AI-guided point-of-care ultrasound to diagnose deep vein thrombosis in primary care

(Diagnostic test accuracy and qualitative study)

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This protocol has regard for the HRA guidance

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Study summary	
Project title	AI-guided point-of-care ultrasound to diagnose deep vein thrombosis in primary care
Short title	AI-guided DVT diagnostic in primary care
Chief investigator	Kerstin Nothnagel
Sponsor	University of Bristol (UoB)
Funder	School for Primary Care Research (SPCR)/ Research Capability Funding (RCF)
Aim	• To assess the accuracy and acceptability of AI-guided DVT diagnosis in primary care <u>Quantitative objectives are:</u> • To estimate the accuracy of HCA reported AI-guided DVT diagnosis against the reference standard of sonographer scan • To estimate the accuracy of AI provided DVT diagnosis against the reference standard of sonographer scan • To estimate the accuracy of remote specialist diagnosis using AI-guided acquired ultrasound images compared to the reference standard of sonographer scan • To determine the proportion of HCA acquired images that are of inadequate quality • To explore which factors are associated with inadequate image quality • To investigate patient satisfaction with AI-guided DVT diagnosis <u>Qualitative objectives:</u> • Explore patient reservations, obstacles, and confidence in relation to their experience of AI-guided point- of-care US undertaking as diagnostic scan for DVT • Explore the confidence of the HCAs in the index scan • Explore the experience of HCAs in delivering the scan
Project design	Diagnostic cross sectional cohort study, with qualitative evaluation.
Sample size	Quantitative: 500 GP Care eligible patients (See exclusion criteria in flowchart) Qualitative: 25 participants (20 patients/ 5 HCAs)
Number of project sites	<u>4 GP Care DVT Clinics in Bristol, North Somerset and South Gloucestershire (BNSSG):</u> • Concord Medical Centre, Braydon Avenue, Little Stoke, Bristol BS34 6BQ • Crest Family Practice, William Budd Health Centre, Knowle West Health Park, Downton Road, Bristol, BS4 1WH • East Trees Health Centre, 100a Fishponds Road, Bristol BS5 6SA • New site at Weston-Super-Mare from October 2023
Index test	AI-guided (popliteal region, and groin region) 2-region compression ultrasound (US) of proximal leg with handheld US probe Clarius L7 (“AutoDVT”) operated by GP Care HCA with no previous US experience.
Reference test	Standard DVT US scan of the proximal leg performed by the GP Care sonographer

Inclusion criteria	Patients are eligible if (all of): • Eligible for GP Care DVT Services †1 flowchart • Participant has capacity to consent to study participation.
Exclusion criteria	A patient will not be eligible if (any of): • Unable to communicate in English (spoken or written) and there is no translator available. • For the qualitative study, patients who have a hearing impairment that would hinder the feasibility of an e-interview.
Project duration	Funding start date: 01.06.2023 with 12 months in total but subject to change Project start date: 01.12.23 Anticipated end date: 04.07.2025 (subject to change)
Lay summary	In this study, we aim to investigate a new approach with the overarching goal of enhancing the detection of deep vein thrombosis (DVT). DVT is a medical condition characterised by the formation of blood clots within the deep veins, most commonly occurring in the legs. The current standard for diagnosing DVT involves utilising the Wells Score, a scoring system, in conjunction with a blood test called D-dimer, followed by an ultrasound scan (USS) administered by specialised healthcare professionals (HCP). However, this study explores the potential of a transformative technology that could change this paradigm. A scenario has been envisioned in which ordinary individuals, without specialised ultrasound (US) training, could employ a smartphone application (app) to perform a DVT scan of the leg. This innovative app serves as a comprehensive guide, leading users through the steps necessary to conduct a leg US examination. The significance of this research becomes apparent when considering the potential implications. If successful, this approach has the capacity to revolutionise DVT diagnosis, enabling patients to receive prompt assessments in the convenience of their primary care provider's office or even within their own homes. Such a development could substantially expedite the diagnosis process, offering enhanced convenience to patients and potentially reducing the number of emergency department (ED) visits. Additionally, this innovation holds the promise of alleviating some of the financial strain on healthcare systems like the National Health Service (NHS) by optimising DVT diagnostic services. In essence, this study seeks to pave the way for a future in which DVT diagnosis becomes more accessible, efficient, and financially sustainable for HCPs.

Key contacts

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ThinkSono GmbH c/o HPI Seed Fund GmbH August-Bebel-Str 88 14482 Potsdam Germany And local supplier: ThinkSono Ltd, Flat 35 Mercury House, Heathcroft, London, UK W5 3BF Email: Fouad@thinksono.com	Third Party: • Provision of AI-software device and Clarius L7 Ultrasound Probe • Support with trouble-shooting problems with equipment (e.g., servicing/providing replacement units) • Ensuring accurate description of AI-software and training material • Cover of any loss or damage of research kits
GP Care UK Limited, 160 Aztec West, BS32 4TU Bristol	Third party and hosting project at DVT Clinic (diverse locations): • Concord Medical Centre, Braydon Avenue, Little Stoke, Bristol BS34 6BQ • Crest Family Practice, William Budd Health Centre, Knowle West Health Park, Downton Road, Bristol, BS4 1WH • East Trees Health Centre, 100a Fishponds Road, Bristol BS5 6SA • Clinic at Weston-super-Mare (Planned opening in October 2023)

Glossary of abbreviations

A&E	Accident and Emergency
ACEP	American College of Emergency Physicians
AI	Artificial Intelligence
AutoDVT	Automated Software to diagnose Deep Vein Thrombosis, AI-guidance through App
BMI	Body Mass Index
CI	Confidence Interval
DVT	Deep Vein Thrombosis
DTA	Diagnostic Test Accuracy
FFT	Friends and Family Test
FN	False Negative
FP	False Positive
GCP	Good Clinical Practice
GP	General Practitioner
HCA	Health Care Assistant
HCP	Health Care Professional
HRA	Health Research Authority
IRAS	Integrated Research Application System
NHS	National Health Service
NPV	Negative Predictive Value
ML	Machine Learning
PE	Pulmonary Embolism
PIS	Participant Information Sheet
POCUS	Point-of-care Ultrasound
PPI	Patient and Public Involvement
PPV	Positive Predictive Value
PTS	Post Thrombotic Syndrome
REC	Research Ethics Committee
TN	True Negative
TP	True Positive
UID	Unique Identifier
UoB	University of Bristol

US	Ultrasound
VTE	Venous Thromboembolism

Glossary of medical terms

Anticoagulants - are medicines that help prevent blood clots. They are prescribed to reduce the risk of a blood clot and to treat blood clots.

D-dimer test - measures the level of fibrin degradation in the body. It can indicate whether there may have been a significant blood clot (thrombus), but it does not show the location or cause of the blood clot.

Doppler ultrasound - is a test that uses high-frequency sound waves to measure the amount of blood flow through your arteries and veins, usually those that supply blood to your arms and legs.

DVT - deep vein thrombosis is a blood clot that develops in a deep vein on the body, most commonly the leg, but it can occur anywhere in the body.

Embolism - is the lodging of an embolus, a blockage-causing piece of material, inside a blood vessel. The embolus may be a blood clot (thrombus), a fat globule (fat embolism), a bubble of air or other gas (gas embolism), or foreign material.

PE - Pulmonary Embolism, this is when a blood clot elsewhere in your body has broken off and travelled in the blood stream to your lungs and causes a blockage that can be extremely dangerous and requires urgent medical attention.

PTS - Post-thrombotic syndrome refers to symptoms and signs of chronic venous insufficiency that develop following deep vein thrombosis (DVT) and is a common, burdensome, and costly complication.

Thrombosis - is the formation of a blood clot inside a blood vessel, obstructing the flow of blood through the circulatory system.

US - Ultrasound scan is a medical test that uses high-frequency sound waves to capture live images from the inside of your body. It is also known as sonography.

Veins - are blood vessels that carry blood toward the heart. Most veins carry deoxygenated blood from the tissues back to the heart (exceptions are the pulmonary and umbilical veins, both of which carry oxygenated blood to the heart).

VTE - venous thromboembolism is a condition in which a blood clot forms most often in the deep veins of the leg, groin, or arm (known as deep vein thrombosis, DVT) and travels in the circulation, lodging in the lungs (known as pulmonary embolism, PE), a DVT and PE together are known as a VTE.

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1 Introduction

DVT is a serious medical condition identified by the development of blood clots in the deep veins, frequently found in the lower limbs. These clots can dislodge and travel through the blood vessels, leading to potentially life-threatening pulmonary embolism (PE). DVT and PE collectively form venous thromboembolism (VTE) and represent a significant cause of morbidity and mortality (Mousavi-Roknabadi et al., 2019). Numerous factors contribute to DVT formation, including blood flow stasis, hypercoagulability, and vascular endothelial injury, collectively known as the Virchow triad (Anderson, 2003).

Diagnosing DVT can be challenging due to its symptom overlap with other conditions, and only about 15% of patients with DVT-like symptoms have DVT. US has firmly established itself as the gold standard test for evaluating DVT. This non-invasive imaging modality offers high sensitivity and specificity in detecting DVT, making it a preferred method for accurate diagnosis and effective patient management. Its accuracy may vary due to factors like patients' anatomy, which can be more challenging in obese individuals and the operator's experience with the US examination. Timely and accurate diagnosis is crucial to prevent severe complications such as PE or post-thrombotic syndrome (PTS) leading to chronic venous insufficiency (CVI). General practitioners (GPs) typically start the diagnostic process using the Wells Score and D-dimer tests, but further investigation often requires referral to specialists via EDs or DVT clinics.

DVT poses a significant burden on both patients and healthcare systems, with long-term complications like PTS impacting quality of life and increasing the risk of fatal PE. To address these challenges, Artificial intelligence (AI)-guided US devices have the potential to enable non-specialist HCPs to scan suspected DVT patients in primary care settings. The implementation of AI-guided point-of-care US (POCUS) DVT diagnostics can reduce unnecessary hospital admissions, alleviate the workload of specialists, and improve accessibility and convenience for patients (Kainz et al.).

1.1 The need for research

As the global population ages, the incidence of DVT increases significantly, particularly among individuals aged 65 and above. However, the existing diagnostic pathway for DVT varies across the UK and often involves a time-consuming process from GP to a vascular clinic or an ED, causing delays and potential complications (Thrombosis UK, 2020). This has put a financial burden on healthcare systems and led to ED overcrowding.

Two meta-analyses suggest that a two-region POCUS exam is comparable to full leg compression US in patient management and failure rates (Kraajipoel et al. and Bernardi).

Studies have shown that even non-specialist operators can perform reliable point-of-care compression US (Mumoli et al.).

The meta-analysis conducted by Bhatt et al. in 2020, encompassing 43 studies involving patients with suspected DVT, yielded pooled sensitivity and specificity estimates for proximal compression US of 90.1% (95% confidence interval (CI), 86.5-92.8) and 98.5% (95% CI, 97.6-99.1), respectively. In the case of whole-leg US, the combined estimates were 94.0% (95% CI, 91.3-95.9) for sensitivity and 97.3% (95% CI, 94.8-98.6) for specificity (Bhatt et al.).

An extensive review of the existing literature revealed that the approach to treating distal (below the knee) DVT lacks clear consensus. Distal DVT management options include anticoagulation or monitoring, as highlighted by Kabashneh et al. in 2020. In accordance with the National Institute for Health and Care Excellence (NICE) guidelines, patients presenting with symptoms of DVT will undergo a proximal leg scan, with no specific directive for a distal leg scan. Moreover, the NICE guidelines suggest that if symptoms persist, a repeat proximal leg scan is recommended after six to eight days (NICE, 2021). A 2020 systematic review and meta-analysis found standard DVT US scan to have high sensitivity (97%) and specificity (98%) for proximal DVT, but lower sensitivity (50% to 75%) and specificity (90% to 95%) for distal DVT (Kraaijpoel et al.).

In this primary care research study, the comparison will be made between AI-guided 2-region compression US conducted by a healthcare assistant (HCA) and the standard US diagnostic for DVT performed by a sonographer.

A new smartphone application called "AutoDVT " (also called ThinkSono Guidance) has been developed to aid individuals without specialised expertise in performing proximal leg DVT scans using the '2-region' compression US technique. The software uses machine learning (ML) algorithms and a user-friendly interface, along with a compatible US probe, to support non-specialists in performing POCUS DVT scans.

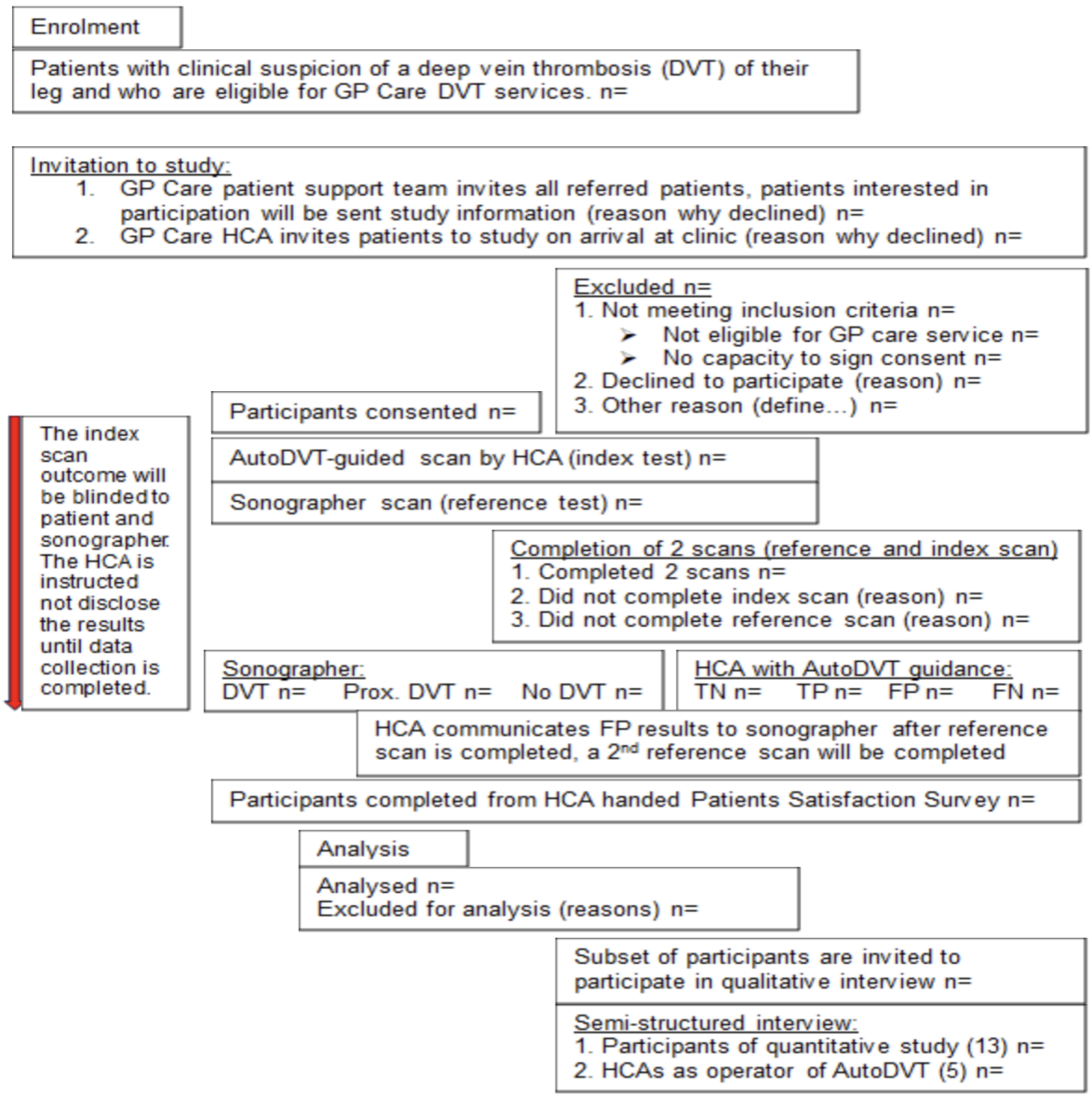
Two preliminary pilot studies were conducted in secondary care: one involving 30 participants at Oxford Haemophilia and Thrombosis Centre (Ethics: 18/SC/0220, IRAS 234007) and another with 53 participants at a hospital in Germany (Ethics: S7(a)/2020). The outcomes were published in npj Digital Medicine in 2021 (Kainz et al., 2021). The index scan, which involves a remote radiographer diagnosing US images taken by a non-specialist, demonstrated sensitivity within a 95% CI range of (0.82, 0.94), specificity of (0.70, 0.82), and a positive predictive value (PPV) of (0.65, 0.89) when compared to the diagnosis from a standard DVT diagnostic USS (Kainz et al.). The AutoDVT app has received Conformité Européene (CE) marking for data collection, and ongoing updates are being informed by new data. This study aims to confirm the accuracy and efficiency of appl-guided DVT diagnosis in primary care settings.

Subsequently, the AI app has undergone enhancements through continuous data input. Additionally, a recent multi-centre pilot study is conducted across multiple UK hospitals. This study is led by Dr Nicola Curry and sponsored by Oxford University Hospitals NHS Foundation Trust. The results have not yet been published, the study's reference is Ethics: 21/ES/0070, IRAS 285274.

This study aims to explore the accuracy of app-guided POCUS DVT diagnosis when the scans are conducted by HCAs in primary care settings using app guidance.

The potential benefits of app-guided POCUS DVT diagnostics include quicker diagnosis, expedited treatment, improved patient outcomes, and reduced costs. App-guided POCUS takes only a few minutes and can be conducted in various community settings, such as GP surgeries, patients' homes, or nursing homes.

2 Flowchart 1



GP Care DVT Exclusion Criteria†[1]

Patients presenting with the following exclusion criteria should be referred immediately to secondary care as they are currently:
Patients unable to transfer themselves on and off a bed without assistance. Patients may use their own portable hoist if able to do so with assistance from their own carer.
Suspected as having upper limb DVT
Patients under 18 years of age
Housebound patients with significant manual handling implications e.g., requiring hoisting. The provider will need to ensure that the needs of eligible housebound patients are taken into account within the specified timescales. If housebound patients require scanning transport this should be arranged for them by the current process. Primary diagnosis of pulmonary embolism
(https://gpcare.org.uk/information-for-clinicians/deep-vein-thrombosis/)

3 Study methods

3.1 Population

The quantitative phase of the study will take place at the primary care GP Care DVT clinics (GP Care, 2022). For the qualitative interviews, a diverse subset of participants will be invited to participate until around 20 participants have been interviewed or data saturation has been achieved. Additionally, five GP Care HCAs, as the operator of the app-guided US device, will be invited for semi-structured interviews.

3.2 Recruitment

The study aims to recruit 500 GP Care patients for the quantitative aspect of the study.

Participants are eligible if they have the capacity to consent.
Participants will not be eligible if they are unable to communicate in English (spoken or written) and there is no translator available.

GP Care eligible patients will receive information about the study in two ways:

- All patients referred to the GP Care DVT clinics routinely receive a call to arrange a scan appointment from the GP Care patient support team. During this interaction, patients will be asked if they are interested in knowing more about the study. Those who express interest will be provided with study information through their preferred method, either via text message or email. Because DVT scans are intended to be scheduled on the same day, sending study information by mail is impractical. However, patients who wish to participate but cannot receive study information via message or email will receive physical copies of the study documents during their clinic appointment. These patients will be encouraged to arrive at least 30 minutes before their appointment to have time to review the study documents and ask the team any questions. Patients who choose not to participate will be indicated by the letter 'R' attached to their study unique identifier (UID), such as RA 152 (R for declined, A for Concord Medical Centre, and 152 for participant number).

- Our aim is for all patients to receive an invitation to participate in the study as soon as they arrive at the GP Care clinic. However, it is important to acknowledge that recruitment could face challenges, such as a crowded DVT clinic, staffing constraints, or equipment-related technical issues. This will be highlighted in flowchart. If patients who initially declined participation later decide to join, the research team will denote this by adding the letter 'A' before the UID, for example, ARA 152 (A for accepted, R for declined, A for Concord Medical Centre, and 152 for participant number). A more detailed explanation of the study codes will be provided in section 5.1.

3.3 Consent

Once the participant is escorted to the treatment room, a good clinical practice (GCP) trained team member will address any questions or concerns the participant may have about the study and the patient information sheet (PIS). Following this, a member of the team. will ask the participant to complete and then sign the consent form. Under the consent heading, the patient will be prompted to provide their personal information, including name, age, gender, and the postcode of their residence within the BNSSG.

The research team will include the UID on the patient satisfaction survey (PSS) and provide it to the participant after they have received the scans, both the reference and index scan, for them to complete. To guarantee precision, the research team will confirm that the UID on the consent form matches the one on the PSS. Any additional questions or concerns expressed by the patient regarding the study will be carefully addressed by the research team.

3.4 Index test

While the patient readies for the scan by uncovering the affected leg, the HCA triggers the initiation of a new scan using the AI app AutoDVT. Following the app's cues, the HCA will input the operator ID, the patient UID, specify the affected leg (right or left), and provide the patient's height and weight for automatic body mass index (BMI) calculation. No personal data will be entered into the app.

The HCA will position the patient on the treatment table with the affected leg exposed. Subsequently, the HCA will conduct a compression US guided by the app.

To maintain blinding of the sonographer and ensure the participant's privacy, the US scan will take place behind medical curtains and the HCA will be advised not to make any verbal comments regarding the procedure and result.

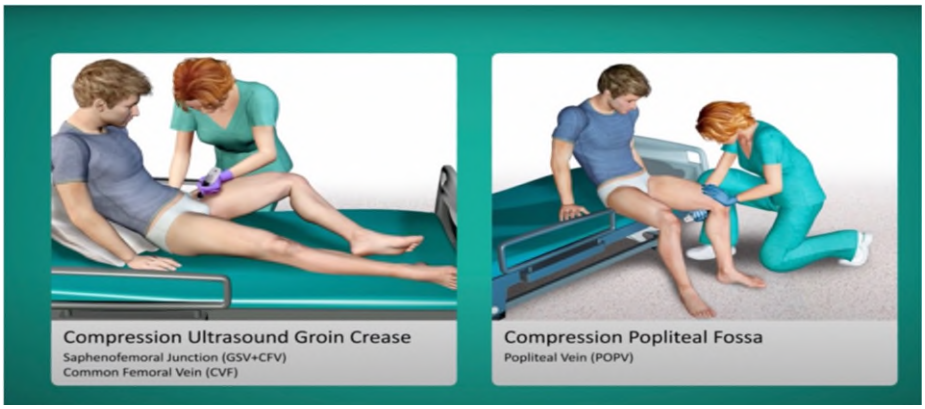


Figure 1, Compression region groin crease and popliteal fossa

The app provides the operator with step-by-step guidance through an US examination of the proximal leg. For example, when the veins are not centred on the screen, the mobile app reminds the operator with 'veins are not centred, when veins are in optimal position, the app will prompt the operator with a beep sound and displays 'recommended area for compression' and instructs to perform compressions. The examination includes scanning of two compression regions, the inguinal crease, and the popliteal fossa.

Inguinal crease

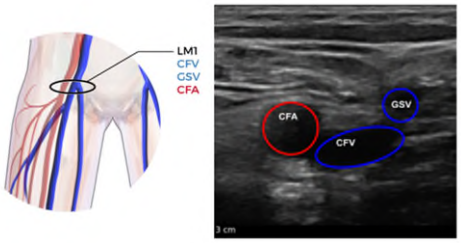


Figure 2, Compression point at the saphenofemoral junction (SFJ)
(These images have been added to help understanding of the protocol)

The US probe will be placed in the groin region. The probe will be advanced proximally until the point where the Great Saphenous Vein (GSV) joins the Common Femoral Vein (CFV). At the SFJ consistent downward pressure is applied to compress both the CFV and proximal GSV. It is worth noting that even though the GSV is superficial, a clot detected in its proximal segment can extend into the deep venous system, necessitating treatment similar to a DVT. A healthy vein will fully collapse under this pressure.

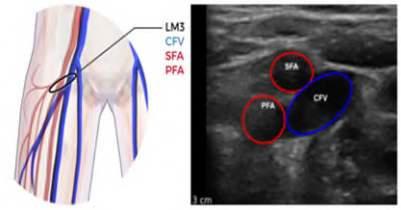


Figure 3, Compression point, at the bifurcation of Common Femoral Artery (CFA) and Profunda Artery (PFA)

The image above shows the CFV at the level of the CFA bifurcation into PFA and Superficial Femoral Artery (SFA). After the first compression in the inguinal crease of the CFV and GSV, the probe is advanced distally to the femoral triangle, following the CFV. The image on the screen will show the CFV medially and the SFA and PFA laterally. Firm pressure is applied to compress the CFV.

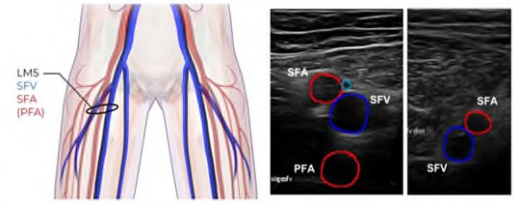


Figure 4, Compression point on the SFV

Then, the scan is continued distally until after the CFV has splits into Superficial Femoral Vein (SFV) and deep femoral vein(s). Firm pressure is applied downward to compress the proximal SFV.

Popliteal fossa

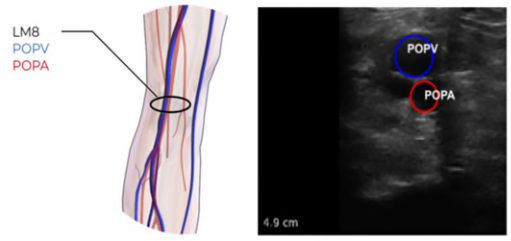


Figure 5, Compression point, proximal popliteal fossa

The US probe is shifted to the back of the knee's crease and a scan is performed that covers a 2 cm area both above and below to locate the popliteal vein. The probe is positioned precisely between the two hamstring tendons situated behind the knee. In this view, the popliteal vein is positioned above, while the popliteal artery is below.

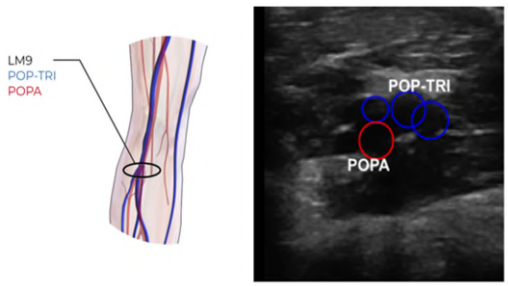


Figure 6, Compression point, popliteal vein (PopV) at the level of the popliteal trifurcation

The US probe is glided downward until the point where the popliteal vein splits into the anterior tibial, peroneal, and posterior tibial veins is reached. This juncture marks the final compression point.

During the examination, the HCAs will be prompted by the app after each compression point with the question, "Are the veins fully compressible?" The HCAs will have three options to choose from: "Compressible," indicating no clot in the vein, the vein fully collapses when pressure is applied, "Not

Compressible," indicating a clot in the vein, or "Retry" if unsure about the finding. It's possible that the HCA might continuously opt for "retry" due to uncertainty regarding the presence of DVT. In such instances, the compression point would be marked as "unsure." In a clinical setting, patients falling into this category would typically necessitate a conventional ultrasound scan conducted by a specialist. An “unsure” result could be caused by inadequate compression by the HCA, challenges in identifying the correct anatomical landmarks, or technical complications with the AutoDVT device, as indicated in flowchart two.
If the HCA selects "Compressible," but the AI app assesses the vein as "Not Compressible," the selected option will appear in red, and the operator will be asked if they wish to "Override" the AI diagnosis.
This is in detailed explained in the AutoDVT training clip ‘https://thinksono.com/training/‘(ThinkSono, 2021).
It is essential to highlight that the software will store both the AI diagnosis and the HCA's decision. The HCAs final decision about whether the veins are ‘compressible’ (no DVT) or ‘not compressible’ (DVT) will be taken as the primary outcome for assessing the sensitivity of the device (see objective 1).
However, it's important to emphasise that the current intended clinical application relies on the app guiding non-specialists through a proximal leg DVT scan and collecting US images of sufficient quality for remote diagnosis.

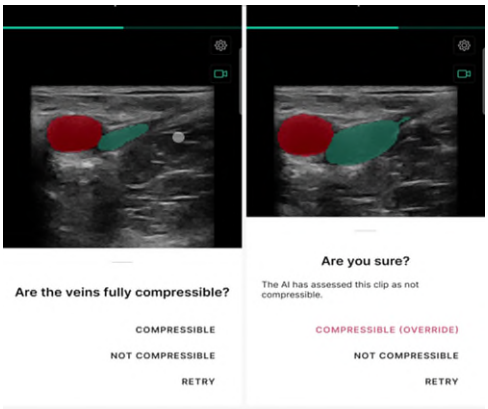


Figure 7, AutoDVT assessment of veins: ‘compressible’, ‘not compressible’, ‘retry’

A "compressible vein" indicates the absence of DVT. It means that the vein can fully collapse or compress when pressure is applied using an US probe. If a vein is compressible, it suggests that there are no blood clots obstructing the vein's lumen, allowing it to easily collapse and return to its original shape when pressure is released. This characteristic is used as a diagnostic criterion to rule out the presence of DVT.

In the context of the index scan, it is defined as a two-region compression US with three compression areas located in the inguinal crease and two compression points in the popliteal fossa region, demonstrated in figure two to figure six. During the index scan, the compressibility of the veins within these specified areas is assessed to determine if there are any indications of DVT. If the HCA notes that the vein cannot be compressed in any of the compression areas, this will be categorised as a positive result in the index scan test.

3.5 Reference test

The patient remains on the treatment table after the completion of the index scan. The sonographer, who is unaware of the index scan outcome, will enter the treatment area and perform the standard DVT scan with a GE Versana Active US machine.

The reference scan is defined as scan of the proximal leg reaching form the inguinal crease to the popliteal fossa, to the trifurcation of the popliteal vein, covering the same or more regions as defined in the index scan.

If the app-guided USS demonstrates a DVT but the sonographers standard DVT scan is negative (i.e., a false positive (FP) result), the HCA will inform the sonographer after the completion of the reference scan. Subsequently, the sonographer will conduct a second scan. If a second scan is conducted the results of both scans will be recorded; the sonographers final clinical opinion based on the results of both the initial

and the repeat scan will be used to determine the final presence or absence of proximal DVT (reference standard). Regardless, if the sonographer is uncertain about the presence of a DVT, the patient would be categorised as 'DVT positive' as in the clinical setting and managed accordingly. Certain sonographers may conduct a full leg scan, which incorporates a more thorough proximal and an additional distal USS (although this is not in accordance with NICE recommendations). If a distal DVT is identified during the scan but no proximal DVT is found, it will be considered negative reference test. Any detected distal DVT will be documented and analysed according to the details outlined in section six.

3.6 Patient satisfaction survey

Upon completing both scans, the HCA will kindly request participants to fill out the PSS for GP Care service and the app-guided scan. Participants will then be encouraged to hand the completed form to the surgery receptionist before leaving the surgery. The research team will be able to assist with the completion of the survey if requested by the participant.

An existing research gap has been identified around PSSs regarding AI medical appliances and related subjects. Despite an exhaustive literature search, no validated surveys exploring patient satisfaction with AI and ultrasound or novel US devices, point of care US have been discovered (Fritsch et al., 2022). In response to this gap, a survey tailored to this specific research project has been developed.

The survey is structured around the Friends and Family Test (FFT) YouTube and Audio promotion, a crucial feedback tool supporting the core principle that individuals using NHS services should have the opportunity to share their experiences (NHS, 2020).
The first question in the survey, introduced with a frame clarifying that it pertains to the AutoDVT scan service, seeks to gauge participants' overall experiences: " Thinking about your scan with the AutoDVT, overall, how was your experience of our service?" Participants can choose from six response options: ‘Very good’, ‘Good’, ‘Neither good nor poor’, ‘Poor’, ‘Very poor’, and ‘Don't know’.

The FFT guidelines stipulate the inclusion of at least one open-ended question alongside standard fixed questions. The FFT has chosen to focus on the following question, as it has been proven to elicit high-quality feedback. However, the specific wording of the questions is left to the survey provider. "Please tell us about anything that we could have done better." This open-ended query is presented as question number four in the survey.

Questions two and three have been formulated based on insights gained from a literature review examining validated PSSs. An example includes a survey conducted by William Durston et al., which assessed patient satisfaction with POCUS performed by physicians in the ED compared to US performed by the medical imaging department. By adopting the FFT framework, our survey benefits from its status as a continuous improvement tool. It is designed to be quick and accessible for all patients and service users, in contrast to national validated surveys, which are often one-time or periodic snapshots of experiences or opinions, typically relying on lengthy structured questionnaires.

Participants will have the opportunity to provide their email address on the PSS if they wish to receive a £10 voucher as compensation for their time. They can also indicate on the form if they are interested in participating in the second part of the study, which involves an interview.

4 Index test equipment

There are two main pieces of equipment:

1. The AI app connected to

2. The handheld US probe Clarius L7 HD3.


Figure 8 and 9, AutoDVT: AI-app and Clarius L7 HD3 handheld ultrasound probe (ThinkSono, 2021)

The clinical study will make use of an AI app known as "AutoDVT", which is specially designed to assist non-specialist operators like nurses, GPs, and other allied health professionals (AHP) in diagnosing DVT. This app employs a "machine learning" (ML) algorithm and a user-friendly graphical interface that works in conjunction with a compatible handheld US probe called the "Clarius L7 HD3."
The purpose is to support non-specialists in accurately identifying cases of DVT. ThinkSono Ltd will provide two device sets for this study enabling flexible use of the devices in between the different GP Care DVT Clinics.
To ensure accessibility and proper maintenance of the study equipment, it will be stored at the secure GP Care base along with the GP Care standard US equipment during the week. GP Care utilises the courier service Go-Getters to facilitate the transportation of US equipment between its storage at the GP Care base and the DVT Clinics. The phone, on which the AI app is stored will be charged overnight at GP Care base to ensure it is fully operational during clinic hours. Likewise, the Clarius US probe will be charged in a terminal overnight. The charger also serves as a stand for the US probe and can be used as charging point in between patients, ensuring the device is always fully charged and ready for use.
It is recommended to bring both device sets to the DVT clinic to ensure readiness in case of any technical issues. If one device encounters problems, the second device can be used for scanning while the CI provides technical support for the affected device.
There are four GP Care DVT Clinic sites, and clinics are typically held on consecutive days at different locations. However, on Wednesdays, a clinic will be held simultaneously at Weston-Super-Mare and the East Tree Health Centre, and only one device set will be available for each clinic. In the event of a technical issue that cannot be immediately resolved, the study may be paused for that specific day.

4.1 Training in the use of the AI-guided handheld ultrasound device

Kerstin Nothnagel, the CI with extensive experience in sonography as an Emergency Care Physician Associate (PA) and qualified Vascular Scientist, will conduct a comprehensive 1.5-hour training session for the five GP Care HCAs. The training will include a practical session, tutorial videos, e.g., https://thinksono.com/training/ and user guidance to ensure proficiency in using app. Prior to the study commencement, the HCAs will have the opportunity to practice up to five app-guided scans during the training (ThinkSono, 2021).

Furthermore, the HCAs will receive instructions on how to follow the study protocol and properly obtain consent according to their Good Clinical Practice (GCP) training. The CI will be present at the clinics during the initial two weeks to address any questions from the HCAs and ensure the smooth integration of study procedures within the DVT Clinic workflow. After the pilot weeks the CI will only be onsite if there are specific indications.

4.2 Image quality checks

The index scans will be retrospectively uploaded by the CI after completion of the recruitment to a cloud dashboard managed by ThinkSono Ltd., the company responsible for the app.
The app-guided scans will subsequently undergo assessment by five certified remote clinicians, including radiologists, sonographers, or other qualified practitioners, each with a minimum of one year of experience in DVT diagnosis through compression ultrasound (US). These clinicians will evaluate the scans without

knowledge of the AI diagnosis, the HCA's reported diagnosis, or the GP Care sonographer's diagnosis, and they will not have access to patient information. The uploaded scans will be organised under the participant's unique UID.

Each remote clinician will rate the quality of each app-guided scan using the American College of Emergency Physicians (ACEP) image quality scale, which ranges from one to five. A rating of three or higher will indicate that the image data meets or exceeds the minimal criteria for a diagnosis ("diagnostic quality scan").

ACEP Score	Grading Scale Definition
1	No recognisable structure, no objective data can be gathered
2	Minimally recognisable structures but insufficient for diagnosis
3	Minimal criteria met for diagnosis, recognisable structures but with some technical or other flaws
4	Minimal criteria met for diagnosis, all structures imaged well and diagnosed easily
5	Minimal criteria met for diagnosis, all structured imaged with excellent image quality and diagnosis completely supported

Table 1, ACEP Score

Preceding investigations carried out in secondary care environments, including the ADVENT study led by Dr Nicola Curry in Oxford (though its outcomes are not yet publicly accessible as per IRAS 285274), unveiled that around ten percent of the acquired US images failed to meet the criterion of an ACEP score of three or above. Consequently, scans that do not offer the requisite quality for remote diagnosis will be categorised as inconclusive data. Inconclusive scans will not be included in the primary analysis but will be clearly indicated and reported separately, as illustrated in flowchart 2.

4.3 Remote diagnosis

Following this, each remote clinician will individually provide their diagnosis for scans that have been rated with an ACEP image quality score of three or higher (indicating one or more relevant veins are incompressible) or a diagnosis of no DVT (indicating all relevant veins are compressible).

The diagnoses offered through majority consensus from all five qualified remote clinicians will then be retrospectively compared with the participant's standard compression USS (considered the reference scan, point 3.5). Agreement between the external clinician's diagnosis and the reference diagnosis will be assessed using appropriate statistical methods, such as Cohen's kappa.
Scans that do not meet the minimum criteria for remote diagnosis will undergo analysis and their outcomes will be reported. In clinical settings, inconclusive scans will necessitate a standard DVT diagnostic scan.

5 Study data

5.1 Study codes

In this study, each participant will be assigned a UID. This UID will consist of a three-digit number ranging from 001 to XXX, preceded by a letter identifying the site of the DVT clinic. Specifically, "A" represents Concord Medical Centre, "B" stands for Crest Family Practice, "C" is for East Trees Health Centre, and "D" designates the clinic at Weston-Super-Mare.

The research team will record this participant UID on the consent form, the AI app (here only the last three digits of the UID will be used), and the PSS. Furthermore, for a subset of patients involved in qualitative data collection, the UID will also be documented on relevant forms.

In situations where patients are contacted by the patient support team, invited to their scan appointment, and offered participation in the study but choose not to take part, the letter "R" will be added to the UID for example, RA152. Those participants who altered their decision to join the study upon arriving at the GP Care DVT Clinic, their UID will be modified with the letter "A," for instance, ARA152.
If patients were not invited to participate in the study by the HCA, this will be denoted by the following codes: 'B' = Clinic too busy, 'T' = Technical issues with AutoDVT or 'O' = Other reasons (e.g., TA XXX). The CI will regularly communicate with the DVT clinics to record any of those occurrences that may have disrupted the adherence to the study protocol. The CI will provide necessary support, when possible, to ensure the study runs smoothly. This approach allows for systematic recording of the patient UID who declined participation, patients who agreed to participate but could not undergo the study, and participants who were recruited but did not receive an index scan due to the aforementioned difficulties will be documented separately and analysed.

5.2 Data sharing

Patients' data, entered onto the app before the exam is started, is stored under the last three digits of their UID number. No information about patient history or patient demographics is communicated with ThinkSono Ltd.

Participant data, including US images of the blood vessels, the patient's BMI, and the affected leg (left or right), will be pseudo-anonymised and transmitted from the app to the cloud dashboard for remote radiology review, following the protocol. This data will be encrypted.

Cloud dashboard

The backend and database are kept on a Linux virtual machine in AWS. It's well-protected, with only http/https ports accessible, and external access to the database is limited.

Data from the US is securely stored in an encrypted S3 bucket in the EU Ireland region. This guarantees encryption while it's stored and when it's sent. US data is kept anonymous by default. Any identifiable information, like patient UIDs, is stored in the database, which isn't accessible from outside. Also, we have a HIPAA-compliant agreement with AWS. The website uses TLS encryption, ensuring all interactions are secure, whether you're viewing or uploading data.

AI app

The AI app is designed as an android app. The data within the app is restricted and can only be accessed by the app itself. Without the proper user credentials for both the phone and the app, access to the app and stored US data is not possible. The app's data cannot be extracted when the phone is connected to a personal computer (PC).

The app establishes a direct and encrypted Wi-Fi connection with the Clarius US hardware. This connection facilitates the streaming of pseudo-anonymised US images to the app. US videos are stored in an anonymised format, with identifiable metadata solely available within the app's database.
For transmitting stored US data to the cloud dashboard, the app requires an internet connection. This transmission is facilitated through TLS-encrypted S3 and backend endpoints.

5.3 Withdrawal from the study

Participants have the freedom to withdraw their consent for the study at any time, and this decision will not impact their care. There is no obligation for participants to provide a reason for their withdrawal. In the event of withdrawal, participants can choose to either withdraw completely from the study or allow data collection to continue without their active participation. Any data collected up to the point of withdrawal will be retained and used for the purposes of the study.

5.4 Quantitative data collection

Data collection will occur at five different stages.

Prior to Scan:

1. All patients referred to GP Care DVT services will be consecutively invited to participate in the study by the patient support team and will be allocated an UID at the time of invitation.
2. Patients will receive the consent form, participation sheet, and a link to the video clip either by message or email based on their preference. The video will explain the importance of research in general. Hard copies of the documents are available at the clinic, where participants will provide consent during their appointment. The consent process covers various aspects, including access to medical notes and sharing US images with ThinkSono for device optimisation.

During the Scan:

3. Data collection will involve the HCA entering patient information into the app before starting the scan. This includes the HCA operator ID, the last three digits of the participant UID, the affected limb site (right or left), and the participant's height and weight to calculate the BMI and optimise scanner settings.

After the Scan:

4. After completing both scans, the PSS will be given to the participant by the HCA. The HCA ensures that the correct UID is recorded on the survey. Participants are asked to return the completed survey at the surgery reception along with the GP Care satisfaction survey. The survey will collect patient details like the UID and their name. Participants can provide their email address to receive a £10 voucher as compensation for their time. They can express interest in participating in the second part of the study, involving an interview. The survey assesses patient satisfaction with the AI-guided scan.

5. The GP care sonographer will complete the sonographer data collection sheet which includes data collection such as the duration of the standard diagnostic DVT scan, repeat scans after a FP event, finding of a DVT or SVT in the proximal or distal leg and the opportunity to document inconclusive compression regions.

5.5 Study closure

The study will reach its closure point when the following conditions are met: the targeted number of 500 participants has been attained, the study data have undergone thorough cleaning, the database has been locked, and appropriate arrangements for archiving have been established. The Research Ethics Committee (REC) will be duly notified of the study's closure.

5.6 Sample size

The sample size calculation is derived from the data collected at the GP Care DVT Clinics from January to June 2023. During this period, 1868 patients underwent DVT scans. 271 patients were positive for DVT, constituting 15% of the total scanned population.

The goal of this study is to enrol approximately 500 participants, as determined by a calculated sample size of 487 participants (refer to table two below). This sample size aims to achieve a 95% CI with a margin of error of +/- 5% around an assumed sensitivity of 95% (i.e., a 95% CI ranging from 90% to 100%). This assumption is based on the performance of 2-point compression US in previous studies (Mousavi-Roknabadi et al., 2019 and Hannula et al., 2021) and an assumed DVT prevalence of 15%.

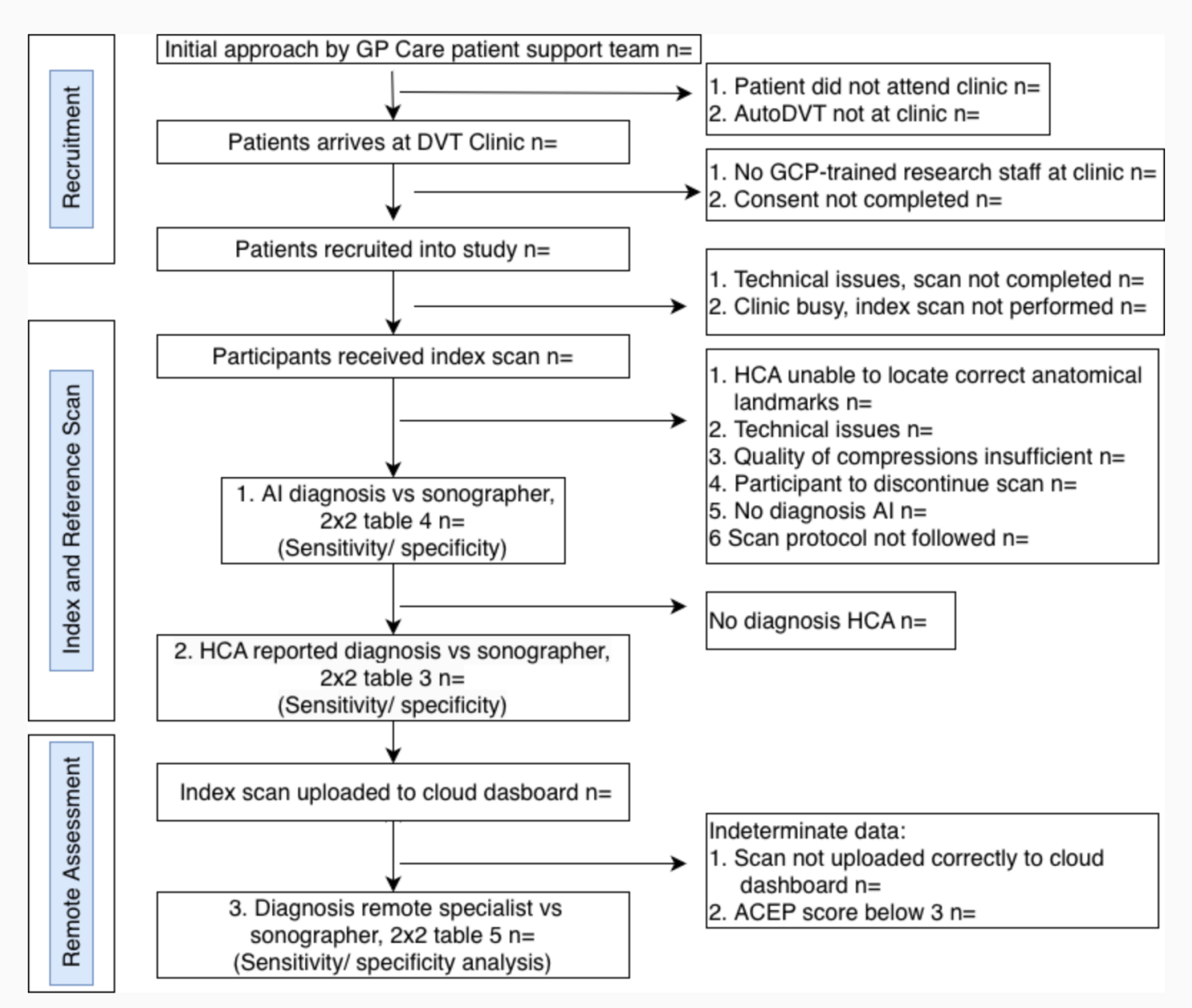
Table below further demonstrates that with 500 participants, a maximum precision of +/- 5% (or even better) can be attained across various sensitivities and DVT prevalence rates.

		Assumed prevalence			
		10%	15%	20%	25%
Assumed true sensitivity	92%	-	-	-	452
	95%	-	487	365	292
	97%	447	298	224	179
	98%	301	201	151	120

Table 2, Sample size calculation based on assumed prevalence of DVT

6 Analysis

A flowchart illustrating missing and inconclusive data, presented below, will provide an overview of the number of participants screened, exclusions (along with explanations), and relevant details.



Flowchart 2: Missing and indeterminate data

6.1 Diagnostic accuracy analysis

The data analysis plan will involve the following steps:
(Statistical analysis of the sensitivity, specificity, PPV, negative predictive value (NPV))

1. To estimate the sensitivity of HCA reported app guided DVT diagnosis against the reference standard of sonographer scan.

The GP Care HCA's reported diagnosis from the app guided scan (index scan) will be compared to the diagnosis from the standard DVT diagnostic scan conducted by the sonographer. The sonographer will not have knowledge of the index scan's outcome, until after recording he reference scan result.

However, in the event of index scan positive with reference scan negative (a FP result) occurs, the HCA will promptly notify the sonographer about the index scan's diagnosis after completion of the reference scan. Subsequently, the sonographer will perform the reference scan again to verify or disprove the initial diagnosis from the reference scan.

If the HCA is unable to determine if the vein is 'compressible' or 'not compressible,' the number of attempts will be recorded. However, since no diagnosis is provided, the data for this compression point will be considered as missing data. This scan will not be included in the 2x2 table three (as shown below) but will be separately documented and analysed, as indicated in flowchart two.

1. To estimate the accuracy of HCA reported AI-guided DVT diagnosis against the reference standard of sonographer scan

Contingency	Reference (sonographer) Positive*	Reference (sonographer) Negative**
Index (HCA reported) Positive	TP	FP
Index (HCA reported) Negative	FN	TN

Table 3, 2x2 table, HCA reported diagnosis as index test and sonographer diagnosis as reference test.

(*If a repeat scan is conducted because of a FP, the outcome of this scan is considered the reference standard, **If a distal DVT is identified during the scan but no proximal DVT is found, it will be considered a negative reference test. See section 3.5
If the HCA is unable to determine whether the vein was compressible or not, even after attempting multiple times, the scan without a diagnosis will be documented as inconclusive data, as illustrated in the flowchart above. This inconclusive data will be analysed separately. This will also apply for table 4 below.)

2. To estimate the accuracy of AI provided DVT diagnosis against the reference standard test.

Contingency	Reference (sonographer) Positive	Reference (sonographer) Negative
Index (AI) Positive	TP	FP
Index (AI) Negative	FN	TN

Table 4, 2x2 table, AI outcome as index test and sonographer outcome as reference test.

Previous pilot studies involving the AutoDVT focused on the current intended use of the device:
App-guidance to enable non-specialist to perform a 2-region DVT scan of the proximal leg, collecting high-quality ultrasound images for remote specialist diagnosis. Nevertheless, the app not only assists the operator in locating the correct anatomical landmarks for compression but also provides feedback whether the vein had been fully compressible or not. In this context, the app diagnosis will be observed as the index test, while the sonographer's diagnosis will be considered the reference test.

3. The third 2x2 table will focus on the intended use of the device, as discussed above.
To estimate the accuracy of remote specialist diagnosis using app guided acquired US images with an ACEP score of ≥ 3 compared to the reference standard of the sonographer scan.

Contingency	Reference (sonographer) Positive	Reference (sonographer) Negative
Index (Remote) Positive & undetermined *	TP	FP
Index (Remote) Negative	FN	TN

Table 5, 2x2 table, diagnosis of remote specialist as index test and sonographer outcome as reference test.

(*An indeterminant compression will require in the clinical world a scan by a sonographer, hence will be classified as a positive DVT scan)

Index scan with ACEP score < 3	Calculating a secondary sensitivity for scans with an ACEP score of less than 3 as positive for DVT. It implies that such scans would necessitate a standard US scan in a clinical context.

Table 6, Remote diagnosis of images with ACEP of 3 and above

For each US clip rated as ACEP score ≥ three, a diagnosis will be given by the remote specialist. Prior research indicates that approximately ten percent of the obtained US images receive an ACEP score <

three (Kainz et al., 2021) and will therefore be omitted from this table, as depicted in flowchart two above. The remote specialist has the options to select:

- Compressible: The veins compress fully and the vein walls fully touch.
- Not compressible: A proper compression has been carried out though the vein does not compress the vein walls don't touch.
- Other: An indeterminant compression will require in the clinical world a scan by a sonographer, hence will be classified as a positive DVT scan in the 2x2 table five.

All patients whose imaging data was deemed adequate for interpretation (ACEP score ≥ three) were included in the sensitivity and specificity analysis in table five. The number of scans that were assessed as insufficient quality subsequently will be analysed but not incorporated for the sensitivity calculations for the qualified reviewers.

It's essential to note that in a clinical context, findings of other pathologies like a Baker Cyst would typically necessitate a rescan. However, for the specific purpose of constructing the 2x2 table, our focus will solely be on assessing the compressibility of the veins. These scans will be included as either compressible or not compressible in the analysis.

The diagnostic accuracy of the remote specialist will then be compared between patients with BMI > 30 and those ≤ 30 to assess any variations in diagnostic performance.

The proportion of HCA acquired images that are of inadequate quality for remote diagnosis, hence with a ACEP below three, will be reported (see section 6.2)

Distal DVTs found during the reference scan, without any extra proximal DVT, will be considered as not having a DVT. Both the index and reference scans focus on the upper leg. However, we will report the distal DVTs separately. This data will be collected on the sonographer data collection sheet. Although, the primary analysis will specifically look at the upper leg scan protocol to make comparisons.

Missing, inconclusive data and data excluded for analysis in the 2x2 table will be carefully assessed. Sensitivity analyses will be conducted to evaluate the potential impact this data on the precision and dependability estimates. The quantity of data caused by usage or technical errors, such as missing data or data corruption will be analysed.

6.2 Image quality assessment and comparison with diagnosis from external clinician

App guided US is used to guide and train HCP in collecting and storing US images for DVT. Several clinical investigations have demonstrated the effectiveness and safety of app guided USS in acquiring qualitative images, allowing non-specialists in DVT US to follow a POCUS DVT scanning protocol and share data with remote specialists for decision making (Kainz et al., 2021).

Scans that are uploaded will be evaluated for their image quality using an ACEP scale ranging from one to five. A scan with an ACEP image quality score of three or above by three or more remote specialists will be considered a 'diagnostic quality scan'. The proportion of app guided scans meeting these criteria will be presented with a 95% confidence interval, along with the median and interquartile range of ACEP scores. USS data collected at the four GP Care DVT Clinics will be uploaded to the cloud dashboard by the CI.

USS that deviates from the study protocol or encountered technical issues leading to inconclusive data will be documented and flagged as invalid, similar to how they would necessitate review by a sonographer in a clinical setting. Scans earmarked for analysis will undergo evaluation by five remote specialists using the ACEP image quality scale, as depicted in table one. USS scans with an ACEP score of three or higher will be utilised for sensitivity and specificity analysis, as indicated in table five. Scans with an ACEP rating below three will be documented and examined, mirroring the approach in clinical settings that would warrant specialist review.

Prior pilot studies have demonstrated that 89% (ISRCTN 55099449, ISRCTN 24147434) and pivotal studies 91% (ISRTCN 24293748) of US data collected by non-specialists achieved an ACEP score of three or above, signifying sufficient quality for remote diagnosis. Subsequently, the AutoDVT has undergone enhancements, and it is anticipated that a greater portion of USS will achieve an ACEP score of three or higher.

6.3 Patient satisfaction analysis

Analysing the PSS, which is based on the FFT and includes the two FFT questions and the additional two questions to provide valuable insights into patient experiences (NHS, 2020).

Data Collection:
This phase involves collecting all survey responses and organising the data for further analysis.

Data Preparation:
During this step, the data is cleaned by checking for any missing or incomplete responses.
Responses for questions with a rating scale are converted into numerical values, with 'Very good' assigned a score of one, 'Good' a score of two, 'Neither good nor poor' a score of three, 'Poor' a score of four, 'Very poor' a score of five, and 'Don't know' as a score of six. This processed data is then entered into an Excel data collection sheet.

Descriptive Analysis:
In this phase, summary statistics are calculated for each question. This includes mean, median, mode, and standard deviation for the rating scale questions, such as assessing caring attitude and being informed about the purpose.
For the open-ended question ('Please tell us about anything that we could have done better'), a qualitative analysis is conducted to identify recurring themes and patterns within the responses.

Frequency Analysis:
Tables and charts are created to visually represent the distribution of responses for each question.

Cross-tabulation
Relationships between questions are analysed. For instance, responses to 'Overall experience' might be cross tabulated with 'Caring attitude' and 'Informed about the purpose' to explore potential correlations.

Reporting
Findings are summarised, emphasising key insights, trends, and any actionable recommendations.
Charts, graphs, and qualitative examples are used to support the analysis.

Action Planning:
Based on the analysis, areas for improvement are identified, and an action plan is developed to address issues highlighted by the survey. For example, addressing the literature gap concerning PPS regarding AI and new diagnostic devices.

7 Qualitative aims and outcomes

7.1 Aim

The qualitative component of the study seeks to understand the viewpoints and firsthand experiences of both patients and HCAs concerning the utilisation of app guided US. It aims to identify any potential concerns, obstacles, and levels of confidence associated with the use of this diagnostic tool.

Objective interview with patients:

- Explore patient reservations, obstacles, and confidence in relation to their experience of AI-guided point- of-care US undertaking as diagnostic scan for DVT

Objective interview with HCAs:

- Explore the confidence of the HCAs in the index scan
- Explore the experience of HCAs in delivering the scan

7.2 Study design

The qualitative part of the research will utilise a semi-structured interview format, allowing for open-ended exploration of participants' perspectives.

7.3 Sample method and recruitment

The sample size for the qualitative study will be determined through data saturation, guided by insights from previous research studies. The objective is to enrol 20 patients across the four GP Care DVT clinics and diverse representation in terms of gender, age, and BNSSG residence. Patients will receive a £25 voucher as compensation for their time.

As per Clarke and Braun (2013), qualitative studies typically necessitate a minimum sample size of 12 participants for data saturation (Braun and Clarke). Consequently, a participant cohort of 20 individuals was deemed suitable for the qualitative analysis in this study. However, recruitment will continue until we reach data saturation or as close to saturation as is practically feasible given time and financial constraints.

Patient recruitment for the qualitative segment of the study will commence subsequent to the patient receiving the index and reference scans. During the initial phase of the research project, patients can express their interest in participating in the qualitative research on the PSS. The aim is to conduct the interviews as soon as possible following the scan and within three weeks. Furthermore, interviews will be carried out with the five GP Care HCAs responsible for operating the AI-guided handheld US probe during the study. HCAs will receive a £45 voucher as compensation for their time. Costs are determined based on the principles of SoECAT ensuring accurate cost allocation during the research cost funding application process.

A diverse group of patients from the BNSSG area, considering factors like age (table 8), gender, and postcode (figure 8 and table 7), and those who expressed their interest in participating in the second phase of the project through the PSS, will receive invitations for interviews. This patient information was gathered during the initial phase of the study.

The interview invitations will come with an electronic consent form and the PIS attached. Nevertheless, for participants who prefer it, the CI will send physical copies of the consent form and PIS by mail. For scheduled in-person interviews, hard copies of these documents will also be provided at the interview. Additionally, the invitation email will provide a brief summary outlining the purpose of the interview.

A recruitment matrix has been established to ensure a diverse patient group is recruited from six locations within BNSSG.

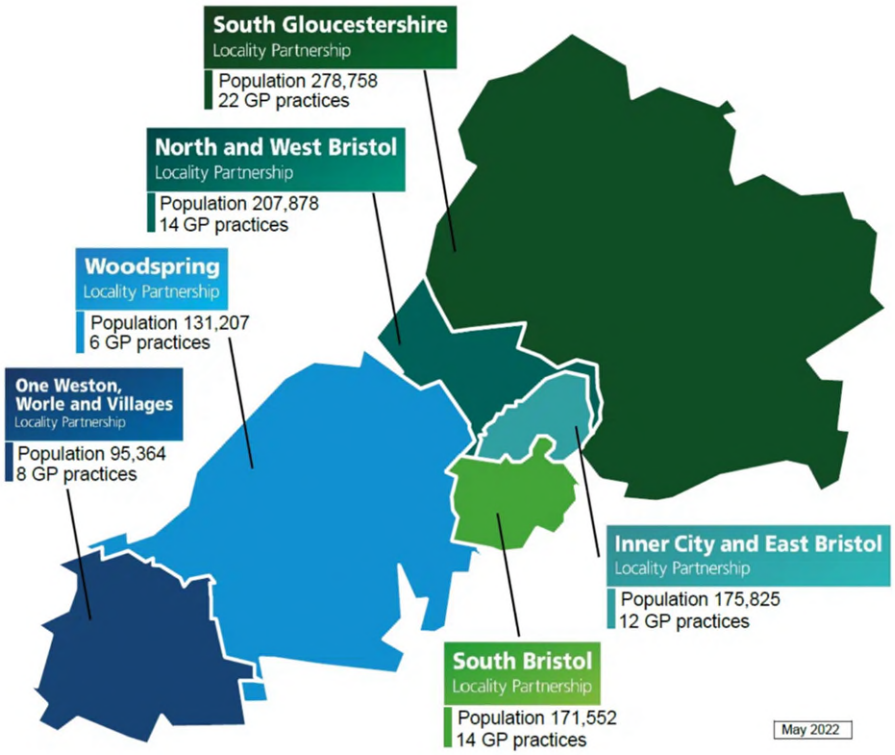


Figure 8, 6 Locality Partnerships in BNSSG ICB (BNSSG ICB, 2022)

Locality Partnership in BNSSG	
South Gloucestershire	1
North and West Bristol	2
Inner City and East Bristol	3
South Bristol	4
Woodspring	5
Westin, Worle and Villages	6

Table 7, 6 Locality Partnerships in BNSSG ICB

This includes both genders (male and female) and spans five age groups, which have been predefined in the quantitative part of the research project.

Participant age	
18-30	1
31-50	2
51-69	3
70-85	4
86-100	5

Table 8, Age groups

The prevalence of DVT increases with age, which means that there will be fewer patients with suspected DVT in the younger age groups one and two, seen in table eight. To ensure that the matrix below reflects this, age groups one and two have been combined.

Location	Age Group 1/2	Age Group 3	Age Group 4	Age Group 5	Total F	Total M	Total
1 Female							
1 Male							
2 Female							
2 Male							
3 Female							
3 Male							
4 Female							
4 Male							
5 Female							
5 Male							
6 Female							
6 Male							
Total F							
Total M							
Total							

Table 9, Recruitment matrix

Recruiting for every combination of location, gender, and age group is not feasible. However, the matrix will serve as a visual aid assuring recruitment from a maximum variety. The recruitment process will be influenced by the prevalence of specific combinations and the successful recruitment of various patient groups. The matrix will be regularly reviewed to ensure that it represents the desired distribution of participants and will enable targeting of particular groups if they are underrepresented.

7.4 Data collection method

Recruitment is planned to run parallel to the DTA intervention at the GP Care DVT clinics, assuring that time between the intervention and the interview is as soon as possible following the scan and within three weeks.

Patient and staff interviews will last approximately 30-45 minutes, scheduled at a convenient time for participants. These interviews will be conducted either face-to-face, phone or through e-interviews, providing flexibility and accommodating participants' preferences for the mode of communication.

The interviews will follow a topic guide, exploring the participants' experiences with the intervention, the confidence levels in the use of the app guided US, and any perceived barriers to app guided DVT diagnostics. Separate topic guides will be used for HCAs and patients. The topic guides can be found in the study materials' appendix.

Interviews will be recorded for qualitative data collection using both secure video or voice recording (telephone interview) via Teams and an encrypted digital audio recorder. This approach provides redundancy, ensuring data collection even if one of the recording methods encounters issues. After each interview, the recordings will be securely transferred and stored on the UoB's servers. All data, including audio recordings and participant contact information, will be kept on these secure servers in compliance with the Data Protection Act and General Data Protection Regulation (GDPR) legislation. Participants

contact information and any identifiable information will only be accessible by the researcher and the supervisory team named on this protocol.

7.5 Data preparation

Two methods for transcribing interview data will be employed:
1. For face-to-face interviews, the interviews will be simultaneously recorded and transcribed on Teams software accessed through the UoB system while the interview takes place and and an encrypted digital audio recorder.
2. For video (e-)-interviews or telephone interviews (which will take place over loudspeaker and recorded on open Teams software) the transcriptions will be produced directly by the Teams or Zoom software within the secure UoB account. All transfer of audio files and transcripts will be in accordance with UoB protocols for data security.

When conducting the interview, it is essential to ensure the best possible audio quality. The interviewee will be asked to help achieve this with an 'E-interview guide' which will be send out with the invite to the e-interview and the consent form.

1. E-interviews:
Checking and correcting transcribed qualitative data over Microsoft Teams or Zoom:

Step 1: Transcription Process
The simultaneous transcription of the interview on Teams/ Zoom software whilst holding e-interview.

Step 2: Corrections and Revisions
Transcribed data will be revised and corrected, by carefully reviewing the transcript against the original video and audio recording to identify any inaccuracies or omissions.
Then, make necessary corrections to ensure the transcribed text accurately represents the intended content while maintaining grammar and clarity.

2. In-person:

Step 1: Transcription Process
During the interview, the Teams software will be active to record and transcribe simultaneously. Additionally, as a precaution, the interview will be recorded on an encrypted digital audio recorder. All data will be stored using the participant's UID generated during the initial study phase, maintaining participant anonymity.

Step 2: Recording and Transcribing
The transcribed data will undergo a thorough review and correction process. The transcript will be carefully compared to the original audio from the digital audio recorder to detect any errors or omissions. Necessary corrections will be applied to ensure the transcript accurately reflects the intended content while adhering to proper grammar and clarity.

3. Telephone interview

Step 1: Transcription Process
Telephone interviews will be conducted using loudspeakers in the designated PODs at Canynge Hall. Similar to face-to-face interviews, the interviews will be recorded and transcribed simultaneously through Teams software. In addition, a secure digital audio recorder will be used to record the interview. All data will be organised under the participant's UID, which was generated during the initial study phase, ensuring participant information remains anonymous.

Step 2: Recording and Transcribing

Transcribed data will undergo careful review and correction. The transcript will be cross-checked with the original audio from the digital audio recorder to identify any inaccuracies or omissions. Necessary revisions will be made to ensure the transcribed text faithfully represents the intended content while maintaining proper grammar and clarity.

PPI has been employed to support the development of qualitative patient-oriented materials and interview topic guides. Additionally, PPI will be involved in piloting both the participant-facing documents and the interview itself. Furthermore, a pilot interviews will be conducted with PPI contributors to facilitate additional adjustments.

7.6 Analysis

To conduct reflexive thematic analysis, a structured flow will be followed: immersing in the data, reading and familiarising with it thoroughly. Next, creating a coding frame, which will be a combination of inductive and deductive, and will serve as the foundation for coding the data.

This coding frame will be applied to a small number of transcripts. During this initial coding phase, the codes will be revised and refined to ensure accuracy. It will be engaged in a collaborative process with colleagues and supervisors to implement the coding frame on an additional transcript. This collaborative approach will play a crucial role in ensuring the interpretation remains consistent and bolsters the overall reliability of the analysis. The coding frame will be worked on outside of until it is complete and stable. Once achieved, the dataset will be imported into NVIVO to support organisation and analysis of data.

The coding frame will be applied to the entire dataset within NVIVO. It will be explored how codes relate to each other, emerging themes will be examined, and it will be considered how these themes connect both to each other and the research questions.

7.7 Data sharing

Upon obtaining participant consent, we will place the anonymised interview transcripts into the University of Bristol Data Repository. These transcripts will be accessible to legitimate researchers. Any requests for access will be evaluated by the University of Bristol's Data Access Committee to determine their validity as genuine research inquiries.

8 Patient and public involvement

PPI is a crucial component of this research protocol on utilising app guided US for diagnosing DVT in primary care. It recognises the value of engaging patients, their caregivers, and the wider public in shaping the research design, methodology, and dissemination of findings. A PPI panel consisting of nine members with diverse ethical and age backgrounds has been assembled to offer support. This PPI panel has convened on three occasions and provided input into study design, patient information materials, topic guides, funding application and lay summary.
In this section, the plans for PPI are outlined, aiming to ensure that the research is patient-centred, ethically sound, and meets the needs and perspectives of those affected by DVT.

The primary objectives of the PPI panel consisting of nine contributors is:

- To define research priorities, ensuring that the study addresses their needs and concerns, e.g. added qualitative part to this project to assess patients' perspective.
- To collaborate to develop the research design, including the use of AI-guided US, and in determining the most appropriate outcome measures.
- To involve PPI in the recruitment and consent processes, ensuring that their experiences and perspectives are considered.

- To comment on and edit patient facing materials for the qualitative study such as, lay summary (protocol), the PIS and topic guides
- To seek input from patients, caregivers, and the public in interpreting study findings, assessing their implications, and identifying potential limitations or areas for improvement.

A PPI advisory group meets regularly throughout the study, providing valuable input on various aspects of the research. The group is involved in reviewing study materials, discussing recruitment strategies, refining data collection methods, and interpreting study findings.

By actively involving PPI in the research protocol, it is aimed to ensure that the study is patient-centered, impactful, and responsive to the needs and perspectives of those affected by DVT. Their involvement will enhance the research quality, validity, and relevance, ultimately contributing to improved healthcare outcomes in primary care settings.

9 Ethical considerations

Prior to the initiation of the study, the protocol, informed consent forms, and any other relevant information to be provided to prospective participants will be submitted to the Health Research Authority (HRA) for approval, which involves ethical review by a REC. Any subsequent amendments to these documents will also be submitted to the HRA and require approval from the same REC.

10 Anticipated timetable (Please see the Gantt chart in Appendix for more details.)

September 23:	Finalise Protocol
Oct -Dec 23:	Finalise IRAS and Ethic Application
Dec 23- Feb 24:	Patient recruitment at GP Care & start qualitative interviews.
March 24:	Captured quantitative data to analysis
April-May 24:	Patient recruitment for qualitative interviews, data coding & capture data on NVIVO
June- Nov 24:	Qualitative data analysis (NVIVO)
Dec 24- March 25:	Finalise qualitative and quantitative data analysis.
July 24 – June 25:	Literature Review
July- Oct 25:	Write-up results for publication and presentation at conferences, PPI meetings for interpretation of results and input for future study design, dissemination of result

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