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Frailty Assessment in Vascular OUtpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.

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TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

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Abstract

Introduction:Frailty has consistently demonstrated associations with poorer healthcare outcomes. Vascular guidelines have recognised the importance of frailty assessment and improved access to frailty-related healthcare services. However, an abundance of frailty tools and a relative lack of prospective trials confirming suitability of routine frailty assessment in clinical practice has delayed the uptake of these guidelines. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study speaks to this evidence gap. The primary aim is to assess feasibility and acceptability of implementing routine frailty assessment in a reproducible outpatient setting. Secondary objectives include comparing prognostic values and inter-user agreement across five frailty assessment tools.

Methods and analysis:This single-centre prospective cohort study of feasibility, is conducted in a rapid-referral vascular surgery clinic, serving a population of 2 million. Capax adults (>18years), attending clinic for any reason are eligible for inclusion. Five frailty assessments are completed at the clinic by patient (CFS and FiND), clinician (CFS, HIS FRAIL and ICE) and researcher (mFI-11). Consistent with feasibility objectives, outcome measures include recruitment rates, frailty assessment completion rates, time-to-complete assessments and interrater variability. Electronic follow-up at 30-days and 1-year will assess home-time and mortality as prognostic indicators. Patients treated surgically/endovascularly will undergo additional 30-day and 1-year post-operative follow-up, outcome measures include: surgical procedure, mortality, complications (according to Clavien-Dindo Classification), length-of-stay, readmission rates, non-home discharge, home-time, higher social care requirements on discharge and amputation-free survival. Prognostic value will be compared by area under ROC curves. Continuous outcome variables will be analysed using Spearman's rank correlation coefficient. Inter-user agreement will be compared by percentage agreement in Cohen's Kappa coefficient.

Ethics and dissemination:Study sponsored by NHS Greater Glasgow & Clyde (R&IUGN23CE014). London–Riverside REC (23/PR/0062) granted ethical approval. Results will be disseminated through publication in peer-reviewed vascular surgery and geriatric medicine themed journals and presentation at similar scientific conferences.

Strengths and limitations of this study

- This study includes all consultant vascular surgeons in a 'hub' vascular surgery site acting as fair representative of stakeholders in the exploration of feasibility and suitability of routine frailty assessment in clinical practice.
- Clinical relevance and research impact is further enhanced through this study incorporating measurements of prognostic value as well as novel direct head-to-head comparison of frailty assessment tools enabling clinicians and policy makers to design evidence-based frailty-centric clinical service adaptations.
- Although the setting is based on a vascular 'hub' site serving three NHS healthboards, this is a single-centre study which excludes patients who lack capacity (e.g., dementia), which may affect the generalisability of results.

Introduction

Background and rationale

Frailty is common in vascular patients with an estimated prevalence three times that of the general population.[1] An association between the clinical syndrome of frailty and adverse surgical outcomes in vascular surgery has been described.[2] For the person living with frailty, adaptations to the traditional surgical approach may be necessary on an individual and wider service-model level to improve healthcare outcomes, ensure equity in healthcare delivery and guide resource allocation. The critical first step is assessment and recognition of frailty in practice, an approach that is advocated by national guidelines.[3]

Despite this, approximately one third of vascular surgeons do not formally assess patients for frailty. The most commonly cited reasons including unfamiliarity with tools and concerns over tool validity.[4] Perhaps the downside to frailty gaining important visibility, in the absence of a gold standard diagnostic tool, is the subsequent accumulation of disparate methods for assessing and diagnosing frailty. A recent review identified 42 separate frailty assessment tools used across 111 vascular surgery related studies, but with limited data on how these tools perform in clinical practice.[1]

To optimise service provision, it is important to identify methods for assessing frailty which lend themselves to practical application in busy clinical services. It is desirable to detect frailty at the earliest opportunity but recognise that this can be challenging to deliver in time pressured acute situations. The available literature does not allow for the identification of a preferred approach to frailty assessment in the vascular surgical context. Limitations of studies to date, include potential biases from retrospective design, poor generalizability to the UK NHS, lack of head to head comparisons of tools and limited assessment of properties such as feasibility and acceptability.

The ideal study design would include a real world, unselected cohort and prospectively compare differing methods for frailty assessment. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study is designed to speak to this gap in the evidence using five frailty assessments that have been carefully selected after reviewing format, relevance, anticipated ease of use and, where possible, are recommended by the Healthcare Improvement Scotland.

Objectives

The primary aim will be to assess the feasibility of implementing routine frailty assessments into an urgent-referral vascular outpatient clinic setting ('Vascular Hot Clinic'). Secondary objectives are to assess and compare the reliability and prognostic value of selected frailty assessments.

Trial design

The FAVOUR study (IRAS ID 322086, NHS R&I reference UGN23CE014/REC reference 23/PR/0062) is a single-centre, non-randomised, observational cohort study of feasibility which will be conducted and reported in line with the guidance presented in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[5]

Methods and analysis

This protocol is reported according to the Standard Protocol Items for Randomized Trials (SPIRIT) statement.[6]

Study setting

This study will take place during a Vascular 'Hot' Clinic at the 'hub' Queen Elizabeth University Hospital (QEUH), Scotland. This is a consultant-led outpatient clinic responsible for delivering urgent vascular care for a population of approximately 1.5 million patients in NHS Greater Glasgow & Clyde and other 'spoke' sites including: NHS Highlands and NHS Forth Valley. Referrals are received from primary care physicians, community podiatrists and secondary care teams. Referrals are triaged within 24 hours of receipt by a consultant vascular surgeon, and if medically appropriate, patients are appointed to the next available appointment (same day to within 1 week). The ethos of the clinic is to provide urgent care for patients with suspected vascular pathology which requires prompt, but not immediate, medical assessment.

Three clinics are held weekly with a capacity of up to ten patients per clinic. The clinics are also served by multidisciplinary team members, including vascular nurse specialists, podiatrists and specialist sonographers who provide a dedicated duplex service.

Population

Participants must provide written informed consent prior to study participation (appendix 1). All referrals to vascular hot clinic are eligible for inclusion, preferentially recruiting new referrals. As frailty is related to age, but does not directly correlate with it, no age cut-off has been defined.[3, 7] As this is primarily a study of feasibility, patients will not be excluded/included based on presenting symptom or diagnosed pathology.

A proxy (relative/friend/carer), if present, will also be invited to participate and assist with frailty assessments of the patients, where suitable. The participation of the proxy is dependent on the patient providing written consent agreeing to their participation, as well as the proxy being eligible to participate, according to the same inclusion/exclusion criteria set out for patients below.

Inclusion criteria:

- Adults (aged 18 years or older)
- Attending Vascular Hot Clinic

Exclusion criteria:

- Lacking capacity to provide informed consent
- Parent clinical team feel frailty assessment not suitable
- Non-English speaker without qualified translator present
- Prisoners

Intervention

Five frailty assessment techniques will be compared: Rockwood 9-item Clinical Frailty Scale (CFS)[8], 11-item Modified Frailty Index (11-mFI)[9], Frailty non-Disabled Questionnaire (FiND)[10], Healthcare Improvement Scotland (HIS) FRAIL assessment tool and Initial Clinical Evaluation (ICE), Table 1. As frailty assessment is recommended, there will be no control, rather differing tools will be compared to one another.

These tools were selected as most likely to be suited to the acute clinic context, after reviewing their content, format, ease of use, training requirements and anticipated time required to complete. This study deliberately selected tools with an emphasis on brevity while incorporating tools that are constructed based on differing theories of frailty and, where possible, are recommended by Scottish healthcare governing body, Healthcare Improvement Scotland. Within vascular surgery, the CFS and mFI-11 are the most commonly used tools; demonstrating international familiarity.[1] By continuing their use, the research impact of this study is enhanced. A primary criterion was that the selected tools should not require additional equipment, external training or have copyright restrictions. This was to ensure ease of implementation at scale, both in the UK NHS and other healthcare settings. Appendix 2-4 display the case report forms (CFFs) with various frailty assessment to be completed by patient/proxy, clinician and researcher.

Participation in this study does not preclude any aspect of concomitant care and/or intervention for patients. To ensure routine care provided by this service remains unaffected, clinicians will perform frailty assessments at the conclusion of each clinic, minimising possible biases in assessment and care provision.

Table 1. Selected frailty assessment tool summaries

CFS	**Definition:** The CFS is an ordinal, hierarchical 9-item person-assessed scale where patients score more highly if more frail. The scale scores run between 1 ('Very Fit') and 9 ('Terminally Ill') with each score having a picture and succinct written definitions This tool is recommended for use in clinical practice by Healthcare Improvement Scotland (HIS). **Personnel:** Vascular surgeon, patient and proxy if present will complete. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, another investigator will score the patient instead. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded. **Training requirement:** While not necessary, there is a short online module available to develop understanding in how the CSF is applied. To ensure internal rigour, clinician's contributing to this study will be requested to complete this training. **Duration**: It is expected this tool will take < 1 minute for clinicians once they are familiar with the tool. For patient's or proxy's completing the tool, it is expected this will take 5 minutes. **Application:** A copy of the CFS chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by one of the research team and asked to score included patients. For patients/proxy's a modified CFS chart will be displayed at the end of their clinic appointment. The patient/proxy will be asked to read each the definition for each score (1-8) before selecting the one they feel most accurately describes them. To reduce the risk of bias, the title and image for each score will be hidden from patient/proxy, leaving only the text description.

	Modifications for study: A CFS score of 9 describes a terminally ill patient, regardless of frailty status. As this is not relevant to this trial, and to reduce the risk of participants becoming upset, this score will not be considered by this trial and therefore not displayed to the participant.
mFI-11	**Definition:** This frailty index assessment is based on the frailty theory of cumulative deficits.[11] Healthcare records are accessed to determine the presence, or absence, of 11 variables across multiple domains (Non-independent function status, cognitive impairment and the following co-morbidities: congestive cardiac failure, myocardial infarction, previous percutaneous coronary intervention/cardiac surgery or angina, hypertension, diabetes mellitus, severe chronic obstructive pulmonary disease/active pneumonia, peripheral arterial disease, stroke/transient ischaemic attack without residual neurological deficit or with deficit). Each variable is scored 1 point when present with the end score divided by the total number of variables (11), giving a score between 0 – 1. The greater the value, the greater the risk of frailty. **Personnel:** A member of the research team will complete this assessment. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded **Training requirement:** No training required for application. **Duration**: This tool has been piloted and found to take < 5 minutes per participant to derive from electronic health record. **Application:** This is a frailty index which is calculated by extracting relevant data through accessing national health service (NHS) electronic records. **Modifications for study:** Nil.
FiND	**Definition:** This is a 5-item self-assessment questionnaire. The first two questions relate to disability while the remaining three relate to frailty. Patients reporting one or more of the three frailty symptoms, in the absence of disability, are defined as frail. The scale's design reflects principles of the Fried frailty phenotype which defines frailty as the presence of three or more of the following energy-negative components: unintentional weight loss ('shrinking'), poor grip strength, exhaustion, slowness and low physical activity levels.[12] This questionnaire is recommended for use by Healthcare Improvement Scotland. The original questionnaire uses metric measurements of distance and weight, an imperial conversion will be added to relevant parts of the questionnaire to assist with patient comprehension. **Personnel:** The patient, and proxy if present, will be completing the questionnaire themselves. **Training requirement:** No training required for application. **Duration**: The questionnaire takes 2 minutes to complete. **Application:** A copy of the FiND will be displayed to the patient/proxy at the end of their clinic. They will be asked to read each of the 5-items closely and select the option that most accurately describes their situation (scoring either 0 or 1 per point). **Modifications for study**: Nil.
HIS FRAIL assessment	**Definition:** This is a five-item frailty screening tool which has been developed by HIS and is currently recommended to be used in all unscheduled older adult admissions. The format is based on the theory of cumulative deficits across multiple domains (function, cognition, social). It's

	selection, in part is due to the novel aspect of this tool not considering co-morbidity as part of the assessment. **Personnel:** The consultant leading the clinic will be asked to complete the HIS FRAIL assessment. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: Completion of the HIS tool takes < two minutes. **Application:** A copy of the HIS FRAIL chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by the chief investigators and asked to score included patients. **Modifications for study:** Nil.
ICE	**Definition:** Also known as the 'end of bed test'. Clinicians will report a subjective and binary assessment of the patient; 'frail' or 'non-frail'. **Personnel:** The consultant leading the clinic will be asked to provide an ICE. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a clinical member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: This assessment takes part as routine practice during a clinical interaction between clinician and patient. No additional time is required. **Application:** The consultants will be approached at the end of the clinic and asked to provide their subjective opinion (ICE) on patient's frailty status to the chief investigator. This assessment will be performed first to minimise bias in clinician responses from completing alternate assessments prior. **Modifications for study:** Nil.

Primary outcome

The primary outcome of this study is to assess the feasibility of implementing routine frailty assessment in a vascular clinic setting. For this, the following data will be collected: number of patients attending hot clinic, number eligible for inclusion, number of eligible patients approached for recruitment, number of patients recruited, time taken to complete assessments, number and nature of assessments with non-completion, reasons for non-completion and if assistance was required to complete the tool. These parameters are clinically relevant as they will allow valid and reproducible calculations of the proportion of eligible patients recruited and time taken to complete assessments which will enable clinicians to consider the feasibility and suitability of implementing routine frailty assessment in a controlled clinical environment, encouraging uptake of current guidance.

Secondary outcomes

The secondary objectives pertain to assessing the prognostic value of selected frailty assessment tools and their value over standard clinical demographic information. All patients will be electronically followed-up at 30-days and 1-year from recruitment, collecting data on home time[13] (defined by the number of full days the patient spends not as an inpatient) and mortality. An additional electronic follow-up will be applied to patients who undergo surgical or endovascular intervention, at 30-day and 1-year post-operatively. For this, the following data will be collected: surgical procedure, mortality, post-operative complications (according to the Clavien-Dindo Classification)[14], length of hospital stay (full days), readmission rates (to any speciality), non-home discharge, home time, discharge with a higher level of social care requirements and amputation free survival for patients with end stage peripheral arterial disease of the lower limbs. As current practice for reporting post-operative outcomes is to report outcomes according to the number of days that has passed since the index intervention, introducing additional 30-day and 1-year follow up periods for patients who undergo interventions (compared to those who do not) allows the collection of clinically relevant data without introducing bias in the mode of data collection. Comparing prognostic validity and interuser variability may be of clinical relevance when considering which frailty assessment tool is best suited for implementation in the described setting.

Baseline assessments

Baseline characteristics will be collected, including patient demographics, social/functional circumstances, polypharmacy and relevant comorbidities to calculate a Charlson comorbidity Index.[15]

Participant timeline

Prospective participants will be identified on the day by reviewing the electronic health care records of patients due to attend a Vascular 'hot' clinic and applying the inclusion and exclusion criteria. Due to the emergent nature of the referrals to the vascular hot clinic, patients (and their proxy, if present) will be approached, recruited and complete frailty assessments on the day of attending their clinic appointment, Figure 1. No ongoing participation is required, follow up will be through accessing electronic health care records.

Sample size

As this is primarily a study of feasibility, a power calculation has not been performed. The vascular hot clinic offers up to 30 appointments weekly across three clinics. Where possible, all eligible patients will be approached for participation with an emphasis on targeting 'new referrals'.

Recruitment

Patient recruitment began in March 2023. Prospective patients will be approached for study participation by the research team upon registering for their clinic appointment. If expressing interest, they will receive a participant information sheet. Patients are required to complete their clinic appointments (where their medical care will remain unaffected by (non-)participation in this

study) prior to participating in the study. The prospective participant will be re-approached at the conclusion of their clinic appointment to confirm willingness to participate and provide written consent. Thereafter, the frailty assessments are completed by the patient. Where a patient attends with a suitable proxy, they will be approached in an identical fashion provided the patient provides written consent for this. Where a patient is eligible for participation but a proxy is ineligible/declines participation, the patient will be recruited without proxy contribution. Where the patient is not eligible for participation, the proxy will not be invited to participate on their behalf. Staggering the consent process by approaching the patient either side of their clinic appointment maximises the time for the patient to consider participating. It is recognised that ideally patients should have a period of at least 24 hours with a patient information sheet prior to expressing a wish to participate in a study however, due to the emergent nature of the clinic and the presenting pathology, this will not be possible. Clinician and research team complete frailty assessments of recruited patients at the end of the clinic to minimising clinic disruption.

Data collection

Data will be collected in person and through review of electronic health care records. On the day of recruitment, frailty assessments scores will be performed in the clinic and collected by patient/proxy, clinician and researcher on relevant paper based CRFs (appendix 2-4). On the same day, the research team will review electronic health care records of recruited patients and extract data for baseline assessments to an electronic data extraction template. All electronic follow up will be extracted to the same electronic data extraction template.

Data management

Data management, processing and handling will be conducted in line with General Data Protection Regulation principles (EU 2016/679). The research team will allocate pseudonymised participant identification numbers then remove and securely destroy personal identifiable information before transcribing data from the paper based CRFs to an electronic data extraction template for storage. Transcribed data will undergo quality checking by a second member of the research team. Data for baseline demographics and electronic follow up will be extracted and stored on Excel Version 2304. SW will be primarily responsible for storing study dataset with sharing through secure means with authors for the purpose of analysis, write-up only. Data will not be shared with third parties.

Statistical methods

Baseline demographics and feasibility parameters will be described using descriptive statistics, including, percentages, ranges, means and standard deviations or medians and interquartile ranges. The prognostic value of frailty assessment tools on binary outcome variables will be displayed through calculating receiver operating characteristic (ROC) curves. Frailty tool comparisons will be performed by comparing the area under the ROC curve. Continuous outcome variables will be analysed using Spearman's rank correlation coefficient. Levels of inter-user agreement between patient and clinician assessments will be calculated with a percentage agreement and Cohen's Kappa coefficient. Subgroup analysis will be performed to compare outcomes for patients undergoing surgical treatment, endovascular treatment and those who do not undergo intervention. Patients lost to follow up, or with incomplete data, will be excluded.

Data monitoring

This observational cohort study will not be subject to a data monitoring or trial management committee. The study may be subject to study monitoring visits and subsequent monitoring reports which will be conducted and reviewed in accordance with a study-specific monitoring plan devised by the study sponsor. The sponsor audits a randomly selected 10% of studies conducted under the Research Governance Framework per annum, as well as those identified using a risk assessment tool as specifically requiring assessment.

Harm

There are no adverse events anticipated to occur secondary to the intervention which falls in line with national guidelines. For this reason, no ancillary and post-trial care has been designed.

Patient and public involvement

A group of five non-medically trained adult volunteers (aged 25 – 65 years) contributed toward the study design through piloting both questionnaires (CFS and FiND) and all took less than 5 minutes to complete both questionnaires, without requiring assistance. There was no further involvement in the development of this study by patients or the public. Patients will not be contacted directly with the results of this study however contact details for the PI have been supplied to participants so that they can request information on study progress/results as they become available.

Ethics and dissemination

Research ethics approval

This study is sponsored by NHS Greater Glasgow & Clyde (Research & Innovation reference UGN23CE014) and has received a favourable opinion by the London – Riverside Research and Ethics Committee (23/PR/0062). This study will be performed according to the Research Governance Framework for Health and Community Care (Second edition, 2006) and WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI Ethical Principles for Medical Research Involving Human Subjects 1964 (as amended).

Amendments

Any amendments to the protocol will be submitted to the IRAS Amendment Portal to the responsible ethics committee and/or NHS GG&C Research & Innovation for review. Changes will only be implemented following the approval of proposed amendments by the original reviewing Research and Ethics Committee and Greater Glasgow & Clyde Health Board Research and Innovation office. All protocol amendments will be appropriately stored, cited and explained in future manuscripts.

Consent

The principal investigatory (PI) (SW) is responsible for obtaining informed written consent from participants. For this, participant information sheets (PIS) will be provided to all prospective participants as well as conducting an informed discussion detailing study design, confidentiality and rights to withdraw. The contact details for the PI are supplied in the PIS which participants will be pointed to and they will be encouraged to make contact with any questions, concerns or if wishing to withdraw. A copy of the consent form will also be provided for participants to keep.

Confidentiality

Participant confidentiality will be upheld through participant pseudonymisation during data collection. To endorse data minimisation, only data relevant for the described outcome measures will be collected and stored. Consent forms and pseudonymised paper based CRFs and will be stored separately in locked filing cabinets, accessible only to the research personnel. Electronic data will be extracted and stored on Excel Version 2304 with personal and research generated data stored on separate databases on different servers. Research data storage will comply with the University of Glasgow's data retention policy.

Access to data

Only members of the core research team will have access to the final dataset with the exception of review by sponsors to ensure proper study conduct. Data will not be shared with third parties for analysis or write-up.

Dissemination

Study results will be disseminated through publication in peer-reviewed journals and presentation to relevant scientific conferences, targeting those with a focus on geriatric medicine and vascular surgery, in particular the Vascular Societies' Annual Scientific Meeting to enhance visibility of the results and assist with knowledge translation.

Discussion

Frailty-centric adaptations to established clinical service models are crucial as the anticipated demographic changes associated with an ageing population means it is likely frailty, with its inherent clinical and financial implications, will become increasingly commonplace.[2] An abundance of frailty assessment tools have confirmed the prognostic value of frailty, hence guidelines advocating the importance of its recognition in clinical practice.[3] However, a relative lack of evidence in measurements of feasibility and suitability of frailty assessment in clinical practice, or head to head comparisons of tools, has contributed toward a delay in uptake of guidelines.[4] For this reason, the prospective assessment of frailty in a reproducible and controlled vascular outpatient department (OPD) environment has been identified as a key area of research interest, which the study presented in this protocol targets.[2, 4]

From a previous systematic review we identify only four relevant studies prospectively assessing frailty in vascular surgery OPD.[1] The first compared the correlation between clinician-assessed CFS scores and patient reported outcome measures of frailty (including FiND and patient-reported outcome measurement information systems v1.2 and v2.0) and its effect on 1-year mortality.[16]

Another examined the effect of frailty as assessed by the Groningen Frailty Indicator on postoperative delirium.[17] One study used the Fried frailty index to compare the effect of frailty status on gait parameters in patients with peripheral arterial disease compared to control[18], while another examined the association of grip strength as a marker of frailty with measures of sarcopenia and co-morbidity.[19] However, the research impact of these data are limited by a paucity in feasibility measurements and direct comparison between selected tools.

The study presented in this protocol builds on current evidence through including and comparing a greater number of commonly used frailty assessment tools that have been specifically selected for their format (assessing frailty according to different theories of frailty), relevance (based on clinician familiarity and compliance with guidance from local healthcare governance) and anticipated rapid time to complete, making them suitable for application in busy OPDs. By incorporating measurements of prognostic value, it is anticipated data generated by this study will bear direct clinical relevance and will contribute toward the generation of evidence based recommendations for an optimum standardised, and reproducible approach to diagnosing frailty in an outpatient setting.

The primary aim of this study is novel within vascular surgery. The major strength in this study is the prospective and longitudinal design. As surgeons increasingly aim to identify patients who would sooner benefit from a conservative approach, the short- and long-term follow-up for all patients managed operatively or not, stratified by frailty status, is of clinical relevance. Limitations to this study are acknowledged, including the single-centre design and the exclusion of patients who lack capacity (e.g., dementia) which may impact generalisability of results.

Study status

Participant recruitment concluded in July, data collection is ongoing.

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Author contributions

TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

Funding statement

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Competing interests statement

Authors declare no conflict of interest or further financial disclosures.

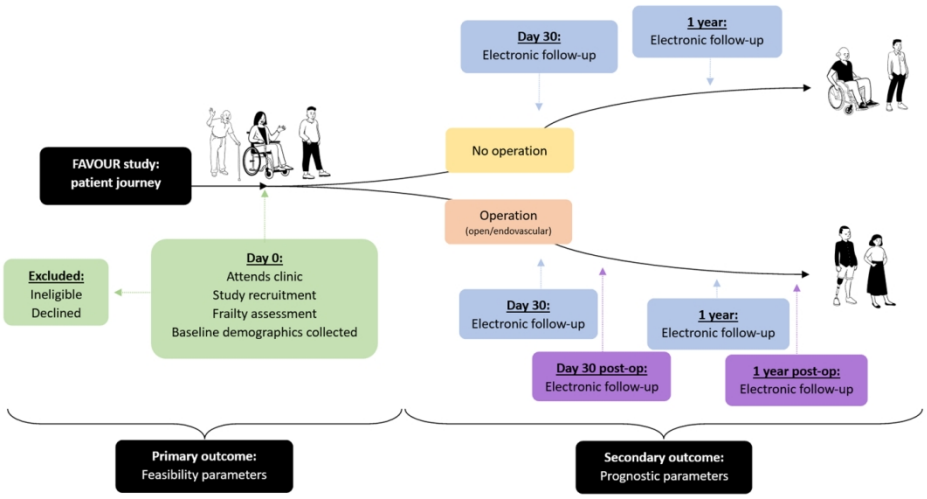

Figure 1. Timeline summarising patient timeline and study methodology

Figure 1 - Summary of patient timeline and study methodology

1044x580mm (38 x 38 DPI)

Appendix 1 – Participant consent form

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

NHS Greater Glasgow and Clyde

Participant Identification Number for this trial: ______________________

Title of Project: **Frailty Assessment in Vascular OUtpatients Review (FAVOUR Trial) – comparing feasibility and prognostic value of commonly used assessments.**

Name of Researcher(s): Miss Silje Welsh

CONSENT FORM (Patient)

Please initial box

1. **I confirm that I have read and understood the Participant Information Sheet (patient) version 1.3 dated 13/02/2023.** ☐
2. **I have had the opportunity to think about the information and ask questions and understand the answers I have been given.** ☐
3. **I understand that my participation is voluntary and that I am free to withdraw at any time during data collection, without giving any reason, without my legal rights being affected. Data collection is expected to conclude 13 months after my recruitment to this study.** ☐
4. **I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.** ☐
5. **I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.** ☐
6. **I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project only and securely destroyed within 3 months of the end of this study.** ☐
7. **I understand that if I withdraw from the study, I will be asked to clarify how I would like the data collected from me up to that point to be handled. There will be the option to retain it for the remainder of the study, or for it to be securely destroyed.** ☐
8. **If relevant, I agree to a proxy (friend/relative/care-giver) contributing towards my participation in this study. Their participation will require them to complete a separate consent form. I also understand that a proxy's decision to participate, or not, will in no way affect my participation in this study.** ☐
9. **I agree that the study team can access my electronic health record for the purposes of the study.** ☐
10. **I understand that electronic follow-up will occur at 30-days and 1-year after my recruitment to this study. Further, I understand that if I undergo surgical treatment, an additional follow-up will occur at 30-days and 1-year after the first treatment/surgery.** ☐

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11. I agree to the dissemination of study results through publication in scientific journals and presentation at relevant conferences. For the purposes of dissemination, I understand that my data will be anonymised. ☐

12. I understand that the results from this study will not be communicated directly to me. However, I have received the contact details for lead researcher (in the Participant Information Sheet), whom I can contact should I want to enquire about progress of the study/study results. ☐

13. I agree to take part in the study. ☐

Name of participant	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher; 1 copy for case notes)

To be completed if participant wishes to withdraw, initial relevant boxes:

14. I confirm that the patient expresses a wish to withdraw from the study. ☐

15. On withdrawal, the patient wishes the following regarding their personal and research data:

(a) All data collected up until the point of withdrawal is to be deleted and not used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

OR

(b) All data collected up until the point of withdrawal can be kept by the researchers and used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

Signed by Principal Investigator on behalf of the patient

Principle Investigator	Date	Signature

Appendix 2 – Case report Form (Patient)

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____

Study participant number: _____

Patient ☐

Sticker/CHI NO:

(Please tear off before transfer)

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Please take time and read through each description before selecting the option which most accurately describes you. The responses to this questionnaire will in no way impact the medical care you have received today or may receive in the future.

	CFS – Questions about activity and function. Which one of the following is most like you:	**Select one option**
1	People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	These people often have **more evident slowing**, and need help in **high order activities** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
X	**Unsure/unable to answer**	

TO BE COMPLETED BY RESEARCH TEAM

Time taken to complete _____ **seconds**

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

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Version 1.1

Date 16/12/2022

PLEASE TURN OVER

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____

Study participant number: _____

Patient ☐

Sticker/CHI NO:

(Please tear off before posting)

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

FiND – Questions about activity and function		
Questions	**Answers**	**Select option**
A. Have you any difficulties walking 400 metres (¼ mile)?	No or some difficulties	
	A lot of difficulties or unable	
B. Have you any difficulties at climbing up a flight of stairs?	No or some difficulties	
	A lot of difficulties or unable	
C. During the last year, have you involuntarily lost more than 4.5 kg (10 lbs)?	No	
	Yes	
D. How often in the last week did you feel that everything you did was an effort or that you could not get going?	Twice or less	
	Three or more	
E. Which is your level of physical activity?	At least 2 – 4 hours per week	
	None or mainly sedentary	

TO BE COMPLETED BY RESEARCH TEAM

A+B ≥ 1: Y☐ N☐

C+D+E ≥ 1: Y☐ N☐

A+B+C+D+E = 0: Y☐ N☐

Time taken to complete _____ seconds

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

Version 1.1
Date 16/12/2022

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Appendix 3 – Case report form (Clinician)

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator □

Surgeon □

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q1. Initial Clinical Evaluation	YES	NO
Is this patient frail?		

Time taken: _____ seconds

Q2. Clinical Frailty Scale (Please select the most appropriate description)		Tick
1	**Very fit** - People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	**Well** - People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	**Managing well** - People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	**Vulnerable** - While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	**Mildly frail** - These people often have **more evident slowing**, and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	**Moderately frail** - People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Severely frail - Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	**Very severely frail** - Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
9	**Terminally ill** Approaching end of life. This applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail**.	
X	**X Unable to score**	

Time taken: _____ seconds

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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator □

Surgeon □

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q3. HIS FRAIL Assessment Tool		YES	NO	UNSURE
F	Functional impairment (new or worsening) e.g. difficulty with self-care			
R	Resident in a care-home?			
A	Altered mental state such as confusion or dementia (use the 4AT)			
I	Immobility/Instability. New decline in mobility, difficulty mobilising without help or fall leading up to admission			
L	Living at home with daily support (homecare; one or more visits per day)			

Time taken: _____ seconds

THIS SECTION IS TO BE COMPLETED BY THE RESEARCHER

For Q1. ICE
If non-completion, why?
- Time restriction □
- Patient not suitable □
- Forgot □
- Other □

Please specify:

_____

For Q2. Clinical Frailty Scale
If non-completion, why?
- Time restriction □
- Patient not suitable □
- Forgot □
- Other □

Please specify:

_____

For Q3. HIS FRAIL Assessment
If non-completion, why?
- Time restriction □
- Patient not suitable □
- Forgot □
- Other □

Please specify:

_____

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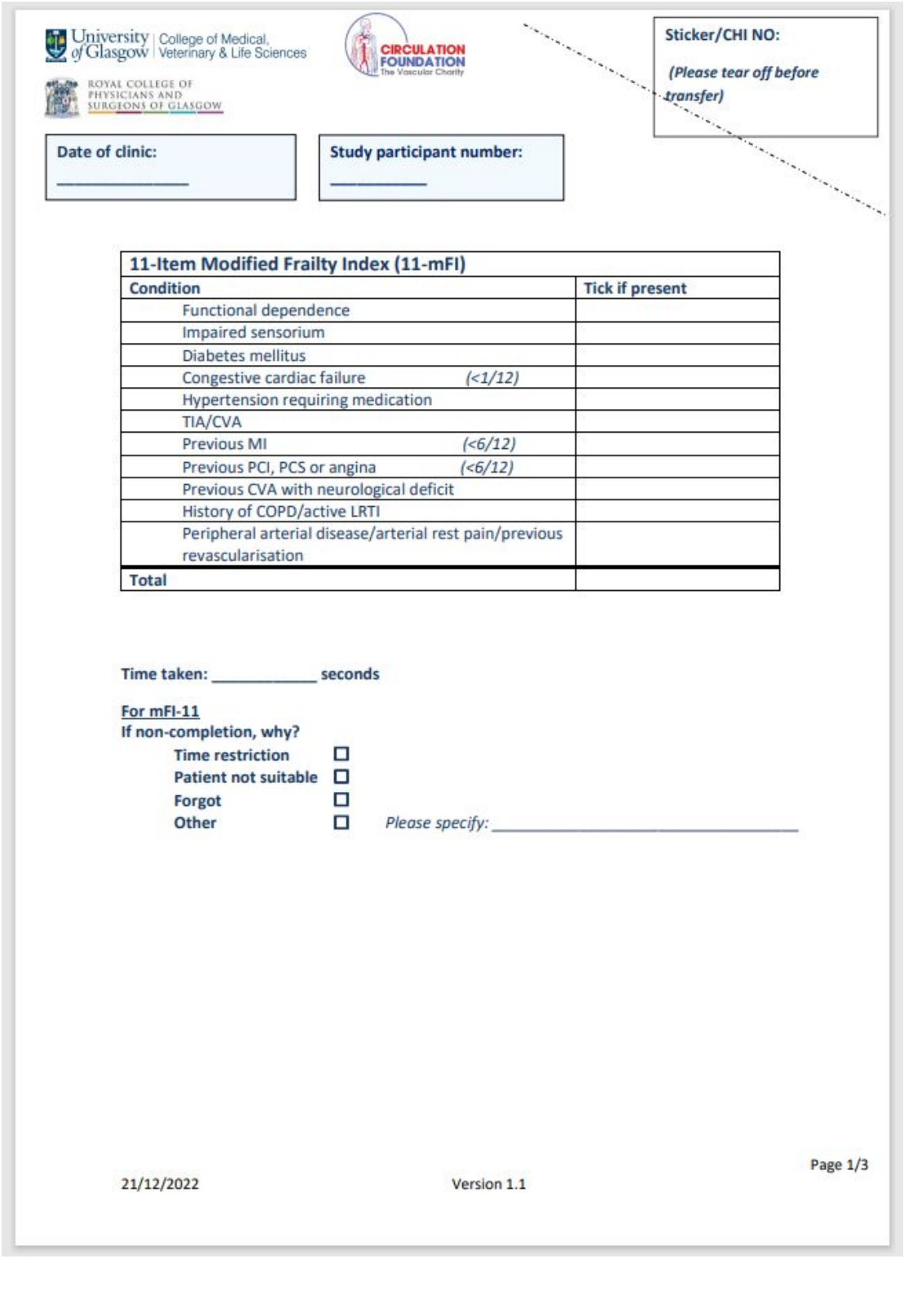
Appendix 4 – Case report form (researcher)



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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic: _____

Study participant number: _____

11-Item Modified Frailty Index (11-mFI)	
Condition	**Tick if present**
Functional dependence	
Impaired sensorium	
Diabetes mellitus	
Congestive cardiac failure *(<1/12)*	
Hypertension requiring medication	
TIA/CVA	
Previous MI *(<6/12)*	
Previous PCI, PCS or angina *(<6/12)*	
Previous CVA with neurological deficit	
History of COPD/active LRTI	
Peripheral arterial disease/arterial rest pain/previous revascularisation	
Total	

Time taken: _____ **seconds**

For mFI-11

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* _____

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University of Glasgow | College of Medical, Veterinary & Life Sciences

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Charslon Comorbidity Index		
Variable	**Score**	**Points**
Age (years)		
< 50	0	
50 - 59	1	
60 – 69	2	
70 – 79	3	
≥ 80	4	
Myocardial infarction		
No	0	
Yes	1	
Congestive cardiac failure		
Exertional/paroxysmal/nocturnal dyspnoea responding to treatment		
No	0	
Yes	1	
Peripheral vascular disease		
Claudicant/rest pain/prev bypass/untreated AAA (>6cm)	0	
No	1	
Yes		
CVA/TIA		
With minor/no neurological sequelae		
No	0	
Yes	1	
Dementia		
No	0	
Yes	1	
COPD		
No	0	
Yes	1	
Connective tissue disease		
No	0	
Yes	1	
Peptic ulcer disease		
Any history of treatment		
No	0	
Yes	1	
Liver disease		
None	0	
Mild *(chronic hepatitis/cirrhosis without complication)*	1	
Mod/Severe *(Cirrhosis, portal hypertension +/- bleeding varices)*	3	

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University of Glasgow | College of Medical, Veterinary & Life Sciences

Royal College of Physicians and Surgeons of Glasgow

Circulation Foundation — The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic____________

Study participant number: ____________

CCI Continued

Diabetes mellitus None/diet-controlled Uncomplicated End-organ damage	 0 1 2	
Hemiplegia No Yes	 0 2	
Moderate/severe CKD *Dialysis/previous renal transplant/Creatinine >265 umol/L* No Yes	 0 2	
Solid tumour None Localised Metastatic	 0 2 6	
Leukaemia No Yes	 0 2	
Lymphoma No Yes	 0 2	
AIDS No Yes	 0 6	
TOTAL SCORE		

For CCI

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* ________________________

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	____n/a____
	2b	All items from the World Health Organization Trial Registration Data Set	_____n/a_____
Protocol version	3	Date and version identifier	____1_____
Funding	4	Sources and types of financial, material, and other support	____1_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	____1_____
	5b	Name and contact information for the trial sponsor	____1_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	____1_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	____n/a_____

Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
	6b	Explanation for choice of comparators	6-8
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	n/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8-9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	9, Figure 1

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9-10
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	n/a
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	n/a
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	n/a
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	10
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	11
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	11
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	11

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	12
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	15
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	10
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	12
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendices 1-4
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Frailty Assessment in Vascular OUtpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-079387.R1
Article Type:	Protocol
Date Submitted by the Author:	31-Oct-2023
Complete List of Authors:	Welsh, Silje; University of Glasgow, College of Medical, Veterinary and Life Sciences; Queen Elizabeth University Hospital, Department of Vascular Surgery Hussey, Keith; Queen Elizabeth University Hospital, Department of Vascular Surgery Brittenden, Julie; University of Glasgow, College of Medical, Veterinary and Life Sciences; Queen Elizabeth University Hospital, Department of Vascular Surgery Orr, Douglas J; University of Glasgow, College of Medical, Veterinary and Life Sciences; Queen Elizabeth University Hospital, Department of Vascular Surgery Quinn, Terry; University of Glasgow, College of Medical, Veterinary and Life Sciences
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Geriatric medicine
Keywords:	Aged, Aging, VASCULAR SURGERY, Surveys and Questionnaires

Frailty Assessment in Vascular OUtpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.

Silje A Welsh[1,2] (MBChB), Keith Hussey[2] (MD), Julie Brittenden[1,2] (MD), Douglas J Orr[1,2] (MD) and Terry Quinn[1] (MD)
[1] – College of Medical, Veterinary and Life Sciences, University of Glasgow, Scotland. [2] – Department of Vascular Surgery, Queen Elizabeth University Hospital.

Issue Date: 16th February 2023
Protocol version: 1.3

ClinicalTrials.gov Identifier: NCT06040658

The study is being conducted as part of a clinical research fellowship. This fellowship is jointly funded by the Royal College of Physicians and Surgeons of Glasgow and the Circulation Foundation. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

Trial Sponsor: NHS Greater Glasgow & Clyde
Sponsor's Reference: NHS GG&C R&I reference number **GN23CE014**
Address: Ward 11, 1st Floor, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE

The sponsor ensures study conduct falls in line with local NHS policies and ethical requirements for studies involving patients. The sponsor will not contribute toward, or control, any aspects of data collection, data analysis, interpretation, manuscript writing or dissemination of results.

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84 Castle Street, Glasgow, G4 0SF, United Kingdom.

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Abstract

Introduction:Frailty has consistently demonstrated associations with poorer healthcare outcomes. Vascular guidelines have recognised the importance of frailty assessment. However, an abundance of frailty tools and a lack of prospective studies confirming suitability of routine frailty assessment in clinical practice has delayed the uptake of these guidelines. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study speaks to this evidence gap. The primary aim is to assess feasibility of implementing routine frailty assessment in a reproducible outpatient setting. Secondary objectives include comparing prognostic values and inter-user agreement across five frailty assessment tools.

Methods and analysis:This single-centre prospective cohort study of feasibility, is conducted in a rapid-referral vascular surgery clinic, serving a population of 2 million. Adults with capacity (>18years), attending clinic for any reason are eligible for inclusion. Five assessments are completed by patient (Rockwood Clinical Frailty Scale [CFS] and Frail NonDisabled Questionnaire), clinician (CFS, Healthcare Improvement Scotland FRAIL tool and 'Initial Clinical Evaluation') and researcher (11-item modified Frailty Index). Consistent with feasibility objectives, outcome measures include recruitment rates, frailty assessment completion rates, time-to-complete assessments and interuser variability. Electronic follow-up at 30-days and 1-year will assess home-time and mortality as prognostic indicators. Patients treated surgically/endovascularly will undergo additional 30-day and 1-year post-operative follow-up, outcome measures include: surgical procedure, mortality, complications (according to Clavien-Dindo Classification), length-of-stay, readmission rates, non-home discharge, home-time, higher social care requirements on discharge and amputation-free survival. Prognostic value will be compared by area under ROC curves. Continuous outcome variables will be analysed using Spearman's rank correlation coefficient. Inter-user agreement will be compared by percentage agreement in Cohen's Kappa coefficient.

Ethics and dissemination:Study sponsored by NHS Greater Glasgow & Clyde (R&IUGN23CE014). London–Riverside REC (23/PR/0062) granted ethical approval. Results will be disseminated through publication in peer-reviewed vascular surgery and geriatric medicine themed journals and presentation at similar scientific conferences.

Strengths and limitations of this study

- By including all consultant vascular surgeons working in a 'hub' site, this study acts as a real world example of typical Vascular Surgery services in the United Kingdom in the exploration of feasibility and suitability of routine frailty assessment in clinical practice which promotes generalisability of study results.
- Clinical relevance and research impact is further enhanced through this study incorporating measurements of prognostic value as well as novel direct head-to-head comparison of frailty assessment tools enabling clinicians and policy makers to design evidence-based frailty-centric clinical service adaptations.
- Although the setting is based on a vascular 'hub' site serving three NHS healthboards, this is a single-centre study which excludes patients who lack capacity (e.g., dementia), which may affect the generalisability of results.

Introduction

Background and rationale

In the absence of a universally agreed definition, frailty can be considered a syndrome of increased vulnerability to even minor stressors due to the accumulation of age-associated deficits across multiple domains.[1] Frailty is common in vascular patients with an estimated prevalence three times that of the general population.[2] An association between the clinical syndrome of frailty and adverse surgical outcomes in vascular surgery has been described.[1] For the person living with frailty, adaptations to the traditional surgical approach may be necessary on an individual and wider service-model level to improve healthcare outcomes, ensure equity in healthcare delivery and guide resource allocation. The critical first step is assessment and recognition of frailty in practice, an approach that is advocated by national guidelines.[3]

Despite this, approximately one third of vascular surgeons do not formally assess patients for frailty with the most commonly cited reasons including unfamiliarity with tools and concerns over tool validity.[4] This issue is not isolated to Vascular Surgery, a similar problem has been demonstrated by a European survey in emergency surgery which demonstrated only 1.2% of clinicians routinely perform frailty screening despite 98% agreeing frailty influences outcomes. Among the reasons cited for this discrepancy were a lack of knowledge on frailty assessment, lack of training and a lack of evidence supporting a single best frailty tool.[5] Perhaps the downside to frailty gaining important visibility, in the absence of a gold standard diagnostic tool, is the subsequent accumulation of disparate methods for assessing and diagnosing frailty. A recent review identified 42 separate frailty assessment tools used across 111 vascular surgery related studies, but with limited data on how these tools perform in clinical practice.[2] The heterogeneity in frailty tools has been labelled as 'immaturity' in this area of research, where a call has been made for direct tool comparisons to help identify if a superior tool exists so that we can better meet the expectations of the vascular population.[6, 7]

Identification of frailty early in the perioperative pathway enables risk stratification, joint decision making and, with the support of appropriate specialist input, syndrome modification.[8] Early evidence confirms the identification and targeted treatment of frailty-related problems during acute vascular admissions, confers both cost and therapeutic benefit, as inferred from a reduced length of stay.[9] Yet these results need corroborated with larger and long-term studies across multiple centres. The well demonstrated heterogeneity in frailty assessment tools complicates the ability to do so by challenging comparison of services and data pooling. Identifying a preferred frailty tool will enable researchers, clinicians and managers to speak one language around frailty and act as a prelude to (inter)national harmonisation in frailty research and approaches to improving its management in clinical practice. With this in mind, it is important to identify methods for assessing frailty which lend themselves to practical application in busy, time-pressured, clinical services. Our previous research demonstrates an evidence gap around the ability to identify a preferred approach to frailty assessment in the vascular surgical context.[2] Limitations of studies to date, include potential biases from retrospective design, poor generalizability to the UK NHS, lack of head to head comparisons of tools and limited assessment of properties such as feasibility and acceptability.

The ideal study design would include a real world, unselected cohort and prospectively compare differing methods for frailty assessment. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study is designed to speak to this gap in the evidence using five frailty assessments that

have been carefully selected after reviewing format, relevance, anticipated ease of use and, where possible, are recommended by the Healthcare Improvement Scotland.

Objectives

The primary aim will be to assess the feasibility of implementing routine frailty assessments into an urgent-referral vascular outpatient clinic setting ('Vascular Hot Clinic'). Secondary objectives are to assess and compare the variability and prognostic value of selected frailty assessments.

Trial design

The FAVOUR study (IRAS ID 322086, NHS R&I reference UGN23CE014/REC reference 23/PR/0062) is a single-centre, non-randomised, observational cohort study of feasibility which will be conducted and reported in line with the guidance presented in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[10]

Methods and analysis

This Standard Protocol Items for Randomized Trials (SPIRIT) guidelines have been followed in the generation of this study protocol.[11]

Study setting

This study will take place during a Vascular 'Hot' Clinic at the 'hub' Queen Elizabeth University Hospital (QEUH), Scotland. This is a consultant-led outpatient clinic responsible for delivering urgent vascular care for a population of approximately 2 million patients in NHS Greater Glasgow & Clyde and other 'spoke' sites including: NHS Forth Valley and part of NHS Highlands. Referrals are received from primary care physicians, community podiatrists and secondary care teams. Referrals are triaged within 24 hours of receipt by a consultant vascular surgeon, and if medically appropriate, patients are appointed to the next available appointment (same day to within 1 week). The ethos of the clinic is to provide urgent care for patients with suspected vascular pathology which requires prompt, but not immediate, medical assessment. This clinic does not provide a vascular access service which is instead offered through a separate renal transplant service.

Three clinics are held weekly with a capacity of up to ten patients per clinic. The clinics are also served by multidisciplinary team members, including vascular nurse specialists, podiatrists and clinical scientists who provide a dedicated duplex service.

Population

Participants must provide written informed consent prior to study participation (appendix 1). All referrals to vascular hot clinic are eligible for inclusion, preferentially recruiting new referrals. As frailty is related to age, but does not directly correlate with it, no age cut-off has been defined.[3, 12] As this is primarily a study of feasibility, patients will not be excluded/included based on presenting symptom or diagnosed pathology.

A proxy (relative/friend/carer), if present, will also be invited to participate and assist with frailty assessments of the patients, where suitable. The participation of the proxy is dependent on the patient providing written consent agreeing to their participation, as well as the proxy being eligible to participate, according to the same inclusion/exclusion criteria set out for patients below.

The lead researcher (SW) is a medical clinician and will assess prospective participants' capacity to consent to study participation on a case-by-case basis.

Inclusion criteria:

- Adults (aged 18 years or older)
- Attending Vascular Hot Clinic

Exclusion criteria:

- Lacking capacity to provide informed consent, as defined in the Mental Capacity Act, 2005.
- Parent clinical team feel frailty assessment not suitable
- Non-English speaker without qualified translator present

- Prisoners

Intervention

Five frailty assessment techniques will be compared: Rockwood 9-item Clinical Frailty Scale (CFS)[13], 11-item Modified Frailty Index (11-mFI)[14], Frailty non-Disabled Questionnaire (FiND)[15], Healthcare Improvement Scotland (HIS) 'Think Frailty' FRAIL assessment tool[16] and Initial Clinical Evaluation (ICE)[17], Table 1. As frailty assessment is recommended, there will be no control, rather differing tools will be compared to one another. The patient, and proxy where applicable, will complete CFS and FiND self-assessment. The clinician will complete CFS, HIS FRAIL and ICE assessment. The researcher will complete the mFI-11 assessment.

These tools were selected as most likely to be suited to the acute clinic context, after reviewing their content, format, ease of use, training requirements and anticipated time required to complete. This study deliberately selected tools with an emphasis on brevity while incorporating tools that are constructed based on differing theories of frailty and, where possible, are recommended by Scottish healthcare governing body, Healthcare Improvement Scotland. Within vascular surgery, the CFS and mFI-11 are the most commonly used tools; demonstrating international familiarity.[2] By continuing their use, the research impact of this study is enhanced. A primary criterion was that the selected tools should not require additional equipment, external training or have copyright restrictions. This was to ensure ease of implementation at scale, both in the UK NHS and other healthcare settings. Appendix 2-4 display the case report forms (CRFs) with various frailty assessment to be completed by patient/proxy, clinician and researcher.

Participation in this study does not preclude any aspect of concomitant care and/or intervention for patients. To ensure routine care provided by this service remains unaffected, clinicians will perform frailty assessments at the conclusion of each clinic, minimising possible biases in assessment and care provision.

Table 1. Selected frailty assessment tool summaries

CFS	**Definition:** The CFS is an ordinal, hierarchical 9-item person-assessed scale where patients score more highly if more frail. The scale scores run between 1 ('Very Fit') and 9 ('Terminally Ill') with each score having a picture and succinct written definitions This tool is recommended for use in clinical practice by Healthcare Improvement Scotland (HIS). **Personnel:** Vascular surgeon, patient and proxy if present will complete. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, another investigator will score the patient instead. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded. **Training requirement:** While not necessary, there is a short online module available to develop understanding in how the CSF is applied. To ensure internal rigour, clinician's contributing to this study will be requested to complete this training. **Duration**: It is expected this tool will take < 1 minute for clinicians once they are familiar with the tool. For patient's or proxy's completing the tool, it is expected this will take 5 minutes. **Application:** A copy of the CFS chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by one of the research team and asked to score included patients. For patients/proxy's a modified CFS chart will be displayed at the end of their clinic

	appointment. The patient/proxy will be asked to read each the definition for each score (1-8) before selecting the one they feel most accurately describes them. To reduce the risk of bias, the title and image for each score will be hidden from patient/proxy, leaving only the text description. **Modifications for study:** A CFS score of 9 describes a terminally ill patient, regardless of frailty status. As this is not relevant to this trial, and to reduce the risk of participants becoming upset, this score will not be considered by this trial and therefore not displayed to the participant.
mFI-11	**Definition:** This frailty index assessment is based on the frailty theory of cumulative deficits.[18] Healthcare records are accessed to determine the presence, or absence, of 11 variables across multiple domains (Non-independent function status, cognitive impairment and the following co-morbidities: congestive cardiac failure, myocardial infarction, previous percutaneous coronary intervention/cardiac surgery or angina, hypertension, diabetes mellitus, severe chronic obstructive pulmonary disease/active pneumonia, peripheral arterial disease, stroke/transient ischaemic attack without residual neurological deficit or with deficit). Each variable is scored 1 point when present with the end score divided by the total number of variables (11), giving a score between 0 – 1. The greater the value, the greater the risk of frailty. **Personnel:** A member of the research team will complete this assessment. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded **Training requirement:** No training required for application. **Duration**: This tool has been piloted and found to take < 5 minutes per participant to derive from electronic health record. **Application:** This is a frailty index which is calculated by extracting relevant data through accessing national health service (NHS) electronic records. **Modifications for study:** Nil.
FiND	**Definition:** This is a 5-item self-assessment questionnaire. The first two questions relate to disability while the remaining three relate to frailty. Patients reporting one or more of the three frailty symptoms, in the absence of disability, are defined as frail. The scale's design reflects principles of the Fried frailty phenotype which defines frailty as the presence of three or more of the following energy-negative components: unintentional weight loss ('shrinking'), poor grip strength, exhaustion, slowness and low physical activity levels.[19] This questionnaire is recommended for use by Healthcare Improvement Scotland. The original questionnaire uses metric measurements of distance and weight, an imperial conversion will be added to relevant parts of the questionnaire to assist with patient comprehension. **Personnel:** The patient, and proxy if present, will be completing the questionnaire themselves. **Training requirement:** No training required for application. **Duration**: The questionnaire takes 2 minutes to complete. **Application:** A copy of the FiND will be displayed to the patient/proxy at the end of their clinic. They will be asked to read each of the 5-items closely and select the option that most accurately describes their situation (scoring either 0 or 1 per point). **Modifications for study**: Nil.

HIS 'Think Frailty' FRAIL assessment	**Definition:** This is a five-item frailty screening tool which has been developed by HIS and is currently recommended to be used in all unscheduled older adult admissions. The format is based on the theory of cumulative deficits across multiple domains (function, cognition, social). It's selection, in part is due to the novel aspect of this tool not considering co-morbidity as part of the assessment. **Personnel:** The consultant leading the clinic will be asked to complete the HIS FRAIL assessment. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: Completion of the HIS tool takes < two minutes. **Application:** A copy of the HIS FRAIL chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by the chief investigators and asked to score included patients. **Modifications for study:** Nil.
ICE	**Definition:** Also known as the 'end of bed test'. Clinicians will report a subjective and binary assessment of the patient; 'frail' or 'non-frail'. **Personnel:** The consultant leading the clinic will be asked to provide an ICE. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a clinical member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: This assessment takes part as routine practice during a clinical interaction between clinician and patient. No additional time is required. **Application:** The consultants will be approached at the end of the clinic and asked to provide their subjective opinion (ICE) on patient's frailty status to the chief investigator. This assessment will be performed first to minimise bias in clinician responses from completing alternate assessments prior. **Modifications for study:** Nil.

Primary aim

The primary aim of this study is to assess the feasibility of implementing routine frailty assessment in a vascular clinic setting. For this, the following data will be collected: number of patients attending hot clinic, number eligible for inclusion, number of eligible patients approached for recruitment, number of patients recruited, time taken to complete assessments, number and nature of assessments with non-completion, reasons for non-completion and if assistance was required to complete the tool. These parameters are clinically relevant as they will allow valid and reproducible calculations of the proportion of eligible patients recruited and time taken to complete assessments which will enable clinicians to consider the feasibility and suitability of implementing routine frailty assessment in a controlled clinical environment, encouraging uptake of current guidance.

Secondary outcomes

The secondary objectives pertain to assessing the prognostic value of selected frailty assessment tools and their value over standard clinical demographic information. All patients will be electronically followed-up at 30-days and 1-year from recruitment, collecting data on home time[20] (defined by the number of full days the patient spends not as an inpatient) and mortality. An additional electronic follow-up will be applied to patients who undergo surgical or endovascular intervention, at 30-day and 1-year post-operatively. For this, the following data will be collected: surgical procedure, mortality, post-operative complications (according to the Clavien-Dindo Classification)[21], length of hospital stay (full days), readmission rates (to any speciality), non-home discharge, home time, discharge with a higher level of social care requirements and amputation free survival for patients with end stage peripheral arterial disease of the lower limbs. As current practice for reporting post-operative outcomes is to report outcomes according to the number of days that has passed since the index intervention, introducing additional 30-day and 1-year follow up periods for patients who undergo interventions (compared to those who do not) allows the collection of clinically relevant data without introducing bias in the mode of data collection. Despite the vascular network declaring a national interest in frailty,[3] there is a lack of evidence directly comparing the prognostic validity and variability of frailty assessment tools. The data from this study will help guide standardisation in the approach to frailty assessment in clinical practice.

Baseline assessments

Baseline characteristics will be collected, including patient demographics, social/functional circumstances, polypharmacy and relevant comorbidities to calculate a Charlson comorbidity Index.[22]

Participant timeline

Prospective participants will be identified on the day by reviewing the electronic health care records of patients due to attend a Vascular 'hot' clinic and applying the inclusion and exclusion criteria. Due to the emergent nature of the referrals to the vascular hot clinic, patients (and their proxy, if present) will be approached, recruited and complete frailty assessments on the day of attending their clinic appointment, Figure 1. No ongoing participation is required, follow up will be through accessing electronic health care records.

Sample size

As this is primarily a study of feasibility, a power calculation has not been performed. The vascular hot clinic offers up to 30 appointments weekly across three clinics. Where possible, all eligible patients will be approached for participation with an emphasis on targeting 'new referrals'.

Recruitment

Patient recruitment began in March 2023. Prospective patients will be approached for study participation by the research team upon registering for their clinic appointment. If expressing interest, they will receive a participant information sheet. Patients are required to complete their clinic appointments (where their medical care will remain unaffected by (non-)participation in this study) prior to participating in the study. The prospective participant will be re-approached at the conclusion of their clinic appointment to confirm willingness to participate and provide written consent. Thereafter, the frailty assessments are completed by the patient. Where a patient attends with a suitable proxy, they will be approached in an identical fashion provided the patient provides written consent for this. Where a patient is eligible for participation, but a proxy is ineligible/declines participation, the patient will be recruited without proxy contribution. Where the patient is not eligible for participation, the proxy will not be invited to participate on their behalf. Staggering the consent process by approaching the patient either side of their clinic appointment maximises the time for the patient to consider participating. It is recognised that ideally patients should have a period of at least 24 hours with a patient information sheet prior to expressing a wish to participate in a study however, due to the emergent nature of the clinic and the presenting pathology, this will not be possible. Clinician and research team complete frailty assessments of recruited patients at the end of the clinic to minimising clinic disruption.

Data collection

Data will be collected in person and through review of electronic health care records. On the day of recruitment, frailty assessments scores will be performed in the clinic and collected by patient/proxy, clinician and researcher on relevant paper based CRFs (appendix 2-4). On the same day, the research team will review electronic health care records of recruited patients and extract data for baseline assessments to an electronic data extraction template. All electronic follow up will be extracted to the same electronic data extraction template.

Data management

Data management, processing and handling will be conducted in line with General Data Protection Regulation principles (EU 2016/679). The research team will allocate pseudonymised participant identification numbers then remove and securely destroy personal identifiable information before transcribing data from the paper based CRFs to an electronic data extraction template for storage. Transcribed data will undergo quality checking by a second member of the research team. Data for baseline demographics and electronic follow up will be extracted and stored on Excel Version 2304. SW will be primarily responsible for storing study dataset with sharing through secure means with authors for the purpose of analysis, write-up only. Data will not be shared with third parties.

Statistical methods

Baseline demographics and feasibility parameters will be described using descriptive statistics, including, percentages, ranges, means and standard deviations or medians and interquartile ranges. The prognostic value of frailty assessment tools on binary outcome variables will be displayed through calculating receiver operating characteristic (ROC) curves. Frailty tool comparisons will be performed by comparing the area under the ROC curve. The CFS is endorsed by healthcare policy throughout the UK and will be used as the gold standard for comparisons. Continuous

outcome variables will be analysed using Spearman's rank correlation coefficient. Levels of inter-user agreement between patient and clinician assessments will be calculated with a percentage agreement and Cohen's Kappa coefficient. Subgroup analysis will be performed to compare outcomes for patients undergoing surgical treatment, endovascular treatment and those who do not undergo intervention. Patients lost to follow up, or with incomplete data, will be excluded. In addition to accuracy and reliability analyses, we will create models to estimate the association of frailty, measured using different approaches, with our outcomes of interest. The primary analysis will be adjusted for age and sex.

Data monitoring

This observational cohort study will not be subject to a data monitoring or trial management committee. The study may be subject to study monitoring visits and subsequent monitoring reports which will be conducted and reviewed in accordance with a study-specific monitoring plan devised by the study sponsor. The sponsor audits a randomly selected 10% of studies conducted under the Research Governance Framework per annum, as well as those identified using a risk assessment tool as specifically requiring assessment.

Harm

There are no adverse events anticipated to occur secondary to the intervention which falls in line with national guidelines. For this reason, no ancillary and post-trial care has been designed.

Patient and public involvement

A group of five non-medically trained adult volunteers (aged 25 – 65 years) contributed toward the study design through piloting both questionnaires (CFS and FiND) and all took less than 5 minutes to complete both questionnaires, without requiring assistance. There was no further involvement in the development of this study by patients or the public. Patients will not be contacted directly with the results of this study however contact details for the PI have been supplied to participants so that they can request information on study progress/results as they become available.

Ethics and dissemination

Research ethics approval

This study is sponsored by NHS Greater Glasgow & Clyde (Research & Innovation reference UGN23CE014) and has received a favourable opinion by the London – Riverside Research and Ethics Committee (23/PR/0062). This study will be performed according to the Research Governance Framework for Health and Community Care (Second edition, 2006) and WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI Ethical Principles for Medical Research Involving Human Subjects 1964 (as amended).

Amendments

Any amendments to the protocol will be submitted to the IRAS Amendment Portal to the responsible ethics committee and/or NHS GG&C Research & Innovation for review. Changes will only be implemented following the approval of proposed amendments by the original reviewing Research and Ethics Committee and Greater Glasgow & Clyde Health Board Research and Innovation office. All protocol amendments will be appropriately stored, cited and explained in future manuscripts.

Consent

The principal investigatory (PI) (SW) is responsible for obtaining informed written consent from participants. For this, participant information sheets (PIS) will be provided to all prospective participants as well as conducting an informed discussion detailing study design, confidentiality and rights to withdraw. The contact details for the PI are supplied in the PIS which participants will be pointed to and they will be encouraged to make contact with any questions, concerns or if wishing to withdraw. A copy of the consent form will also be provided for participants to keep.

Confidentiality

Participant confidentiality will be upheld through participant pseudonymisation during data collection. To endorse data minimisation, only data relevant for the described outcome measures will be collected and stored. Consent forms and pseudonymised paper based CRFs and will be stored separately in locked filing cabinets, accessible only to the research personnel. Electronic data will be extracted and stored on Excel Version 2304 with personal and research generated data stored on separate databases on different servers. Research data storage will comply with the University of Glasgow's data retention policy.

Access to data

Only members of the core research team will have access to the final dataset with the exception of review by sponsors to ensure proper study conduct. Data will not be shared with third parties for analysis or write-up.

Dissemination

Study results will be disseminated through publication in peer-reviewed journals and presentation to relevant scientific conferences, targeting those with a focus on geriatric medicine and vascular surgery, in particular the Vascular Societies' Annual Scientific Meeting to enhance visibility of the results and assist with knowledge translation.

Discussion

Frailty-centric adaptations to established clinical service models are crucial as the anticipated demographic changes associated with an ageing population means it is likely frailty, with its inherent clinical and financial implications, will become increasingly commonplace.[1] An abundance of frailty assessment tools have confirmed the prognostic value of frailty, hence guidelines advocating the importance of its recognition in clinical practice.[3] However, a relative lack of evidence in measurements of feasibility and suitability of frailty assessment in clinical practice, or head to head

comparisons of tools, has contributed toward a delay in uptake of guidelines.[4] For this reason, the prospective assessment of frailty in a reproducible and controlled vascular outpatient department (OPD) environment has been identified as a key area of research interest, which the study presented in this protocol targets.[1, 4]

From a previous systematic review we identify only four relevant studies prospectively assessing frailty in vascular surgery OPD.[2] The first compared the correlation between clinician-assessed CFS scores and patient reported outcome measures of frailty (including FiND and patient-reported outcome measurement information systems v1.2 and v2.0) and its effect on 1-year mortality.[23] Another examined the effect of frailty as assessed by the Groningen Frailty Indicator on postoperative delirium.[24] One study used the Fried frailty index to compare the effect of frailty status on gait parameters in patients with peripheral arterial disease compared to control[25], while another examined the association of grip strength as a marker of frailty with measures of sarcopenia and co-morbidity.[26] However, the research impact of these data are limited by a paucity in feasibility measurements and direct comparison between selected tools.

The study presented in this protocol builds on current evidence through including and comparing a greater number of commonly used frailty assessment tools that have been specifically selected for their format (assessing frailty according to different theories of frailty), relevance (based on clinician familiarity and compliance with guidance from local healthcare governance) and anticipated rapid time to complete, making them suitable for application in busy OPDs. By incorporating measurements of prognostic value, it is anticipated data generated by this study will bear direct clinical relevance and will contribute toward the generation of evidence based recommendations for an optimum standardised, and reproducible approach to diagnosing frailty in an outpatient setting.

The primary aim of this study is novel within vascular surgery. The major strength in this study is the prospective and longitudinal design. As surgeons increasingly aim to identify patients who would sooner benefit from a conservative approach, the short- and long-term follow-up for all patients managed operatively or not, stratified by frailty status, is of clinical relevance. Limitations to this study are acknowledged, including the single-centre design and the exclusion of patients who lack capacity (e.g., dementia) which may impact generalisability of results.

Study status

Participant recruitment concluded in July 2023, data collection is ongoing.

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Author contributions

TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

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Competing interests statement

Authors declare no conflict of interest or further financial disclosures.

Figure 1. Summary of patient timeline and study methodology.

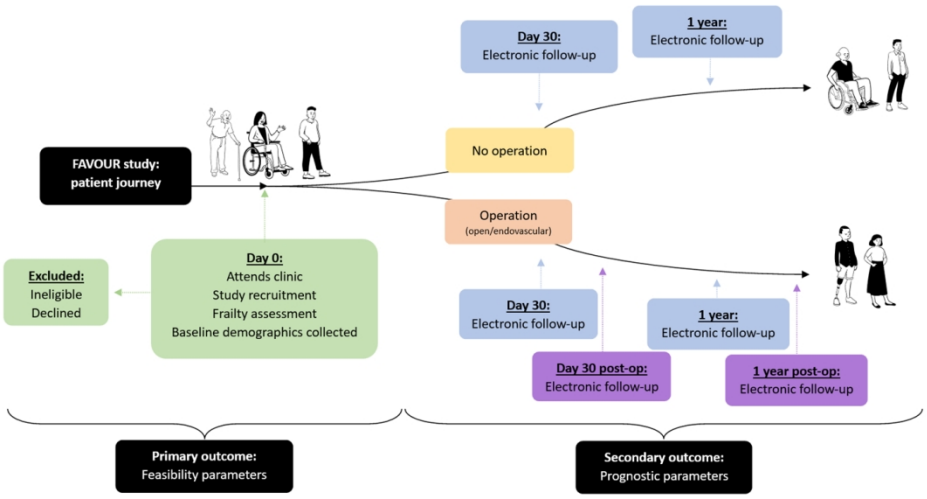

Figure 1. Timeline summarising patient timeline and study methodology

Figure 1 - Summary of patient timeline and study methodology

1044x580mm (38 x 38 DPI)

Appendix 1 – Participant consent form

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

NHS Greater Glasgow and Clyde

Participant Identification Number for this trial: _____

Title of Project: **Frailty Assessment in Vascular OUtpatients Review (FAVOUR Trial) – comparing feasibility and prognostic value of commonly used assessments.**

Name of Researcher(s): Miss Silje Welsh

CONSENT FORM (Patient)

	Please initial box
1. I confirm that I have read and understood the Participant Information Sheet (patient) version 1.3 dated 13/02/2023.	☐
2. I have had the opportunity to think about the information and ask questions and understand the answers I have been given.	☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time during data collection, without giving any reason, without my legal rights being affected. Data collection is expected to conclude 13 months after my recruitment to this study.	☐
4. I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	☐
5. I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐
6. I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project only and securely destroyed within 3 months of the end of this study.	☐
7. I understand that if I withdraw from the study, I will be asked to clarify how I would like the data collected from me up to that point to be handled. There will be the option to retain it for the remainder of the study, or for it to be securely destroyed.	☐
8. If relevant, I agree to a proxy (friend/relative/care-giver) contributing towards my participation in this study. Their participation will require them to complete a separate consent form. I also understand that a proxy's decision to participate, or not, will in no way affect my participation in this study.	☐
9. I agree that the study team can access my electronic health record for the purposes of the study.	☐
10. I understand that electronic follow-up will occur at 30-days and 1-year after my recruitment to this study. Further, I understand that if I undergo surgical treatment, an additional follow-up will occur at 30-days and 1-year after the first treatment/surgery.	☐

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11. I agree to the dissemination of study results through publication in scientific journals and presentation at relevant conferences. For the purposes of dissemination, I understand that my data will be anonymised. ☐

12. I understand that the results from this study will not be communicated directly to me. However, I have received the contact details for lead researcher (in the Participant Information Sheet), whom I can contact should I want to enquire about progress of the study/study results. ☐

13. I agree to take part in the study. ☐

Name of participant	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher; 1 copy for case notes)

To be completed if participant wishes to withdraw, initial relevant boxes:

14. I confirm that the patient expresses a wish to withdraw from the study. ☐

15. On withdrawal, the patient wishes the following regarding their personal and research data:

(a) All data collected up until the point of withdrawal is to be deleted and not used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

OR

(b) All data collected up until the point of withdrawal can be kept by the researchers and used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

Signed by Principal Investigator on behalf of the patient

Principle Investigator	Date	Signature

Appendix 2 – Case report Form (Patient)

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____

Study participant number: _____

Patient ☐

Sticker/CHI NO:

(Please tear off before transfer)

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Please take time and read through each description before selecting the option which most accurately describes you. The responses to this questionnaire will in no way impact the medical care you have received today or may receive in the future.

	CFS – Questions about activity and function. Which one of the following is most like you:	**Select one option**
1	People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	These people often have **more evident slowing**, and need help in **high order activities** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
X	**Unsure/unable to answer**	

TO BE COMPLETED BY RESEARCH TEAM

Time taken to complete _____ **seconds**

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

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Version 1.1

Date 16/12/2022

PLEASE TURN OVER

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____

Study participant number: _____

Patient ☐

Sticker/CHI NO:

(Please tear off before posting)

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

FiND – Questions about activity and function		
Questions	**Answers**	**Select option**
A. Have you any difficulties walking 400 metres (¼ mile)?	No or some difficulties	
	A lot of difficulties or unable	
B. Have you any difficulties at climbing up a flight of stairs?	No or some difficulties	
	A lot of difficulties or unable	
C. During the last year, have you involuntarily lost more than 4.5 kg (10 lbs)?	No	
	Yes	
D. How often in the last week did you feel that everything you did was an effort or that you could not get going?	Twice or less	
	Three or more	
E. Which is your level of physical activity?	At least 2 – 4 hours per week	
	None or mainly sedentary	

TO BE COMPLETED BY RESEARCH TEAM

A+B ≥ 1: Y☐ N☐

C+D+E ≥ 1: Y☐ N☐

A+B+C+D+E = 0: Y☐ N☐

Time taken to complete _____ seconds

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

Version 1.1
Date 16/12/2022

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Appendix 3 – Case report form (Clinician)

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator □

Surgeon □

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q1. Initial Clinical Evaluation	**YES**	**NO**
Is this patient frail?		

Time taken: _____ **seconds**

Q2. Clinical Frailty Scale (Please select the most appropriate description)		**Tick**
1	**Very fit -** People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	**Well -** People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	**Managing well -** People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	**Vulnerable -** While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	**Mildly frail -** These people often have **more evident slowing**, and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	**Moderately frail -** People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Severely frail - Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	**Very severely frail -** Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
9	**Terminally ill** Approaching end of life. This applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail**.	
X	**X Unable to score**	

Time taken: _____ **seconds**

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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator ☐

Surgeon ☐

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q3. HIS FRAIL Assessment Tool		YES	NO	UNSURE
F	Functional impairment (new or worsening) e.g. difficulty with self-care			
R	Resident in a care-home?			
A	Altered mental state such as confusion or dementia (use the 4AT)			
I	Immobility/Instability. New decline in mobility, difficulty mobilising without help or fall leading up to admission			
L	Living at home with daily support (homecare; one or more visits per day)			

Time taken: _____ seconds

THIS SECTION IS TO BE COMPLETED BY THE RESEARCHER

For Q1. ICE
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

For Q2. Clinical Frailty Scale
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

For Q3. HIS FRAIL Assessment
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

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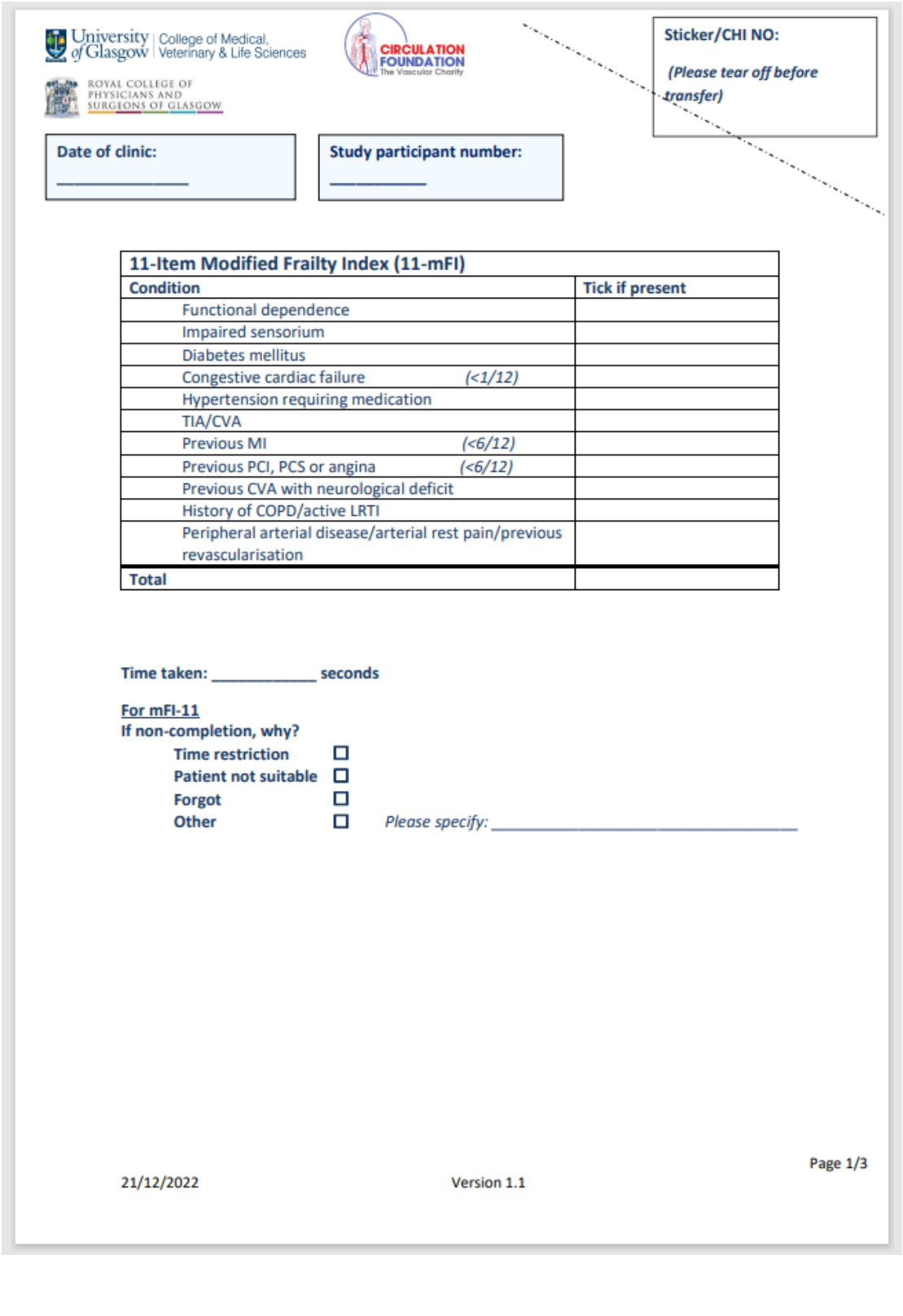
Appendix 4 – Case report form (researcher)



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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic: _____

Study participant number: _____

11-Item Modified Frailty Index (11-mFI)	
Condition	**Tick if present**
Functional dependence	
Impaired sensorium	
Diabetes mellitus	
Congestive cardiac failure *(<1/12)*	
Hypertension requiring medication	
TIA/CVA	
Previous MI *(<6/12)*	
Previous PCI, PCS or angina *(<6/12)*	
Previous CVA with neurological deficit	
History of COPD/active LRTI	
Peripheral arterial disease/arterial rest pain/previous revascularisation	
Total	

Time taken: _____ **seconds**

For mFI-11

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* _____

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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Charslon Comorbidity Index		
Variable	**Score**	**Points**
Age (years)		
< 50	0	
50 - 59	1	
60 – 69	2	
70 – 79	3	
≥ 80	4	
Myocardial infarction		
No	0	
Yes	1	
Congestive cardiac failure		
Exertional/paroxysmal/nocturnal dyspnoea responding to treatment		
No	0	
Yes	1	
Peripheral vascular disease		
Claudicant/rest pain/prev bypass/untreated AAA (>6cm)	0	
No	1	
Yes		
CVA/TIA		
With minor/no neurological sequelae		
No	0	
Yes	1	
Dementia		
No	0	
Yes	1	
COPD		
No	0	
Yes	1	
Connective tissue disease		
No	0	
Yes	1	
Peptic ulcer disease		
Any history of treatment		
No	0	
Yes	1	
Liver disease		
None	0	
Mild *(chronic hepatitis/cirrhosis without complication)*	1	
Mod/Severe *(Cirrhosis, portal hypertension +/- bleeding varices)*	3	

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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number:

_____

CCI Continued

Diabetes mellitus		
None/diet-controlled	0	
Uncomplicated	1	
End-organ damage	2	
Hemiplegia		
No	0	
Yes	2	
Moderate/severe CKD		
Dialysis/previous renal transplant/Creatinine >265 umol/L		
No	0	
Yes	2	
Solid tumour		
None	0	
Localised	2	
Metastatic	6	
Leukaemia		
No	0	
Yes	2	
Lymphoma		
No	0	
Yes	2	
AIDS		
No	0	
Yes	6	
TOTAL SCORE		

For CCI

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* _____

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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

NHS Greater Glasgow and Clyde

Participant Identification Number for this trial: _____

Title of Project: **Frailty Assessment in Vascular OUtpatients Review (FAVOUR Trial) – comparing feasibility and prognostic value of commonly used assessments.**

Name of Researcher(s): Miss Silje Welsh

CONSENT FORM (Patient)

	Please initial box
1. I confirm that I have read and understood the Participant Information Sheet (patient) version 1.3 dated 13/02/2023.	
2. I have had the opportunity to think about the information and ask questions and understand the answers I have been given.	
3. I understand that my participation is voluntary and that I am free to withdraw at any time during data collection, without giving any reason, without my legal rights being affected. Data collection is expected to conclude 13 months after my recruitment to this study.	
4. I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	
5. I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	
6. I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project only and securely destroyed within 3 months of the end of this study.	
7. I understand that if I withdraw from the study, I will be asked to clarify how I would like the data collected from me up to that point to be handled. There will be the option to retain it for the remainder of the study, or for it to be securely destroyed.	
8. If relevant, I agree to a proxy (friend/relative/care-giver) contributing towards my participation in this study. Their participation will require them to complete a separate consent form. I also understand that a proxy's decision to participate, or not, will in no way affect my participation in this study.	
9. I agree that the study team can access my electronic health record for the purposes of the study.	
10. I understand that electronic follow-up will occur at 30-days and 1-year after my recruitment to this study. Further, I understand that if I undergo surgical treatment, an additional follow-up will occur at 30-days and 1-year after the first treatment/surgery.	

11. I agree to the dissemination of study results through publication in scientific journals and presentation at relevant conferences. For the purposes of dissemination, I understand that my data will be anonymised. ☐

12. I understand that the results from this study will not be communicated directly to me. However, I have received the contact details for lead researcher (in the Participant Information Sheet), whom I can contact should I want to enquire about progress of the study/study results. ☐

13. I agree to take part in the study. ☐

Name of participant	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher; 1 copy for case notes)

To be completed if participant wishes to withdraw, initial relevant boxes:

14. I confirm that the patient expresses a wish to withdraw from the study. ☐

15. On withdrawal, the patient wishes the following regarding their personal and research data:

(a) All data collected up until the point of withdrawal is to be deleted and not used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

OR

(b) All data collected up until the point of withdrawal can be kept by the researchers and used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

Signed by Principal Investigator on behalf of the patient

Principle Investigator	Date	Signature

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	___1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	____ ClinicalTrials.gov Identifier: NCT06040658 _____
	2b	All items from the World Health Organization Trial Registration Data Set	_____n/a_____
Protocol version	3	Date and version identifier	____1_____
Funding	4	Sources and types of financial, material, and other support	____1_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	____1_____
	5b	Name and contact information for the trial sponsor	____1_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	____1_____

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	7-9
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	n/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-10
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10, Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	10-11
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	n/a
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	n/a
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	n/a
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11-12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11-12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11-12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12
Ethics and dissemination			

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	16
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
	31b	Authorship eligibility guidelines and any intended use of professional writers	13
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendices 1-4

Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____n/a_____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Frailty Assessment in Vascular OUtpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.

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Frailty Assessment in Vascular OUtpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.

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TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

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The sponsor ensures study conduct falls in line with local NHS policies and ethical requirements for studies involving patients. The sponsor will not contribute toward, or control, any aspects of data collection, data analysis, interpretation, manuscript writing or dissemination of results.

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Abstract

Introduction:Frailty has consistently demonstrated associations with poorer healthcare outcomes. Vascular guidelines have recognised the importance of frailty assessment. However, an abundance of frailty tools and a lack of prospective studies confirming suitability of routine frailty assessment in clinical practice has delayed the uptake of these guidelines. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study speaks to this evidence gap. The primary aim is to assess feasibility of implementing routine frailty assessment in a reproducible outpatient setting. Secondary objectives include comparing prognostic values and inter-user agreement across five frailty assessment tools.

Methods and analysis:This single-centre prospective cohort study of feasibility, is conducted in a rapid-referral vascular surgery clinic, serving a population of 2 million. Adults with capacity (>18years), attending clinic for any reason are eligible for inclusion. Five assessments are completed by patient (Rockwood Clinical Frailty Scale [CFS] and Frail NonDisabled Questionnaire), clinician (CFS, Healthcare Improvement Scotland FRAIL tool and 'Initial Clinical Evaluation') and researcher (11-item modified Frailty Index). Consistent with feasibility objectives, outcome measures include recruitment rates, frailty assessment completion rates, time-to-complete assessments and interuser variability. Electronic follow-up at 30-days and 1-year will assess home-time and mortality as prognostic indicators. Patients treated surgically/endovascularly will undergo additional 30-day and 1-year post-operative follow-up, outcome measures include: surgical procedure, mortality, complications (according to Clavien-Dindo Classification), length-of-stay, readmission rates, non-home discharge, home-time, higher social care requirements on discharge and amputation-free survival. Prognostic value will be compared by area under ROC curves. Continuous outcome variables will be analysed using Spearman's rank correlation coefficient. Inter-user agreement will be compared by percentage agreement in Cohen's Kappa coefficient.

Ethics and dissemination:Study sponsored by NHS Greater Glasgow & Clyde (R&IUGN23CE014). London–Riverside REC (23/PR/0062) granted ethical approval. Results will be disseminated through publication in peer-reviewed vascular surgery and geriatric medicine themed journals and presentation at similar scientific conferences.

Strengths and limitations of this study

- By including all consultant vascular surgeons working in a 'hub' site, this study acts as a real world example of typical Vascular Surgery services in the United Kingdom in the exploration of feasibility and suitability of routine frailty assessment in clinical practice which promotes generalisability of study results.
- Clinical relevance and research impact is further enhanced through this study incorporating measurements of prognostic value as well as novel direct head-to-head comparison of frailty assessment tools enabling clinicians and policy makers to design evidence-based frailty-centric clinical service adaptations.
- Although the setting is based on a vascular 'hub' site serving three NHS healthboards, this is a single-centre study which excludes patients who lack capacity (e.g., dementia), which may affect the generalisability of results.

Introduction

Background and rationale

In the absence of a universally agreed definition, frailty can be considered a syndrome of increased vulnerability to even minor stressors due to the accumulation of age-associated deficits across multiple domains.[1] Frailty is common in vascular patients with an estimated prevalence three times that of the general population.[2] An association between the clinical syndrome of frailty and adverse surgical outcomes in vascular surgery has been described.[1] For the person living with frailty, adaptations to the traditional surgical approach may be necessary on an individual and wider service-model level to improve healthcare outcomes, ensure equity in healthcare delivery and guide resource allocation. The critical first step is assessment and recognition of frailty in practice, an approach that is advocated by national guidelines.[3]

Despite this, approximately one third of vascular surgeons do not formally assess patients for frailty with the most commonly cited reasons including unfamiliarity with tools and concerns over tool validity.[4] This issue is not isolated to Vascular Surgery, a similar problem has been demonstrated by a European survey in emergency surgery which demonstrated only 1.2% of clinicians routinely perform frailty screening despite 98% agreeing frailty influences outcomes. Among the reasons cited for this discrepancy were a lack of knowledge on frailty assessment, lack of training and a lack of evidence supporting a single best frailty tool.[5] Perhaps the downside to frailty gaining important visibility, in the absence of a gold standard diagnostic tool, is the subsequent accumulation of disparate methods for assessing and diagnosing frailty. A recent review identified 42 separate frailty assessment tools used across 111 vascular surgery related studies, but with limited data on how these tools perform in clinical practice.[2] The heterogeneity in frailty tools has been labelled as 'immaturity' in this area of research, where a call has been made for direct tool comparisons to help identify if a superior tool exists so that we can better meet the expectations of the vascular population.[6, 7]

Identification of frailty early in the perioperative pathway enables risk stratification, joint decision making and, with the support of appropriate specialist input, syndrome modification.[8] Early evidence confirms the identification and targeted treatment of frailty-related problems during acute vascular admissions, confers both cost and therapeutic benefit, as inferred from a reduced length of stay.[9] Yet these results need corroborated with larger and long-term studies across multiple centres. The well demonstrated heterogeneity in frailty assessment tools complicates the ability to do so by challenging comparison of services and data pooling. Identifying a preferred frailty tool will enable researchers, clinicians and managers to speak one language around frailty and act as a prelude to (inter)national harmonisation in frailty research and approaches to improving its management in clinical practice. With this in mind, it is important to identify methods for assessing frailty which lend themselves to practical application in busy, time-pressured, clinical services. Our previous research demonstrates an evidence gap around the ability to identify a preferred approach to frailty assessment in the vascular surgical context.[2] Limitations of studies to date, include potential biases from retrospective design, poor generalizability to the UK NHS, lack of head to head comparisons of tools and limited assessment of properties such as feasibility and acceptability.

The ideal study design would include a real world, unselected cohort and prospectively compare differing methods for frailty assessment. The Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study is designed to speak to this gap in the evidence using five frailty assessments that

have been carefully selected after reviewing format, relevance, anticipated ease of use and, where possible, are recommended by the Healthcare Improvement Scotland.

Objectives

The primary aim will be to assess the feasibility of implementing routine frailty assessments into an urgent-referral vascular outpatient clinic setting ('Vascular Hot Clinic'). Secondary objectives are to assess and compare the variability and prognostic value of selected frailty assessments.

Trial design

The FAVOUR study (IRAS ID 322086, NHS R&I reference UGN23CE014/REC reference 23/PR/0062) is a single-centre, non-randomised, observational cohort study of feasibility which will be conducted and reported in line with the guidance presented in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[10]

Methods and analysis

Study setting

This study will take place during a Vascular 'Hot' Clinic at the 'hub' Queen Elizabeth University Hospital (QEUH), Scotland. This is a consultant-led outpatient clinic responsible for delivering urgent vascular care for a population of approximately 2 million patients in NHS Greater Glasgow & Clyde and other 'spoke' sites including: NHS Forth Valley and part of NHS Highlands. Referrals are received from primary care physicians, community podiatrists and secondary care teams. Referrals are triaged within 24 hours of receipt by a consultant vascular surgeon, and if medically appropriate, patients are appointed to the next available appointment (same day to within 1 week). The ethos of the clinic is to provide urgent care for patients with suspected vascular pathology which requires prompt, but not immediate, medical assessment. This clinic does not provide a vascular access service which is instead offered through a separate renal transplant service.

Three clinics are held weekly with a capacity of up to ten patients per clinic. The clinics are also served by multidisciplinary team members, including vascular nurse specialists, podiatrists and clinical scientists who provide a dedicated duplex service.

Population

Participants must provide written informed consent prior to study participation (appendix 1). All referrals to vascular hot clinic are eligible for inclusion, preferentially recruiting new referrals. As frailty is related to age, but does not directly correlate with it, no age cut-off has been defined.[3, 11] As this is primarily a study of feasibility, patients will not be excluded/included based on presenting symptom or diagnosed pathology.

A proxy (relative/friend/carer), if present, will also be invited to participate and assist with frailty assessments of the patients, where suitable. The participation of the proxy is dependent on the patient providing written consent agreeing to their participation, as well as the proxy being eligible to participate, according to the same inclusion/exclusion criteria set out for patients below.

The lead researcher (SW) is a medical clinician and will assess prospective participants' capacity to consent to study participation on a case-by-case basis.

Inclusion criteria:

- Adults (aged 18 years or older)
- Attending Vascular Hot Clinic

Exclusion criteria:

- Lacking capacity to provide informed consent, as defined in the Mental Capacity Act, 2005.
- Parent clinical team feel frailty assessment not suitable
- Non-English speaker without qualified translator present
- Prisoners

Intervention

Five frailty assessment techniques will be compared: Rockwood 9-item Clinical Frailty Scale (CFS)[12], 11-item Modified Frailty Index (11-mFI)[13], Frailty non-Disabled Questionnaire (FiND)[14], Healthcare Improvement Scotland (HIS) 'Think Frailty' FRAIL assessment tool[15] and Initial Clinical Evaluation (ICE)[16], Table 1. As frailty assessment is recommended, there will be no control, rather differing tools will be compared to one another. The patient, and proxy where applicable, will complete CFS and FiND self-assessment. The clinician will complete CFS, HIS FRAIL and ICE assessment. The researcher will complete the mFI-11 assessment.

These tools were selected as most likely to be suited to the acute clinic context, after reviewing their content, format, ease of use, training requirements and anticipated time required to complete. This study deliberately selected tools with an emphasis on brevity while incorporating tools that are constructed based on differing theories of frailty and, where possible, are recommended by Scottish healthcare governing body, Healthcare Improvement Scotland. Within vascular surgery, the CFS and mFI-11 are the most commonly used tools; demonstrating international familiarity.[2] By continuing their use, the research impact of this study is enhanced. A primary criterion was that the selected tools should not require additional equipment, external training or have copyright restrictions. This was to ensure ease of implementation at scale, both in the UK NHS and other healthcare settings. Appendix 2-4 display the case report forms (CRFs) with various frailty assessment to be completed by patient/proxy, clinician and researcher.

Participation in this study does not preclude any aspect of concomitant care and/or intervention for patients. To ensure routine care provided by this service remains unaffected, clinicians will perform frailty assessments at the conclusion of each clinic, minimising possible biases in assessment and care provision.

Table 1. Selected frailty assessment tool summaries

CFS	**Definition:** The CFS is an ordinal, hierarchical 9-item person-assessed scale where patients score more highly if more frail. The scale scores run between 1 ('Very Fit') and 9 ('Terminally Ill') with each score having a picture and succinct written definitions This tool is recommended for use in clinical practice by Healthcare Improvement Scotland (HIS). **Personnel:** Vascular surgeon, patient and proxy if present will complete. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, another investigator will score the patient instead. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded. **Training requirement:** While not necessary, there is a short online module available to develop understanding in how the CSF is applied. To ensure internal rigour, clinician's contributing to this study will be requested to complete this training. **Duration**: It is expected this tool will take < 1 minute for clinicians once they are familiar with the tool. For patient's or proxy's completing the tool, it is expected this will take 5 minutes. **Application:** A copy of the CFS chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by one of the research team and asked to score included patients. For patients/proxy's a modified CFS chart will be displayed at the end of their clinic

	appointment. The patient/proxy will be asked to read each the definition for each score (1-8) before selecting the one they feel most accurately describes them. To reduce the risk of bias, the title and image for each score will be hidden from patient/proxy, leaving only the text description. **Modifications for study:** A CFS score of 9 describes a terminally ill patient, regardless of frailty status. As this is not relevant to this trial, and to reduce the risk of participants becoming upset, this score will not be considered by this trial and therefore not displayed to the participant.
mFI-11	**Definition:** This frailty index assessment is based on the frailty theory of cumulative deficits.[17] Healthcare records are accessed to determine the presence, or absence, of 11 variables across multiple domains (Non-independent function status, cognitive impairment and the following co-morbidities: congestive cardiac failure, myocardial infarction, previous percutaneous coronary intervention/cardiac surgery or angina, hypertension, diabetes mellitus, severe chronic obstructive pulmonary disease/active pneumonia, peripheral arterial disease, stroke/transient ischaemic attack without residual neurological deficit or with deficit). Each variable is scored 1 point when present with the end score divided by the total number of variables (11), giving a score between 0 – 1. The greater the value, the greater the risk of frailty. **Personnel:** A member of the research team will complete this assessment. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, will be recorded **Training requirement:** No training required for application. **Duration**: This tool has been piloted and found to take < 5 minutes per participant to derive from electronic health record. **Application:** This is a frailty index which is calculated by extracting relevant data through accessing national health service (NHS) electronic records. **Modifications for study:** Nil.
FiND	**Definition:** This is a 5-item self-assessment questionnaire. The first two questions relate to disability while the remaining three relate to frailty. Patients reporting one or more of the three frailty symptoms, in the absence of disability, are defined as frail. The scale's design reflects principles of the Fried frailty phenotype which defines frailty as the presence of three or more of the following energy-negative components: unintentional weight loss ('shrinking'), poor grip strength, exhaustion, slowness and low physical activity levels.[18] This questionnaire is recommended for use by Healthcare Improvement Scotland. The original questionnaire uses metric measurements of distance and weight, an imperial conversion will be added to relevant parts of the questionnaire to assist with patient comprehension. **Personnel:** The patient, and proxy if present, will be completing the questionnaire themselves. **Training requirement:** No training required for application. **Duration**: The questionnaire takes 2 minutes to complete. **Application:** A copy of the FiND will be displayed to the patient/proxy at the end of their clinic. They will be asked to read each of the 5-items closely and select the option that most accurately describes their situation (scoring either 0 or 1 per point). **Modifications for study**: Nil.

HIS 'Think Frailty' FRAIL assessment	**Definition:** This is a five-item frailty screening tool which has been developed by HIS and is currently recommended to be used in all unscheduled older adult admissions. The format is based on the theory of cumulative deficits across multiple domains (function, cognition, social). It's selection, in part is due to the novel aspect of this tool not considering co-morbidity as part of the assessment. **Personnel:** The consultant leading the clinic will be asked to complete the HIS FRAIL assessment. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: Completion of the HIS tool takes < two minutes. **Application:** A copy of the HIS FRAIL chart will be available in the outpatient department. At the end of clinic, the consultant will be approached by the chief investigators and asked to score included patients. **Modifications for study:** Nil.
ICE	**Definition:** Also known as the 'end of bed test'. Clinicians will report a subjective and binary assessment of the patient; 'frail' or 'non-frail'. **Personnel:** The consultant leading the clinic will be asked to provide an ICE. In the unlikely event where the surgeon is unwilling or unable to provide the frailty assessment score for the patient, a clinical member of the research team will score the patient instead. Non-completion of frailty assessment by surgeon will be recorded. **Training requirement:** No training required for application. **Duration**: This assessment takes part as routine practice during a clinical interaction between clinician and patient. No additional time is required. **Application:** The consultants will be approached at the end of the clinic and asked to provide their subjective opinion (ICE) on patient's frailty status to the chief investigator. This assessment will be performed first to minimise bias in clinician responses from completing alternate assessments prior. **Modifications for study:** Nil.

Primary aim

The primary aim of this study is to assess the feasibility of implementing routine frailty assessment in a vascular clinic setting. For this, the following data will be collected: number of patients attending hot clinic, number eligible for inclusion, number of eligible patients approached for recruitment, number of patients recruited, time taken to complete assessments, number and nature of assessments with non-completion, reasons for non-completion and if assistance was required to complete the tool. These parameters are clinically relevant as they will allow valid and reproducible calculations of the proportion of eligible patients recruited and time taken to complete assessments which will enable clinicians to consider the feasibility and suitability of implementing routine frailty assessment in a controlled clinical environment, encouraging uptake of current guidance.

Secondary outcomes

The secondary objectives pertain to assessing the prognostic value of selected frailty assessment tools and their value over standard clinical demographic information. All patients will be electronically followed-up at 30-days and 1-year from recruitment, collecting data on home time[19] (defined by the number of full days the patient spends not as an inpatient) and mortality. An additional electronic follow-up will be applied to patients who undergo surgical or endovascular intervention, at 30-day and 1-year post-operatively. For this, the following data will be collected: surgical procedure, mortality, post-operative complications (according to the Clavien-Dindo Classification)[20], length of hospital stay (full days), readmission rates (to any speciality), non-home discharge, home time, discharge with a higher level of social care requirements and amputation free survival for patients with end stage peripheral arterial disease of the lower limbs. As current practice for reporting post-operative outcomes is to report outcomes according to the number of days that has passed since the index intervention, introducing additional 30-day and 1-year follow up periods for patients who undergo interventions (compared to those who do not) allows the collection of clinically relevant data without introducing bias in the mode of data collection. Despite the vascular network declaring a national interest in frailty,[3] there is a lack of evidence directly comparing the prognostic validity and variability of frailty assessment tools. The data from this study will help guide standardisation in the approach to frailty assessment in clinical practice.

Baseline assessments

Baseline characteristics will be collected, including patient demographics, social/functional circumstances, polypharmacy and relevant comorbidities to calculate a Charlson comorbidity Index.[21]

Participant timeline

Prospective participants will be identified on the day by reviewing the electronic health care records of patients due to attend a Vascular 'hot' clinic and applying the inclusion and exclusion criteria. Due to the emergent nature of the referrals to the vascular hot clinic, patients (and their proxy, if present) will be approached, recruited and complete frailty assessments on the day of attending their clinic appointment, Figure 1. No ongoing participation is required, follow up will be through accessing electronic health care records.

Sample size

As this is primarily a study of feasibility, a power calculation has not been performed. The vascular hot clinic offers up to 30 appointments weekly across three clinics. Where possible, all eligible patients will be approached for participation with an emphasis on targeting 'new referrals'.

Recruitment

Patient recruitment began in March 2023. Prospective patients will be approached for study participation by the research team upon registering for their clinic appointment. If expressing interest, they will receive a participant information sheet. Patients are required to complete their clinic appointments (where their medical care will remain unaffected by (non-)participation in this study) prior to participating in the study. The prospective participant will be re-approached at the conclusion of their clinic appointment to confirm willingness to participate and provide written consent. Thereafter, the frailty assessments are completed by the patient. Where a patient attends with a suitable proxy, they will be approached in an identical fashion provided the patient provides written consent for this. Where a patient is eligible for participation, but a proxy is ineligible/declines participation, the patient will be recruited without proxy contribution. Where the patient is not eligible for participation, the proxy will not be invited to participate on their behalf. Staggering the consent process by approaching the patient either side of their clinic appointment maximises the time for the patient to consider participating. It is recognised that ideally patients should have a period of at least 24 hours with a patient information sheet prior to expressing a wish to participate in a study however, due to the emergent nature of the clinic and the presenting pathology, this will not be possible. Clinician and research team complete frailty assessments of recruited patients at the end of the clinic to minimising clinic disruption.

Data collection

Data will be collected in person and through review of electronic health care records. On the day of recruitment, frailty assessments scores will be performed in the clinic and collected by patient/proxy, clinician and researcher on relevant paper based CRFs (appendix 2-4). On the same day, the research team will review electronic health care records of recruited patients and extract data for baseline assessments to an electronic data extraction template. All electronic follow up will be extracted to the same electronic data extraction template.

Data management

Data management, processing and handling will be conducted in line with General Data Protection Regulation principles (EU 2016/679). The research team will allocate pseudonymised participant identification numbers then remove and securely destroy personal identifiable information before transcribing data from the paper based CRFs to an electronic data extraction template for storage. Transcribed data will undergo quality checking by a second member of the research team. Data for baseline demographics and electronic follow up will be extracted and stored on Excel Version 2304. SW will be primarily responsible for storing study dataset with sharing through secure means with authors for the purpose of analysis, write-up only. Data will not be shared with third parties.

Statistical methods

Baseline demographics and feasibility parameters will be described using descriptive statistics, including, percentages, ranges, means and standard deviations or medians and interquartile ranges. The prognostic value of frailty assessment tools on binary outcome variables will be displayed through calculating receiver operating characteristic (ROC) curves. Frailty tool comparisons will be performed by comparing the area under the ROC curve. The CFS is endorsed by healthcare policy throughout the UK and will be used as the gold standard for comparisons. Continuous

outcome variables will be analysed using Spearman's rank correlation coefficient. Levels of inter-user agreement between patient and clinician assessments will be calculated with a percentage agreement and Cohen's Kappa coefficient. Subgroup analysis will be performed to compare outcomes for patients undergoing surgical treatment, endovascular treatment and those who do not undergo intervention. Patients lost to follow up, or with incomplete data, will be excluded. In addition to accuracy and reliability analyses, we will create models to estimate the association of frailty, measured using different approaches, with our outcomes of interest. The primary analysis will be adjusted for age and sex.

Data monitoring

This observational cohort study will not be subject to a data monitoring or trial management committee. The study may be subject to study monitoring visits and subsequent monitoring reports which will be conducted and reviewed in accordance with a study-specific monitoring plan devised by the study sponsor. The sponsor audits a randomly selected 10% of studies conducted under the Research Governance Framework per annum, as well as those identified using a risk assessment tool as specifically requiring assessment.

Harm

There are no adverse events anticipated to occur secondary to the intervention which falls in line with national guidelines. For this reason, no ancillary and post-trial care has been designed.

Patient and public involvement

A group of five non-medically trained adult volunteers (aged 25 – 65 years) contributed toward the study design through piloting both questionnaires (CFS and FiND) and all took less than 5 minutes to complete both questionnaires, without requiring assistance. There was no further involvement in the development of this study by patients or the public. Patients will not be contacted directly with the results of this study however contact details for the PI have been supplied to participants so that they can request information on study progress/results as they become available.

Ethics and dissemination

Research ethics approval

This study is sponsored by NHS Greater Glasgow & Clyde (Research & Innovation reference UGN23CE014) and has received a favourable opinion by the London – Riverside Research and Ethics Committee (23/PR/0062). This study will be performed according to the Research Governance Framework for Health and Community Care (Second edition, 2006) and WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI Ethical Principles for Medical Research Involving Human Subjects 1964 (as amended).

Amendments

Any amendments to the protocol will be submitted to the IRAS Amendment Portal to the responsible ethics committee and/or NHS GG&C Research & Innovation for review. Changes will only be implemented following the approval of proposed amendments by the original reviewing Research and Ethics Committee and Greater Glasgow & Clyde Health Board Research and Innovation office. All protocol amendments will be appropriately stored, cited and explained in future manuscripts.

Consent

The principal investigatory (PI) (SW) is responsible for obtaining informed written consent from participants. For this, participant information sheets (PIS) will be provided to all prospective participants as well as conducting an informed discussion detailing study design, confidentiality and rights to withdraw. The contact details for the PI are supplied in the PIS which participants will be pointed to and they will be encouraged to make contact with any questions, concerns or if wishing to withdraw. A copy of the consent form will also be provided for participants to keep.

Confidentiality

Participant confidentiality will be upheld through participant pseudonymisation during data collection. To endorse data minimisation, only data relevant for the described outcome measures will be collected and stored. Consent forms and pseudonymised paper based CRFs and will be stored separately in locked filing cabinets, accessible only to the research personnel. Electronic data will be extracted and stored on Excel Version 2304 with personal and research generated data stored on separate databases on different servers. Research data storage will comply with the University of Glasgow's data retention policy.

Access to data

Only members of the core research team will have access to the final dataset with the exception of review by sponsors to ensure proper study conduct. Data will not be shared with third parties for analysis or write-up.

Dissemination

Study results will be disseminated through publication in peer-reviewed journals and presentation to relevant scientific conferences, targeting those with a focus on geriatric medicine and vascular surgery, in particular the Vascular Societies' Annual Scientific Meeting to enhance visibility of the results and assist with knowledge translation.

Discussion

Frailty-centric adaptations to established clinical service models are crucial as the anticipated demographic changes associated with an ageing population means it is likely frailty, with its inherent clinical and financial implications, will become increasingly commonplace.[1] An abundance of frailty assessment tools have confirmed the prognostic value of frailty, hence guidelines advocating the importance of its recognition in clinical practice.[3] However, a relative lack of evidence in measurements of feasibility and suitability of frailty assessment in clinical practice, or head to head

comparisons of tools, has contributed toward a delay in uptake of guidelines.[4] For this reason, the prospective assessment of frailty in a reproducible and controlled vascular outpatient department (OPD) environment has been identified as a key area of research interest, which the study presented in this protocol targets.[1, 4]

From a previous systematic review we identify only four relevant studies prospectively assessing frailty in vascular surgery OPD.[2] The first compared the correlation between clinician-assessed CFS scores and patient reported outcome measures of frailty (including FiND and patient-reported outcome measurement information systems v1.2 and v2.0) and its effect on 1-year mortality.[22] Another examined the effect of frailty as assessed by the Groningen Frailty Indicator on postoperative delirium.[23] One study used the Fried frailty index to compare the effect of frailty status on gait parameters in patients with peripheral arterial disease compared to control[24], while another examined the association of grip strength as a marker of frailty with measures of sarcopenia and co-morbidity.[25] However, the research impact of these data are limited by a paucity in feasibility measurements and direct comparison between selected tools.

The study presented in this protocol builds on current evidence through including and comparing a greater number of commonly used frailty assessment tools that have been specifically selected for their format (assessing frailty according to different theories of frailty), relevance (based on clinician familiarity and compliance with guidance from local healthcare governance) and anticipated rapid time to complete, making them suitable for application in busy OPDs. By incorporating measurements of prognostic value, it is anticipated data generated by this study will bear direct clinical relevance and will contribute toward the generation of evidence based recommendations for an optimum standardised, and reproducible approach to diagnosing frailty in an outpatient setting.

The primary aim of this study is novel within vascular surgery. The major strength in this study is the prospective and longitudinal design. As surgeons increasingly aim to identify patients who would sooner benefit from a conservative approach, the short- and long-term follow-up for all patients managed operatively or not, stratified by frailty status, is of clinical relevance. Limitations to this study are acknowledged, including the single-centre design and the exclusion of patients who lack capacity (e.g., dementia) which may impact generalisability of results.

Study status

Participant recruitment concluded in July 2023, data collection is ongoing.

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Author contributions

TQ, was responsible for study conception. *TQ, DO* and *SW* formulated the study methodology, design and are responsible for obtaining ethical approval. *KH* and *JB* helped with implementation. Statistical expertise appropriate for the proposed study methodology was provided by *TQ*. *SW* is responsible for participant recruitment, data collection and analysis. All authors contributed toward the refinement of the study protocol and approve the final manuscript.

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Competing interests statement

Authors declare no conflict of interest or further financial disclosures.

Figure 1. Summary of patient timeline and study methodology.

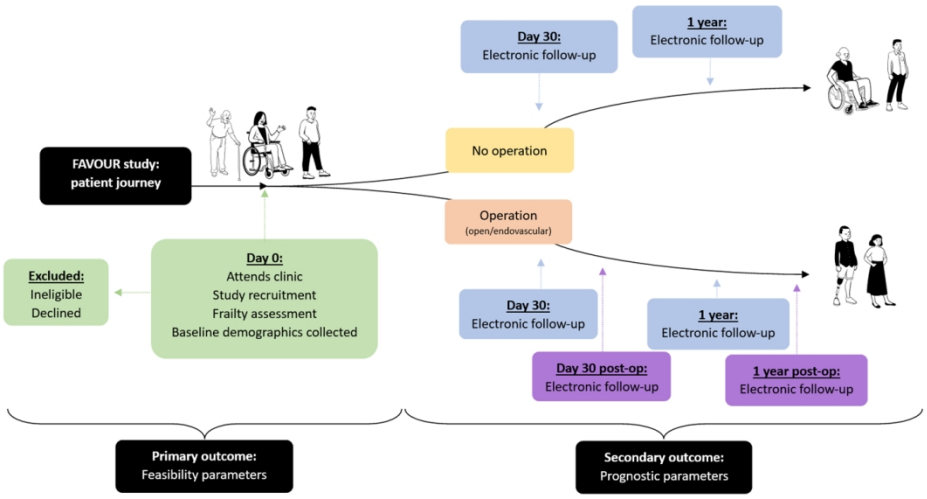

Figure 1. Timeline summarising patient timeline and study methodology

Figure 1 - Summary of patient timeline and study methodology

1044x580mm (38 x 38 DPI)

Appendix 1 – Participant consent form

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

CIRCULATION FOUNDATION The Vascular Charity

NHS Greater Glasgow and Clyde

Participant Identification Number for this trial: _____

Title of Project: **Frailty Assessment in Vascular OUtpatients Review (FAVOUR Trial) – comparing feasibility and prognostic value of commonly used assessments.**

Name of Researcher(s): Miss Silje Welsh

CONSENT FORM (Patient)

	Please initial box
1. I confirm that I have read and understood the Participant Information Sheet (patient) version 1.3 dated 13/02/2023.	☐
2. I have had the opportunity to think about the information and ask questions and understand the answers I have been given.	☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time during data collection, without giving any reason, without my legal rights being affected. Data collection is expected to conclude 13 months after my recruitment to this study.	☐
4. I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	☐
5. I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐
6. I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project only and securely destroyed within 3 months of the end of this study.	☐
7. I understand that if I withdraw from the study, I will be asked to clarify how I would like the data collected from me up to that point to be handled. There will be the option to retain it for the remainder of the study, or for it to be securely destroyed.	☐
8. If relevant, I agree to a proxy (friend/relative/care-giver) contributing towards my participation in this study. Their participation will require them to complete a separate consent form. I also understand that a proxy's decision to participate, or not, will in no way affect my participation in this study.	☐
9. I agree that the study team can access my electronic health record for the purposes of the study.	☐
10. I understand that electronic follow-up will occur at 30-days and 1-year after my recruitment to this study. Further, I understand that if I undergo surgical treatment, an additional follow-up will occur at 30-days and 1-year after the first treatment/surgery.	☐

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11. I agree to the dissemination of study results through publication in scientific journals and presentation at relevant conferences. For the purposes of dissemination, I understand that my data will be anonymised. ☐

12. I understand that the results from this study will not be communicated directly to me. However, I have received the contact details for lead researcher (in the Participant Information Sheet), whom I can contact should I want to enquire about progress of the study/study results. ☐

13. I agree to take part in the study. ☐

Name of participant	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher; 1 copy for case notes)

To be completed if participant wishes to withdraw, initial relevant boxes:

14. I confirm that the patient expresses a wish to withdraw from the study. ☐

15. On withdrawal, the patient wishes the following regarding their personal and research data:

(a) All data collected up until the point of withdrawal is to be deleted and not used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

OR

(b) All data collected up until the point of withdrawal can be kept by the researchers and used in the study results. No further data (i.e. at any remaining follow-up points) may be collected. ☐

Signed by Principal Investigator on behalf of the patient

Principle Investigator	Date	Signature

Appendix 2 – Case report Form (Patient)

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____	Study participant number: _____	Patient ☐	Sticker/CHI NO: *(Please tear off before transfer)*

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Please take time and read through each description before selecting the option which most accurately describes you. The responses to this questionnaire will in no way impact the medical care you have received today or may receive in the future.

	CFS – Questions about activity and function. Which one of the following is most like you:	**Select one option**
1	People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	These people often have **more evident slowing**, and need help in **high order activities** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
X	**Unsure/unable to answer**	

TO BE COMPLETED BY RESEARCH TEAM

Time taken to complete _____ **seconds**

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

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Version 1.1

Date 16/12/2022

PLEASE TURN OVER

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

University of Glasgow | College of Medical, Veterinary & Life Sciences

Date of clinic_____

Study participant number: _____

Patient ☐

Sticker/CHI NO:

(Please tear off before posting)

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

FiND – Questions about activity and function		
Questions	**Answers**	**Select option**
A. Have you any difficulties walking 400 metres (¼ mile)?	No or some difficulties	
	A lot of difficulties or unable	
B. Have you any difficulties at climbing up a flight of stairs?	No or some difficulties	
	A lot of difficulties or unable	
C. During the last year, have you involuntarily lost more than 4.5 kg (10 lbs)?	No	
	Yes	
D. How often in the last week did you feel that everything you did was an effort or that you could not get going?	Twice or less	
	Three or more	
E. Which is your level of physical activity?	At least 2 – 4 hours per week	
	None or mainly sedentary	

TO BE COMPLETED BY RESEARCH TEAM

A+B ≥ 1: Y☐ N☐

C+D+E ≥ 1: Y☐ N☐

A+B+C+D+E = 0: Y☐ N☐

Time taken to complete _____ seconds

Assistance required: Y☐ N☐ *If yes:* **Verbal assistance**☐ **Hands on assistance** ☐

Non-completion: Y☐ N☐ *If yes:* **Time limitation**☐ **Task comprehension**☐ **Other**☐, *please specify* _____

Version 1.1
Date 16/12/2022

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Appendix 3 – Case report form (Clinician)

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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator □

Surgeon □

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q1. Initial Clinical Evaluation	**YES**	**NO**
Is this patient frail?		

Time taken: _____ **seconds**

Q2. Clinical Frailty Scale (Please select the most appropriate description)		**Tick**
1	**Very fit -** People who are robust, active, energetic and motivated. These people commonly exercise regularly. Among the fittest for age.	
2	**Well -** People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.	
3	**Managing well -** People whose **medical problems are well controlled** but are **not regularly active** beyond routine walking.	
4	**Vulnerable -** While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.	
5	**Mildly frail -** These people often have **more evident slowing**, and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
6	**Moderately frail -** People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.	
7	**Severely frail - Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).	
8	**Very severely frail -** Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.	
9	**Terminally ill** Approaching end of life. This applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail**.	
X	**X Unable to score**	

Time taken: _____ **seconds**

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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Assessor's initials: _____

Principal Investigator ☐

Surgeon ☐

ABOVE THIS LINE TO BE COMPLETED BY RESEARCH TEAM

Q3. HIS FRAIL Assessment Tool		YES	NO	UNSURE
F	Functional impairment (new or worsening) e.g. difficulty with self-care			
R	Resident in a care-home?			
A	Altered mental state such as confusion or dementia (use the 4AT)			
I	Immobility/Instability. New decline in mobility, difficulty mobilising without help or fall leading up to admission			
L	Living at home with daily support (homecare; one or more visits per day)			

Time taken: _____ seconds

THIS SECTION IS TO BE COMPLETED BY THE RESEARCHER

For Q1. ICE
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

For Q2. Clinical Frailty Scale
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

For Q3. HIS FRAIL Assessment
If non-completion, why?
- Time restriction ☐
- Patient not suitable ☐
- Forgot ☐
- Other ☐

Please specify:

_____

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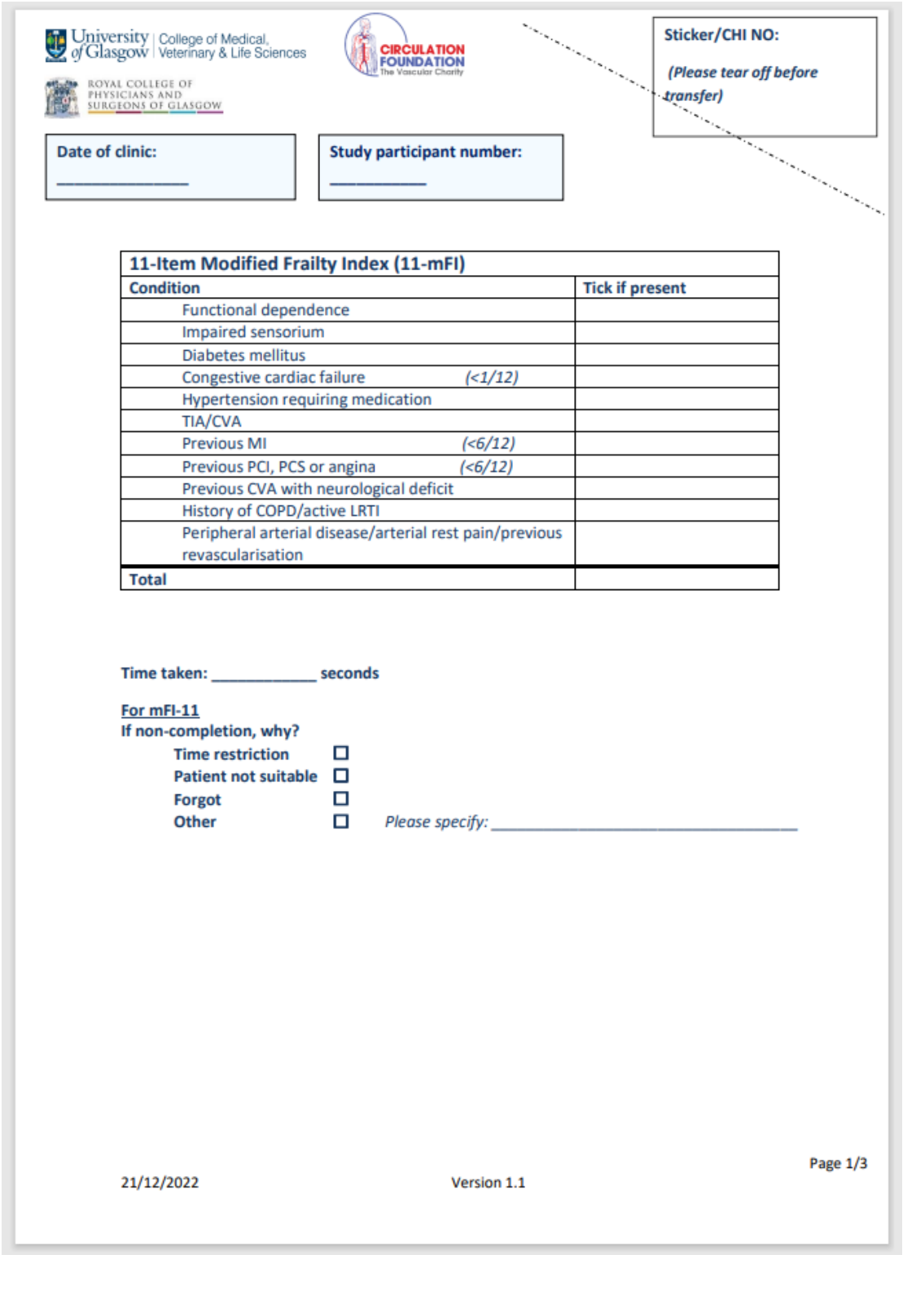
Appendix 4 – Case report form (researcher)



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CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic: _____

Study participant number: _____

11-Item Modified Frailty Index (11-mFI)

Condition		Tick if present
Functional dependence		
Impaired sensorium		
Diabetes mellitus		
Congestive cardiac failure	*(<1/12)*	
Hypertension requiring medication		
TIA/CVA		
Previous MI	*(<6/12)*	
Previous PCI, PCS or angina	*(<6/12)*	
Previous CVA with neurological deficit		
History of COPD/active LRTI		
Peripheral arterial disease/arterial rest pain/previous revascularisation		
Total		

Time taken: _____ **seconds**

For mFI-11

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* _____

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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number: _____

Charslon Comorbidity Index		
Variable	**Score**	**Points**
Age (years)		
< 50	0	
50 - 59	1	
60 – 69	2	
70 – 79	3	
≥ 80	4	
Myocardial infarction		
No	0	
Yes	1	
Congestive cardiac failure		
Exertional/paroxysmal/nocturnal dyspnoea responding to treatment		
No	0	
Yes	1	
Peripheral vascular disease		
Claudicant/rest pain/prev bypass/untreated AAA (>6cm)	0	
No	1	
Yes		
CVA/TIA		
With minor/no neurological sequelae		
No	0	
Yes	1	
Dementia		
No	0	
Yes	1	
COPD		
No	0	
Yes	1	
Connective tissue disease		
No	0	
Yes	1	
Peptic ulcer disease		
Any history of treatment		
No	0	
Yes	1	
Liver disease		
None	0	
Mild *(chronic hepatitis/cirrhosis without complication)*	1	
Mod/Severe *(Cirrhosis, portal hypertension +/- bleeding varices)*	3	

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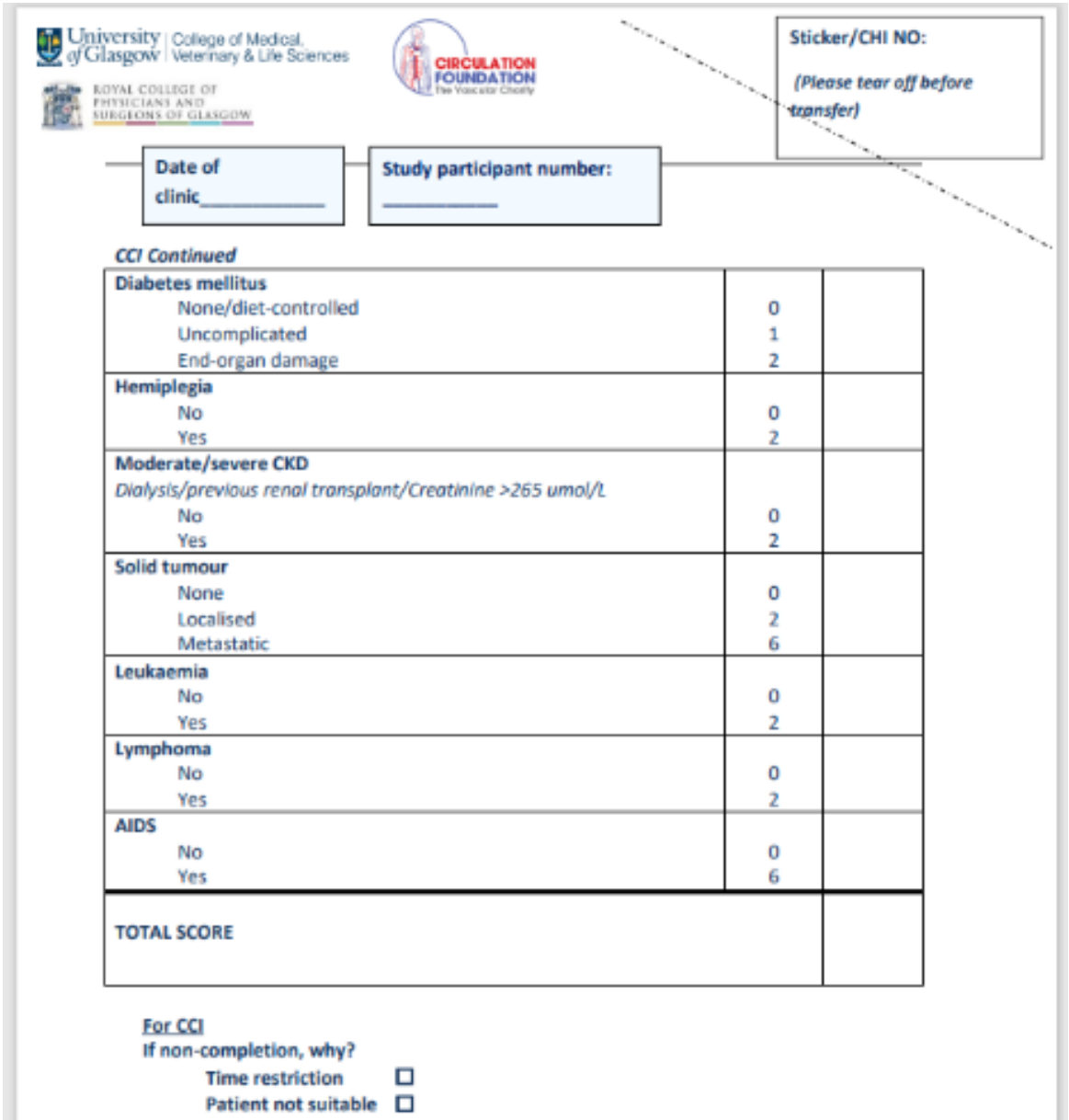

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ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

CIRCULATION FOUNDATION The Vascular Charity

Sticker/CHI NO:

(Please tear off before transfer)

Date of clinic_____

Study participant number:

_____

CCI Continued

Diabetes mellitus		
None/diet-controlled	0	
Uncomplicated	1	
End-organ damage	2	
Hemiplegia		
No	0	
Yes	2	
Moderate/severe CKD		
Dialysis/previous renal transplant/Creatinine >265 umol/L		
No	0	
Yes	2	
Solid tumour		
None	0	
Localised	2	
Metastatic	6	
Leukaemia		
No	0	
Yes	2	
Lymphoma		
No	0	
Yes	2	
AIDS		
No	0	
Yes	6	
TOTAL SCORE		

For CCI

If non-completion, why?

- **Time restriction** ☐
- **Patient not suitable** ☐
- **Forgot** ☐
- **Other** ☐ *Please specify:* _____

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