

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Frailty Assessment in Vascular Outpatients Review (FAVOUR) PROTOCOL – single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools.
AUTHORS	Welsh, Silje; Hussey, Keith; Brittenden, Julie; Orr, Douglas J; Quinn, Terry

VERSION 1 – REVIEW

REVIEWER	Beilby, Justin National Health and Medical Research Council of Australia Centre of Research Excellence Frailty Trans-disciplinary Research To Achieve Healthy Ageing, Torrens University
REVIEW RETURNED	27-Sep-2023

GENERAL COMMENTS	<p>The protocol paper is well argued and logically presented. I have a couple of clarification questions:</p> <ul style="list-style-type: none"> + the authors talk about all consultant vascular surgeons acting as "fair" representation of stakeholders - this wide ranging statement needs more justification. + in the methods I was confused if all enrolled patients would use all tools or self select. This needs clarification + recruitment began in March 2023. It ended in July and is there an estimate/target for recruitment and data collection. + the primary outcomes make sense but in essence the secondary outcomes may also be insightful. The authors talk about "reproducible approach to diagnosing frailty in an outpatient setting" - could the authors expand to what that may mean to actual clinical care on a day to day basis.
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REVIEWER	Kennard, Alice Canberra Hospital
REVIEW RETURNED	09-Oct-2023

GENERAL COMMENTS	<p>This is a novel area of research interest with clinical relevance. There are a few clarifications required to improve readability and comprehension.</p> <p>1. The primary aim as defined by the Abstract is to explore the feasibility and acceptability (line 6) of implementing routine frailty assessment in the outpatient department. It appears feasibility will be assessed based on uptake. How will acceptability be assessed? And acceptability by whom? Will the participating patients and their caregivers be asked about the acceptability of participating in frailty screening? Will refusal to participate in assessment (ie poor recruitment) be interpreted as poor acceptability to consumers?</p>
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	<p>2. The term "capax" is used in line 2 of methods section within the abstract. Presumably this is meant to mean "adults with capacity" but needs some clarification as this is an unusual term. How will capacity be assessed? How will lack of capacity (which is an exclusion criteria) be defined? This component requires clarification.</p> <p>3. Abstract: please provide full names for CFS, FiND, HIS FRail and ICE within Abstract.</p> <p>4. Introduction; background and rationale. Please provide a definition of frailty.</p> <p>5. Introduction; line 17; spelling error: time-pressured should be hyphenated.</p> <p>6. Objectives: in this section aims seem to have been altered slightly to focus on feasibility, with no mention of acceptability. See comments earlier regarding acceptability. Reliability would imply comparison of a novel frailty assessment against a gold standard. What will be the gold standard frailty assessment to answer this question?</p> <p>7. Does the vascular Hot clinic cater to patients with ESKD requiring vascular access? Will this patient cohort be eligible for participation? If so, perhaps consider inclusion of other patient outcomes including vascular access use at first dialysis/failure to mature and progression of CKD to dialysis requirement. How will admissions related to dialysis treatments be distinguished from other hospital admissions? If this patient population is not included, please state explicitly and provide rationale.</p> <p>8. Exclusion criteria. Please provide further detail regarding the following: 1. How will lack of capacity to provide informed consent be assessed, 2. Why might the clinical team feel frailty assessment is not suitable? Would you envisage patients are precluded from frailty assessment if the clinical team feels them to be particularly robust, or because patients are overtly frail and actively dying/receiving palliative care? Please comment on how this selection bias might alter observed findings. 3. Please describe availability of translation services and what efforts will be made to offer culturally-safe research inclusion of participants with cultural and linguistic diversity. Please comment on how this exclusion criterion might influence external validity of study findings.</p> <p>9. Primary outcome. See comments earlier with respect to acceptability. This section either needs addition of how acceptability of frailty screening will be assessed from clinical staff perspective and participant/caregiver perspective, or acceptability term need to be clarified within the abstract.</p> <p>10. Secondary outcomes. The discussion notes that some patients might benefit sooner from a conservative approach. Perhaps consider including utilisation of palliative care services as a relevant secondary outcome. Why are patients who do not undergo surgical management not going to be followed-up for the outcomes described? Suggest justification for this methodological choice.</p> <p>11. Statistical methods. Frailty tools will be compared using ROC analysis but the manuscript does not define the gold standard comparator. Please define what the Gold Standard of frailty will be and how this will be assessed.</p>
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REVIEWER	Hurst, Christopher Newcastle University, Institute of Neuroscience
REVIEW RETURNED	19-Oct-2023

GENERAL COMMENTS	<p>Thank you to authors for giving me the opportunity to review this interesting manuscript. Please see below for some general comments.</p> <p>General comments</p> <p>The manuscript is well written, and the protocol is clear and well described.</p> <p>Please see below for some specific comments.</p> <p>Abstract</p> <ul style="list-style-type: none"> • In the introduction section of the abstract the primary aim is described as being 'feasibility and acceptability' However, this is the only mention of acceptability in the abstract (the method section of the abstract only talks about feasibility). Please clarify this – is this work feasibility and acceptability or just feasibility? • There are several abbreviations used in the abstract which are not explained – this could present a challenge to the non-specialist reader (the frailty measures and ROC are not explained). <p>Introduction</p> <ul style="list-style-type: none"> • Although the rationale and justification for the study is well illustrated in the introduction, it is not particularly well evidenced. I would like to see a little more evidence-based justification of the proposed work (which exists) to support the points that are made throughout the introduction. <p>Objectives</p> <ul style="list-style-type: none"> • As previous comment, no mention of acceptability in the objectives section. Should this be removed? <p>Primary outcome</p> <ul style="list-style-type: none"> • I think the first sentence of this section describes the primary aim of the study not the primary outcome. Please can this be reworded for clarity. The key outcomes are then well articulated in the remainder of the paragraph. <p>Secondary outcomes</p> <ul style="list-style-type: none"> • Inter-rater reliability (mentioned in the abstract), reliability (mentioned in the objectives section) and interuser variability (mentioned in the secondary outcomes paragraph) are not described here (apologies if I have missed this). I am not clear how / when reliability is being assessed and reliability of what? Please can this be clarified.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Prof. Justin Beilby, National Health and Medical Research Council of Australia Centre of Research Excellence Frailty Trans-disciplinary Research To Achieve Healthy Ageing, Torrens University Australia

Comments to the Author:

The protocol paper is well argued and logically presented. I have a couple of clarification questions:

+ the authors talk about all consultant vascular surgeons acting as "fair" representation of stakeholders - this wide ranging statement needs more justification. The first point in 'Strengths and limitations' has been amended in favour of describing the study setting as a typical example of how vascular surgery services work within the UK which better describes how the results from this study will be applicable to a large patient population.

+ in the methods I was confused if all enrolled patients would use all tools or self select. This needs clarification. For clarity, we have added a brief elaboration on who is to complete which tool in the 'Intervention' section. This falls in line with the summary that is provided in the abstract.

+ recruitment began in March 2023. It ended in July and is there an estimate/target for recruitment and data collection. As this study is primarily designed as an observational study of feasibility, there were no preceding power calculations to endorse a desired sample size. For this reason, a desired sample size has not been detailed in the protocol. The research team had anticipated a 100 patient recruitment which was exceeded when recruiting 150.

+ the primary outcomes make sense but in essence the secondary outcomes may also be insightful. The authors talk about "reproducible approach to diagnosing frailty in an outpatient setting" - could the authors expand to what that may mean to actual clinical care on a day to day basis. From the research team's ongoing, unpublished, qualitative work there is an appetite in Vascular services to institute frailty screening, but a limitation has been the large number of tools produced, with a lack of data on feasibility and utility. This study is specifically designed to speak to this evidence gap. We benefit from being part of a national network of Vascular Surgeons with a national interest in frailty and would hope that our data can form a standardised approach across the UK to its assessment in clinical practice. We include this explanation in the 'secondary outcomes' section.

Reviewer: 2

Dr. Alice Kennard, Canberra Hospital

Comments to the Author:

This is a novel area of research interest with clinical relevance.

There are a few clarifications required to improve readability and comprehension.

1. The primary aim as defined by the Abstract is to explore the feasibility and acceptability (line 6) of implementing routine frailty assessment in the outpatient department. It appears feasibility will be assessed based on uptake. How will acceptability be assessed? And acceptability by whom? Will the participating patients and their caregivers be asked about the acceptability of participating in frailty screening? Will refusal to participate in assessment (ie poor recruitment) be interpreted as poor acceptability to consumers? We thank the reviewer for highlighting the important distinction between feasibility and acceptability. While a poor recruitment rate may be considered a surrogate marker of acceptability, in the absence of authentic acceptability parameters being measured the word acceptability has been removed to avoid further confusion. Instead, recruitment rate will be discussed within the context of feasibility parameters.
2. The term "capax" is used in line 2 of methods section within the abstract. Presumably this is meant to mean "adults with capacity" but needs some clarification as this is an unusual term. How will capacity be assessed? How will lack of capacity (which is an exclusion criteria) be defined? This component requires clarification. Thank you for identifying this, non-abbreviated terminology has been added to the abstract. A lack of capacity definition has been added to the exclusion criteria.
3. Abstract: please provide full names for CFS, FiND, HIS FRAIL and ICE within Abstract. The abstract has been updated accordingly.
4. Introduction; background and rationale. Please provide a definition of frailty. A definition has been added.
5. Introduction; line 17; spelling error: time-pressured should be hyphenated. Grammatical correction made accordingly.
6. Objectives: in this section aims seem to have been altered slightly to focus on feasibility, with no mention of acceptability. See comments earlier regarding acceptability. Reliability would imply comparison of a novel frailty assessment against a gold standard. What will be the gold standard frailty assessment to answer this question? Acceptability term removed. See answer to point 11 re 'gold standard' assessment.
7. Does the vascular Hot clinic cater to patients with ESKD requiring vascular access? Will this patient cohort be eligible for participation? If so, perhaps consider inclusion of other patient outcomes including vascular access use at first dialysis/failure to mature and progression of CKD to dialysis requirement. How will admissions related to dialysis treatments be distinguished from other hospital

admissions? If this patient population is not included, please state explicitly and provide rationale. Patients with end stage kidney disease, with or without renal replacement therapy, are eligible for study participation as this is representative of the vascular population. However, the clinic within this vascular service is not designed to provide a vascular access service. Rather, this is overseen and delivered by the renal transplant service which operates independently in the same site. However, the renal/vascular access service also have an interest in frailty and so the data from this study may be of interest to this speciality. In patients who dialyse, where this is performed on an ambulatory/outpatient basis, this will not be considered an admission.

8. Exclusion criteria. Please provide further detail regarding the following: 1. How will lack of capacity to provide informed consent be assessed, The investigator is a clinician with experience in assessing capacity and each participant is assessed on a case by case basis. This is now detailed in 'Population' 2. Why might the clinical team feel frailty assessment is not suitable? Would you envisage patients are precluded from frailty assessment if the clinical team feels them to be particularly robust, or because patients are overtly frail and actively dying/receiving palliative care? Please comment on how this selection bias might alter observed findings. We can speculate as to the reasons why; some may include palliative patients. An accompanying qualitative study is being conducted examining stakeholders views on frailty and its assessment in vascular surgery, this study will explore this question in more detail. The open inclusion criteria to this study has been designed in a deliberate attempt to reduce the described type of selection bias. 'New referrals' to clinic are preferentially approached for study inclusion and once recruited, regardless of perceived frailty status (by clinician, researcher or patient's self-perception) frailty assessments are required. 3. Please describe availability of translation services and what efforts will be made to offer culturally-safe research inclusion of participants with cultural and linguistic diversity Please comment on how this exclusion criterion might influence external validity of study findings. All patients who are known to require a formal translation service (through medical history or referral letter) are offered in-person qualified translators to attend their clinic appointment. Patients who declined a qualified translator in favour of bringing a relative or personal friend were excluded due to inability to ensure rigour in the translation process. Of note, the Glasgow population is not as ethnically, and culturally diverse as other areas of the UK and so added consideration and care will be required in the future application of study results.

9. Primary outcome. See comments earlier with respect to acceptability. This section either needs addition of how acceptability of frailty screening will be assessed from clinical staff perspective and participant/caregiver perspective, or acceptability term need to be clarified within the abstract. This has been removed.

10. Secondary outcomes. The discussion notes that some patients might benefit sooner from a conservative approach. Perhaps consider including utilisation of palliative care services as a relevant secondary outcome. Why are patients who do not undergo surgical management not going to be followed-up for the outcomes described? Suggest justification for this methodological choice. We thank the reviewed for this interesting point regarding access to palliative care services for conservatively managed patients. While this is an area that would be of interest, the referral of patients from outpatient clinic to palliative care services is not an established pathway in this service and is done infrequently and variably by the consultant body overseeing this outpatient clinic. Due to these inconsistencies, this variable is not included. All patients will undergo 30-day and 1-year follow-up for home time and mortality. The introduction of additional parameters (i.e., post-operative complications, readmission rates, discharge destination and postoperative mortality) has been designed specifically to capture data that is reported as a standard for perioperative outcomes and is therefore only relevant to patients who proceed to surgical or endovascular treatment. Figure 1 has been included to clarify the follow-up process across the two arms (conservatively versus operatively managed patients).

11. Statistical methods. Frailty tools will be compared using ROC analysis but the manuscript does not define the gold standard comparator. Please define what the Gold Standard of frailty will be and how this will be assessed. In the absence of a universally agreed gold standard definition for frailty,

there is no gold standard frailty assessment tool. However, the Rockwood Clinical Frailty Scale is endorsed by healthcare policy across the UK and so this will be used as a comparator for the purpose of RoC analysis; this has been elaborated upon in the 'statistical methods' section.

Reviewer: 3

Dr. Christopher Hurst , Newcastle University

Comments to the Author:

Dear authors

Thank you to authors for giving me the opportunity to review this interesting manuscript. Please see below for some general comments.

General comments

The manuscript is well written, and the protocol is clear and well described.

Please see below for some specific comments.

Abstract

- In the introduction section of the abstract the primary aim is described as being 'feasibility and acceptability' However, this is the only mention of acceptability in the abstract (the method section of the abstract only talks about feasibility). Please clarify this – is this work feasibility and acceptability or just feasibility? In accordance with the valid points raised by previous reviewer as well, the term 'acceptability' has been removed from the protocol.
- There are several abbreviations used in the abstract which are not explained – this could present a challenge to the non-specialist reader (the frailty measures and ROC are not explained). The full, non-abbreviated, names have been included in the abstract which has been modified slightly to adhere to the word limit.

Introduction

- Although the rationale and justification for the study is well illustrated in the introduction, it is not particularly well evidenced. I would like to see a little more evidence-based justification of the proposed work (which exists) to support the points that are made throughout the introduction. The introduction has been expanded with more evidence justifying the rationale and purpose of this study.

Objectives

- As previous comment, no mention of acceptability in the objectives section. Should this be removed? This has been removed.

Primary outcome

- I think the first sentence of this section describes the primary aim of the study not the primary outcome. Please can this be reworded for clarity. The key outcomes are then well articulated in the remainder of the paragraph. This has been changed.

Secondary outcomes

- Inter-rater reliability (mentioned in the abstract), reliability (mentioned in the objectives section) and interuser variability (mentioned in the secondary outcomes paragraph) are not described here (apologies if I have missed this). I am not clear how / when reliability is being assessed and reliability of what? Please can this be clarified. The protocol has been amended so that the term 'variability' is consistently used to describe how the tools perform when used by clinicians, compared to patient self-assessment, for the tool (CFS) that is completed by more than one assessor.