met on a weekly basis. The project manager ensured effective communications, maintained the risk register and action lists, and provided the contact point with the project funder when reporting or when project variations were required.

The Study commenced later than planned due to the time taken to develop and approve the Study Protocol. As a result, the testing period was extended into 2024 as at least one test setting started their testing later than planned (Ridgacre Pharmacy) when the study testing period clashed with the annual flu jab schedule.

The Governance structures were consistent in their cadence, reporting and decision making. There was evidence of effective day to day decision making, and the ability to take into consideration exceptional situations such as the assessment of "Amber" results requiring the re-calibration of the Cardisio test to allow for this, as well as the extensions to the testing periods. These were all agreed through project variation change requests agreed with SBRI.

18	11	68	100+	3	25	7	2
Months for the Study Duration	Study SteerCo Meetings	Study Management Group Meetings	Team Meetings	Test Administration Teams	Test Administrators trained	Geographical areas served	Formal Change requests

A8. Lessons learned and opportunities identified

In common with many companies introducing innovative technology into the NHS, the SBRI Study Team gained significant insights and lessons on how to deal with the complexity, sensitivity and opportunity for change within the NHS.

Lessons Learned

A number of lessons were learned primarily on how a study should be conducted for a novel healthcare solution, and secondarily on the CVD care pathways and the considerations for future pathways:

A. **Do not underestimate the effort and time required to develop and sign-off a Study Protocol.** The Cardisio test is well established in other healthcare settings, and the development of the protocol should therefore have been straightforward. However, it is novel to the NHS, and a comprehensive study requires a diverse and wide group of stakeholders and contributors. Coordination, combined with early and wide ranging consultation made a great difference to the smooth running of the study which required the extra time taken in finalising the Study Protocol. It is challenging to complete protocol development and study delivery within the 12 month timescales set for the funding.

B. **The value of Communication.** With so many moving parts and different teams in the NHS, and the commitment to data security and patient safety, there are many groups who needed to be convinced of the value of the Cardisio test. The Study Team adopted a transparent and inclusive approach which paid dividends when in discussions with, for example, Patient and Public Engagement teams, Clinicians, Information Management Departments and Ethics Committees. Whilst this can be time consuming and, for the study, this delayed the start of testing, it ultimately led to a better study outcome.

C. **Appreciate that innovation requires change to be accepted.** The complexity for this study arose in the interactions between Primary and Secondary Care. However, different NHS teams, encountering Cardisio and the Study for the first time, assumed a clinical trial was being undertaken. This resulted in a number of challenges that needed to be addressed, from being asked to use a Protocol template designed for clinical trials, to negotiations on how the current care pathways needed to be adapted for the study, and the creation of new interactions between Primary and Secondary Care.

D. **Innovations are likely to meet further challenges to widespread adoption.**
A series of existing and potential pathways, including the study pathway, have been documented in the Study Pathway Document. These demonstrate how the Cardisio Test can integrate within existing Pathways, with the opportunity for future optimisation once the test is fully established and clinicians have accepted this with confidence.
It has become clear that whilst the Cardisio Test provided sufficient quality information for a referral that future Primary Care pathways, such as a Pharmacy directly making a referral to Secondary Care, which has been shown by the Study to be possible and effective, will take considerable time to be assessed and implemented. The Study also shows that even the current Primary Care pathways (via GP referral) are varied and will take considerable time and effort to achieve adoption of the Cardisio test on an individual ICB and Trust basis.

E. **Federated and diverse structure of the NHS need to be factored into the plans for introducing new innovations.** Different parts of the NHS are large enough to be completely independent with distinct processes that do not necessarily rely on each other. In future, further scoping of stakeholders, governance bodies and their requirements should clarified in advance with a time contingency added to achieve their sign off.

F. **Central planning is only as good as the quality of the Local teams.** The Study managed the diversity of the settings in terms of their practices, facilities and capability to support the testing. The PI's suggested that their teams should be allowed to manage their activities to ensure that the study protocol was being followed. The two areas where this was evident were:

    i. The processes required participants to be included or excluded based on information that the Pharmacy or the GP Surgery held. For the Community Pharmacy this was not possible and there was concern how participants might find out about the test, read the introductory pamphlets and give their informed consent. In fact some of the "walk-in" participants did not receive information in advance, but trusted the NHS staff, gave their consent and reported back that they were happy to have been included.

    ii. Data sharing while preserving patient confidentiality was a challenge at first, with the Cardisio system and team outside of the NHS Firewall, and the tests being recorded against patient data within the firewall. Members of the PI teams supported the Study Team, using Microsoft Teams Channels, to enable this data to be anonymised and ensure only relevant data was shared securely.

Opportunities identified

Over more than 18 months, as well as learning about SBRI Study management in the NHS, a number of areas have emerged where the Cardisio test can add further value, and provide opportunities for future improvements in the treatment of CVD.

1. Removing the need for patients to travel to Secondary Care for the quality of diagnostic information that the Cardisio Test provides, reduces the carbon footprint, in terms of travel alone by 60.7%. Potentially fewer people could be referred as a result of a Cardisio test than is current practice, there is a further saving to be gained in terms of carbon reduction during a future roll out.

2. More specific referrals leads to better use of the expertise and time of Secondary Care specialists and should shorten waiting lists. Testing all patients on a waiting list should in fact identify those incorrectly referred, providing a quick win in reducing waiting lists, and reducing the wait time for those in actual need of CVD treatment.

3. With fewer patients being potentially referred for CVD, there could be a significant reduction of patients on long waiting lists. Instead those patients can more quickly explore alternative diagnosis and treatment for whatever ails them. This will improve patient wellbeing and care.

PART B – CARE PATHWAYS

B1 Care Pathways

The NHS has a "Cardiovascular Disease (CVD) prevention pathway" for the public and practitioners in Primary Care". Pathways are designed to ensure that the right person has the right care, in the right place, at the right time, making the best use of available resources as shown on page 4 of the "Cardisio Care Pathways" Report. These provide the current, standard Care Pathways (shown in the table below as Care Pathways #1 and #2).****

In line with the NHS aim to improve Cardiovascular health outcomes through early-detection and prevention, the Cardisio test can be deployed in Primary Care. For the purposes of the SBRI study, the standard Care Pathway was modified to accommodate patients who are "at risk" but otherwise considered asymptomatic for CVD (this is shown in the table below as Care Pathway #3). The Study has shown how the Cardisio test can be incorporated into the standard Care Pathways to achieve improved health outcomes, with the intention to potentially reduce the burden on Secondary Care by carrying out the diagnostic test in Primary Care and avoid unnecessary referrals. In cases where patients present in Primary Care with serious chest pains, they will still be immediately referred to Secondary Care or will be required to go straight to Accident & Emergency (A&E).

Based upon the Study outcomes, the standard Care Pathways can be adapted to incorporate the Cardisio test, and three potential pathway scenarios are shown in the table below as Care Pathways #5A, #5B and #5C.

Table of Care Pathways by Type

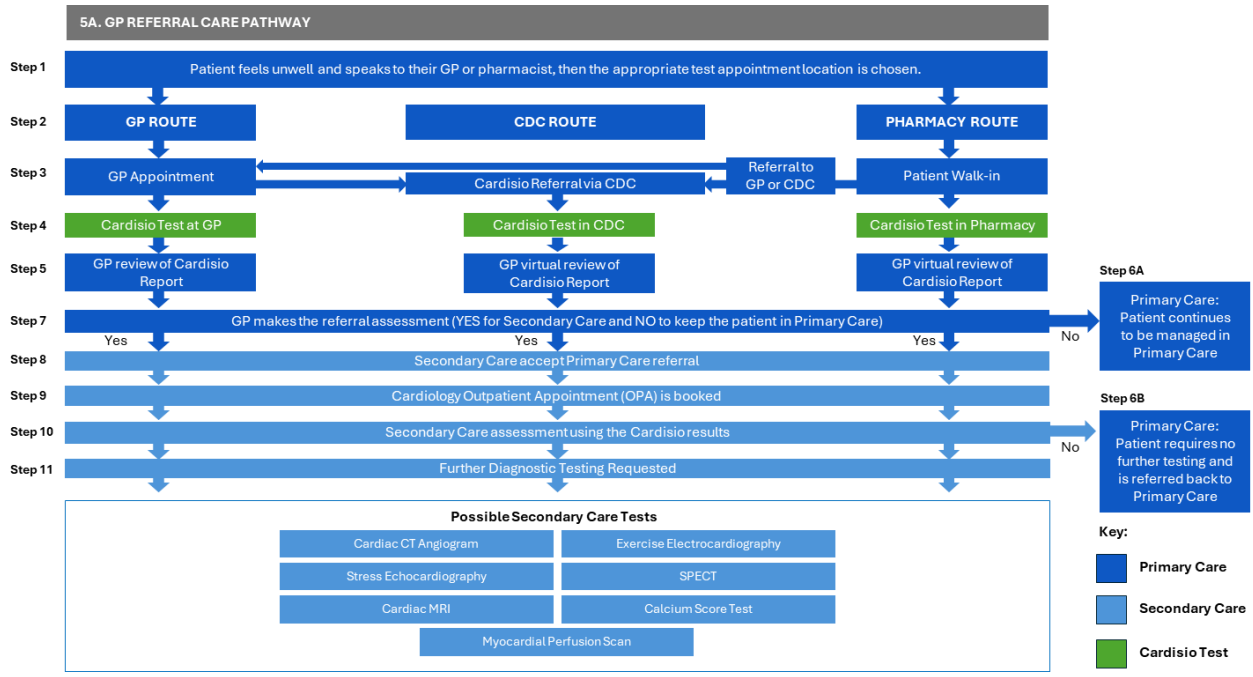
The following table sets out the current Care Pathways and those which are being proposed with Cardisio testing:

#	Type of Pathway	Pathway	Description	Source
1	**Standard & Current**	NHS CVD Prevention Care Pathway	The NHS CVD Prevention Schematic published by the NHS website	NHS
2	**Standard & Current**	Current CVD Care Pathway	This is the current care pathway without Cardisio	NHS/Corevitas
3	**Study Pathway**	SBRI Study Protocol Pathway	The care pathway shown in the study protocol document. Specifically only used in the study	Study Protocol Document
5A	**Possible to-be model –** test in Primary Care, then GP referral	GP Referral Care Pathway **(5A)**	GP to Secondary Care with Cardisio testing at GP/Pharmacy/CDC	Corevitas
5B	**Possible to-be model –** test in Primary Care, invite from Secondary Care	Secondary Care Referral Care Pathway **(5B)**	Secondary Care invites patients in based on their Cardisio test results database	Team
5C	**Possible to-be model –** test in Primary Care, then direct referral	Pharmacy Referral Care Pathway **(5C)**	Pharmacy testing then direct referral to Secondary Care	Team

Care Pathways #5B and #5C require a change in Secondary Care, whereby Secondary Care proactively review all Red and Amber Cardisio Test results or accept referrals from a pharmacy; this is therefore not immediately recommended.

Pathway #5A, however, can be implemented quickly and easily with the Cardisio Test being made available to GPs, and/or Pharmacies to administer, and GPs to then make higher quality referrals to Secondary Care, supporting GP decision making and reducing the number of unnecessary referrals to Secondary Care and so improving efficient use of resources.

Pathway #5A is shown below;



Further details of all Pathways considered can be found in the “Cardisio Care Pathways” Report.

PART C - MARKET ACCESS PLAN

C1 Market Access Plan

The Market Access Plan document, written by HIE and summarised here, which accompanies this report details insights and perspectives on the possible strategies and pathways for Cardisio to gain access to the NHS. The aim is to show the positive impact on factors such as cost-effectiveness, clinical benefits, and patient outcomes.

C1.1 The Cardisio value proposition for the NHS

The Cardisio test responds to the challenges of determining the heart health of an individual in a consistent way using advanced digital technologies specifically.

A. **Addressing NHS Challenges:** unprecedented healthcare pressures that include increased patient demand, long wait times, and economic constraints. Innovation is seen as a way to improve efficiency and patient outcomes and Cardisio aligns perfectly with these objectives with regard to CVD testing.

B. **Innovative Technology:** Cardisio leverages advanced artificial intelligence and 3D vectorcardiography to accurately and non-invasively detect heart diseases.

C. **Proven Efficacy:** High sensitivity and specificity in diagnosing coronary artery disease reduces misdiagnosis compared to traditional methods. For example, Cardisio has shown a sensitivity of 95.4% and specificity of 90% in detecting CAD, outperforming conventional electrocardiography.

D. **Competitive Advantage:** Compared to diagnostic tools like ECG, Holter monitors, CT-Calcium scores, and MRIs, Cardisio stands out as a non-invasive, cost-effective, and highly accurate solution, combing multiple diagnostic methods into a single, streamlined process that is both patient-friendly and efficient.

E. **Cost-Effectiveness:** Implementing Cardisio can lead to significant cost savings by reducing unnecessary referrals, and the need for expensive diagnostic procedures. Over a five-year period, Cardisio is projected to save the NHS approximately £9.7 million and reduce GP referrals to cardiology by 27,789, while also shortening wait times for secondary care diagnostics.

F. **Enhanced Patient Outcomes:** Early and accurate diagnosis using Cardisio can improve patient outcomes and quality of life (QoL), supporting the NHS's strategic goals of enhancing patient care, reducing health inequalities, and optimising resource utilisation.

G. **Alignment with NHS Policies:** In line with the NHS Long Term Plan's emphasis on early detection and treatment of CVD, Cardisio aligns with key NHS guidelines and initiatives, such as the CORE20PLUS5 framework and the NHS Outcomes Framework.

H. **Sustainability and Future Growth:** Cardisio is committed to ongoing innovation and regulatory compliance, continuous improvement and adaptation to evolving healthcare needs. The company also emphasises sustainability, aligning with NHS goals for reducing carbon emissions and promoting environmental responsibility.

C2 Product Aim

Cardisio was developed to support primary care with a better tools to determine if a patient is developing heart disease, improving referrals to Secondary Care, or advise on lifestyle modifications and/or medications. The product including the digital services are cost effective, scalable and present a minimal carbon footprint in use.

C2.1 Benefits

C2.1.1 Tester/Test Administrator/Examiner Independent Evaluations

Cardisio Webservices uses AI-based algorithms, supervised machine-learning and feed-forward neural networks to derive the results in the Cardisio Reports. The service is completely automated and independent of the skills of the tester/test administrator/examiner to produce the results, compile the measurements and highlight areas of concern.

C2.1.2 Three-in-One Test

The Cardisio test analyses the heartbeats in three broad categories, that of Coronary Artery Disease (specifically minor perfusion); arrythmias and Structural Heart Diseases. Each category is analysed independently by the Cardisio system allowing all three to be considered in the round as some categories impact others. Areas of concern are highlighted by category, so a healthcare specialist would be able to refer with confidence and the patient can be more rapidly provided with the appropriate first-line diagnostic tests.

C2.1.3 High Accuracy

Coronary Artery Disease is difficult to detect in Primary Care through the use of a 12- lead ECG alone, unless patient presents with typical symptoms and/or compatible ECG changes. The Cardisio test performs approximately 3.2 million calculations on each 4 minute dataset, looking for minute changes in the wavelets that make up a heartbeat. This produces a highly accurate pattern recognition for CAD for the Cardisio system to analyse.

Classic symptoms of CAD, normally involve chest pain/jaw pain and/or breathlessness, but not in all cases. Further, there are some 40 medical conditions that can cause chest pain, one of which is CAD. The Cardisio test is able to determine if chest pain is of cardiac origin and whether the patient has a myocardial infarction (STEMI or NSTEMI).

C2.1.4 Flexible care pathway architecture

The Cardisio System is designed for use in a variety of Primary Care Settings including General Practice, Community Pharmacy, Community Diagnostic Centres, Care Homes or District Nursing and can be configured to suit each ICSs Care Pathways.

For the SBRI Study Cardisio was configured for three Primary Care settings connecting to a local hospital's cardiology department. Red tests were reviewed by a consultant cardiologist who determined if the patient should be referred to a clinic for further assessment. In the future, with the appropriate agreement on changes to care pathways, potentially a pharmacy could even refer a Red condition patient test results to their local cardiology department for review and onward referral.

The care pathways could also accommodate “pull” referral models where either Primary or Secondary Care specialists invite patients in for testing if assessment of their health risk is of concern.

C3 Cardiovascular Diseases (CVD) – Impacted Population Size

Cardiovascular diseases (CVD) remain a significant health burden in the UK. The following statistics provide an overview of the population sizes affected by various heart and circulatory conditions in the UK:

- Circulatory System Diseases: 2018/19, approximately 1.8 million individuals were diagnosed
- Coronary Heart Disease: 2018/19, around 480,000 individuals in 2019/20 were diagnosed
- Coronary Artery Bypass Surgeries: 2018/19, 14,187 coronary artery bypass surgeries performed
- Inpatient Episodes: 2019/20, over 1.8 million inpatient episodes with a main diagnosis of circulatory system disease
- Mortality Rate: CVD mortality rate in 2019 was 255 deaths per 100,000 population. Scotland 326 deaths per 100,000. Scotland also had the highest mortality frequency for coronary heart disease, with 134 deaths per 100,000 compared to the UK average of 108 per 100,000.
- Atrial Fibrillation (AF): AF the most common arrhythmia, prevalent in approximately 3% of the population increases the risk of stroke by five times and is associated with heart failure. As many as 300,000 people may be living with undiagnosed AF in the UK.
- Heart Procedures and Operations: Around 371,000 heart procedures and operations were performed in England in 2020, marking a 22% drop from 2019 when more than 473,000 were carried out.
- Coexisting Health Conditions: Approximately 80% of people with heart and circulatory diseases have at least one other health condition.

These statistics highlight the significant impact of cardiovascular diseases on the population and the healthcare system in the UK, emphasising the need for effective early detection and management strategies.

C4 Policy and Guidelines Alignment

The Cardisio proposition is aligned with current NHS policies, guidelines, and strategic priorities in cardiology care, including digital health innovations. The Study Market Access Report outlines how Cardisio's technology aligns with these policy directives by improving early detection, supporting timely intervention, and enhancing overall patient care quality in alignment with the NHS's strategic goals and guidelines.

C4.1 NHS Long Term Plan 2019

(https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/)

NHS Long Term Plan emphasises early detection and treatment of cardiovascular diseases (CVD) to help patients live longer, healthier lives.

C4.2 NHS Outcomes Framework 2024

(https://digital.nhs.uk/data-and-information/publications/statistical/nhs-outcomes-framework)

The **NHS Outcomes Framework (NHS OF)** is a set of **68 indicators** that measure performance in the health and care system at a national level, driving transparency, quality improvement, and outcome measurement.

C5 Cardisio Carbon Reduction Plan and Net Zero Commitment

Cardisio has a published Net Zero carbon emissions statement which is currently being actioned with a Baseline Assessment for 2023.

During this SBRI Study CO2e was monitored and calculated. A 61% lower level of carbon compared to the use of standard care pathways was identified due to the digital technology used and the proximity of testing to the Study Participants.

Future deployment can yield significant benefits for NHS England's carbon reduction plan. Integration into current care pathways will leverage the supply of Cardisio devices and accessories as part of carbon reduction plans, with the ability to train, set-up and deliver the environment remotely using carbon neutral 3rd party logistics companies, remote working and digital training media as a significant advantage of the Cardisio proposition.

Please refer to the SBRI Cardisio End of Study ESG Report for further details.

PART D - BUDGET IMPACT MODEL

D1 Budget Impact Model

A Budget Impact Model (BIM) was developed comparing the diagnostic pathways for patients with suspected Arrhythmias, Structural Heart Disease and Coronary Artery Disease with and without the use of the Cardisio test in a Primary Care setting**.** The model inputs are based on the SBRI funded study on the use of Cardisio testing for "at risk" patients in Primary Care (GP and Pharmacy settings), Hospital Episode Statistics (HES) Data for England, a review of literature and information sourced from expert clinicians in the field.

D1.1 Summary of the Impact of Cardisio over 5 years in England

The implementation of the Cardisio test over a five-year period in England is projected to result in significant cost savings and a substantial reduction in GP referrals to cardiology. Additionally, the BIM highlights considerable monthly reductions in various secondary care diagnostic tests and procedures, along with the current average waiting times for these services.

It is important to note that the SBRI funded study was designed around the selection of participants with a high CVD risk profile who were asymptomatic of classic CVD symptoms whereas in the Budget Impact Model it focuses on the diagnosis pathway for symptomatic patients highlighting the budget impact as well as the impact of Cardisio testing on Secondary Care diagnostic capacity.

D1.2 Key findings

Reduction in Total Cost:	£9,701,036 over five years.
Reduction in GP Referrals into Cardiology:	27,789 referrals over five years.

Monthly Reductions in Secondary Care:

- Cardiologist Face-to-Face Consultations: Decrease by 182.8 consultations per month
- Stress Echocardiographies: Decrease by 120.4 tests per month
- Exercise Electrocardiographies: Decrease by 91.2 tests per month
- Cardiac CT Angiographies: Decrease by 76.5 tests per month
- Cardiac MRIs: Decrease by 62.8 tests per month
- SPECT: Decrease by 5.6 tests per month
- Myocardial Perfusion Scans: Decrease by 14.7 tests per month
- Calcium Score Tests: Decrease by 25.3 tests per month

Current Average Waiting Times (Days):

- Cardiologist Face-to-Face Consultations: 213.5 days
- Stress Echocardiographies: 174.9 days
- Exercise Electrocardiographies: 186 days
- Cardiac CT Angiographies: 186 days
- Cardiac MRIs: 244.4 days
- SPECT: 244.4 days
- Myocardial Perfusion Scans: 169 days
- Calcium Score Tests: 170.1 days

This detailed analysis emphasises the potential of Cardisio in streamlining cardiovascular care and alleviating pressure on secondary care resources

Note: The default value is 10 sites per ICB; however, this number may be too high for ICBs with low referral numbers. Another critical input to monitor is the percentage of referrals that did not require specialist attention.

APPENDICES

Key Facts

- Study Period of 18 months
- 79 formal Study meetings
- 25 test administrators trained
- 7 geographical areas served

- 628 candidates selected and tested with 134 requiring OPAs
- 91% of referrals correctly referred
- Net promoter score of 88%

- 49%:51% - Women:Men – Gender balance achieved
- 71.6% of participants were from diverse ethnic minorities
- 60.7% Potential CO_2e emission reduction identified

- £9.7M of savings projected over 5 years projected
- 27,789 fewer referrals to secondary care projected

Deliverable & Key Document List

SBRI Cardisio Study Report – Final August 2024.pdf

SBRI Cardisio Study Overview and Key Results 2024 06 03 (005 FINAL).pdf

SBRI Cardisio Study Cardisio Care Pathways 2024 07 10 (003).pdf

SBRI Cardisio STUDY ESG Report 2024 06 21 v1 FINAL.pdf

Cardisio End of Study BIM Summary 2024.pdf

HIE Cardisio Market Access Plan V2.0 REVIEW DOCUMENT.pdf

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