Frailty Assessment in Vascular Surgery

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Abstract

Background: Frailty describes a syndrome characterised by reduced physiological reserve and increased vulnerability to even minor stressors due to age-associated changes in physiological substrate. Frailty is common in vascular surgery populations and has demonstrated associations with adverse health outcomes and increased risk of mortality. However, in the absence of clear guidelines there is uncertainty over the approach to frailty identification and its management. Frailty identification can be considered the critical first step to improving health outcomes for this vulnerable population. A role is identified for exploring approaches to frailty assessment and the implications this might bring to vascular surgery services.

Aims: This thesis addresses the following aims:

1. To explore the methodological approaches to frailty assessment described in vascular surgery research and clinical practice.

2. To explore the practical utility of frailty in vascular surgery clinical practice.

3. To explore stakeholders perceptions of frailty assessment in clinical practice.

Methods: Three approaches were adopted to target research questions. First a two-part systematic review was performed. The first part included any study describing any form of frailty assessment in vascular surgery populations for any reason. Data collection included which frailty assessment tools were used, the methodological application of each tool and how data was analysed. The second review set out to explore how the clinimetric properties have been assessed for the ten most commonly used frailty assessment tools identified in the aforementioned review. Any study with the aim of exploring any clinimetric property was included. The search criteria was expanded to include studies of any surgical population as initial search strategy found restricting to vascular surgery populations only yielded a low number of eligible studies.

Secondly, a prospective observational study was conducted to explore the practical utility of frailty assessments in clinical practice. Patients were recruited from a vascular rapid-access clinic, baseline data were collected and five different frailty assessments were performed (Clinical Frailty Scale, Healthcare Improvement Scotland FRAIL, Frail NonDisabled questionnaire, subjective clinical assessment and 11-item modified frailty index). Outcome measures include feasibility parameters, comparisons of the demographic differences between robust and frail patients and clinimetric property assessment (interrater reliability and convergent validity), using clinician-assessed CFS as reference standard. A short-term (30-day) follow-up explores prognostic properties of frailty assessment tools.

Finally, a national mixed methods study recruited vascular surgeons and allied healthcare professionals and explored their perceptions and utilisation of frailty assessment in clinical practice. An 18-item questionnaire was distributed purposively by email with respondents given the option to volunteer for follow-up interview/focus groups through the questionnaire.

Results:

Research aim 1: Screening 5358 records identified 111 eligible studies. Forty-three differing frailty assessment tools were identified. One-third of these failed to assess frailty as a multidomain deficit and there was a reliance on assessing function and presence of comorbidity. Substantial methodological variability in data analysis and lack of methodological description was also identified. Published psychometric and/or clinimetric assessment was available for only 4 of the 10 most commonly used frailty tools. The Clinical Frailty Scale (CFS) was most studied and demonstrated good clinimetric properties within a surgical population.

Research aim 2: A total of 150 patients were recruited. Most were young, male and from areas of greatest social deprivation. Seventy-six (51%) were frail (CFS 5+). Frailty was significantly associated with age, polypharmacy and comorbidity. Clinicians were more likely to consider women frail on end-of bed, this was not replicated in remaining instruments. Compared to CFS, there was excellent

agreement with end-of-bed assessment and moderate agreement with HIS FRAIL. The mFI-11 and FiND demonstrated poor agreement and correlation with the remaining frailty assessment instruments which suggests these tools measure different constructs. Due to small numbers, no significant differences were observed on 30-day follow-up, including: mortality, morbidity, length of stay, readmission rate, or nonhome discharge.

Research aim 3: A total of 160 questionnaires were distributed with 60 (37.5%) responses. Respondents were primarily consultant or trainee vascular surgeons but contributions were comprehensive and involved most members of vascular surgery multidisciplinary team members. Responses were received from ten of fourteen Scottish regional health boards. A total of 20 respondents volunteered for follow-up interviews/focus groups across four regional health boards and totalling over 8 hours of recorded interview time. Healthcare workers recognise the importance of identifying and treating frailty. However, assessment lacks a unified approach with clinicians primarily performing subjective assessments. A call for standardising the approach to frailty assessment was made primarily due to a feeling that this would assist in unifying the necessary, and currently, disjointed services into a collaborative multidisciplinary approach to improving health outcomes for patients living with frailty.

Conclusion: Despite frailty being recognised by vascular healthcare professionals as a relevant construct with important clinical considerations, there is substantial heterogeneity in approaches to frailty assessment within vascular surgery research and clinical practice. This might be associated with variability in diagnostic and prognostic accuracy and has generated uncertainty around tool selection. For this reason, a call has been made for adopting a standardised approach to frailty assessment. To support such a movement, the work in this thesis presents data supporting the feasibility of routine frailty screening using standardised tools in an outpatient setting. Surgeons prioritise a prognostic role for such tools while allied healthcare professionals consider frailty in a broader sense, recognising the need for collaborative multidisciplinary approaches to its management as part of improving health care outcomes. Introducing a standardised approach to frailty identification is felt supportive in this movement primarily through guiding

unification of language, awareness of a growing problem and to redirect the attention and priorities of multidisciplinary services. As part of achieving shared care goals, a deepened understanding of early-onset frailty and the interplay with mobility-limiting pathology, particularly in considering frailty phenotypically, is recommended.

Acknowledgments

I am exceptionally grateful for the expert guidance and support that I received from my supervisors Professor Terry Quinn and Mr Douglas Orr on both professional and personal levels from the beginning right through to the end of this project. I feel both honoured and humbled to have been awarded this inaugural fellowship and I know the work wouldn't have been possible in the absence of their enthusiasm, positivity and wisdom.

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Finally, thank you to my friends and family for the constant support they have provided me with. Juggling this work and the arrival of my son, Oliver, would not have been possible without them.

Author's declaration

The work presented in this thesis was completed during a Postgraduate Research Fellowship which was jointly sponsored by the Royal College of Physicians and Surgeons of Glasgow and the Circulation Foundation, a charity affiliated with the Vascular Society of Great Britain and Ireland.

I declare that I am the primary author of this thesis, and under the guidance of my supervisors, am responsible for conceptualisation, design, implementation and conduct of studies including participant recruitment, as well as conducting all aspects of data analysis. Where chapters have been published in scientific journals, I wrote the first draft of each manuscript which I then revised following feedback from my supervisors and additional co-authors. Co-authors for published chapters are mentioned in the introduction section of the chapter which contains the full citation. Specific contributions are listed below.

In Chapter 2 Dr Paul Martin and Dr Sasi Pathmanathan provide insights in to the frailty services they are part of delivering in their units. Further, as co-authors in the published manuscript, they reviewed the first draft prior to publication.

Chapter 3 contains a systematic review, I acted as first reviewer for all aspects of the review process (search, screening, data extraction and analysis). Dr R Claire Pearson acted as second author by independently conducting screening and data extraction.

For the prospective cohort study (Chapters 4 – 6), I conceptualised and designed the study under the guidance of my supervisors. I created all relevant data

extraction forms, recruited participants and was responsible for all aspects of data transcription and analysis. Dr Fariha Naeem assisted with quality control of transcribed data, as set out in chapter 4.

The mixed method study (Chapter 7) contains both questionnaire and interview data. I designed the questionnaire and interview guide under the guidance of my supervisor Professor Terry Quinn. I performed all aspects of participant recruitment, acted as interviewer for all interviews/focus groups and was responsible for all aspects of data collection/transcription. I acted as first reviewer in data analysis, reviewing my transcripts and coding quotes. Data analysis was complemented by Dr Jenni Burton who independently coded quotes from transcripts. Together we reviewed and collated quotes into specific themes and subthemes. Dr Burton also provided feedback on the thesis chapter.

I am the author of Chapter 8 which summarises the work in the thesis and has not been submitted for publication to any journal.

This work has not been submitted for any other degree at the University of Glasgow or any other institution.

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Published work arising from this thesis

1. Welsh SA, Pearson RC, Hussey K, Brittenden J, Orr DJ, Quinn T. A systematic review of frailty assessment tools used in vascular surgery research. J Vasc Surg. 2023 Dec;78(6):1567-1579.e14. DOI: 10.1016/j.jvs.2023.06.010. Epub 2023 Jun 19. PMID: 37343731.

2. Welsh SA, Hussey K, Brittenden J, Orr DJ, Quinn T. Frailty Assessment in Vascular OUtpatients Review (FAVOUR) protocol: single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools. BMJ Open. 2023 Dec 9;13(12):e079387. DOI: 10.1136/bmjopen-2023-079387 PMID: 38070914; PMCID: PMC10729052.

3. Welsh SA, Martin P, Pathmanathan S, Hussey K, Brittenden J, Orr DJ, Quinn T. Frailty in peripheral arterial disease. J.Vasc.Soc.G.B.Irel. 2023;2(3):128-133, http://doi.org/10.54522/jvsgbi.2023.077

Published work achieved during research period but not directly relating to this thesis

1. Sarah Kelly, Andy Cowan, Gizdem Akdur, Lisa Irvine, Guy Peryer, Silje Welsh, Stacey Rand, Iain A Lang, Ann-Marie Towers, Karen Spilsbury, Anne Killett, Adam Lee Gordon, Barbara Hanratty, Liz Jones, Julienne Meyer, Claire Goodman, Jennifer Kirsty Burton, Outcome measures from international older adult care home intervention research: a scoping review, Age and Ageing, Volume 52, Issue 5, May 2023, afad069, https://doi.org/10.1093/ageing/afad069. PMID: 37192505

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Oral conference presentations arising from this thesis

1. Frailty Assessment in Vascular OUtpatient Review (FAVOUR) Study – feasibility results
   The Vascular Societies' Annual Scientific Meeting, 2024
2. Frailty in Vascular Disease
   British Geriatric Society, 2023
3. Frailty Assessment in Vascular OUtpatient Review (FAVOUR) Study – early results
   The Vascular Societies' Annual Scientific Meeting, 2023
4. Frailty in Vascular Patients
   The Vascular Societies' Annual Scientific Meeting, 2022

List of accompanying material

Appendix 1: Supplementary material for Chapter 2 and 3: Search syntaxes for literature and systematic review.

Appendix 2: Supplementary material for Chapter 3: Systematic review protocol registration.

Appendix 3: Supplementary material for Chapter 3: Comprehensive taxonomy of COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) definitions.

Appendix 4: Supplementary material for Chapter 3: Search syntax for second (COSMIN) systematic review.

Appendix 5: Supplementary material for Chapter 3: Complete list of all Risk Analysis Index tools identified in the first systematic review.

Appendix 6: Supplementary material for Chapter 4: Frailty Assessment in Vascular Outpatient Review (FAVOUR) study registration and ethical approval

Appendix 7: Supplementary material for Chapter 4: Example of FAVOUR consent form.

Appendix 8: Supplementary material for Chapter 4: List of case report forms (CRFs) completed by clinicians, patients, proxies and researcher in FAVOUR study.

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Appendix 10: Supplementary material for Chapter 5: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

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Appendix 13 : Supplementary material for Chapter 7: 18-item questionnaire used in the study.

Appendix 14: Supplementary material for Chapter 7: The semi structured interview guide used during interview and focus group sessions and ethical approval for study.

List of abbreviations

ADL	Activities of Daily Living
AUC	Area Under Curve
BACPAR	British Association of Chartered Physiotherapists in limb Absence Rehabilitation
BGS	British Geriatrics Society
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CD	Clavien-Dindo
CEA	Carotid Endarterectomy
CFAE	Common Femoral Artery Endarterectomy
CFS	Clinical Frailty Scale
CGA	Comprehensive Geriatric Assessment
CHERRIES	CHEcklist for Reporting Results of Internet and E-Surveys
CI	Confidence Interval
CLTI	Critical Limb Threatening Ischaemia
COREQ	COnsolidated criteria for REporting Qualitative studies
COSMIN	COnsensus-based Standards for the selection of health Measurement Instruments
CPOC	Centre for Perioperative Care
CRF	Case Report Form
CVD	Cardiovascular Disease
CVS	Consultant Vascular Surgeon
ECOG	Eastern Cooperative Oncology Group
EFS	Edmonton Frail Scale
ELF	Emergency Laparotomy and Frailty
ERAS	Enhanced Recovery After Surgery
FAVOUR	Frailty Assessment in Vascular OUtpatient Review
FI	Frailty Index
FiND	Frail NonDisabled questionnaire
GFI	Grongingen Frailty Indicator
HCP	Healthcare Professional
HIS	Healthcare Improvement Scotland
ICE	Initial Clinical Evaluation
IQR	Interquartile Range
JD	Junior Doctor
JHACGS	Johns Hopkins Adjusted Clinical Group System
MD	Doctor of Medicine
mEFT	Modified Essential Frailty Toolset
mFI-11	11-item modified Frailty Index
MoSCoW	‘Must have’, ‘Should have’, ‘Could have’, ‘Won’t have’
MPI	Multidimensional Prognostic Index
NHS	National Health Service
OR	Odds Ratio
PAD	Peripheral Arterial Disease
PIS	Participant Information Sheet
POPS	Perioperative care for Older Patients undergoing Surgery
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses

RAVES	Relevant, Accessible, Validated, Evidenced, Standardised
QEUH	Queen Elizabeth University Hospital
RAI	Risk Analysis Index
ROC	Receiver Operating Characteristics
SD	Standard Deviation
SN	Staff Nurse
SIMD	Scottish Index of Multiple Deprivation
STROBE	Strengthening The Reporting of Observational Studies in Epidemiology
UK	United Kingdom
VNS	Vascular Nurse Specialist

Chapter 1 Introduction to thesis

1.1 Chapter summary

This chapter presents a summary of the content, aims/objectives and research questions of the thesis. This is followed by a brief summary of the work presented in each chapter and how this was designed to answer the component parts of the research questions.

1.2 Research objectives

This thesis aims to understand the implications of frailty within a vascular surgery population. Specifically, it aims to explore frailty assessment within vascular research and clinical practice with a view to informing clinicians, researchers and policy makers on how this can be used to improve health outcomes. The main aims are :

1. To explore the methodological approaches to frailty assessment described in vascular surgery research and clinical practice.

2. To explore the practical utility of frailty in vascular surgery clinical practice.

3. To explore stakeholders perceptions of frailty assessment in clinical practice.

1.3 Research questions

The research questions that will be addressed in this thesis are:

1. What are the methodological approaches to frailty assessment in vascular surgery related research.

2. Can frailty assessment be implemented as part of routine care in clinical practice, and if so;

    a. What is the feasibility of routinely measuring frailty in an outpatient setting.

    b. How do clinimetric properties of frailty assessment tools compare in prospective frailty assessment.

    c. How do the prognostic properties of frailty assessment compare in prospective frailty assessment.

3. What are stakeholder's perception and utilisation of frailty assessments in a vascular surgery setting.

1.4 Outline of chapters

This thesis is presented in monograph/traditional format. Where the work presented in chapters has resulted in journal publication, this has been made clear in the respective chapter summary with the chapter presented in the style of the journal publication.

Chapter 2: Frailty assessment in a vascular surgery population

This chapter presents a published literature review defining arterial disease relevant to vascular surgery speciality and summarising frailty and its implications in vascular surgery practice. The relevance of frailty assessment and its role in improving healthcare outcomes is explored, acting to justify the research questions described in section '1.3. Research questions'.

Chapter 3: A systematic review of frailty assessment tools used in vascular surgery research.

This chapter contains a published two-part systematic review addressing research question 1 (What are the methodological approaches to frailty assessment in vascular surgery related research). The first systematic review collates and describes the varying frailty assessment instruments applied in vascular surgery research. The second systematic review explores the clinimetric properties, where assessed, of popular frailty assessment instruments. Finally, the chapter discusses challenges in frailty assessment relevant to a vascular surgical population. Areas for further work are identified which are addressed in subsequent chapters.

Chapter 4: Materials and methods for 'Frailty Assessment in Vascular OUtpatient Review' (FAVOUR) study

This chapter contains a published methodological summary of the approach to a prospective observational study of feasibility, addressing research question 2 (Can frailty assessment be implemented as part of routine care in clinical practice). It describes the approach to assessment of frailty in an outpatient vascular department setting. Different frailty tools are described and their selection justified.

Chapter 5: FAVOUR study results: feasibility measures and clinimetric properties

This chapter presents the early results of the FAVOUR study, specifically addressing research questions 2a (what is the feasibility of routinely measuring frailty in an outpatient setting) and 2b (How do clinimetric properties of frailty assessment tools compare in prospective frailty assessment). The proposed role routine frailty assessment may have in clinical practice is explored as well as discussing suitable instruments/approaches for doing this.

Chapter 6: FAVOUR study results: 30-day outcomes

This chapter presents the early results from the FAVOUR study and addresses research question 2c (How do the prognostic properties of frailty assessment compare in prospective frailty assessment). This chapter explores the prognostic properties of selected frailty assessment instruments in the context of identifying a preferred instrument for routine assessment of vascular surgery patients.

Chapter 7: Assessing stakeholder's perception and utilisation of frailty assessment in a Vascular Surgery setting – A mixed methods study.

In addressing research question 3 (What are stakeholder's perception and utilisation of frailty assessments in a vascular surgery setting), this chapter explores the role that frailty assessment currently has in modern management of vascular patients. The contrast between research practices and clinical practices is explored and stakeholders opinions on future directions of travel to improve the care of patients living with frailty and vascular disease is discussed.

Chapter 8: Discussion

The final chapter summarises the work presented in this thesis, emphasising key learning points. Strengths and limitations of the presented work are discussed before putting the thesis findings in the context of current literature. Finally, implications for future research and clinical practice are discussed.

Chapter 2 Frailty assessment in a vascular surgery population

2.1 Chapter summary

This chapter presents a literature review of frailty and its implications in vascular surgical practice. Firstly, this chapter summarises the definition of arterial disease relevant to vascular surgery speciality practices. This is followed by presenting definitions of frailty, its biology and epidemiology within a vascular surgery setting and its implications on patient care, health care resources and sustainability. This chapter rationalises the importance of frailty recognition within this speciality, providing evidence to support the research questions presented in this section 1.3. The resultant challenges associated with heterogeneity in frailty assessment are touched upon in this chapter, however a comprehensive discussion is continued in Chapter 3.

The work presented in this chapter, alongside figures 2.3 - 2.7, has been published as Welsh SA MP, Pathmanathan S, Hussey K, Brittenden J, Orr DJ, Quinn T. Frailty in peripheral arterial disease. J Vasc Soc G B 2023;2(3):128-33.[1]

2.2 Introduction

It has been consistently demonstrated that compared to robust counterparts, vascular patients living with frailty have poorer perioperative outcomes, with increased morbidity and mortality.[2] Consideration of frailty is particularly important, not only as our population continues to age, but as advances in anaesthetic, surgical and endovascular techniques are enabling a broader range of interventional options for those people who may have traditionally been labelled as unsuitable for surgery.[3]

Frailty has implications for health and social care at the micro and macro level and a failure to consider the differing needs and natural histories of people living with frailty could result in avoidable harm and suboptimal resource allocation. The growing urgency in the need to recognise and manage frailty has been acknowledged in national guidelines[4], however, a standardised method for doing so has yet to be identified and agreed upon. Despite its undeniable prognostic value, the predisposing risk factors and pathophysiological mechanisms of frailty in vascular disease remain poorly understood, albeit new data are emerging. This in turn has challenged a uniform approach to assessment and management. This heterogeneity complicates translation of research into routine clinical practice and guidelines. This chapter will consider the theories and biology of frailty and apply these to the assessment and management of the vascular surgical patient.

2.3 Methods

Biomedical databases were searched for high quality original research or reviews pertinent to vascular surgery and frailty. Full search terms can be found in appendix 1 (this is the same search syntax as for the systematic review presented in Chapter 3). This was complemented by feedback from vascular surgical teams who are developing frailty services across the United Kingdom. These services were contacted purposively with information gathered through unstructured telephone interview (Hull Royal Infirmary) or through email communication (Ninewells Hospital). Field notes were taken and a summary of described services were generated with the spokesperson for each service invited to comment.

2.4 Definition of arterial disease in vascular surgery

Vascular disease describes disorders of vascular (arterial and venous) anatomy. The vascular surgery subspeciality oversees the management of non-cardiac and extracerebral vascular pathology. Specifically, the work presented in this thesis encompasses arterial disease of any aetiology (with the exception of trauma) of the abdominal aorta, aortoiliac segments, mesenteric, femoral, upper/lower limb and carotid arteries. Disease of the thoracic or thoraco-abdominal aorta was considered if the proposed treatment did not involve aortic root or aortic arch repair as the latter two procedures can involve cardiothoracic speciality. Further, the management of vascular access procedures varies between health boards between vascular surgery or renal transplant specialities so to ensure consistency, vascular access is excluded. These criteria were defined to incorporate arterial disease typically managed by a vascular surgery speciality. Venous disease is out with the scope of this thesis.

Pathophysiological processes of arterial inflow will result in end-organ hypoperfusion and tissue/organ dysfunction with signs and symptoms dependent on the tissue affected. Diseases that require specialised vascular surgery care include: peripheral arterial disease of the lower (and upper) limbs, mesenteric/visceral arterial disease, carotid artery disease, thoraco-abdominal aortic syndromes (including aneurysms, dissections, intramural haematomas and penetrating aortic ulcers)[5], renovascular disease (including renal access in certain centres), vascular trauma and vascular malformations.[6]

There are multiple aetiological risk factors for arterial disease with the most common cause being atherosclerotic disease.[7] Atherosclerotic disease describes a chronic, progressive systemic disease resulting in flow-limiting stenosis of the arterial tree due to the progressive development of atherosclerotic plaque deposition.[8] The aetiological risk factors are multifactorial and can be classified into modifiable and non-modifiable categories. Modifiable risk factors include

arterial hypertension, hyperlipidaemia, diabetes mellitus, obesity and smoking. Non-modifiable risk factors include rising age, male sex and a family history.[9] Less common arterial pathophysiological disease processes include, but are not limited to: inflammatory vasculitides[10], infective vasculitides[11], iatrogenic injury, congenital disease[12] and trauma.

The demand for vascular services is set to increase due to the continuing global rise in life expectancy, particularly in men, alongside the obesity epidemic and rising incidence in diabetes mellitus.[10, 13, 14]

2.4.1 Management of arterial vascular disease

There are several approaches to the management of arterial disease depending on the anatomical configuration of the disease, degree of end-organ dysfunction and physiological disturbance as well as 'host factors', such as the presence of frailty which can affect physiological reserves and ability to tolerate the stress imposed by various treatment options.

Treatment can be classified into medical and surgical management with treatment options given concurrently where appropriate. Medical management encompasses all aspects of non-surgical treatment, including pharmaceutical treatment and lifestyle modifications for primary prevention of disease onset, active treatment of diagnosed pathology and/or aetiological risk factors for atherosclerotic disease or medical palliation of symptomatic end stage arterial disease.[15] Surgical treatment considers both open surgical intervention and minimally invasive endovascular revascularisation techniques performed with the intention of augmenting arterial inflow and arrest/reverse symptoms and signs of malperfused tissues. Open surgical and endovascular techniques can be employed concurrently as part of a 'hybrid' approach, enabling the treatment of multiple levels of arterial

disease. There are anatomical and 'host factors' to consider when selecting appropriate mode of surgical intervention.

2.4.2 Key management considerations

- **Host factors**: Different management options impose varying degrees of physiological stress. The decision to offer one treatment option over another will depend on the perceived likelihood of achieving satisfactory revascularisation against the individual's ability to tolerate the stress imposed by the proposed treatment. This thesis will consider the role of frailty in the management of arterial disease typically managed by a vascular surgery subspeciality.

- **Timing considerations**: Management can be offered on an elective, urgent or emergent basis, according to the Society for Vascular Surgery reporting standards.[16] A substantial proportion of the workload in vascular surgery is emergent or urgent with patients presenting with varying degrees of acute physiological stress and/or chronic physiological deconditioning. This thesis will consider how frailty, and its impact on physiological reserves, may influence treatment.

2.5 Definitions and theories of frailty

In the absence of a globally accepted standardised definition, frailty can be considered a syndrome of increased vulnerability to even minor stressors due to a failure in homeostatic reserves brought about by age-associated deficits accrued across multiple domains. Two main theories underpinning frailty have been accepted:

- Fried phenotypic model.

- Rockwood theory of cumulative deficits.

The two theories are not necessarily mutually exclusive.

2.5.1 Fried Phenotypic model of frailty

The Fried phenotype of frailty is characterised by progressive age-related deterioration in underlying physical substrate.[17] It is defined by the presence of three or more of the following energy-negative components existing in a self-perpetuating cycle: unintentional weight loss, weakness, slow walking speed, low physical activity levels and self-reported exhaustion, Figure 2.1. Additionally, those without these characteristics are considered ‘robust’, while displaying one or two characteristics is considered a ‘pre-frail’ state.

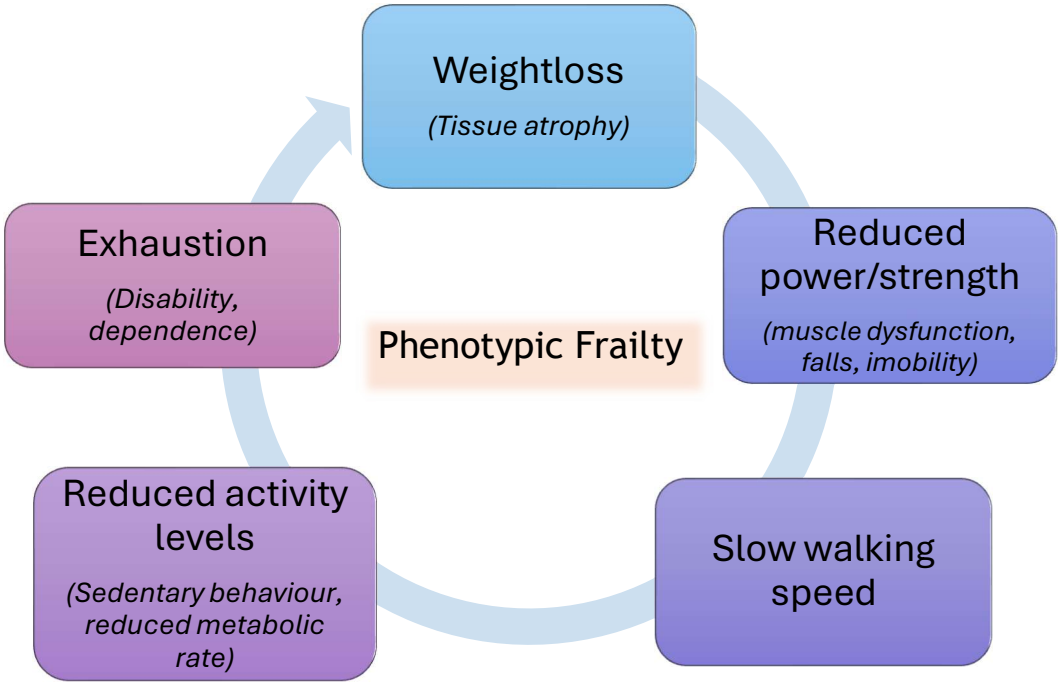


Figure 2.1 - Five components of Fried's phenotypic model of frailty. Figure is as presented in Welsh et al.[1]

2.5.2 Rockwood cumulative deficit model of frailty

By contrast, Rockwood's cumulative deficit theory of frailty describes frailty as a multifactorial and dynamic biological construct where frailty is graded by the progressive accrual of deficits across multiple, undefined, domains.[18] Authors created a Frailty Index (FI) which quantifies risk of frailty, through a quantitative summation of the number of deficits, rather than a qualitative consideration of the type of deficit, such that the greater the number of deficits, the greater the risk of frailty and associated risk of morbidity, Figure 2.2. Of note, the model was found to have improved construct, predictive validity and reduced variance once factors surplus to the traditional foci of physical deficits were incorporated.

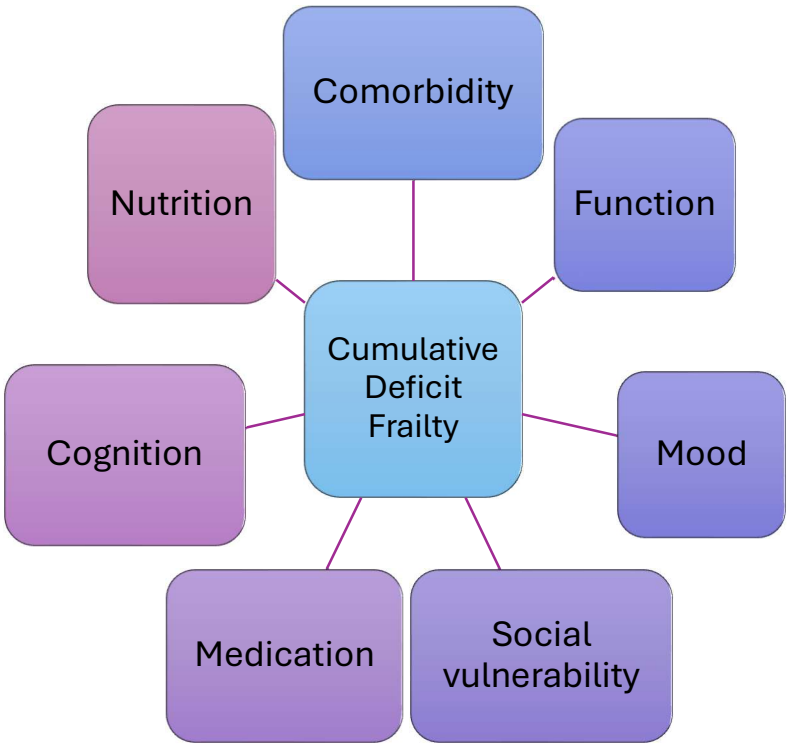


Figure 2.2 - Cumulative deficit frailty model A non-exhaustive example of the domains that could be incorporated into a frailty index based on the cumulative deficit model of frailty. Figure is as presented in Welsh et al.[1]

2.5.3 Key frailty considerations

- **Age association**: Frailty is associated with increasing age but is not synonymous with ageing.[19] Research has historically described and assessed frailty in populations aged 65 years and older. However, it has increasingly been recognised that frailty affects middle-aged patients. Further, the observed negative prognostic implications of frailty in older adults is similarly observed in younger populations with early onset frailty.[20, 21]

- **Dynamic state**: Historically frailty may have been considered a progressive physiological decline in the context of unsuccessful ageing.[22] However, literature exploring methods for mitigating the impact of frailty on adverse health outcomes have suggested a dynamic state with the ability for one person's frailty to fluctuate across a bidirectional spectrum of frailty severity, with the potential to delay, or reverse, its progression.[23, 24]

- **Interplay with comorbidity**: Similar to frailty, co-morbidity is similarly positively associated with increasing age.[25] The relationship between frailty and comorbidity is variable. Although commonly co-existent, the two entities can occur independently. Further, some pathophysiological processes can be considered aetiological risk factors for frailty. This will be explored in more detail later in this chapter.

2.5.4 Similar constructs

Due in part to similarities, co-existence and suspected interactions, frailty has previously been considered equivalent to co-morbidity, disability and/or sarcopenia. While these entities may be related, and often coexist, they should be considered separate constructs.

To differentiate, co-morbidity describes the co-existence of two or more chronic conditions. It is estimated that 70% of frail patients are co-morbid, yet only 20% of co-morbid patients are frail.[26] The identification of non-frail co-morbid, and non-comorbid frail patients supports the two constructs as independent entities, at least in part.

Disability refers to a limitation in physical or cognitive ability to perform activities of daily living independently.[27] Whereas frailty describes a vulnerable state, at increased risk of loss of function and independence with potential for developing disability.[17, 22] Fried *et al*. have demonstrated that while 72% of frail persons report difficulty in mobility, only 27% had difficulty in completing the disability-assessing activities of daily living.[17] Furthermore, of those classified as disabled, only 28% could be described as frail thus confirming a degree of diagnostic independence between the two constructs. There is also the consideration that frail patients may not report a disability as they may no longer attempt more demanding tasks of daily living.

Lastly, sarcopenia is a biological syndrome characterised by the generalised and progressive loss of skeletal muscle mass and quality and can occur as a primary or secondary condition.[28] Primary sarcopenia describes tissue loss associated with old age in the absence of other pathological causes. Secondary sarcopenia occurs in states of catabolism (malnutrition, malabsorption, chronic inflammatory or

malignant conditions) as well as in sedentary lifestyles (‘sarcopenic obesity’).[28] The loss in muscle mass and quality is thought to be driven by a disruption in muscular homeostatic mechanisms resulting in type II muscle fibres being replaced by type I muscle fibres as well as fat infiltration.[29] Contributing factors are thought to include dysregulated inflammatory cytokines, oxidative stress, insulin resistance and neuromuscular junction dysfunction. Some of these pathways, as well as decreased concentrations of hormones responsible for muscle mass maintenance (i.e. insulin-like growth factor 1, testosterone and the steroid dehydroepiandrosterone sulphate), have also been hypothesised to contribute toward the development of frailty and are elaborated on later in this chapter (see section 2.6 Biology of frailty).[30] In comparing sarcopenia and frailty definitions according to Fried’s phenotype, on a macrocellular level, low grip strength and slow gait speed are characteristic of both frailty and sarcopenia, while low physical activity levels and weight loss are physical manifestations of frailty and aetiological risk factors for sarcopenia.[31] It is clear sarcopenia and frailty have overlapping features and can coexist in patients. Yet frailty does not guarantee sarcopenia, as sarcopenia does not guarantee frailty. In its assessment, sarcopenia should only be considered part of, but not wholly responsible for, the frailty syndrome. The interplay of these constructs is summarised in Figure 2.3.

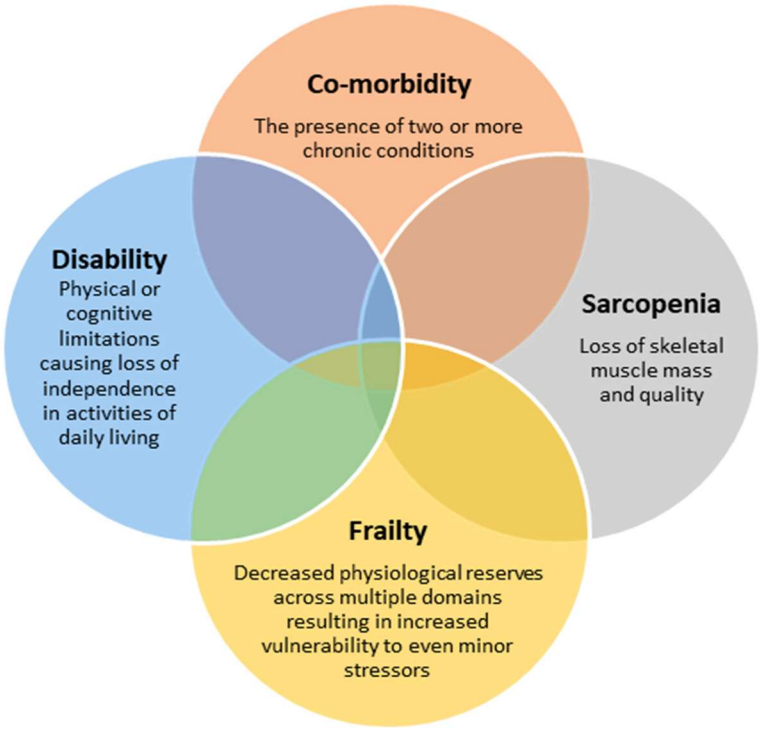


Figure 2.3 - Venn Diagram representing the simultaneous co-existence and independence of co-morbidity, disability, sarcopenia and frailty as descriptive entities. Figure is as presented in Welsh et al.[1]

2.6 Biology of frailty

Similar to sarcopenia, frailty is thought to develop primarily (as an intrinsic process) or secondary to alternate disease processes. Primary frailty describes an accelerated ageing process due to intrinsic dysregulation of proposed neuromuscular, metabolic, immunomodulatory or inflammatory pathways that create organ deficits without necessarily progressing to clinically detectable disease.[32, 33] Secondary frailty describes similar pathway dysregulations, but these are instigated or perpetuated by the physiological burden imposed by alternate diseases and/or their treatment. It is, however, unclear if this distinction bears significant relevance when translated to research or clinical practice.[34] In considering frailty as an accelerated, or unsuccessful, ageing process, several hallmarks of ageing have been defined, including altered intercellular communication, mitochondrial dysfunction, genomic instability, telomere shortening, epigenetic changes and cellular senescence.[35] Underpinning these age-related changes are chronic inflammation, oxidative stress and environmental exposures which will be explored further in this section, Figure 2.4

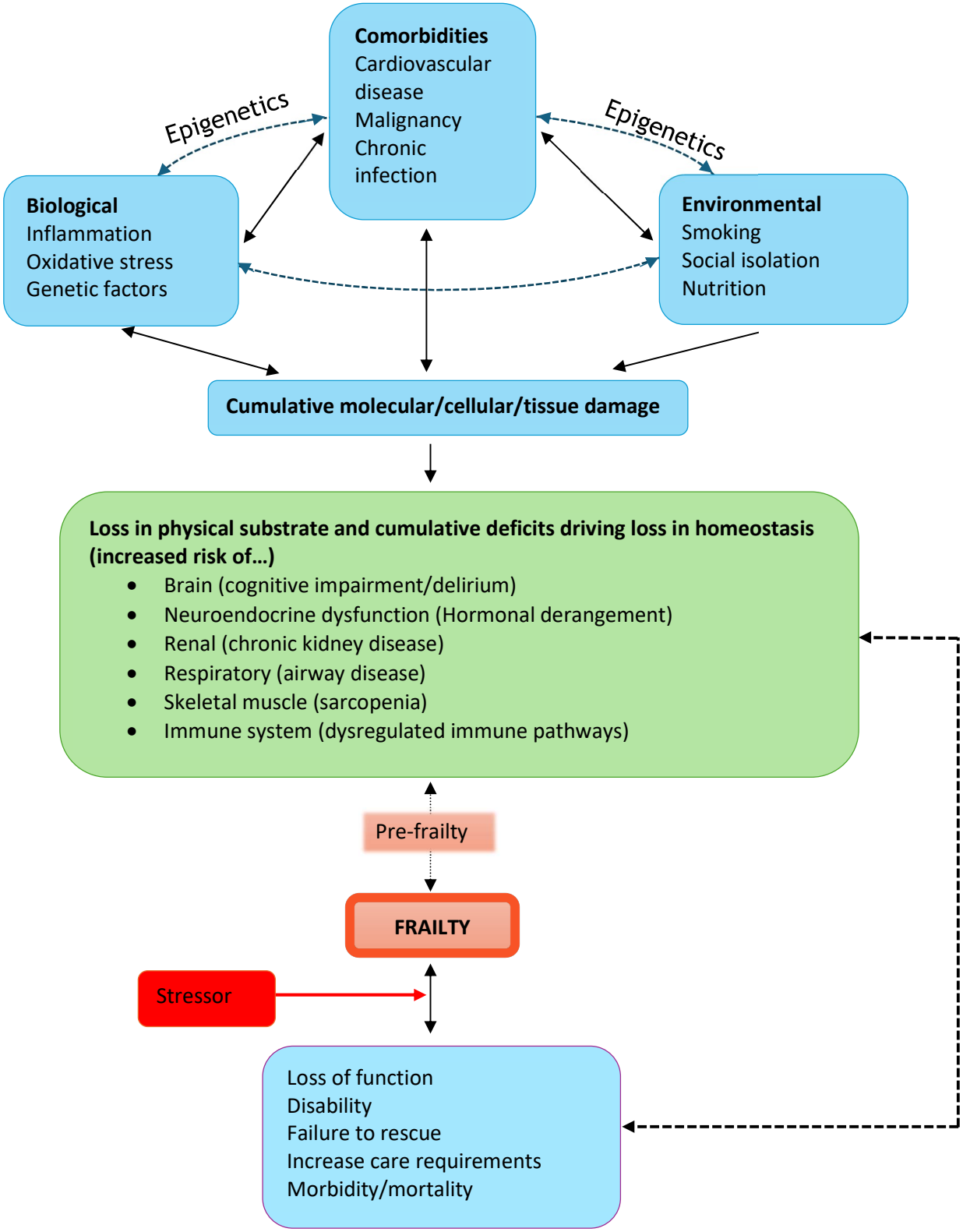


Figure 2.4 - Schematic representation of frailty pathophysiological mechanisms. Figure is as presented in Welsh et al.[1]

2.6.1 Chronic inflammation ('Inflammaging')

This describes an age related, chronic, sterile increase and dysregulation of inflammatory processes, that have been suggested as underlying the frailty syndrome. A meta-analysis demonstrated that 21 of 22 relevant published studies demonstrated a significant relationship between frailty and (pro-)inflammatory biomarkers.[36] Significant and positive correlations have been demonstrated between frailty and concentrations of C-reactive protein and interleukin-6. To a lesser extent, elevated levels of constituents of clotting pathways (D-dimer, Factor 8 and fibrinogen), tumour necrosis factor-alpha and total white blood cells, or reduced levels of haemoglobin and haematocrit have also been correlated with frailty, even after correcting for factors such as age, sex, smoking status, relevant pro-inflammatory co-morbidities and some medications.[37, 38]

2.6.2 Oxidative stress

It has been observed that patients with frailty and 'pre-frailty' demonstrate higher levels of oxidative stress and possibly lower antioxidant levels compared to non-frail counterparts, after adjusting for age and sex[39, 40]. The theory of oxidative stress and frailty describes a cumulative burden of reactive oxygen species causing gradual cell damage, loss of recovery and regeneration and ultimately apoptosis or cellular senescence resulting in progressive decline in tissue and organ function.[32, 33] Depending on which tissue or organ is affected, different effects are felt. For example, oxidative stress and loss in functional reserve of the brain could cause cognitive decline or may affect neuroendocrine function. Frailty-related hormonal changes have also been demonstrated, including low levels of insulin like growth factor-1 and dehydroepiandrosterone sulphate as well as higher levels of cortisol. Overall this reduces muscle and bone strength resulting in the phenotypic changes typically observed in frailty.[41-43]. Moreover, oxidative related stress in age-related diseases such as chronic kidney disease, non-insulin dependent diabetes mellitus and cardiovascular disease (CVD) have been demonstrated.[44] It is proposed when these effects reach an undefined and

varied threshold across multiple organ systems, the person becomes clinically frail.

2.6.3 Environmental exposure

Extrinsic exposures have been proposed as initiators or drivers of frailty. Among a multitude of environmental/modifiable risk factors correlated with frailty are lower levels of income, social isolation, abnormal (high/low) body mass index, poor self-rated health, depressive symptoms, smoking and alcohol use.[45-47] Furthermore, dietary deficiencies in vitamin E as an anti-oxidising agent and vitamin D as a contributor to maintaining muscle strength have also been linked to frailty.[48-50]

2.7 Epidemiology of frailty in peripheral vascular disease

It is currently estimated that 10% of the general population aged 65 years and above live with frailty.[51] In vascular surgery, the estimated prevalence is at least twice this, with reports between 20 - 60%.[52] However, the prevalence may be even higher as the majority of research focuses on peri-operative outcomes which might exclude the frailest patients as they may not be considered suitable candidates for intervention. The greater prevalence of frailty, and its implications, in patients with vascular disease may be particularly pertinant due to shared aetiological risk factors and the possibility of synergistic biological mechanisms.[53-55] Chronic inflammation, increased levels of oxidative stress and shared modifiable risk factors such as smoking and raised BMI have been correlated with both cardiovascular disease (CVD) and frailty.[54, 55] Further, CVD has been identified as an independent risk factor for frailty.[45]

Beyond vascular surgery, a similarly high estimated prevalence of frailty in stroke patients has been described at 24.6%, supporting a proposed biological relationship. Frailty in stroke patients is also associated with increased mortality, prolonged hospital admission and disability.[56]

It is clear that frailty is also significant in patients presenting on an urgent basis to other surgical specialities, as exampled by the Emergency Laparotomy and Frailty (ELF) study which demonstrates a 20% prevalence of frailty in patients undergoing emergency laparotomy in general surgery.[57]

2.7.1 The rise of frailty

The successful advances in health care are driving a rapid rise in global life expectancies. The number of people aged 65 years, or older, is projected to rise from 9% to 16% between 2019 and 2050, equating to 1 in every 6 persons in the global population. Similarly, the number of people aged over 80 years is set to increase three-fold over the same time frame.[58] The demographic changes associated with increased ageing is likely to see an associated rise in the prevalence of frailty. Further, the incidence of surgical intervention in older patients is rising more quickly than the rate at which the population is ageing,[3, 59] likely due to advances in anaesthetic and surgical techniques which enable treatment of patients that traditionally may have been considered unsuitable for surgery.[3] Vascular surgery patients represent a comorbid population with a high prevalence of frailty.[4] The aforementioned considerations will likely dictate vascular surgeons will encounter frailty increasingly commonly. As presented in Chapter 2, this patient cohort is vulnerable and present complex multidisciplinary and resource-intensive health care needs.[60-63] This has been recognised in national guidelines which advocate the importance of identifying frailty in surgical patients as an independent predictive risk factor.[4]

2.8 Implications of frailty in peripheral vascular disease

Frailty has been described as “the most problematic expression of population ageing”.[33] At the individual level, the diminished resilience to physiological insults impairs recovery and complicates return to pre-morbid functional levels, Figure 2.5.

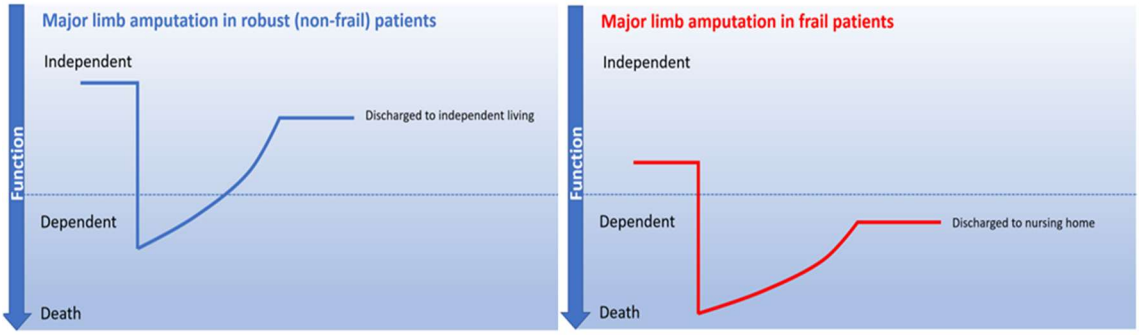


Figure 2.5 - Example of effects of major limb amputation on robust compared to frail patients. Robust patients demonstrate greater rehabilitative potential with capacity to return to a level of functional independence. Frail patients demonstrate poorer rehabilitative potential and a greater likelihood of long-term functional dependence requiring greater levels of social support. Figure is as presented in Welsh et al.[1]

In vascular surgery, frailty is associated with significantly increased risk of morbidity, short- and long-term mortality, prolonged hospital admission, discharge with greater social care requirements and functional decline, see Figure 2.6.[2, 52, 62] These findings have been corroborated in both open vascular surgery and endovascular techniques.[2, 64]

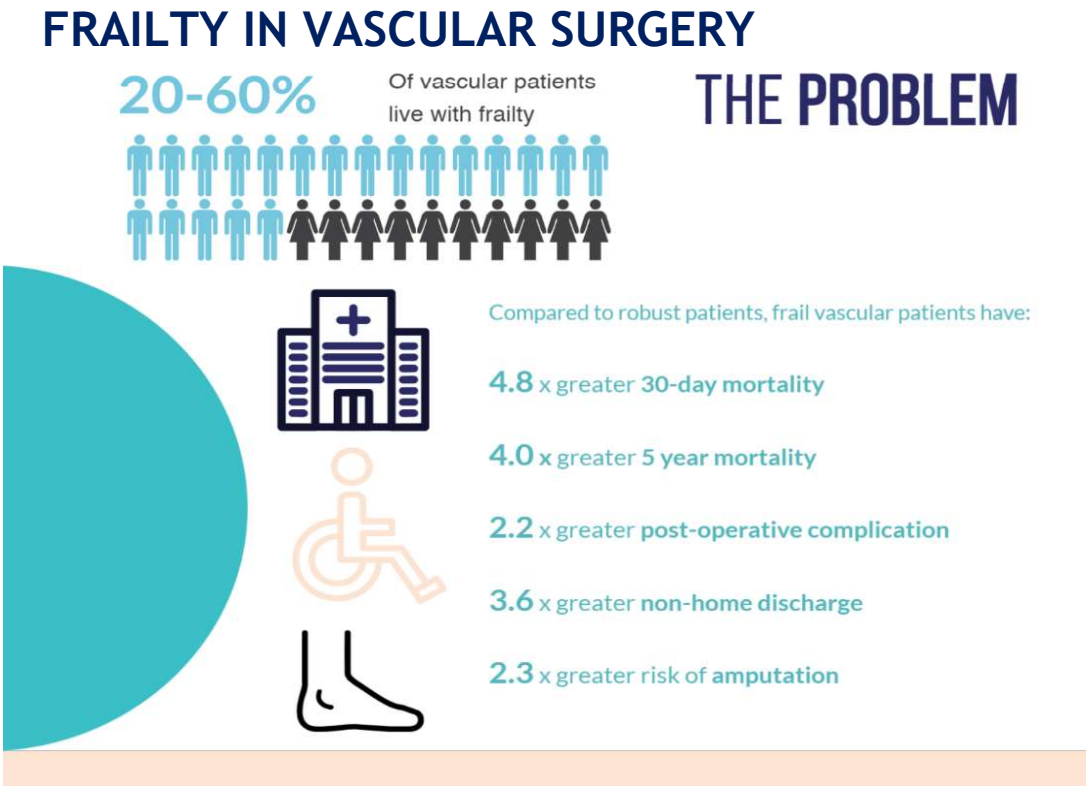


Figure 2.6 - Implications of frailty in vascular surgery outcomes. Figure is as presented in Welsh et al.[1]

While there is a paucity of health economic data specific to frailty and vascular surgery, undifferentiated economic data demonstrate that, after controlling for confounding factors such as age and co-morbidity, frailty significantly increases total healthcare costs by between 54% and 290% based on in-patient and outpatient treatments as well as pharmaceutical and nursing home care costs.[65, 66] The cost of the frail elective surgical patient is also substantially higher than robust counterparts.[67] As frail patients are more likely to be discharged with greater social care requirements, it is important to consider that some estimations suggest a 16-fold increase in costs of providing care for dependent patients compared to robust individuals.[44] In light of changing population demographics and the resulting clinical and economic pressures, maintaining the status quo is not an option. Many vascular services are looking at innovative changes to clinical pathways that facilitate frailty screening and subsequent person-centred management, examples of such clinical service models are summarised in Figure 2.7.

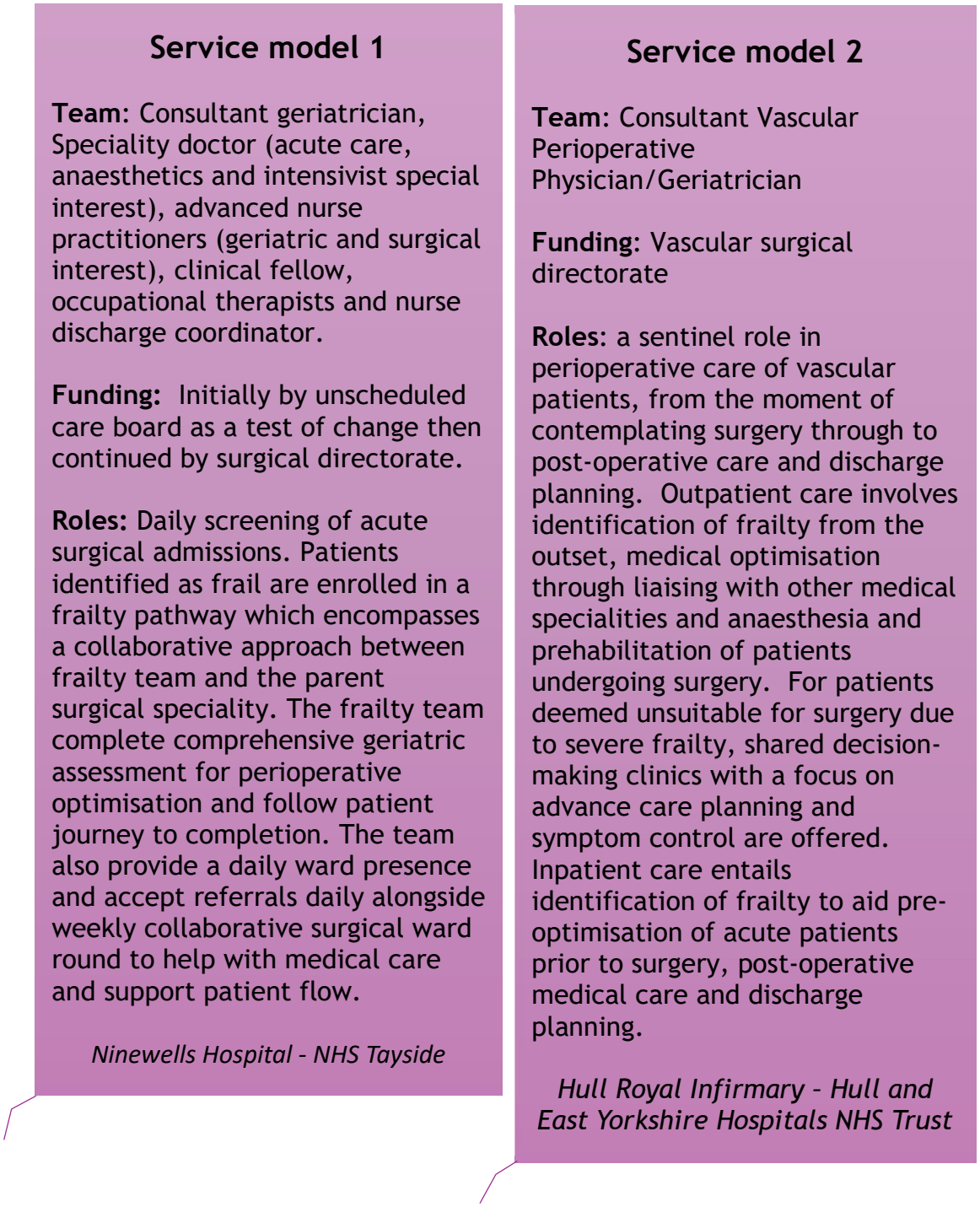


Figure 2.7 - Examples of clinical service model modifications, adapting to meet the needs of frail vascular surgery patients in the United Kingdom. Figure is as presented in Welsh et al.[1]

2.9 Assessment of frailty in peripheral vascular disease

The first step in managing frailty is its identification and quantification. A review confirming the prognostic value of frailty in vascular patients identified the use of 16 different frailty assessment tools.[64] This variety in tools has created heterogeneous research data and is born from a lack of standardised definition, various theories underpinning the syndrome, and a growing number of approaches to its identification. Broadly, frailty assessment tools in vascular patients have been categorised into phenotypic, cumulative deficit/FI and novel measurements.[64]

In vascular surgery, measures used to assess solely phenotypic traits of frailty include grip strength, gait velocity, timed up-and-go test and wearable sensor technology to record upper limb flexion/extension.[68-73] An important consideration is that the majority of vascular-themed frailty research involves revascularisation procedures of patients with peripheral arterial disease.[64] Clearly ischaemic rest pain of the limb will impair mobility, which will skew results if assessing frailty through phenotypic measurements. However, end stage arterial disease is a systemic process with a propensity to produce critical co-morbidities. Given the proposed interactions between CVD and frailty, what remains to be clarified is if this 'skew' in fact represents a true estimation of frailty or a bias in its assessment.

In assessing frailty as a cumulative deficit, the original FI incorporated 70-items, reflecting the themes included in a comprehensive geriatric assessment (CGA).[18] However, this expansive nature was felt overly burdensome for rapid, routine clinical application, so several more concise iterations of the FI have since been produced. The expected standards of an FI are to include at least 30 variables that have an association with health status, increase in prevalence with age without premature saturation and belong to multiple domains to avoid becoming a co-morbidity count.[74] In vascular surgery related research, nine

different FIs have been identified. From these, none conform with these expectations, as they all have fewer than 30 variables.[64] Despite this they demonstrate predictive validity in vascular surgery populations.

Novel markers of frailty include nursing home residency[75], various biomarkers[76-78], nutritional[79] and functional assessments[80] and a functional status coding on a national database[81, 82]. The use of radiologically-detected sarcopenia as a marker of frailty has also been investigated, without evidence of prognostic value[83].

A standardisation of frailty assessment would benefit research and clinical practice through minimising future research data-wastage, improving comparison of services, facilitating data-pooling for meta-analysis to improve the strength of evidence and enhance translatability of results into clinical practice.

In clinical practice, selecting and applying frailty assessment tools mandates considering their intended benefit, the point of the patient care pathway at which the assessments is to take place and who is to complete the assessment. In considering intended benefits, two are identified: frailty recognition for prognostication, and quantifying the individual's frailty-related domain deficits for targeted optimisation. As the prognostic value of several frailty assessment tools have been demonstrated, tools that are reproducible between users, quick to apply and do not require additional training or equipment will naturally fall in to favour in established busy clinical settings. One well-recognised example of such a tool is the Clinical Frailty Scale (CFS). This is a 9-point person-assessed tool with brief descriptions per point (the greater the value, the greater the frailty) can be applied in less than a minute.[18] Incorporating frailty assessment into preoperative decision-making may guide clinicians and patients in formulating a patient-centred management plan. In an elective setting, frailty assessment may

be of particular use when considering the suitability of offering prophylactic surgical treatments such as carotid endarterectomy or open abdominal aortic aneurysm repair. While in urgent settings, frailty scores may aid decision-making around a patients' suitability for invasive treatment compared to palliative measures.

To inform targeted frailty-related optimisation more exhaustive assessments should be considered. However, the maximum benefit of such assessments is only achieved when involving experienced health care professionals in the correct environment, with access to the necessary means to implement and sustain relevant changes. Adequate time is also required for a patient to benefit from these implementations. The Comprehensive Geriatric Assessment (CGA) is a well-recognised frailty centric assessment performed with the view to optimise health outcomes and quality of life.[84] It can be applied pre- and post-operatively, lending itself to elective, urgent and emergency admissions. However, to ensure such a resource intensive service is directed appropriately, it may prove valuable to identify frail and at-risk vascular patients through the introduction of patient frailty-screening.

Incorporating such assessments into a vascular surgery practice mandates establishing service models with regular and reliable interdisciplinary contribution from relevant services like geriatricians, pharmacists, physiotherapists, occupational therapists and secondary care discharge co-ordinators, complemented by direct communication with relevant social support services and links to community follow-up.

2.10 Management of frailty in peripheral vascular disease

Frailty exists along a spectrum of severity with potential for bi-directional transitions, between ageing successfully and vulnerability.[85] At a societal level, public health responses to increasing frailty include health promotion, health education and improving access to health prevention as therapeutic targets are identified. Supporting healthy ageing will drive the biggest benefit to population health with direct benefit to increasingly stretched health and social care resources. However, even if successful preventative measures are implemented, societal demographic changes suggest that frailty will still be prevalent in secondary care. It is therefore imperative secondary care pathways are adjusted for those vascular surgical patients living with frailty.

Important progress has been made in delineating the management of frail patients. The British Geriatrics Society (BGS) has published the 'Silver Book', a best practice guidance on addressing the care requirements of older people living with frailty during the first 72 hours of unscheduled medical and surgical admissions.[86] Further, the BGS and the Centre for Perioperative Care (CPOC) have co-written and published general guidelines on the Perioperative Care for People Living with Frailty.[87] In brief, the guidelines set out a multidisciplinary approach across community, primary, secondary and social care to deliver holistic care across a multicomponent pathway. This incorporates pre-operative risk assessment and optimisation, lifestyle modification, optimised intraoperative techniques, appropriate postoperative rehabilitation, pro-active discharge planning that incorporates links to relevant community and primary care follow-up as well as involving patient and carers in decision-making processes. Naturally there will be challenges in attempting to overcome the anticipated issues of funding, lack of resources and in co-ordinating the synchronisation of such a multidisciplinary approach across all components of health and social care.

Some societies have produced speciality-specific frailty-related guidelines. As an example, the American Society of Colon and Rectal Surgeons' 11-point document advises on the perioperative care of frail adults undergoing colorectal surgery.[88] In addition to describing the importance of considering frailty over age in designing management plans, some recommendations include providing prehabilitative care through a multidisciplinary and multifaceted approach, and to offer access to health care providers with geriatric expertise for peri-operative care and medical optimisation. More specific to colorectal surgery, it advocates the application of established post-operative care (Enhanced Recovery Protocols) in a modified fashion, tailored to the frail elderly's individual care needs. The guidelines recognise that traditional outcome metrics in colorectal surgery (e.g., length of stay, time to first flatus) may not mirror the patient's goals of care. In the recommendation of aligning a patient's care goals with realistic medicine, the case is made to instead consider functional recovery and patient reported outcome measures in addition to traditional post-operative outcomes.

In vascular surgery, the importance of identifying and managing frailty in vascular surgical patients has also been recognised in national guidelines which advocate patients have access to a CGA to "address issues of frailty...".[4] However, there remains a paucity of large volume trials to produce evidence-based guidelines for speciality-specific aspects of this pathway and how best to incorporate this into the variety of patient care pathways that exist in vascular surgery. Preliminary studies confirm clinical and financial advantages to incorporating CGA in perioperative pathways for vascular surgery patients, where applicable. For example, a randomised controlled trial (n=209) confirmed clinical and cost-effectiveness of introducing pre-operative CGA-based pre-habilitation compared to standard care for patients undergoing elective arterial reconstruction.[84] This benefit was primarily through reductions in length of stay, but also due to reductions in intensive care use, postoperative clinical reviews, care packages and community rehabilitation referrals. Importantly, a challenge specific to vascular surgery is that a considerable proportion of patients present with time-sensitive emergent and urgent pathology, precluding meaningful prehabilitation. Yet, the

use of frailty assessments to guide post-operative involvement of a geriatric service for these patients has also demonstrated similar positive effects, with reductions in length of admission and associated improved short-term readmission rates.[89] Large multicentre and longer-term follow-up studies are required to substantiate this evidence and support clinicians and policy makers in driving forward suggested augmentations to clinical practice and service models.

Frailty is significant for patients with end stage arterial disease who are considered for non-operative (medical palliation) management. In this setting - and where relevant- identifying frailty and discussing its prognostic role, may enable the alignment of a patient's care goals with their clinicians', representing an opportunity to use the frailty construct to endorse the delivery of realistic medicine.

As different approaches to improving frailty-related services in vascular surgery continue to be trialled, it is important to make public both successful and unsuccessful designs. This will help delineate a reproducible operational framework that delivers a proactive, holistic and multidisciplinary approach to identifying and treating vascular patients with frailty. This of course, constitutes but one part in the recommended multicomponent approach to managing these patients.

2.11 Conclusion

This chapter summarises the theories and biology of frailty and its relationship with its assessment and management in patients with peripheral vascular disease. Frailty is complex, heterogeneous and multidimensional and the need to approach its identification and management in a multidisciplinary fashion has been identified as a priority for vascular services.[87] Frailty is gaining increasing attention in research, yet despite increasing numbers in frailty studies, the translation of results into clinical practice is lagging. Further, there is a lack of evidence base to support frailty-centric adaptations to vascular health care policy. In a population where frailty is likely to have greater prevalence and implications, there are growing concerns around prospective population morbidity, health care resources and social care sustainability. A collaborative approach between researchers, clinicians and policy makers must be adopted to identify means of optimising clinical service models that safeguard equity in health care provision for frail vascular surgical patients in a secondary care setting.

Exploring heterogeneity in frailty assessment, and understanding why it exists, represents the beginning of translating the academic progress in frailty-research into positive changes to clinical practice. This is discussed in Chapter 3.

Chapter 3 A systematic review of frailty assessment tools used in vascular surgery research.

3.1 Chapter Summary

Frailty is common in vascular patients and is recognised for its prognostic value. In the absence of consensus, a multitude of different instruments exist with the purpose of assessing frailty. This chapter presents a two-part systematic review of published journal manuscripts and conference abstracts of observational studies, trials and quality improvement/audit projects addressing research question 1 (what are the methodological approaches to frailty assessment in vascular surgery related research). This chapter aims to quantify the variety in frailty assessment instruments and describe their content/application.

The first systematic review focuses on the methodological approach to frailty assessment for any vascular surgery population. This is followed by a secondary systematic review which summarises the available literature for the assessment of the psychometric and clinimetric properties of selected frailty assessment instruments within a surgical population.

The work, figures and tables presented in this chapter are published in Welsh SA, Pearson RC, Hussey K, et al. A systematic review of frailty assessment tools used in vascular surgery research. J Vasc Surg. 2023.[90]

The protocol for this study was registered on Open Science Framework (https://osf.io/dtyqv) which is included in Appendix 2.

3.2 Background

3.2.1 Therapeutic benefit to frailty assessment

On an individual level, the proposed clinical relevance of identifying frailty is two-fold, prognostication to guide operative decision-making and peri-operative optimisation for improved peri-procedural and even longer term outcomes.[2] Identifying frailty and appreciating the prognostic significance for vascular pathology and the host of treatment options available will better inform joint decision-making and may help to align patient expectations with those of healthcare professionals. It may also inform discussions when considering non-operative (medical palliation) management of end stage arterial disease. Secondly, frailty represents a transition phase from ageing successfully to vulnerability. It is not a unidirectional trajectory as deficits can be reversed with a targeted multidomain approach.[22] With this in mind, frailty assessment and 'treatment' may help patients reverse this transition phase and ameliorate healthcare outcomes.

On a wider service-level, patients living with frailty have additional resource and cost intensive requirements compared to robust counterparts, as summarised previously in Chapter 2.[44, 65-68] Considering the rapid demographic changes that are occurring on a global scale, it is critical resources are adjusted for this increasing demand to ensure equity in healthcare provision. It is therefore vital that health care pathways are modified to optimise the care provision for this vulnerable and high-demand patient group. The first step in achieving this is to improve how we identify frailty.

3.2.2 Challenges in frailty assessment/identification

The frailty syndrome does not have a gold standard definition, which in turn challenges the formulation of an optimum assessment tool/instrument. As

discussed in Chapter 2, frailty can be considered a syndrome of increased vulnerability to even minor extrinsic stressors due to the accumulation of typically age-associated deficits that impairs physiological reserve.[22] This diminished resilience to physiological insults, such as surgery, results in impaired recovery and can preclude the return to pre-morbid functional levels.

In contradiction to the clear guidance advocating frailty identification, there is a comparative lack of guidance describing optimum methodological approaches for doing so.[4] This is likely born out of the multifaceted and heterogeneous nature of the frailty syndrome, which has generated a multitude of measurable deficits to consider and the subsequent development of a variety of instruments.

The difficulties are confounded by the complex interplay between frailty and similar constructs such as comorbidity and disability, which challenges the ability to isolate and measure each construct discreetly. Albeit some may argue that diagnostic tools focusing on separating these entities may not bear comparative clinical utility if each construct predicts poor clinical outcomes in surgical settings. Over time there has been an accumulation of a multitude of different frailty assessment instruments with historical reviews noting between 14 - 16 different tools used across 23 - 53 studies.[52, 60] Each tool, measuring differing aspects of frailty, will predict varying incidences of frailty and hold different prognostic value. This introduces uncertainty around the clinical applicability of the tools and may discourage their uptake in clinical settings.

As a result, there is currently no consensus on the optimal tool. Further, disparate data from heterogeneous assessment techniques complicates data comparison and pooling which inherently limits research impact and clinical applicability of results.

As frailty has gained increasing visibility in the surgical community it is possible that there is now greater standardisation in frailty assessment. However, with an increasing number of frailty assessment instruments available, it is also possible that inconsistency in assessment has increased. Only by demonstrating and understanding this heterogeneity in frailty assessment techniques can researchers, and clinicians, begin further evidence synthesis which may shed light on the optimum approach to assessing frailty in clinical practice.

3.2.3 Objectives

This chapter presents a systematic review which aims to collate and describe all frailty assessment instruments, tools, and surrogate markers used in vascular surgery research with the intention of quantifying frailty. Secondary objectives were to describe the mode of instrument application, assess the content validity of described frailty assessment techniques as well as critically appraising psychometric and clinimetric properties of the most commonly used instruments. As the prognostic utility of frailty assessment instruments have been reported previously[2, 60, 63], repeating these measurements was not felt to be of additional academic value.

3.3 Methods 1 - Systematic review of frailty assessment instruments in vascular surgery

The review followed best practice in evidence synthesis and is reported using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidance where appropriate.[91]

3.3.1 Participants

The following inclusion criterion were applied:

- Adults (aged ≥ 18 years) diagnosed and/or treated for arterial disease normally treated by vascular surgery speciality, including: abdominal aorta, aortoiliac segment, mesenteric, femoral, upper/lower limb and carotid arteries.

- Treatment for acute, chronic and acute-on-chronic vascular conditions on an emergency, urgent and/or elective basis.

- Patients with arterial disease managed by open surgical techniques, endovascularly or non-operatively were eligible for inclusion.

Studies investigating frailty in mixed surgical patients were eligible if outcomes for vascular surgery patients were reported separately. Disease of the thoracic or thoracoabdominal aorta was considered if the proposed treatment did not involve aortic root, or aortic arch, repair/replacement to avoid inadvertent inclusion of cardiothoracic surgery patients. To ensure consistency in the dataset, vascular access patients were excluded as these can be managed by vascular or renal transplant specialities. Trauma patients were excluded from this analysis as this represents a different patient cohort with different demographics and pathophysiological mechanisms.

3.3.2 Studies

Journal manuscripts and published conference abstracts describing observational studies, trials and quality improvement/audit projects were included. Non-human, non-English, case-reports, unpublished studies and non peer-reviewed pre-prints were excluded. Separate articles accessing the same study population were not collated if the study methodology or research question differed. Separate articles describing the same study, or updated results from a previous study, were collated in favour of selecting the most comprehensively described study. The inclusion of abstracts may be felt to be problematic in some reviews due to limited data available for extraction.[92] However, this review does not intend to perform a meta-analysis on prognostic implications of frailty – as this aspect has been well described[2, 60, 63]-, rather it intends to collate and present methods for frailty assessment, and the relevant data was felt likely to be sufficiently detailed in published abstracts. This methodology was felt pertinent for capturing the full literature in this fast-moving area of research, quantifying the described methodological approaches to frailty assessment within vascular surgery research in its entirety.

3.3.3 Frailty assessment

As discussed previously in this chapter, there is no gold standard definition for the frailty syndrome and there exists a multitude of measurable frailty-related deficits. This review did not enforce a standardised definition of frailty, rather it considered authors' definitions of this construct. This ensured the most comprehensive and inclusive review of literature describing the use of any instrument, tool, or outcome measure, used with the described intention of quantifying the presence, or severity, of frailty in vascular surgical patients.

3.3.4 Sarcopenia as a surrogate marker of frailty

During the first round of literature review it became apparent that some authors were utilising measures of sarcopenia as surrogate markers of frailty. However, this was done so inconsistently with other authors exploring measurements of sarcopenia and its prognostic utility in the absence of consideration of the frailty syndrome. To ensure reproducibility in this reviews methodology, the decision was made to exclude any studies exploring sarcopenia done in the context of frailty, Figure 3.1. Where a study examined multiple frailty assessment tools/techniques, including sarcopenia, this study was included but the sarcopenia measurement was not collected during data extraction.

3.3.5 Search strategy

Embase (OVID), Medline (OVID) and CINAHL (EBSCO) were searched from inception to August 2022 using a combination of MeSH terms for frailty and validated search syntaxes for relevant vascular diseases and treatments, these are presented in full in appendix 1. Systematic/literature reviews and letters of correspondence were not included but were manually reference checked for eligible original studies. Studies published in both conference abstract and journal article formats were collated, in favour of selecting the journal article. All included studies underwent manual reference checking. As the amount of extractable data is limited from conference abstracts, these results are presented separately and only consider the numerical total of frailty assessment instruments.

3.3.6 Study selection

References were imported and deduplicated in EndNote X9 (Clarivate).[93] Following deduplication, I performed a first-pass screen of references to exclude clearly irrelevant references. Thereafter, all further aspects of literature review (title and abstract screening and full text review) and data extraction were performed by myself and another researcher, working independently.

Discrepancies were discussed and resolved, agreeing final outcomes. There was access to a third researcher for independent advice, but this was not required. During title and abstract screening, references were labelled 'include', 'maybe' and 'exclude'. Full articles for those not excluded were then retrieved for full text review to assess eligibility for inclusion.

3.3.7 Data extraction

Data extraction was performed using a standardised template on Microsoft Excel (version 2304). Basic data extraction included study design, publication details, participant demographics and the outcome measures described by included studies. These outcome measures include mortality (timeframe as defined by authors), morbidity (as classified by authors), length of hospital stay, readmission rates, nonhome discharge, limb salvage/amputation free survival, postoperative function, patient reported outcome measures and a category of 'other' for less commonly described outcome measures. These outcome measures were formulated during data extraction as they were encountered.

The instruments and methods for assessing frailty were then collected. Data on frailty tool description and utilisation included instrument format (expanded below), author description of the instrument (defined as 'present' or 'absent'), if a frailty cut-off value was described for the selected instrument (if yes, the value was collected) and whether the author introduced modifications to the selected frailty assessment instrument (defined as 'yes' or 'no').

The instrument format was categorised into 'frailty index', 'person-assessed' and 'other'. A frailty index is born from the Cumulative Deficit Theory of frailty, as described in Chapter 2. A person-assessed tool incorporates frailty assessments that mandate an in-person assessment whether that constitutes an objective measurement of a physical deficit in accordance with Fried's definition of frailty

(e.g., walking speed) or author-defined variables with the intention of quantifying frailty (e.g., Rockwood Clinical Frailty Scale[18, 94]). The category of 'other' was introduced for frailty assessments that could not be categorised into the aforementioned groups. The statistical methods for data analysis were also collected and compared.

Lastly, this review collected data on author descriptions of the methodological application of their selected frailty assessment techniques. This included: who performed the assessment, where in the patient journey the assessment took place and whether there was any requirement for additional training to use the frailty assessment technique.

Where data were absent and could not be derived, primary authors were not contacted. A category of 'not defined' was used if necessary. As the prognostic value of frailty assessment instruments was not assessed, methodological quality assessment of included studies was not indicated.

3.3.8 Assessment of frailty tool content ('content validity')

Frailty instruments were appraised for their content validity by determining if the tool assessed deficits across multiple domains. Where the instrument assessed deficits across multiple and differing domains, the frailty instrument was accepted as assessing the presence of 'frailty', confirming content validity. For instruments primarily assessing singular, or similar domains, the frailty instrument was instead considered a tool that assessed the presence of the preferentially assessed domain, therefore lacking content validity. To do this, I critically appraised all included frailty assessment instruments, identifying eleven common frailty-related domains through which frailty may be assessed, these are presented in Table 3.1 with definitions. Included articles were referenced checked to identify

descriptions of original versions of frailty assessment instruments. Original instruments were then evaluated for the number and type of domains each instrument assessed. In the instance where an instrument describes assessing one domain as part of another (e.g., mobility as part of function), both domains were documented as assessed. A summary of the psychometric definition of content validity is included in section 3.5 of this chapter.

Table 3.1 - The 11 domains included in assessing content validity of frailty assessment techniques. Table is as presented in Welsh et al.[90]

Domain category	Definition
Mobility	Defined according to level of dependence or measurements of physical parameters. This included descriptions of mobility as 'independent', 'requires assistance' (to any extent), and 'dependent'. It also included self-rated scores of perceived abilities to mobilise described distances (e.g. Likert scales or binary answers). Similarly, it included physical measurements, such as gait speed, or measurements of time taken to cover a certain distance. Mobility was at times described as being assessed as part of function, in this instance, both 'Mobility' and 'Function' domain categories were documented as assessed. Where frailty assessment techniques defined independently assessing 'Mobility', in the absence of considering 'Function', only Mobility was documented as assessed.
Function	This was defined as a measurement of any degree of functional (in)dependence according to an (in)ability to perform activities of daily living (ADL). The selected ADLs were accepted according to the definition set out by the frailty assessment tool/technique. Typically, these include descriptions of personal/domestic hygiene, shopping, managing finances and continence.
Cognition	This included any mode of assessment used to quantify the presence, and/or severity, of cognitive impairment. Typically, this includes assessment of mild memory loss through to advanced dementia as well as the presence/absence of delirium. This includes validated techniques (e.g. 4AT), non-validated/novel techniques and self-assessment questionnaires.
Nutrition	This described any anthropometric, biochemical, clinical, or dietary measurement used with the described intention of measuring the physiological state of an individual which results from the relationship between nutritional intake and nutritional requirement.
Mood	This was defined as any measurement of an intrinsic emotional state, psychological description or feeling, differing from assessments of cognition.
Comorbidity	This was defined as any qualitative or quantitative measurement of medical disease. This included a description of a list of medical disease, scored as absent or present. This also incorporated more general assessments, such as nonspecific self-assessment scores for perceived health status (e.g., 'Patient description of overall health: Good, Fair or Poor'.)
Medication	This was defined as the assessment of the need for medication and/or the requirement for multiple medications (the

	definition for multiple medication/pharmacy varied according to different tools).
Social	This definition included any subjective or objective quantification of social vulnerability. These include, but are not limited to socioeconomic class, residential status (e.g., 'residence other than independent living'/'living status'), cohabitation status or self-assessment of the extent to which the participant feels supported or part of a social network.
Nature of admission	The presence or absence of 'emergency hospital' admission being part of the frailty assessment technique. This domain was formulated in the absence of being suitably incorporated into any other domain.
Age	This domain includes and frailty assessment tool which incorporate a description of age either dichotomously or categorically.
Laboratory	This domain includes the use of any serum marker (primarily biochemical but also haematological) as a surrogate marker for frailty. Unless specifically described by the authors, the assessment of different biomarkers was considered independently from other domains. For example, serum albumin is incorporated in some assessments of nutritional status. However, if albumin was described as being independently assessed, as a surrogate marker of frailty without referencing nutrition in the authors definition of frailty, only the 'Laboratory' domain was marked as assessed.

3.4 Results 1 – systematic review of frailty assessment instruments in vascular surgery

A total of 5358 references were identified, from which 1244 underwent abstract screening. There were 110 original studies and 44 published abstracts eligible for inclusion. One additional original study published in journal article form was identified on manual reference checking, Figure 3.1. Table 3.2 presents a complete list of included studies (n = 111) summarising the author, year of publication, study design, if the study only included patients managed operatively ('intervened on'), number of participants, as well as the number and type of frailty instruments used.

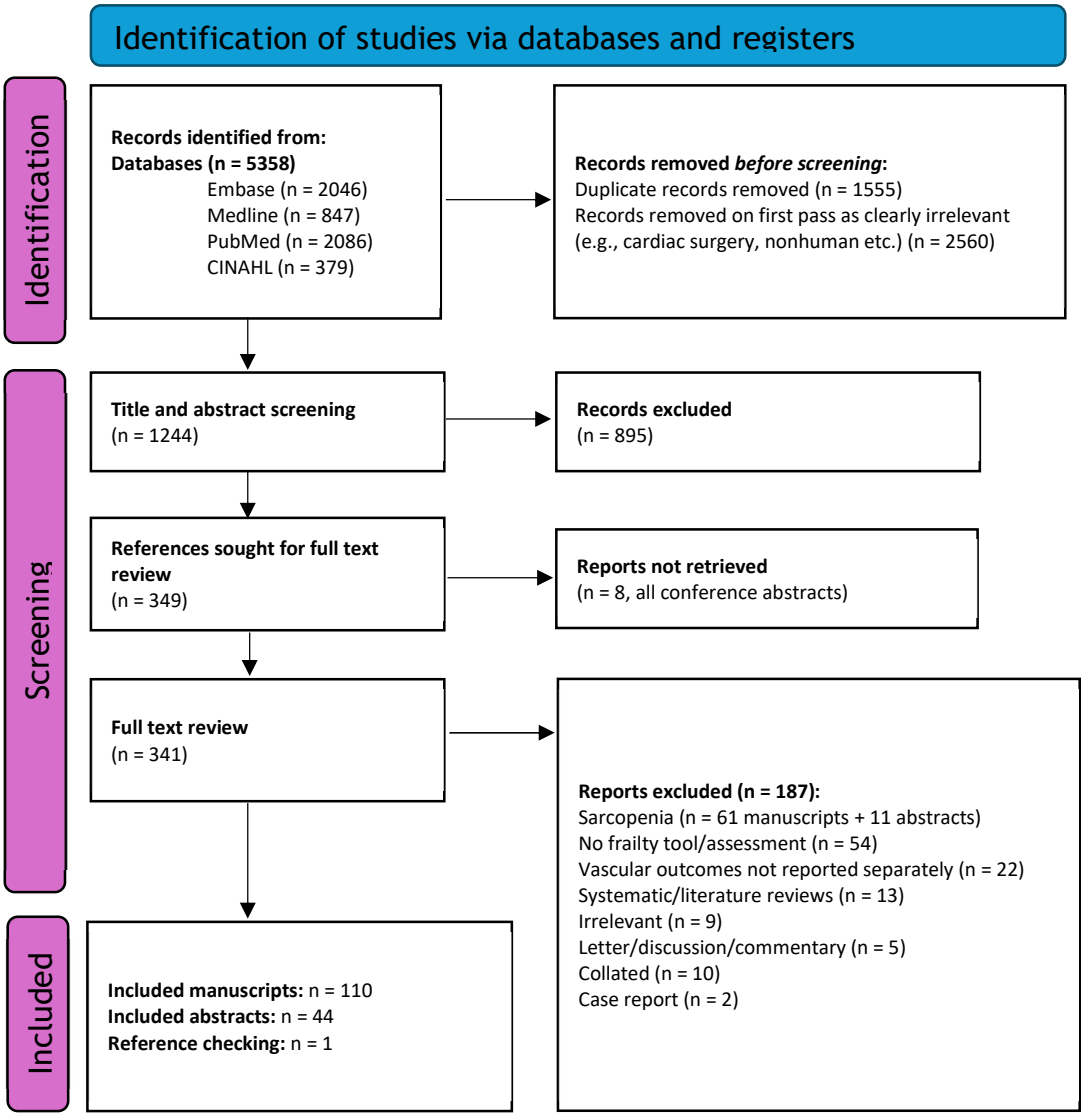


Figure 3.1 - PRISMA diagram for the selection of articles assessing frailty in vascular disease. Figure is as presented in Welsh et al.[90]

Table 3.2 - Characteristics of included studies. Full list of included studies assessing frailty in vascular surgery with results published in journal article format. Table is as presented in Welsh et al.[90]

Study ID	Author	Year	Study Design	Country	Data Source	Included only intervened on	Age cut-off (years)	n		Frailty prevalence (%)	No. frailty tools used	Frailty instrument(s)
								Total	Frail			
1	Aitken[95]	2021	Cohort, R	Australia	Government maintained APDC	Y	75	9752	ND	-	1	Hospital Frailty Risk Score
2	Aitken[96]	2022	Cohort, P	Australia	Prospectively collected data/institutional database	Y	18	917	203	22	1	Clinical Frailty Scale (9 point)
3	Al Shakarchi [97]	2019	Cohort, R	England	NVR	Y	ND	184	26	14	1	Clinical Frailty Scale (9 point)
4	Al-Damluji [98]	2022	Cohort, R	USA	VQI	Y	ND	85517	ND	-	2	5-item modified frailty index (mFI-5) VQI-derived Risk Analysis Index (VQI-RAI)
5	Ali[99]	2018	Cohort, R	USA	ACS-NSQIP	Y	16	4704	ND	-	1	11-item modified frailty index (mFI-11)
6	Ambler [100]	2020	Cohort, R	England	Institutional database	N	65	410	ND	-	2	Addenbrookes Vascular Frailty Score Modified Addenbrookes Vascular Frailty Score
7	Ambler [101]	2015	Cohort, R	England	Institutional database	N	65	410	ND	-	1	Addenbrookes Vascular Frailty Score
8	Andersen [102]	2020	Cohort, R	USA	VQI	Y	18	2040	ND	-	1	5-item modified frailty index (mFI-5)
9	Araujo-Andrade [103]	2020	Cohort, R	Portugal	Institutional database	Y	ND	184	45	24	1	5-item modified frailty index (mFI-5)
10	Arya[104]	2015	Cohort, R	USA	ACS-NSQIP	Y	16	23027	ND	-	1	11-item modified frailty index (mFI-11)
11	Arya[105]	2016	Cohort, R	USA	ACS-NSQIP	Y	ND	15843	ND	-	1	11-item modified frailty index (mFI-11)
12	Ayyash [106]	2022	Cohort, P	England	Prospectively collected data	Y	60	97	ND	-	2	Clinical Frailty Scale (9 point) Edmonton Frail Scale (EFS)
13	Bailey [107]	2022	Cohort, R	Wales	NHS database	Y	ND	127	ND	-	1	Initial Clinical Evaluation (ICE)
14	Banning [108]	2021	Cohort, P	NL	Prospectively collected data	Y	ND	639	183	29	1	Groningen Frailty Index

15	Banning [109]	2020	Cohort, P	NL	Prospectively collected data/institutional database	Y	65	310	129	42	1	Groningen Frailty Index
16	Barbey [110]	2019	Cohort, R	USA	VQI	Y	ND	20750	ND	-	1	11-item modified frailty index (mFI-11)
17	Beffa[75]	2015	Cohort, R	USA	Medicare and Medicaid Services Medicare Provider Analysis and Review Health insurance claims (MedPAR) linked to nursing home datasets	Y	67	213	213	100	1	Nursing home resident as surrogate marker of frailty
18	Boyd[111]	2022	Cohort, R	USA	VASQIP	Y	None	22960	ND	-	1	Risk Analysis Index-A (RAI-A)
19	Braet[112]	2020	Cohort, R	USA	ACS-NSQIP	Y	18	11530	ND	-	1	5-item modified frailty index (mFI-5)
20	Brahmbhatt [113]	2016	Cohort, R	USA	ACS-NSQIP	Y	16	24611	14738	60	1	11-item modified frailty index (mFI-11)
21	Brown [114]	2022	Cohort, P	England	Prospectively collected data	N	ND	84	16	19	1	Clinical Frailty Scale (7 point)
22	Butala [115]	2021	Cohort, R	USA	Medicare and Medicaid Services Medicare Provider Analysis and Review Health insurance claims (MedPAR)	Y	66	85060	35484	42	1	Claims-based Frailty Indicator (CFI)
23	Callahan [116]	2021	Cohort, R	USA	Institutional database	Y	65	269	61	23	1	electronic Frailty Index (eFI)
24	Chopra [117]	2018	Cohort, R	USA	Institutional database	Y	ND	206	ND	-	1	11-item modified frailty index (mFI-11)
25	Ciaramella[118]	2021	Cohort, R	USA	Institutional database	Y	ND	60	21	35	1	11-item modified frailty index (mFI-11)
26	Cotton [119]	2022	Cohort, R	USA	Institutional database	Y	18	298	ND	-	2	11-item modified frailty index (mFI-11) Risk Analysis Index (RAI-A)
27	D'Cruz [120]	2020	Cohort, R	Singapore	Institutional database	Y	ND	211	ND	-	1	11-item modified frailty index (mFI-11)
28	DeAngelo [121]	2021	Cohort, P	USA	Prospectively collected data	Y	18	126	55	44	2	13-item Vulnerable Elders Survey (VES-13) Clinical Frailty Scale (7 point)
29	Dittman [122]	2022	Cohort, R	USA	ACS-NSQIP	Y	ND	8155	ND	-	1	Revised Risk Analysis Index (RAI-Rev)
30	Donald [123]	2018	Cohort, R	USA	Institutional database	Y	ND	134	39	29	1	Clinical Frailty Scale (9 point)
31	Drudi[124]	2019	Cohort, P	Canada	Prospectively collected data/institutional database	y	ND	148	ND	-	6	Edmonton Frail Scale (EFS) Groningen Frailty Index (GFI) 11-item modified frailty index (mFI-11) Risk Analysis Index (RAI-C)

												Modified Essential Frailty Toolset (mEFT) Multidimensional Prognostic Index (MPI)
32	Edman [125]	2022	Cohort, R	USA	Institutional database	N	ND	578	ND	-	2	5-item modified frailty index (mFI-5) Authors own
33	Ehlert [126]	2016	Cohort, R	USA	ACS-NSQIP	Y	18	72106	ND	-	1	11-item modified frailty index (mFI-11)
34	Eslami [127]	2019	Cohort, R	USA	ACS-NSQIP	Y	18	12677	ND	-	1	11-item modified frailty index (mFI-11)
35	Faateh [81]	2021	Cohort, R	USA	VQI	Y	ND	7836	ND	-	2	5-item modified frailty index (mFI-5) Functional status database code ("Good/poor")
36	Fang[128]	2017	Cohort, R	USA	Institutional database	Y	18	379	ND	-	1	5-item modified frailty index (mFI-5)
37	George(a) [129]	2020	Cohort, R	USA	VQI	Y	ND	11647	4034	35	2	VQI-derived Risk Analysis Index (VQI-RAI) Initial Clinical Evaluation (ICE)
38	George(b)[130]	2020	Cohort, R	USA	VQI	Y	18	15803	2010	13	1	VQI-derived Risk Analysis Index (VQI-RAI)
39	George [131]	2021	Cohort, R	USA	ACS-NSQIP/VASQIP	Y	18	217215	ND	-	1	Risk Analysis Index
40	Gilbertson[132]	2021	Cohort, R	USA	Institutional database linked to SVS-PSO VQI	Y	ND	163	44	27	1	Clinical Frailty Scale (9 point)
41	Gonzalez [76]	2019	Cohort, R	USA	Institutional database	Y	ND	431	ND	-	2	11-item modified frailty index (mFI-11) Biomarkers
42	Gouda [133]	2022	Cohort, R	Italy	Multiple linked provincial databases (Alberta)	Y	ND	7861	ND	-	1	Hospital Frailty Risk Score
43	Gray[134]	2020	Cohort, R	England	HES database for England	Y	18	98109	ND	-	1	Hospital Frailty Risk Score
44	Harris [135]	2017	Cohort, R	USA	ACS-NSQIP	Y	ND	13432	389	3	1	Functional status per NSQIP ("dependent/independent")
45	Harris[82]	2020	Cohort, R	USA	ACS-NSQIP	Y	ND	1784	ND	-	1	Authors own
46	Holeman [136]	2020	Cross-sectional, P	USA	Prospectively collected data	n	ND	118	ND	-	3	Clinical Frailty Scale (9 point) Frail Non-Disabled Questionnaire (FiND) Patient-reported outcome measurement information system (PROMIS): a) Physical Function (v1.2), b) Satisfaction with Social Activities (v2.0) and c) Depression (v1.0)
47	Houghton [77]	2019	Case-control, P	England	Prospectively collected data	Y	18	n/a	ND	-	3	Clinical Frailty Scale (9 point) Edmonton Frail Scale (EFS) Biomarkers

48	Houghton [137]	2021	Cohort, R	England	Institutional database	N	50	198	98	49	1	Clinical Frailty Scale (9 point)
49	Hui[138]	2019	Cohort, R	USA	Multiple linked provincial databases (Ontario)	Y	65	17047	7979	47	1	preoperative Frailty Index
50	Iida[68]	2017	Cohort, P	Japan	Prospectively collected data (PRIORITY database)	N	20	625	ND	-	2	5-m gait velocity Grip strength
51	Ishihara [139]	2019	Cohort, R	Japan	Institutional database	Y	ND	71	23	32	1	Cardiovascular Health Study (CHS) Index
52	Itagaki [140]	2021	Cohort, P	Japan	I-PAD registry (regional register)	Y	ND	320	82	26	1	Clinical Frailty Scale (9 point)
53	Karam [141]	2013	Cohort, R	USA	ACS-NSQIP	Y	ND	67308	ND	-	1	11-item modified frailty index (mFI-11)
54	Karim [142]	2022	Cohort, R	USA	NIS	N	18	1414080	332855	24	1	Authors own (CLTI-frailty risk score (CLTI-FRS))
55	Kazaure [143]	2021	Case-control, R	USA	ACS-NSQIP	Y	65	165	ND	-	1	5-item modified frailty index (mFI-5)
56	Khan[144]	2022	Cohort, R	USA	VQI	Y	ND	17983	4524	25	1	5-item Modified Frailty index (5-mFI)
57	Kim[145]	2021	Cohort, R	USA	NIS	Y	18	301869	7729	3	1	Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators
58	Kodama [80]	2018	Cohort, R	Japan	Institutional database	Y	ND	109	ND	-	1	Barthel Index
59	Kraiss [146]	2022	Cohort, R	USA	VQI	Y	ND	265632	ND	-	1	Authors own (simple VQI-Frailty Score (sVQI-FS))
60	Li[79]	2021	Cohort, R	USA	Institutional database	Y	ND	255	137	54	1	Geriatric Nutritional Risk Index (GNRI)
61	Man[147]	2021	Cohort, R	USA	ACS-NSQIP	Y	ND	15839	ND	-	1	Risk Analysis Index (RAI-A)
62	Mandelbaum [148]	2021	Cohort, R	USA	NIS	Y	18	1,426,343	59,158	4	1	Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators
63	McIsaac [149]	2017	Cohort, R	Canada	Multiple linked provincial databases (Ontario)	Y	18	4984	ND	-	1	Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators
64	McRae [150]	2016	Cohort, P	Australia	Prospectively collected data	N	65	110	43	39	1	Authors own
65	Melin[151]	2015	Cohort, R	USA	ACS-NSQIP	Y	ND	44832	ND	-	1	Revised Risk Analysis Index (RAI-Rev)
66	Mirabelli [152]	2018	Cohort, P	USA	Prospectively collected data	N	ND	159	ND	-	3	Frail Non Disabled Questionnaire (FiND) Clinical Frailty Scale (9 point) Friend Frailty Index
67	Modrall [153]	2022	Cohort, R	USA	ACS-NSQIP	Y	ND	2454	ND	-	1	5-item modified frailty index (mFI-5)

68	Morisaki [154]	2017	Cohort, R	Japan	Institutional database	Y	ND	266	92	35	2	Critical Limb Ischaemia Frailty (CLI Frailty) 11-item modified frailty index (mFI-11)
69	Morisaki [155]	2019	Cohort, R	Japan	Institutional database	Y	ND	127	ND	-	2	Critical Limb Ischaemia Frailty (CLI Frailty) Modified Critical Limb Ischaemia Fraitly (Modified CLI Frailty)
70	Morisaki [156]	2020	Cohort, R	Japan	Institutional database	Y	ND	316	30	9	2	Critical Limb Ischaemia Frailty (Modified CLI Frailty) 11-item modified frailty index
71	Najafi[69]	2020	Cohort, P	USA	Prospectively collected data	Y	ND	152	41	27	1	Wearable sensor technology (UL - Najafi)
72	Nishikawa [157]	2021	Cohort, P	Japan	I-PAD registry (regional register)/prospectively collected data	Y	None	352	92	26	1	Clinical Frailty Scale (9 point)
73	Nobrega [158]	2022	Cohort, P	Portugal	Vascular registry/prospectively collected data	Y	ND	109	36	33	1	5-item modified frailty index (mFI-5)
74	O'Neill [159]	2016	Cohort, R	England	Institutional database	Y	None	392	120	31	1	Initial Clinical Evaluation (ICE)
75	Otsuji [160]	2022	Cohort, R	Japan	Institutional database	Y	ND	200	ND	-	1	Clinical Frailty Scale (9 point)
76	Paajanen [161]	2022	Cohort, R	USA	Institutional database	Y	ND	592	ND	-	1	11-item modified frailty index (mFI-11)
77	Pandit(a) [162]	2020	Cohort, R	USA	ACS-NSQIP	Y	ND	37875	10340	27	1	11-item modified frailty index (mFI-11)
78	Pandit(b) [163]	2020	Cohort, R	USA	ACS-NSQIP	Y	18	36000	ND	-	2	11-item modified frailty index (mFI-11) 5-item modified frailty index (mFI-5)
79	Pandit [164]	2021	Cohort, R	USA	ACS-NSQIP	Y	65	8681	ND	-	2	11-item modified frailty index (mFI-11) 5-item modified frailty index (mFI-5)
80	Pandit(c) [165]	2020	Cohort, R	USA	ACS-NSQIP	Y	65	4218	1223	29	1	11-item modified frailty index (mFI-11)
81	Partridge [166]	2014	Cohort, P	England	Prospectively collected data	Y	60	114	ND	-	1	Edmonton Frail Scale (EFS)
82	Partridge [70]	2015	Cohort, P	England	Prospectively collected data	Y	60	125	65	52	4	Edmonton Frail Scale (EFS) Grip Strength Gait Velocity Timed up and go
83	Pol[167]	2011	Cohort, P	NL	Prospectively collected data/institutional database	Y	None	142	50	35	1	Groningen Frailty Index
84	Reeve [168]	2018	Cross-sectional, P	USA	Prospectively collected data	ND	None	311	86	28	1	Grip strength

85	Reijnen [169]	2021	Cohort, R	NL	Institutional database	Y	none	429	ND	-	1	5-item modified frailty index (mFI-5)
86	Reitz[170]	2021	Cohort, R	USA	VASQIP/ACS-NSQIP	Y	None	279115	ND	-	1	Risk Analysis Index
87	Rothenberg(a) [171]	2020	Cohort, R	USA	VQI	Y	None	42869	9993	23	1	Revised Risk Analysis Index (RAI-Rev)
88	Rothenberg(b) [172]	2020	Cohort, R	USA	ACS-NSQIP	Y	none	139569	27015	19	3	Revised Risk Analysis Index (RAI-Rev) Risk Analysis Index-Procedure (RAI-P) Risk Analysis Index-Procedure Complexity (RAI-PC)
89	Ruangsetakit [173]	2022	Cohort, R	Thailand	Institutional database	Y	ND	266	40	15	1	Critical Limb Ischaemia Frailty (CLI Frailty)
90	Ruske [174]	2021	Cross-sectional, P	USA	Prospectively collected data	Y	18	100	ND	-	1	Frail/Nondisabled questionnaire (FiND)
91	Saadeddin[175]	2020	Cohort, R	USA	ACS-NSQIP	Y	18	2612	ND	-	2	5-item modified frailty index (mFI-5) Authors own
92	Sanchez-Garcia [71]	2021	Cohort, R	Spain	Institutional database	N	60	144	9	6	1	Authors own (Preoperative geriatric assessment by geriatrician)
93	Sareh [176]	2020	Cohort, R	USA	Nationwide Readmission Database	Y	ND	302798	45939	15	1	Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators
94	Sarkar [177]	2021	Cohort, R	USA	Institutional database	Y	18	53	46	87	1	11-item modified frailty index (mFI-11)
95	Schaller [178]	2018	Cohort, R	USA	ACS-NSQIP	N	50	129	ND	-	1	11-item modified frailty index (mFI-11)
96	Schweitzer [179]	2022	Cohort, R	USA	ACS-NSQIP	Y	ND	30921	ND	-	1	5-item modified frailty index (mFI-5)
97	Sibona [180]	2022	Cohort, R	USA	Institutional database	N	ND	145	ND	-	1	Clinical frailty scale (9 point)
98	Soon[181]	2022	Cohort, R	Singapore	Institutional database matched ACS-NSQIP	Y	ND	233	ND	-	1	11-item modified frailty index (mFI-11)
99	Spence [78]	2020	Cohort, P	England	Prospectively collected data	ND	ND	33	ND	-	2	Edmonton Frail Scale (EFS) Biomarker
100	Sridharan [182]	2018	Cohort, R	USA	Institutional database	Y	ND	1782	ND	-	1	Authors own
101	Srinivasan [183]	2016	Cohort, R	England	Institutional database	Y	65	184	ND	-	2	Addenbrookes Vascular Frailty Score (AVFS) Authors own
102	Szabó [184]	2021	Cross-sectional, P	Hungary	Prospectively collected data	Y	18	164	ND	-	1	Authors own
103	Takeji [185]	2018	Cohort, P	Japan	Prospectively collected data/institutional database	Y	ND	643	ND	-	1	Clinical Frailty Scale (9 point)

104	Thillainadesan [186]	2021	Cohort, P	Australia	Prospectively collected data/institutional database	N	65	150	ND	-	2	Clinical Frailty Scale (9 point) Authors own
105	Toosizadeh [72]	2016	Case-control, P	USA	Prospectively Collected data	N	60	17	0	0	2	Fried Frailty index Wearable Sensor Technology
106	Tse [187]	2022	Cohort, R	USA	VASQIP	Y	ND	5568	ND	-	1	Risk Analysis Index (RAI-A)
107	Tse[188]	2020	Cohort, R	USA	Institutional database	Y	None	134	44	33	1	Risk analysis Index-A (RAI-A)
108	Velanovich [189]	2013	Cohort, R	USA	ACS-NSQIP	Y	ND	117121	ND	-	1	11-item modified frailty index (mFI-11)
109	Wahl[190]	2017	Cohort, R	USA	VASQIP	Y	ND	42801	ND	-	1	11-item modified frailty index (mFI-11)
110	Wang[191]	2021	Cohort, Both	China	Institutional database	Y	60	749	134	18	1	11-item modified frailty index (mFI-11)
111	Yanquez [73]	2020	Cohort, P	USA	Prospectively collected data	Y	50	37	7	19	1	Wearable sensor technology (upper limb)

Summary table of included articles. R – retrospective. P – prospective. APDC – Admitted Patients Data Collection. NVR - National Vascular Registry. VQI - Vascular Quality Initiative. ACS-NSQIP - American College of Surgeons National Surgical Quality Improvement Program. NHS – National Health Service. VASQIP - Veterans affairs Surgical Quality Improvement Programme. SVS-PSO VQI - Society of Vascular Surgery Patient Safety Organization Vascular Quality Initiative. HES – Hospital Episode Statistics. NIS - National Inpatient Sample. y – Yes. n – No. ND – Not described.

3.4.1 Study characteristics

This systematic review includes an aggregate population of 5,418,236 patients. Of 111 eligible studies, 49 reported the prevalence of frailty with a mean prevalence of 29% (range 0 - 100%).[69-73, 75, 79, 96, 97, 103, 108, 109, 113-116, 118, 121, 123, 129, 130, 132, 135, 137-140, 142, 144, 145, 148, 150, 154, 156-159, 162, 165, 167, 168, 171-173, 176, 177, 188, 191] The majority of included studies were retrospective (n=82, 73.9%) or prospective cohort (n=21, 18.9%) design. One author performed a retrospective study that ran onto a prospective format. Additionally, there were four cross-sectional (3.6%), two case-control studies (1.8%) and one published study protocol (0.9%). From 111 studies published as journal articles most were from the United States of America (n = 68, 61%) and the United Kingdom (n = 14, 13%). Studies primarily reported on elective admissions (n = 51, 46%) and the most common outcome measures were mortality (n = 96, 86%) and morbidity (n = 75, 68%). The most common vascular procedures performed were lower limb revascularisation (n = 81, 73%) and abdominal aortic aneurysm repair (n = 73, 66%), Table 3.3.

Table 3.3 - Study outcome measures and vascular interventions for included studies published as journal articles. Table is as presented in Welsh et al.[90]

Country of research origin (n = 111)	**N (%)**
USA	68 (61)
UK	14 (13)
Japan	10 (9)
EU countries (The Netherlands, Portugal, Hungary, Italy, Spain)	9 (8)
Australia	4 (4)
Canada	2 (2)
Singapore	2 (2)
China	1 (1)
Thailand	1 (1)
Mode of presentation (n = 111)	
Elective	51 (46)
Not specified	35 (32)
Both	21 (19)
Emergency	4 (4)
Study outcome measures (n = 111)	
Mortality	96 (86)
Morbidity (including all medical/surgical complications and re-intervention)	75 (68)
Length of stay	36 (32)
Readmission	30 (27)
Nonhome discharge	22 (20)
Limb salvage/Amputation Free Survival	17 (15)
Postoperative function (functional status/ability to perform activities of daily living/care requirement on discharge/gait speed)	10 (9)
Patient Reported Outcome Measure	4 (4)
Other	14 (13)
Vascular interventions (n = 111)	
Lower limb bypass graft	43 (39)
Endovascular aneurysm repair (including fenestrated and branched endografts)	42 (38)
Lower limb angioplasty +/- stenting	38 (34)
Open repair of abdominal aortic aneurysm	31 (28)
Carotid endarterectomy	23 (21)
Lower limb amputation	20 (18)
Aortoiliac segment	19 (17)
Thoracic endovascular aortic repair	12 (11)
Carotid artery stent	10 (9)
Open thoracoabdominal aortic repair	9 (8)
Mesenteric revascularisation	6 (5)
Vascular access procedures	6 (5)
Thrombo-embolectomy	5 (5)
Other (pseudoaneurysm repair, carotid-subclavian bypass, arteriovenous fistula repair)	4 (4)
Unspecified vascular procedures	16 (14)
**Other - (Ambulatory status (n=3), comparing prognostic value of frailty assessment tools (n = 2), cost of care (n=2), frailty state transition (n = 2), palliative care referral (n = 1), patient comprehension during*	

consent process (n=1), correlation between age and frailty (n=1), correlation between race/ethnicity and frailty (n=1), interuser variability of frailty assessment tool (n = 1)

3.4.2 Frailty assessment techniques

Table 3.4 presents a complete list of the assessment instruments/tools and techniques for assessing frailty in vascular surgery identified by this review. Across 111 studies, there were 42 different assessment tools or methods used to assess frailty, with a total of 147 frailty assessments performed. 85 studies assessed frailty using one tool[69, 71, 73, 75, 79, 80, 82, 95-97, 99, 101-105, 107-118, 120, 122, 123, 126-128, 130-135, 137-151, 153, 157-163, 166-171, 173, 174, 176-182, 184, 185, 187-191], 20 studies used two tools[68, 72, 76, 78, 81, 98, 100, 106, 119, 121, 125, 130, 154-156, 163, 164, 175, 183, 186], four studies used three tools[77, 136, 152, 172], one study used four tools[70] and one used six tools[124]. There were 11 (26%) bespoke tools, designed by the study author for the purpose of their study, these are included in Table 3.4 as 'Authors own'.[71, 125, 135, 141, 146, 150, 175, 182-184, 186] The distribution of person-assessed tools (n = 20) and frailty indexes (n = 19) were similar. Each assessment is presented in order of popularity ('number of assessments') along with a representation of the tool format, content validity and the domains assessed by (original versions) of each tool.

Table 3.4 - Frailty assessment (instruments) used in 111 included studies. Table is as presented in Welsh et al.[90]

Frailty tool	Assessment No. (Total 147)	Instrument format	Content validity	Mobility	Function (dependence) + ability to complete ADLs	Cognition	Nutrition	Mood	Comorbidity	Medication	Social	Nature of admission	Age	Laboratory
11-item Modified Frailty Index (mFI-11)	27	FI	Frailty		●	●			●					
Risk Analysis Index (RAI - combined)	17	FI	Frailty	●	●	●	●		●		●		●	
5-item Modified Frailty Index (mFI-5)	16	FI	Frailty		●				●					
Clinical Frailty Scale (9 point)	15	PA	Frailty		●	●			●					
Edmonton Frail Scale (EFS)	6	FI	Frailty		●	●				●				
Critical Limb Ischaemia Frailty (CLI Frailty)	5	FI	Frailty	●			●							
Addenbrookes Vascular Frailty Score	4	FI	Frailty	●	●			●		●		●		●
Groningen Frailty Index	4	FI	Frailty	●	●	●	●	●		●	●			
Johns Hopkins Adjusted Clinical Group System (JHACGS)	4	PA	Unclear	-	-	-	-	-	-	-	-	-	-	-
Biomarkers	3	Other	No tool											●
Frail Non Disabled Questionnaire (FiND)	3	PA	Frailty	●			●	●						
Hospital Frailty Risk Score	3	FI	Frailty	●	●	●	●	●	●		●			
Initial Clinical Evaluation (ICE)	3	PA	Unclear	-	-	-	-	-	-	-	-	-	-	-
Wearable sensor technology	3	PA	Strength		●									
Grip strength	3	PA	Strength		●									
Clinical Frailty Scale (7 point)	2	PA	Frailty		●				●					
Fried Frailty Index	2	PA	Frailty	●			●	●						
Functional status (per database coding)	2	Other	No tool		●									
Gait velocity measurements	2	PA	Function	●										
13-item Vulnerable Elders Survey (VES-13)	1	PA	Frailty	●	●								●	
Barthel Index	1	PA	Function	●	●									

Cardiovascular Health Study (CHS) Index	1	PA	Frailty	●	●		●							
Claims-based Frailty Indicator (CFI)	1	FI	Frailty	●	●	●		●	●				●	
electronic Frailty Index (eFI)	1	FI	Frailty	●	●	●	●	●	●	●				●
Geriatric Nutritional Risk Index (GNRI)	1	PA	Nutrition				●							
modified Essential Frailty Toolset (mEFT)	1	PA	Frailty	●		●								●
Multidimensional Prognostic Index (MPI)	1	PA	Frailty		●		●	●	●	●	●			
Nursing home resident	1	Other	No tool	-	-	-	-	-	-	-	-	-	-	-
Patient-reported outcome measurement information system (PROMIS): a) Physical Function (v1.2), b) Satisfaction with Social Activities (v2.0) and c) Depression (v1.0)	1	PA	Function/Quality of Life		●			●						
preoperative Frailty Index	1	FI	Frailty	●	●	●	●		●	●	●			
Timed up and go test	1	PA	Function	●	●									
Authors own: Edman[44]	1	FI	Frailty	●	●	●	●							●
Authors own: Harris[57]	1	FI	Frailty		●				●					
Authors own: Karim[66]	1	FI	Frailty				●		●					●
Authors own: Kraiss[71]	1	FI	Frailty	●			●		●		●			●
Authors own: McRae[76]	1	PA	Frailty		●	●	●							
Authors own: Saadeddin[103]	1	FI	Frailty				●		●	●			●	●
Authors own: Sanchez-Garcia[104]	1	PA	Frailty	●		●			●					
Authors own: Sridharan[112]	1	FI	Comorbidity						●					
Authors own: Srinivasan[113]	1	FI	Frailty		●				●	●				●
Authors own: Szabó[114]	1	PA	Frailty			●	●	●	●	●				
Authors own: Thillainadesan[116]	1	FI	Frailty	●	●	●		●	●		●			

Tabular summary of 42 frailty assessment tools, summarising frequency of use, tool type, frailty assessment tool outcome measures and the frailty domains which were assessed. ● Indicates this domain was assessed. – Indicates the frailty tool domains could not be assessed either due to the frailty assessment relying on the subjective opinion of the assessors impression of overall frailty (Initial Clinical Evaluation), lack of description on domain assessment (Johns Hopkins Adjusted Clinical Group System) or using nursing home residency as a surrogate marker of frailty without assessing domain deficits. Blank fields represent domains that were not assessed. Multiple versions of the Risk Analysis Index (RAI) were used across studies, and it was not always possible to identify which RAI was employed (see Appendix 5 for complete list). To simplify presentation, these assessment tools have been collated and presented as 'RAI-combined'. FI – Frailty Index, PA – Person assessed

3.4.3 Frailty instrument domain assessment

Domains assessed by frailty assessment techniques could be determined in 39 (93%) of 42 frailty assessment techniques. The three (7%) frailty assessment techniques where the domains assessed could not be determined, were: the 'Initial Clinical Evaluation' (ICE)[107, 129, 159], the Johns Hopkins Adjusted Clinical Group System' (JHACGS)[148, 149, 176] and the use of nursing home residency[75] as a surrogate marker. ICE could not be assessed as it relies on an undefined subjective assessment performed by a clinician during patient assessment. JHACGS bases its assessment on the Fried phenotypic definition of frailty, describing an assessment that measures the presence or absence of unintentional weight loss, exhaustion, low energy expenditure, low grip strength, and/or slowed walking speed. However, it was not possible to access the technique or variables used to measure these outcomes and so the exact domains assessed could not be confirmed. Similarly, nursing home residency may imply frailty but the justification for this (e.g., physical frailty, cognitive frailty, comorbidity) is incompletely described and so this was also excluded.

The eleven frailty-domains weighted by the frequency of assessment according to the number of times each frailty assessment technique is used, are presented in Figure 3.2. Function was most commonly assessed (23%), followed by comorbidity (20%) and cognition (16%).

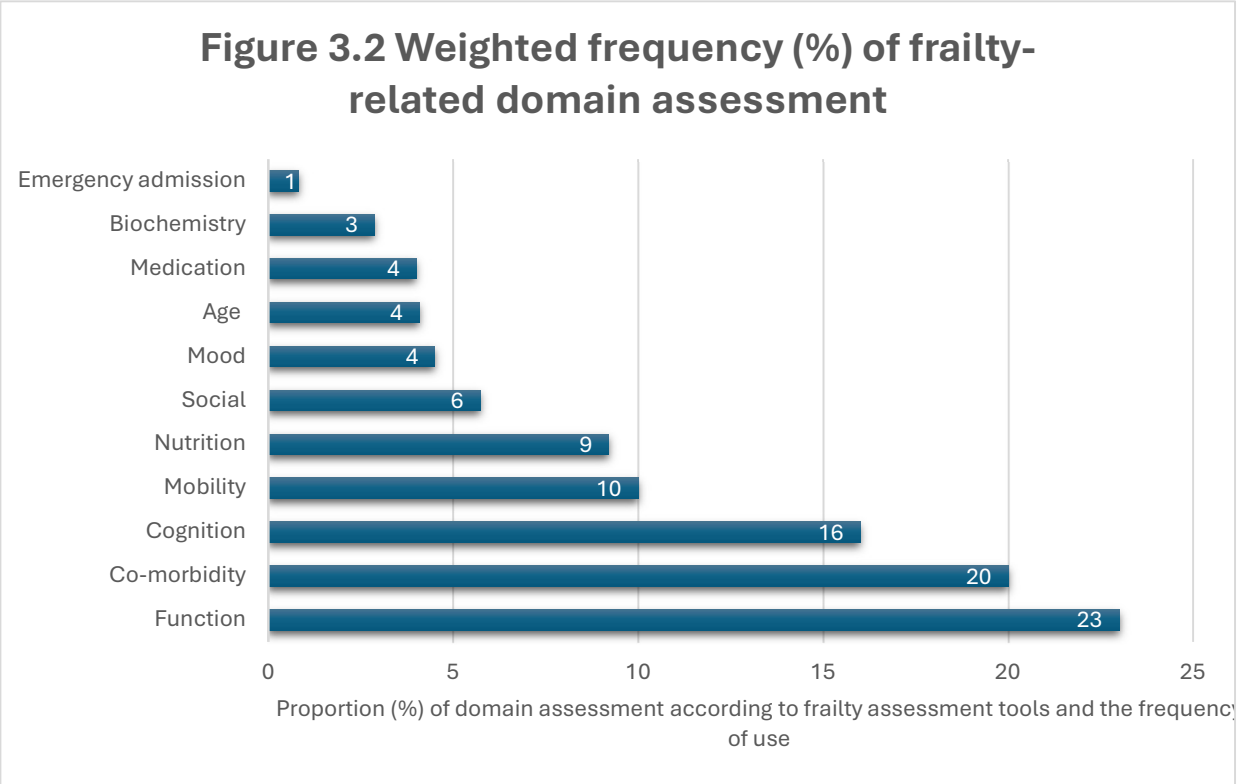


Figure 3.2 - Summary of weighted frequency of the 11 domains assessed by frailty assessment tools. Figure is as presented in Welsh et al.[90]

3.4.4 Frailty instrument content validity

Content validity was assessed for 37 (88%) of 42 frailty assessment techniques, Table 3.4. There were two (5%) frailty assessment techniques where content validity could not be assessed, including: ICE[107, 129, 159] and JHACGS[148, 149, 176] as the domains could not be determined, as discussed earlier in this chapter. The content validity for these tools have been labelled as 'unclear' in Table 3.4. Further, three frailty assessment techniques did not assess domains, rather, measured a single variable described as a surrogate marker of frailty. These are therefore not included in further analysis of content validity and are labelled as 'no tool' in Table 3.4. These variables include: biomarkers[76-78], functional status according to database coding[81, 82] or nursing home residency status[75]

The majority of frailty assessment instruments (n=29/37, 78%) measured frailty as a multidimensional syndrome of cumulative deficits, confirming content validity. Eight assessment techniques (26%) preferentially assessed individual domains, including: Function ± quality of life (n = 4)[68, 70, 80, 136], strength (n = 2)[68-70, 72, 73, 168], nutrition (n = 1)[79], comorbidity (n=1)[182].

There were 11 (26%) bespoke tools, designed by the study author for the purpose of their study.[71, 125, 135, 141, 146, 150, 175, 182-184, 186] The overall content validity of frailty assessment tools used in vascular surgery decreased (n = 19/26, 73%) when these tools were discounted.

3.4.5 Frailty instrument description and utilisation

I selected the ten most commonly used frailty assessment techniques to compare how authors reported on their methodological application of each tool. Some frailty assessment techniques had been used the same number of times, complicating selection. To overcome this, only instruments where domains could be assessed, and content validity was confirmed, were selected for inclusion, Table 3.5.

One hundred frailty assessments were performed with the ten most commonly used frailty assessment instruments. The majority of frailty assessments (n = 84, 84%) were performed using original versions of the selected frailty assessment instrument, as described or referenced by the authors[70, 77, 81, 95, 98-103, 105, 106, 108, 109, 111-113, 118-120, 122, 124-130, 133, 134, 136, 141, 143, 144, 147, 152-156, 158, 162-167, 169, 171, 173-175, 177-179, 181, 187-191]. Twelve assessments (12%) were performed using a modified version of a selected frailty assessment instrument, however, in five of these cases (42%), authors did not describe what the modification was.[76, 100, 104, 110, 151, 155, 156, 161, 171, 172, 183] In four assessments (4%) the authors failed to describe or reference the instrument at all, after naming its application in the study[78, 117, 131, 170].

Table 3.5 - Descriptive and analytical characteristics of the 10 most frequently used frailty assessment (instruments) used in included journal article studies. Table is as presented in Welsh et al.[90]

		Instrument description			Analysis description					
Instrument used to assess frailty	n	Standard tool (%)	Modified version (%)	Not described (%)	Binary	Different cut offs	Continuous	Categorical	Different cut offs	Not described
11-item modified frailty index (mFI-11)[192]	27	22 (81.5)	4 (14.8)	1 (3.70)	10	Yes	5	11	Yes	4
Risk Analysis Index (RAI - combined)[193]	17	11 (64.7)	4 (23.5)	2 (11.8)	12	Yes	2	6	Yes	4
5-item modified frailty index (mFI-5)[194]	16	16 (100)	-	-	4	Yes	5	1	N/A	6
Clinical Frailty Scale (9 point) (CFS)[94]	15	15 (100)	0		9	Yes	2	2	Yes	3
Edmonton Frail Scale (EFS)[195]	6	5 (83.3)	0	1 (16.67)	4	Yes	1	1	N/A	2
Critical Limb Ischaemia Frailty (CLI Frailty)[154]	5	3 (60)	2 (40)	-	5	No	-	-	-	-
Addenbrookes Vascular Frailty Score[101]	4	2 (50)	2 (50)	-	-	-	3	-	-	1
Groningen Frailty Index[196]	4	4 (100)	-	-	4	No	1	-	-	-
Frail Non Disabled Questionnaire (FiND)[197]	3	3 (100)	-	-	3	No	-	-	-	-
Hospital Frailty Risk Score[198]	3	3 (100)	-	-	-	-	-	3	No	-
Total number of assessments	**100**	**84 (84)**	**12 (12)**	**4 (4)**	**51**	**-**	**19**	**24**	**-**	**20**

Table summarising the most 10 commonly used frailty assessment tools in vascular surgery in order of most to least commonly used (n). N/A - Not applicable. The proportion of studies describing use of standard version of the tool, compared to modified or no description is presented, alongside mode of data analysis. Some studies analysed data in more than one way. Values are presented as n (%) unless otherwise indicated. The Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicators tool was used by 4 authors but not presented in this table due to incomplete description. Other tools that were assessed three times but not presented in this table include: biomarkers (not presented as these were isolated variables selected as surrogate markers of frailty rather than an assessment tool), initial clinical evaluation (not presented due to subjective nature of tool), wearable sensor technology and grip strength (not presented due to differences in equipment and methodological application of assessment between authors).

3.4.6 Mode of data analysis

The same data selected for section 3.4.5 was used to compare how authors analysed their data. From the 100 assessments, this review identified three different modes of data analysis: dichotomous, continuous and categorical, Table 3.5. Dichotomous analysis describes a binary classification of patients into 'robust' or 'frail' categories. Continuous data analysis can be applied to frailty assessment techniques that quantify frailty across a scale. Lastly, categorical analysis describes the instance where continuous data were classified into groups, data permitting. For example, the categorical analysis may describe three descriptive cut-offs, including 'robust', 'prefrail' and 'frail'.

Data were most commonly analysed in a dichotomous fashion (n = 51 assessments), where patients were categorised as 'robust' or 'frail'.[70, 96-98, 105, 106, 108, 109, 113, 118, 119, 122-124, 129-132, 136, 137, 140, 144, 147, 152, 154-158, 163, 165-167, 170-174, 177, 179, 186, 188, 191] All eight instruments that underwent dichotomous data analysis were used by multiple authors and there was variation in the descriptive cut-offs where a 'robust' patient became 'frail' in five of these instruments (63%). Thereafter, categorical analysis was the second most common form of data analysis (n = 24 assessments).[76, 95, 99, 104, 106, 110, 112, 119, 120, 127, 131, 133, 134, 161, 170-172, 178, 181, 185, 187, 191] A total of six instruments underwent categorical statistical analysis and substantial variation in descriptive cut-offs was observed again in three of the four (75%) instruments that were used by multiple authors. Analysing data continuously was performed least commonly (n = 19).[100, 101, 122, 124, 126, 128, 141, 143, 153, 160, 169, 175, 180, 183, 189, 190] Mode of data analysis was inadequately described and/or displayed by authors for 20 assessments.[77, 78, 81, 102, 103, 111, 117, 125, 136, 151, 152, 154, 163, 164, 172]

3.4.7 Practical application of frailty assessment tools

From 147 frailty assessments included in this review, most authors did not describe who performed the assessment (68%), Table 3.6.[68, 70-72, 75-79, 81, 82, 98, 100, 110, 112, 113, 115-120, 122, 125-131, 133-135, 137-149, 151, 153-156, 158, 161-165, 169-173, 175-183, 187-191] The majority of authors did not describe whether the use of the selected frailty assessment tool mandated additional training requirements, or not (n = 128, 87%). Where authors did describe the need for additional training requirements (13%),[72, 73, 96, 108, 123, 124, 152, 167, 168, 184, 186] the type of training was uncommonly defined (74%).[72, 73, 96, 124, 152, 167, 168, 186] Most authors did not report the duration of time required to use their selected frailty assessment instrument (93%).[70, 71, 106, 136, 152, 168] Lastly, most authors did report the time in the patient journey where the frailty assessment took place (59%). Where described, all assessments were performed pre-operatively[68-72, 77-81, 95-97, 99-110, 112-124, 126-128, 132, 136-138, 140, 149, 150, 152, 157, 159, 160, 166-168, 174, 178-180, 184-187] with 11% of assessments repeated post-operatively[68, 70, 77, 109, 124]. Where specified, the timing of pre-operative frailty assessments ranged from assessment on the day of admission[70, 78, 80, 96, 100, 160, 166, 180, 186], day of surgery[174], using a pre-morbid frailty status determined 2-weeks before surgery[150], or to assessing relevant data that had been collected up to three years before surgery.[149]

Table 3.6 - The practical application of frailty assessment tools. Table is as presented in Welsh et al.[90]

Total assessments	147 (%)
Authors reported who performed the assessment	47 (32)
Authors reported additional training requirements	19 (13)
From those reporting additional training requirements:	
Training described	5 (26)
No description of training	14 (74)
Authors reported duration of frailty assessment	11 (7)
Authors reported when assessment was performed	86 (59)
Preoperatively	86 (59)
Outpatient department	35 (24)
Hospital records	30 (20)
On admission/inpatient	18 (12)
Unspecified	3 (2)
Postoperatively	16 (11)

Table summarising the description of practical application of frailty assessment tools observed in this review.

3.4.8 Conference abstract frailty tools

Forty-four conference abstracts were included. Forty-one authors used one frailty assessment instrument,[89, 199-238] and three authors used two instruments.[239-241] Three authors did not describe the instrument used.[212, 214, 230]

Figure 3.3 summarises the most commonly used frailty assessment instruments. Similar to published journal articles, the most commonly used instruments were the modified frailty index (5- and 11-point), the Clinical Frailty Scale (7- and 9-point) and a version of the Risk Analysis Index (RAI). Six (14%) published abstracts used a bespoke frailty assessment instrument designed for the purpose of the authors' study.[204, 213, 218, 232, 237, 238]

The inclusion of abstracts identified one additional frailty assessment tool that was not identified in the included journal articles: the FRAIL criteria (Falls, Reduced mobility, Altered cognition, new onset or worsening of previous Incontinence, Lots of medications).[89]

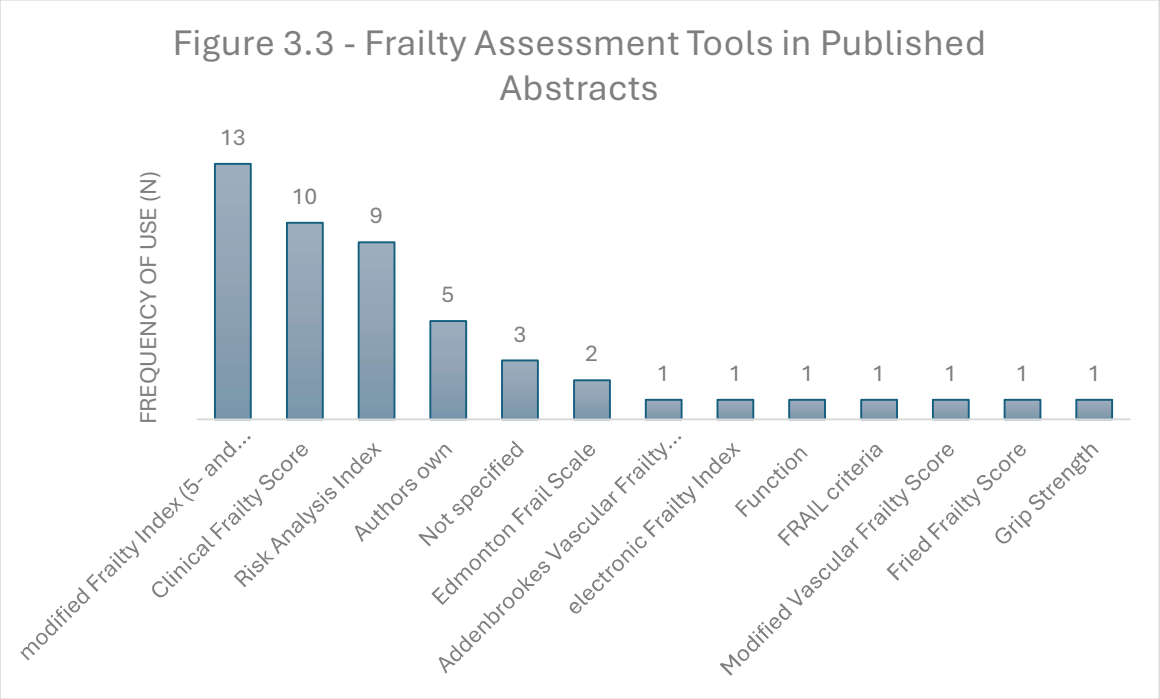


Figure 3.3 - Frailty assessment tools used, according to frequency, in frailty assessments in published abstracts. Figure is as presented in Welsh et al.[90]

3.5 Methods 2 - Systematic review of the psychometric and clinimetric properties of frailty tools in surgical populations

A secondary systematic review was performed to describe the psychometric and clinimetric properties of the ten most commonly used frailty assessment instruments. Psychometric analysis is a field of study designed to assess statistical and structural robustness of assessment instruments. Clinimetric analysis is a related field which assesses the clinical usefulness of an instrument. Criteria for both psychometric and clinimetric assessment are described in the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN).[242, 243] A list of the COSMIN properties that were assessed, and their definitions, is included below. The comprehensive taxonomy is included in appendix 3.

- **Validity (psychometric)**
    - **Content validity**

      This domain considers the relevance, comprehensiveness and comprehensibility of an instrument's content with respect to the construct of interest and the target population it is being applied to.

    - **Criterion validity**

      This domain assesses how correlation of scores from one tool with that of a 'gold standard' tool.

    - **Convergent validity**

      This domain measures the strength of relationship between scores from the tested instrument and those of other instruments considered to be of good quality.

- **Known-groups validity**

  The ability of an instrument to discriminate between two groups known to differ on the variable of interest.

- **Interrater reliability (clinimetric)**

  This domain assesses an instruments ability to reproduce a result consistently in time and space, or from the perspective of different observers/users.

- **Responsiveness**

  This domain measures the ability of an instrument to detect change over time.

Having identified a previous systematic COSMIN review of frailty assessment instruments[244], an updated literature search of Embase (OVID) and Medline (OVID) was performed using modifications of its search syntax to identify additional publications, see appendix 4. The initial literature search had produced a limited number of references when defining the search to include only a vascular population. For this reason, it was felt necessary to broaden the literature search to include articles involving any surgical population.

Included references were restricted to: participants of any age, published journal articles involving any surgical population and presentation of COSMIN properties of original descriptions of selected tools. COSMIN properties were extracted as reported by the original author of included papers with the following standardised cut-offs applied: Cohen's Kappa statistics: ≤ 0.2=poor, 0.21-0.6=moderate, ≥0.601=good; Area Under the Curve Receiver Operating Characteristic: <0.7=poor/inadequate, 0.7-0.8=moderate, >0.8=good and Spearman's correlation co-efficient: <0.5=poor, 0.5-0.7=moderate, >0.7=good. Where multiple papers assessed the same parameter for one tool, the highest score was accepted.

3.6 Results 2 - Assessing psychometric and clinimetric properties of frailty tools in surgical populations

The previous systematic review contained one relevant reference for inclusion. An updated literature search identified ten additional journal articles, producing a total of eleven articles for inclusion in this secondary systematic review, see Figure 3.4. Table 3.7 summarises study characteristics for included journal articles; only one article assessed psychometric properties of a frailty assessment instrument when applied solely to a vascular surgery population.

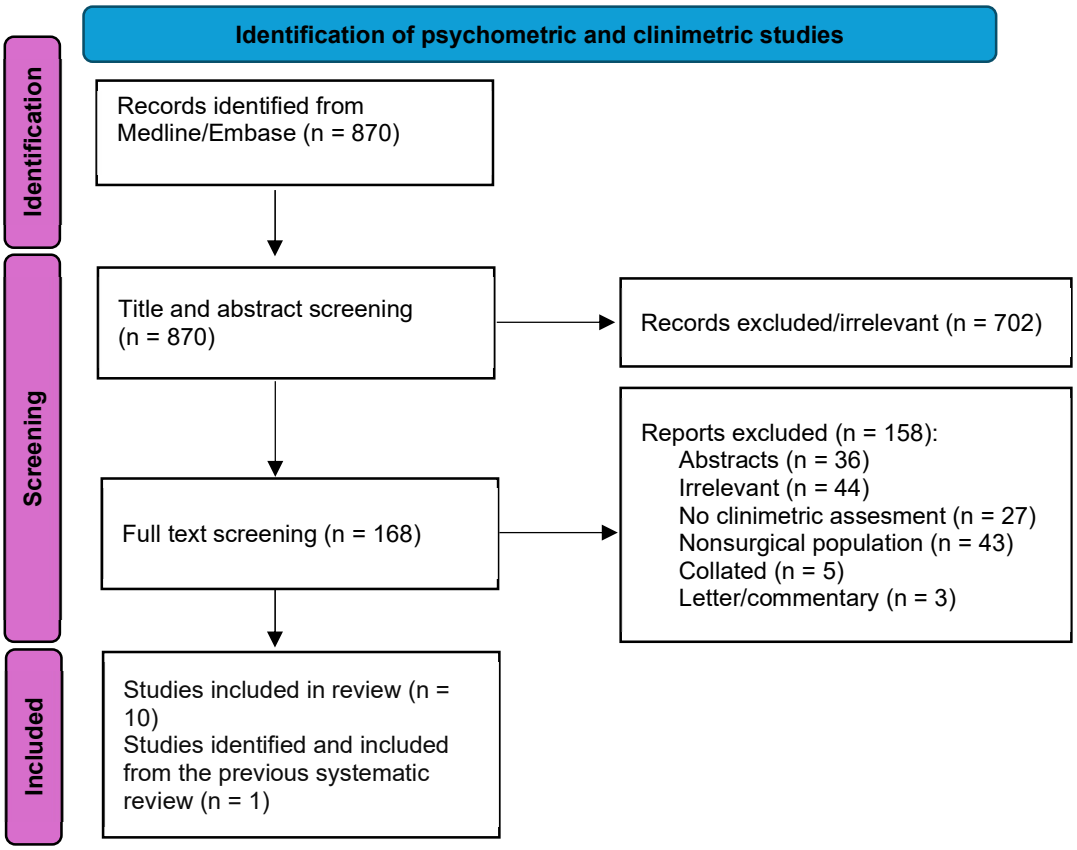


Figure 3.4 - PRISMA diagram for the selection of articles assessing psychometric and clinimetric properties of frailty assessment tools. Figure is as presented in Welsh et al.[90]

Table 3.7 - Summary of articles included in COSMIN review.

Author	Year	Study design	Country	Data source	Population	n	Frailty tool(s)	COSMIN property	Author defined gold standard comparison tool
Ayyash[106]	2022	Cohort, P	England	Prospectively collected data	Vascular surgery	97	Clinical Frailty Scale	Interrater reliability Convergent validity	NA Edmonton Frailty Scale
Chimukangara[245]	2017	Cohort, R	USA	ACS-NQIP	General surgery (paraoesphageal hernia repair)	3711	5-item modified Frailty Index	Criterion validity	mFI-11
Darvall[246]	2020	Cohort, P	Australia	Prospectively collected data	Surgery, unspecified	218	Clinical Frailty Scale	Content validity Criterion validity Convergent validity	NA Edmonton Frailty Scale Edmonton Frailty Scale
Fornaess[247]	2022	Cohort, R	Norway	Institutional database	Emergency abdominal surgery (excluding vascular surgery)	112	Clinical Frailty Scale	Interrater reliability	NA
He[248]	2020	Cohort, P	Singapore	Prospectively collected data	Elective major abdominal surgery (general surgery, urology and gynaecology)	142	Edmonton Frail Scale	Interrater reliability	NA
Kay[249]	2022	Cohort, P	Scotland	Prospectively collected data	Orthopaedic (hip fracture)	57	Clinical Frailty Scale	Interrater reliability	NA
Kerschbaumer[250]	2022	Cohort, R	Austria	Institutional database	Neurosurgery (resection of metastatic brain disease)	205	Clinical Frailty Scale	Construct approach	NA
Pierce[251]	2021	Cohort, R	USA	ACS-NQIP	Orthopaedic (spine surgery)	61,356	5-item modified Frailty Index	Convergent validity	mFI-11
Pulik[252]	2020	Cohort, R	Poland	Institutional database	Orthopaedic (primary total hip arthroplasty)	365	5-item modified Frailty Index	Convergent validity	mFI-11
Yagi[253]	2019	Cohort, R	Japan	Institutional database	Orthopaedic (spine surgery)	281	5-item modified Frailty Index	Convergent validity	mFI-11
Zhao[254]	2022	Cohort, P	China	Prospectively collected data, institutional database	Trauma	101	Hospital Frailty Risk Score	Construct validity	Fried index Trauma-specific frailty index mFI-11

Table summarising the characteristics of articles included in this updated COSMIN review. ACS-NQIP - American College of Surgeons National Surgical Quality Improvement Program. NA – Not applicable.

From eleven articles, COSMIN assessment was performed on four of the ten most commonly used frailty assessment tools: CFS[18, 94], 5-item Modified Frailty Index[194], Edmonton Frail scale[195] and the Hospital Frailty Risk Score[198]. The remaining six frailty assessment tools have not been subject to COSMIN property analysis, Table 3.8.

The most commonly assessed tool was the CFS (n = 5) which demonstrates good content validity, interrater reliability, criterion validity, convergent validity (against the Edmonton Frail Scale) and responsiveness. Thereafter, the mFI-5 was assessed by four authors, all electing to compare criterion or convergent validity of the instrument against the mFI-11, demonstrating good strength in this relationship. The Edmonton Frail Scale was observed to demonstrate good interrater reliability (n = 1), whereas the Hospital Frailty Risk Score demonstrated only poor/moderate convergent and known-groups validity when compared to three other measures of frailty, with others reporting frailty assessment instruments are commonly based on different concepts of frailty and most tools cannot be assumed to be interchangeable.

Table 3.8 - COSMIN assessment of most common frailty assessment tools. Table is as presented in Welsh et al.[90]

Tool	n	Content validity	Criterion validity	Convergent validity	Known-groups validity	Interrater reliability	Responsiveness	Gold standard compared to
11-item Modified Frailty Index (mFI-11)	0							n/a
Risk Analysis Index (RAI - combined)	0							n/a
5-item Modified Frailty Index (mFI-5) [245, 251-253]	4		NV:0 NoS:1	NV:0 NoS:3				mFI-11
Clinical Frailty Scale (9 point) [106, 246, 247, 249, 250]	5	NV:1 NoS:0	NV:0 NoS:1	NV:0 NoS:2		NV:1 NoS:2	NV:0 NoS:1	Edmonton Frail Scale
Edmonton Frail Scale (EFS) [248]	1					NV:0 NoS:1		n/a
Critical Limb Ischaemia Frailty (CLI Frailty)	0							n/a
Addenbrooke's Vascular Frailty Score	0							n/a
Groningen Frailty Index	0							n/a
Frail Non Disabled Questionnaire (FiND)	0							n/a
Hospital Frailty Risk Score [254]	1			NV:0 NoS:1	NV:0 NoS:1			Fried index, Trauma-specific FI and mFI-11

Table summarising reported COSMIN assessment of selected frailty assessment tools within a surgical population. Original descriptions of the frailty assessment tools were used. Where a property was assessed by multiple authors, the highest score was accepted. Blank fields indicate no assessment performed. NV - Number Vascular papers, NoS - Number other Surgical papers. Colours indicate: red - poor/inadequate evidence, yellow - moderate evidence, green - good/excellent evidence. This table summarises COSMIN assessments performed on the most commonly selected frailty assessment tools used in vascular surgery. The following tools were excluded from this analysis due to inadequate tool description, or unsuitability due to the assessment being an isolated variable or a clinician's subjective opinion: Johns Hopkins Adjusted Clinical Group System, biomarkers, Initial clinical evaluation, wearable sensor technology and grip strength.

3.7 Discussion

As summarised in Chapter 2, in open vascular surgery and endovascular techniques alike[60], frail patients experience increased risk of morbidity, short-term and long-term mortality, limb loss, discharge with greater social care requirements, and functional decline.[2, 52, 62] These end points must be recognised and clinical service models modified to ensure equity in health care provision for this vulnerable cohort, the critical first step in achieving this is standardising our approach to its identification. Although guidelines advocate the importance of frailty recognition, recommendations for such standardisations are unfortunately lacking.[4] This review set out to explore variations in practice this with a view to guiding future research and policymakers.

This review identifies a surplus of heterogeneous frailty assessment instruments used within vascular surgery research with a reliance on assessing patient function and comorbidity, substantial variability in data analysis and poor description of methodological application. Almost one third of frailty assessment tools did not evaluate a multi-domain deficit, despite this being the underpinning principle of frailty. There is also widespread use of bespoke frailty assessment tools, which seems counterintuitive given the number of tools available and, while the content validity of frailty assessment tools improved when incorporating bespoke tools (demonstrating author recognition of the importance of multidomain assessment), it challenges comparison between studies. These inconsistencies may imply variation in prognostic value[255], complicate training and service provision and preclude meaningful comparison of services and pooling of data. The notable paucity in psychometric and clinimetric assessment of these tools within a surgical population adds additional complexity as it further complicates the ability to identify preferred frailty assessment tools.

It is estimated that 10% of people over 65-years old are frail[51] and while the purpose of this review was not to summarise prevalence, it identifies a prevalence three times this within a vascular surgery patient population emphasising the importance of frailty recognition. However, confounding factors for this high prevalence are identified. Firstly, the most commonly used tool (mFI-11) is a frailty index which awards one point per variable present across 11-variables; the greater the value the greater the risk of frailty.[192] It is constructed on American national databases which were heavily represented in this review. While the mFI-11 incorporates variables across three domains, it is overly reliant on comorbidities, such that comorbidities alone can result in a 'frail' score. In particular, a history of peripheral arterial disease (PAD) is one of the eleven variables, which may represent a bias in assessment when applying the tool to a vascular surgery population. Second, the most commonly assessed vascular intervention was lower limb revascularization and clearly ischemic rest pain will impair mobility and affect patient function. In this population, using a frailty tool that relies on assessing mobility will give a high absolute number of frailty. However, consideration must be put to end-stage peripheral arterial disease being associated with systemic atherosclerotic disease with associated morbidity risks. Because frailty and comorbidity are closely related, what remains to be clarified is whether this represents a bias in assessment or true estimates of frailty. It is recognized that the content validity of differing tools may change when applied to different vascular populations. However, for the purpose of population screening, a consistent approach is preferable.

3.7.1 Consistency of frailty assessment in other surgical fields

Research to date confirms frailty is associated with poorer peri-operative outcomes across numerous surgical specialities. A review investigating frailty in patients undergoing radical cystectomy included 9 studies with 11 different frailty assessment tools and a reciprocal heterogeneity in frailty definition and mode of analysis was identified.[256] Similarly, a review of frailty in major abdominal surgery described limitations in the clinical applicability of their results, in part,

due to the scope and extent of heterogeneity in the frailty-related variables assessed, of which up to 70-items were reported across 35 studies.[257]

3.7.2 Implications for research and clinical practice

Our data confirm substantial inconsistency in frailty assessment. Available evidence does not suggest a definitive superior tool. It also highlights a lack of research comparing psychometric and clinimetric properties of frailty tools, and a lack of studies examining important methodological considerations such as assessing the feasibility of implementing frailty assessment into routine clinical practice. Surgical teams should look to fill this evidence gap.

The prognostic value of frailty has been confirmed through several iterations of various frailty assessment tools. However, the feasibility of disentangling each tools' clinical usefulness in the granular context of individual vascular conditions and the various treatment options is questionable. Further, expecting a positive uptake of various iterations of frailty assessment tools according to the range of conditions and treatments (e.g., open, endovascular, or medical treatment) in vascular surgery feels overly complicated and perhaps unrealistic. Standardising the approach to frailty identification represents an opportunity to clarify the implications of frailty according to disease and treatment burden (e.g., major and minor procedures or general, regional, or local anaesthesia). Further, standardization in assessment promotes research reproducibility, minimises data wastage, and enhances research impact, which directly informs clinical care. Additional to prognostication, using a frailty assessment tool for population screening may direct resource-intensive, comprehensive, frailty-centric services enabling periprocedural optimisation tailored to the burden of disease and its proposed treatment. As presented in Chapter 2, such clinical service models in vascular surgery have been trialled with limited evidence suggesting improvements in perioperative outcomes and financial advantages when

implemented both pre- and post-operatively.[84, 89] In a speciality where pathology is commonly time-sensitive, the latter is particularly beneficial.

In the absence of a clearly superior tool, it is preferable clinicians refrain from deferring frailty assessment pending original research which may not happen. Considering data presented in this review and relevant reviews demonstrating the prognostic usefulness of frailty, consideration should be put toward standardisation in the approach to frailty assessment. From the data in this review, a recommendation is made for clinicians and national databases to consider adopting the CFS. As detailed in Chapter 2, this 9-item scale, with images and brief descriptions per point, uses information collected routinely as part of preoperative assessment.[18, 94] Its widespread use represents international familiarity, the tool demonstrates good psychometric and clinimetric properties, it does not require additional equipment and the tool can be applied in seconds, making it suitable for use in established busy clinical scenarios.[106] A short online module is available to ensure consistency in application prior to implementation.[258] However, there is a role for further research to perform head to head comparisons of the prognostic utility of the CFS in a surgical setting (see Chapters 4 - 6).Furthermore, although the COSMIN assessment considers classical test properties, issues such as time to complete and ease of administration are equally important when considering the practical implications of implementing frailty assessment in a busy vascular surgery unit. Clarifying these metrics should be considered in future studies.

Another identified issue lies in the analysis of data, where over half of assessments define a binary cut-off (which varies between authors), above which, a patient is diagnosed as frail. Whilst this facilitates data comparisons between ‘frail’ and ‘non-frail’ groups, it fails to recognise that frailty is not a binary condition, rather a transitional state in a dynamic progression from robustness to a state of vulnerability.[259] Data analysis should reflect this continuum and will have

greater clinical applicability if analysed in a categorical and/or continuous fashion.

Lastly, this review identifies a limited number of studies examining the prognostic utility of frailty in patients managed non-operatively. As clinicians increasingly aim to identify those patients who would sooner benefit from a conservative approach, future research should include direct comparisons between patients proceeding to intervention and those managed conservatively.

3.7.3 Strengths and limitations

This systematic review is large, including 111 original studies and 44 conference abstracts, in total identifying 43 different ways to assess frailty within vascular surgery research. The scale of this review is further enhanced by analysing authors' definition of frailty in included studies. This accounts for the large sample population as some authors sampled the same database through overlapping time periods. To fully explore patterns of frailty assessment, the decision was made not to collate these papers when encountered. The analysis was limited to the data as presented, without contacting authors for clarification. While this may overestimate the descriptive problems, this acts as a fair representation of the anticipated challenges that would be encountered by prospective authors wishing to simulate similar trials with differing population groups or compare results across different studies. Further, although content validity was explored in this review, the usefulness of each domain when applied to a vascular surgery population was not, identifying an area for future research.

3.7.4 Conclusion

This review explores the methodology of frailty assessment in vascular surgery research. It identifies significant issues with heterogeneity in tool selection and data analysis, a reliance on assessing patient function and comorbidity as well as poor description of methodological application. Further, there is a stark lack of psychometric and clinimetric assessment of selected frailty assessment tools within a surgical population. To minimise data wastage and enhance research impact, this review recommends a standardisation in the reporting of frailty tool application and that frailty is considered as a continuous construct for analysis. In the absence of a consensus the CFS is recommended for use by surgical teams given proven satisfactory psychometric and clinimetric properties and practical suitability for application in established clinical service models.

Chapter 4 Materials and methods for 'Frailty Assessment in Vascular OUtpatient Review' (FAVOUR) study

4.1 Chapter summary

This chapter summarises the methodological approach to the Frailty Assessment in Vascular OUtpatient Review (FAVOUR) study. This study is designed, in part, to address some of the evidence gaps identified in Chapter 3 which discussed the challenges faced by clinicians in selecting frailty assessment instruments suitable for application in clinical practice. Specifically, this prospective observational study was designed to answer research question 2a-2c (can frailty assessment be implemented as part of routine care in clinical practice). This two-part study aims to: a) assess the feasibility of implementing routine frailty screening in a vascular outpatient setting, and b) compare the prognostic value of five different frailty assessment tools or techniques.

The text, figures and tables presented in this chapter are published in Welsh SA, Hussey K, Brittenden J, Orr DJ, Quinn T. Frailty Assessment in Vascular OUtpatients Review (FAVOUR) protocol: single-centre prospective cohort study comparing feasibility and prognostic value of commonly used frailty assessment tools. *BMJ Open* 2023;13:e079387.[260] doi: 10.1136/bmjopen-2023-079387

This study is registered on ClinicalTrials.gov, Identifier: NCT06040658 which has been included in appendix 6.

4.2 Introduction

4.2.1 Background and rationale

Chapter 2 summarises the growing relevance and implications of frailty for patients with vascular surgery pathology. Chapter 3 identified the abundance of methodologically heterogeneous frailty assessments that exist within vascular surgery research. It then discussed the resultant challenges and implications this brings when attempting to translate progress made to date into meaningful changes to clinical practice. It is clear that current service models will need to adapt their approach to the management of vascular patients living with frailty on an individual and wider service-model level. This is required to ensure equity in healthcare delivery, guide resource allocation and improve healthcare outcomes. The critical first step to this is the definition and optimisation of clinicians' approach to frailty assessment and its recognition in clinical practice. While the importance of recognising frailty (and ensuring access to frailty-related specialist input) has been advocated by national guidelines, guidance on the optimum approach for doing this is lacking.[4]

Approximately one third of vascular surgeons do not formally assess patients for frailty, with common reasons for not doing so including unfamiliarity with tools and concerns over tool validity.[261] Further, of centres in the United Kingdom reporting the use of frailty assessment, over 40% rely to some extent on subjective clinical judgement rather than utilising validated instruments.[261] This issue is not isolated to vascular surgery as 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 perceived lack of evidence supporting a single best frailty tool.[262] 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, with limited data on how these tools perform in clinical practice.[90] The

heterogeneity in frailty tools has been labelled as immaturity in this area of research and a call has been made for direct tool comparisons to help identify whether a superior tool exists in order to better meet the expectations of vascular populations.[263, 264]

Identification of frailty early in the perioperative pathway enables risk stratification, joint decision making and, with the support of appropriate specialist input, syndrome modification.[265] Targeted treatment of this vulnerable population may also confer financial and medical benefit, although larger and long-term studies across multiple centres are required to support this.[89] The well demonstrated heterogeneity in frailty assessment tools complicates the ability to do so by preventing 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 improve approaches to 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 but are still accurate and relevant. Chapter 3 demonstrates an evidence gap around the ability to identify a preferred approach to frailty assessment in the vascular surgical context.[90] Limitations of studies to date include potential biases from retrospective design, poor generalisability to the United Kingdom's National Health Service (NHS), lack of head to head comparisons of tools and limited assessment of properties such as feasibility and acceptability. Despite the vascular community declaring a national interest in frailty,[4] 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.

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 a national governing body: Healthcare Improvement Scotland.

4.2.2 Objectives

The primary aim was to assess the feasibility of implementing routine frailty assessments into an urgent-referral vascular outpatient clinic setting ('Vascular Hot Clinic'). Part of feasibility assessment will also include comparison of interrater reliability (comparing scores when one tool is accessed by different users), as well as assessing convergent validity (comparing scores of different tools accessed by the same user). Secondary objectives were to assess and compare the variability and prognostic value of selected frailty assessments.

4.2.3 Study 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 was conducted and reported in line with the guidance presented in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[266]

4.3 Methods

4.3.1 Study setting

This study was based in the Vascular rapid access ('Hot') clinic at the Queen Elizabeth University Hospital (QEUH), Scotland. Following centralisation of services, vascular surgery services in the United Kingdom operate a 'hub-and-spoke' model. This model describes a tertiary speciality service delivered from a hub/main site with spoke/satellite sites referring patients to the hub site, in the absence of the service being offered locally. The consultant-led outpatient clinic is responsible for delivering urgent vascular care for a population of approximately 1.7 million patients in NHS Greater Glasgow & Clyde and spoke sites including: NHS Forth Valley, part of NHS Highlands and NHS Western Isles. 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 and intervention.

Three clinics are held weekly with a capacity of up to ten patients per clinic. The clinics are also served by a multidisciplinary team, including vascular nurse specialists, podiatrists and clinical scientists who provide complex wound care and a dedicated duplex service. This clinic does not provide a vascular access service which is instead offered through a separate renal transplant service.

4.3.2 Population

Patients were recruited from the Vascular Hot Clinic between March - July 2023 inclusive.[267] This offers a real-world, unselected cohort. Participants were required to provide written informed consent prior to study participation (see Appendix 7 for example consent form). All referrals to vascular hot clinic were eligible for inclusion, preferentially recruiting new referrals. As frailty is related to age, but does not directly correlate with it, no age cut-off was defined.[4, 22] As this was primarily a study of feasibility, patients were not excluded/included based on presenting symptom or diagnosed pathology.

A proxy (relative/friend/carer), if present, was also invited to participate and assist with frailty assessments of the patient, where suitable. The participation of the proxy was 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.

4.3.2.1 Inclusion criteria:

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

4.3.2.2 Exclusion criteria:

- Lacking capacity to provide informed consent, as defined in the Mental Capacity Act, 2005 (I was responsible for assessing capacity as part of participant recruitment)

- Parent clinical team felt frailty assessment was not appropriate for any reason

- Non-English speaker without suitable translator present

- Prisoners

4.3.3 Intervention

Five frailty assessment techniques were compared. These are comprehensively detailed in Table 4.1:

- Rockwood 9-item Clinical Frailty Scale (CFS)[94]
- Initial clinical evaluation (ICE)[159]
- Healthcare Improvement Scotland (HIS) 'Think Frailty' FRAIL assessment tool[268]
- 11-item Modified Frailty Index (11-mFI)[192]
- Frailty non-Disabled Questionnaire (FiND)[269]

As frailty assessment is recommended, there was no control, rather differing tools were compared to one another. The clinician completed CFS, ICE and HIS FRAIL assessment. The patient, and proxy where applicable, completed CFS and FiND self-assessment. The researcher completed the mFI-11 assessment. The CFS is endorsed by healthcare policy throughout the UK and will be used as the reference standard for comparisons.[86]

These tools were selected as most likely to be suited to the acute clinic context after reviewing their relevance, format, cost, anticipated ease of use, training requirements and, where possible, endorsement in local or national healthcare policy. The choice of instruments was also based on their representation of differing theories of frailty. Further, the work presented in Chapter 3 demonstrates the CFS and mFI-11 are the most commonly used tools within vascular surgery which demonstrates international familiarity.[90] By continuing their use, the research impact of this study was enhanced. Key requirements to tool selection were 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 8 displays the case report forms (CRFs) with various frailty assessment to be completed by clinician, patient/proxy, and researcher.

Participation in this study did not preclude any aspect of concomitant care and/or intervention for patients. To ensure routine care provided by this service remained unaffected, clinicians were asked to complete frailty assessments at the conclusion of each clinic, minimising possible biases in assessment and care provision.

Table 4.1 - Selected frailty assessment tool summaries. Table is as presented in Welsh *et al.*[260]

Clinical Frailty Scale (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) completed. In the unlikely event where the surgeon was unwilling or unable to provide the frailty assessment score for the patient, the research team scored the patient instead. Where relevant, non-completion of frailty assessment by surgeon/patient/proxy, and the reason why, was recorded. Incomplete clinician assessments were filled in by the research team. Incomplete patient/proxy scores were left blank. **Training requirement:** While not necessary to use the instrument, there is a short online module available to develop understanding in how the CSF is applied. To ensure internal rigour, clinicians contributing to this study were requested to complete this training. **Duration**: It was expected this tool would take less than one minute for clinicians once they were familiar with the tool. For patients or proxy's completing the tool, it was expected this would take five minutes. **Application:** A copy of the CFS chart was available in the outpatient department. At the end of clinic, the consultants were approached by the research team and asked to score recruited patients. For patients/proxy's, a modified CFS chart was displayed at the end of their clinic appointment. The patient/proxy was asked to read each the definition for each score (1-8) before selecting the one they felt most accurately described them. To reduce the risk of bias, the title and image for each score was hidden from patient/proxy, leaving only the text description. Time taken to complete was calculated by the number of seconds required for clinicians/patients/proxy to read and respond to all sections of the tool. **Modifications for study:** A CFS score of 9 describes a terminally ill patient, regardless of frailty status. As this was not relevant to this study, and to reduce the risk of participants becoming upset, this score was not considered by this study and therefore was not displayed to the participant.
Initial Clinical Evaluation (ICE)	**Definition:** Also known as the 'end of bed test'. Clinicians reported a subjective and binary assessment of the patient; 'frail' or 'non-frail'.

	Personnel: The consultant leading the clinic was asked to provide an ICE. In the unlikely event where the surgeon was unwilling or unable to provide the frailty assessment score for the patient, the research team scored the patient instead. Non-completion of frailty assessment by surgeon was recorded, where relevant. **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 was required. **Application:** The consultant was approached at the end of the clinic and asked to provide their subjective opinion (ICE) on patients frailty status to the research team. This assessment was performed first to minimise bias in clinician responses from completing subsequent structured frailty assessments. Time taken to complete was calculated by the number of seconds required for clinicians to read and respond to all sections of the tool. **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). Its 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 was asked to complete the HIS FRAIL assessment. In the unlikely event where the surgeon was unwilling or unable to provide the frailty assessment score for the patient, the research team scored the patient instead. Non-completion of frailty assessment by surgeon was recorded. **Training requirement:** No training required for application. **Duration**: Completion of the HIS tool was expected to take less than two minutes. **Application:** A copy of the HIS FRAIL chart was available in the outpatient department. At the end of clinic, the consultant was approached by the research team and asked to score recruited patients. Time taken to complete was calculated by the number of seconds required to read and respond to all relevant sections of the tool. **Modifications for study**: Nil.
11-item modified frailty index (mFI-11)	**Definition:** This frailty index assessment is based on the frailty theory of cumulative deficits.[270] Healthcare records were 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:** The research team completed this assessment. Where relevant, non-completion of frailty assessment, and the reason why, was recorded **Training requirement:** No training required for application. **Duration**: This tool was piloted and found to take less than five minutes per participant to extract relevant data from electronic health records. **Application:** This is a frailty index which is calculated by extracting relevant data through accessing national health service (NHS) electronic records. Time taken to complete was calculated by the number of seconds required to extract, and document, relevant data from electronic health records to calculate the overall score. **Modifications for study**: Nil.
Frail NonDisabled (FiND) Questionnaire	**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.[17] This questionnaire is recommended for use by Healthcare Improvement Scotland. The original questionnaire uses metric measurements of distance and weight, an imperial conversion was added to relevant parts of the questionnaire to assist with patient comprehension. **Personnel:** The patient, and proxy if present, completed the questionnaire themselves. Where relevant, non-completion was documented with reasons why. Noncompleted forms were left blank. **Training requirement:** No training required for application. **Duration**: It was expected this questionnaire would take approximately two minutes to complete. **Application:** A copy of the FiND questionnaire was displayed to the patient/proxy at the end of their clinic. They were 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). Time taken to complete was calculated by the number of seconds to read and respond to all relevant sections of the tool, with or without assistance. **Modifications for study**: Nil.

4.3.4 Primary aim

The primary aim of this study was to assess the feasibility of implementing routine frailty assessment in a vascular clinic setting. For this, the following data was 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 (in seconds: see 'Application' in Table 4.1 - Selected frailty assessment tool summaries.), number of assessments with non-completion, reasons for non-completion (defined as: 'time restriction', 'patient not suitable', 'forgot' or 'other') and if assistance was required to complete the tool (defined as: 'verbal assistance' where a verbal prompt/explanation was required or 'hands on' where patients required greater degree of assistance than 'verbal assistance').

Part of feasibility parameters involved assessing clinimetric properties, specifically interrater reliability and convergent validity.[242, 243] Complete COSMIN definitions are presented in 3.4. In brief, interrater reliability describes the difference in measurements between observers when different users apply the same tool. Convergent validity describes how closely a test is related with other tests that measure the same, or similar, constructs.

The described outcome measures were felt to be clinically relevant as they allow valid and reproducible calculations of the proportion of eligible patients recruited and time taken to complete assessments which enables clinicians to consider the feasibility and suitability of implementing routine frailty assessment in a controlled clinical environment, encouraging compliance with current guidance.[4]

4.3.5 Secondary outcomes (follow-up)

The secondary objectives involved assessing the prognostic value of selected frailty assessment tools and their value over standard clinical demographic information. All patients were electronically followed-up at 30-days from recruitment, collecting data on mortality and home time.[271] Home time is defined as the number of full days the patient spends not as an inpatient and thereby acts as a summary of any hospital admissions, length of hospital stay(s), readmission and non-home discharges.

A secondary 30-day post-operative follow-up was applied for those patients who proceeded to surgical and/or endovascular treatment following their attendance at the clinic. This falls in line with current practice for reporting post-operative outcomes according to the number of days that have passed since the index intervention. With this in mind, common post-operative outcomes were selected to encourage applicability and generalisability of results. The following data was collected: surgical procedure [classified by 1) approach: open surgical repair, endovascular or both/hybrid, and 2) anatomy: upper limb, aortic, iliac, common femoral and infrainguinal, the latter encompassing any treatment distal to the common femoral artery], mortality, post-operative complications (according to the Clavien-Dindo Classification, see Table 4.2)[272, 273], length of hospital stay (full days), readmission rates (to any speciality), non-home discharge (defined as discharge to any place of residence other than the patient's pre-operative place of residence) and discharge with a higher level of social care requirement (defined as any increase in formal social care package requirement).

I performed all aspects of data collection for 30-day follow up periods. Participants recruited to the FAVOUR study will undergo an additional 1-year follow-up, these data are not yet complete and will not be presented in this thesis.

Table 4.2 - Summary of Clavien-Dindo grading of post-operative morbidity. Table modified from Clavien *et al.*[273]

Grades	Definition	Modes of therapy
I	Any deviation from normal postoperative course	No additional pharmacological or operative interventions were required beyond those routinely required in postoperative care. Acceptable therapeutic regimens include pharmaceutical agents like anti-emetics, anti-pyretics, analgesics, diuretics, electrolyte replacement and physiotherapy. This grade includes simple wound infections and/or small abscess requiring incision at bedside.
II	Normal course altered	Pharmacological management additional to those described in grade I. Blood transfusions and total parenteral nutrition are included in this grade.
III	Complications requiring interventions	Subclassified into: Grade IIIa – Interventions performed under local anaesthetic. Grade IIIb – Interventions requiring general or regional anaesthetic.
IV	Life threatening complications (including CNS complications), requiring intensive care unit support	Subclassified into: IVa – Single organ dysfunction (including dialysis). IVb – Multi-organ dysfunction.
V	Death	N/A

4.3.6 Baseline assessments

Baseline characteristics were collected, including patient demographics (sex, age, social deprivation status according to the Scottish Index of Multiple Deprivation[274] and vascular diagnosis), social/functional circumstances (defined as: independent, informal care by relatives or friends, formal care package with frequency of visits or care home resident), number of medications and polypharmacy (defined as ≥ 5 medications) and relevant comorbidities to calculate a Charlson comorbidity Index, the latter being one of the most extensively studied comorbidity indexes for predicting mortality.[275, 276]

4.3.7 Participant timeline

Participants eligible for study recruitment were identified on the day they attended clinic by review of electronic health care records and application of the inclusion and exclusion criteria. Due to the urgent nature of the referrals, patients (and their proxy, if present) were approached, recruited, baseline data collected and frailty assessments completed, all on the day of attending their clinic appointment, Figure 4.1. No ongoing participant participation was required for this study and all follow-up was conducted through accessing electronic health care records.

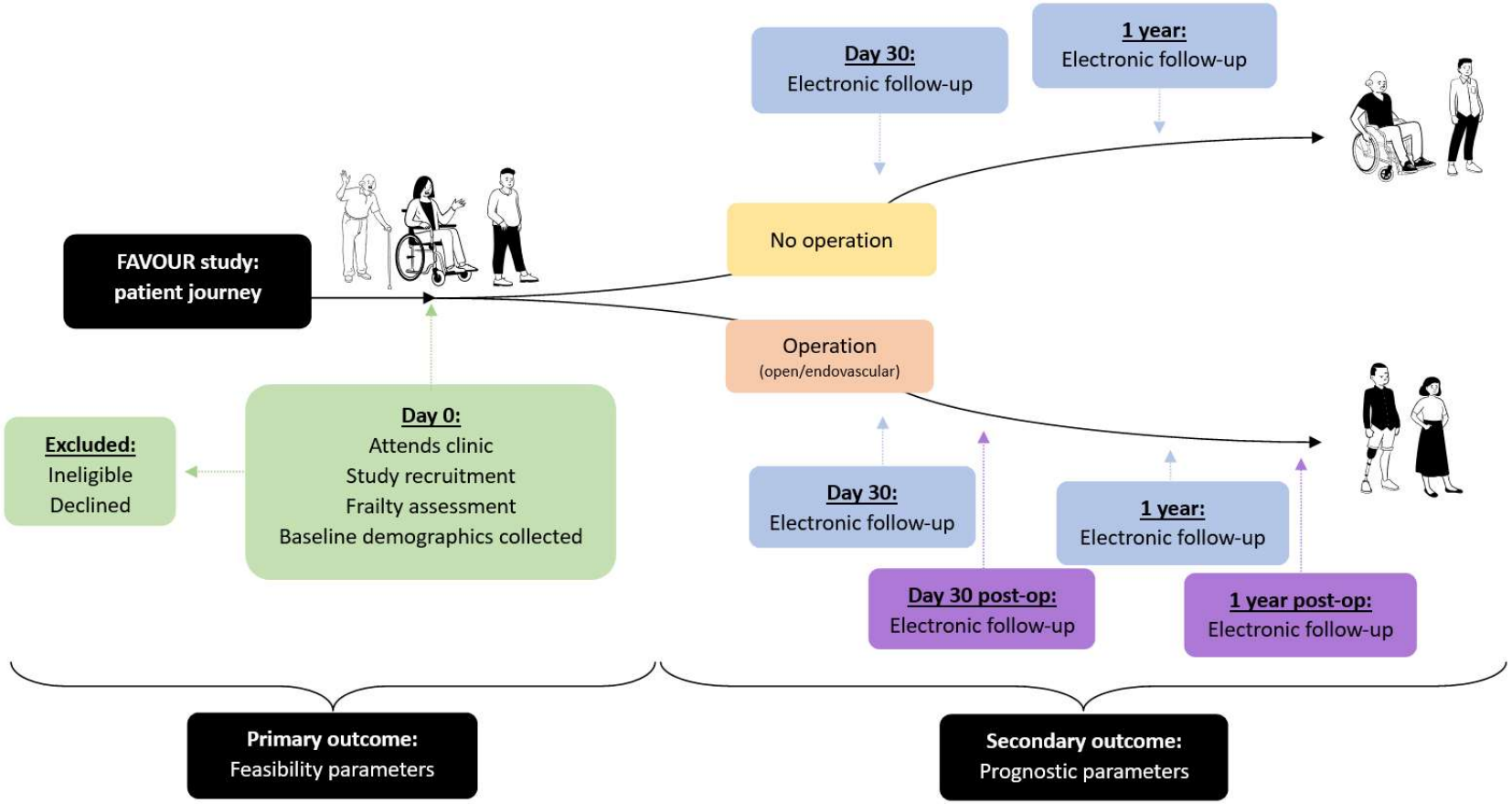


Figure 4.1 - Summary of patient timeline and study methodology.Figure is as presented in Welsh *et al.*[260]

4.3.8 Sample size

As this was primarily a study of feasibility, part of the primary aim involved describing the number of assessments possible to complete within a fixed timeframe. For this reason, a power calculation was not performed.[277]

4.3.9 Recruitment

Patient recruitment ran between March and July 2023. Prospective patients were approached for study recruitment by myself upon registering for their clinic appointment. If expressing interest, they received a participant information sheet. Patients were required to complete their clinic appointments (where their medical care remained unaffected by (non-)participation in this study) prior to participating in the study. Prospective participants were re-approached at the end of their clinic appointment to confirm willingness to participate and provide written consent. Thereafter, frailty assessments were completed by the patient. Where a patient attended with a suitable proxy, they were approached in an identical fashion on the condition the patient provided written consent for this. Where a patient was eligible for participation, but a proxy was ineligible or declined participation, the patient was recruited without proxy contribution. Where the patient was not eligible for participation, the proxy was not invited to participate on their behalf. Staggering the consent process by approaching the patient either side of their clinic appointment maximised the time for the patients to consider their recruitment. It was recognised that ideally patients should have a period of at least 24 hours[278] with a patient information sheet prior to study recruitment however, due to the emergent nature of the clinic and the presenting pathology, this was not considered to be achievable. The clinician and research team completed frailty assessments at the end of each clinic to minimise the disruption of the clinic and reduce bias in care provision.

4.3.10 Data collection

I performed all aspects of data collection. Data was collected both in person and by review of electronic health care records. On the day of recruitment, frailty assessments were performed in the clinic and collected on relevant paper based CRFs. On the same day, I reviewed the electronic health care records of recruited patients and extracted data for baseline demographics to an electronic data extraction template. All electronic follow-up was extracted to the same electronic data extraction template. Feasibility parameters were also collected and stored on the same electronic data extraction template, on the day of each clinic.

4.3.11 Data management

Data management, processing and handling was conducted in line with General Data Protection Regulation principles (EU 2016/679). The research team allocated pseudonymised participant identification numbers, removing and securely destroying any personal identifiable information from paper based CRFs before transcription to the electronic data extraction template for storage. Transcribed data underwent quality control by another researcher. This was performed by the second researcher reviewing 20 CRFs against the transcribed data extraction template. This saw an error margin of <0.001% inconsistencies in transcribed data which was considered acceptable, so quality control of remaining transcribed data was not performed. Data for baseline demographics and electronic follow up was extracted and stored on Excel Version 2304. Data was not shared with third parties for the purpose of data analysis or write-up.

4.3.12 Statistical methods

Most data were analysed using IBM SPSS Statistics v25. Where SPSS did not have available software for statistical calculation (Delong method: see section 4.3.12.3), MedCalc v22.023 was used instead. A p value < 0.05 was considered significant. There was no imputation of missing data. Patients with missing data

had this coded and available data was included in analysis. To facilitate head-to-head comparisons, patients were categorised into dichotomous categories of 'frail' and 'robust'. Table 4.3**Error! Reference source not found.** sets out the criteria according to each frailty assessment instrument. If the assessment score is greater or equal to the threshold value, the patient is categorised as frail. Where the assessment score is less than this value, patients are categorised as robust.

Table 4.3 - Frailty definitions for instruments used in FAVOUR study.

Instrument	Robust	Frail	Comment
CFS	CFS: <5	CFS: 5+	
ICE	'No'	'Yes'	
HIS FRAIL tool	≤1/5 variables present	≥2/5 variables present	Five variables scored as 'yes', 'no' or 'unsure'. Each variable recorded as present scores 1 point. A score of 'unsure' was treated as 'no' and given a value of 0 for the purpose of analysis
11-mFI	≤2/11 variables present	≥3/11 variables present	
FiND	C+D+E = 0	C+D+E ≥1	Five binary categories (A-E), if present a score of 1 is given per variable. Where no variables are present the patient is considered robust. Where a patient scores for categories A or B only, they are considered 'disabled' and where the patient scores in categories C-E, they are considered frail. Patients can be categorised as frailty positive and disability positive concurrently.

4.3.12.1 Baseline demographics

Baseline demographics were reported using descriptive statistics, including: percentages, ranges, means and standard deviations or medians and interquartile ranges. Bivariate comparisons between groups were made using chi-squared tests for categorical data and t-tests for normally distributed continuous data. To assess if patients recruited to the FAVOUR study were representative of the patient population attending the vascular hot clinic, demographic data were compared to a database from an internal audit project (conducted at Queen Elizabeth University Hospital), containing data on unselected cohort of all patients (n = 428) attending the vascular hot clinic between January – June 2021.

4.3.12.2 Feasibility parameters: Interrater reliability (results presented in Chapter 5)

Interrater reliability was calculated using Cohen's Kappa coefficient, with the following pre-defined categories: ≤ 0.4 = poor, 0.41 - 0.6 = moderate, 0.61 - 0.8 = good and ≥ 0.81 = excellent.[279] Bland-Altman plots were also used for direct comparison with linear regression to assess for the presence of proportional bias.[280]

4.3.12.3 Feasibility parameters: Convergent validity (results presented in Chapter 5)

As mentioned earlier, the CFS was selected as reference standard in this study. Specifically, clinician CFS (cCFS) scores were selected over patient self-assessed CFS scores as participating clinicians were requested to complete online training in the use of the instrument prior to study commencement. To compare agreement between tools, a variety of statistical methods were adopted, including: receiver operating characteristic (ROC) curves with area under curve (AUC) analysis, spearman's rank statistical analysis and Cohens Kappa coefficient analysis. For ROC analysis, the following AUC cut-offs were employed: < 0.7 = poor/inadequate, 0.7 – 0.79 = moderate, 0.8 – 0.89 = good and ≥ 0.9 = excellent

predictive accuracy.[281] To compare AUC, the Delong method was used with MedCalc software.[282] Test sensitivity and specificity were also reported with the following defined cut-offs: < 70% = poor/inadequate, 70 - 79% = acceptable, 80 – 89% = good, ≥ 90% = excellent.[283] For Spearman's rank the following cut-offs were accepted: 0.1-0.49 = low, 0.5-0.69 = medium, 0.7-0.89 = high, >0.89 = excellent.[284] The cut-offs for Cohens Kappa coefficient analysis were as described in section 4.3.12.2: Feasibility parameters: Interrater reliability. Post-hoc analysis was also performed to assess the correlation between co-morbidity measure CCI and frailty assessment instruments.

4.3.12.4 Follow-up data (results presented in Chapter 6)

Bivariate comparisons between groups were made using Chi Square test for categorical data. For continuous data, parametric comparisons were performed using student's T test and non-parametric data were analysed by Mann-Whitney U test. Receiver Operator Characteristic (ROC) curves were calculated with area under the curve (AUC) analysis to compare how well each instrument discriminated outcome events in operatively managed patients. The same ROC cut-offs defined in 4.3.12.3 were applied.[281] We calculated both unadjusted and adjusted predictive values, adjusting for age and sex. Subgroup analysis of patients diagnosed and treated for critical limb threatening ischaemia (CLTI) only was also performed and are presented in Appendix 9. Additionally, post-hoc descriptive analysis of the constituents of FiND with CLTI patients was performed to assess the prevalence of mobility issues in this patient population.

4.3.13 Data monitoring

This observational cohort study was not subject to a data monitoring or trial management committee. The study might have been subject to study monitoring visits and subsequent monitoring reports which would have been 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.

4.3.14 Harm

There were no adverse events anticipated to occur secondary to the intervention applied in this study. For this reason, no ancillary and post-study care was designed.

4.3.15 Patient and public involvement

A group of five non-medically trained adult volunteers (aged 25 – 65 years) contributed toward the study design through acting as participants and piloting relevant questionnaires (CFS and FiND). All volunteers took less than five 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 were not contacted directly with the results of this study however my contact details (as Primary Investigator) were supplied to participants so that they could request information on study progress/results as they become available.

4.4 Ethics

4.4.1 Research ethics approval

This study was sponsored by NHS Greater Glasgow & Clyde (Research & Innovation reference UGN23CE014) and received a favourable opinion by the London – Riverside Research and Ethics Committee (23/PR/0062). This study was 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).

4.4.2 Amendments

No amendments were made to this protocol. In the instance where amendments were felt necessary, the protocol would have been submitted to the IRAS Amendment Portal to the responsible ethics committee and/or NHS GG&C Research & Innovation for review. Changes would 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 would have been appropriately stored, cited and explained in future manuscripts.

4.4.3 Consent

I was responsible for obtaining informed written consent from participants. For this, participant information sheets (PIS) were provided to all prospective participants as well as conducting an informed discussion detailing study design, confidentiality and rights to withdraw. My contact details were supplied in the PIS which participants were pointed to, and encouraged to make contact with any questions, concerns or if wishing to withdraw. A copy of the consent form was also provided for participants to keep, see Appendix 7.

4.4.4 Confidentiality

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

4.4.5 Access to data

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

4.4.6 Funding and competing interests statements

The study was 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. Authors declare no conflict of interest or further financial disclosures.

4.5 Discussion

4.5.1 Clinical relevance of study

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] The abundance of frailty assessment tools demonstrated in Chapter 3 has confirmed the prognostic value of frailty and guidelines advocating the importance of its recognition in clinical practice now exist.[4] 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.[261] For this reason, the prospective assessment of frailty in a reproducible and controlled vascular outpatient department environment has been identified as a key area of research interest which the study presented in this chapter targets.[1, 261]

The study presented in this chapter 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 outpatient department settings. By incorporating measurements of prognostic value, it is anticipated the 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.

4.5.2 Current evidence and its limitations

From the 5358 references screened in the systematic review in Chapter 3, I identified only four relevant studies prospectively assessing frailty in a vascular surgery outpatient setting.[90] One 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.[136] Another examined the effect of frailty as assessed by the Groningen Frailty Indicator on postoperative delirium.[167] 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[72], while the last study examined the association of grip strength as a marker of frailty with measures of sarcopenia and co-morbidity.[168] The research impact of the results from these studies are limited by a paucity in feasibility measurements and direct comparison between selected tools.

4.5.3 Strengths and limitations of this study

The primary aim of this study, exploring the feasibility and suitability of routine frailty assessment in clinical practice, is novel within vascular surgery. The major strength in this study was the prospective and longitudinal design. The study design and inclusion of all consultant vascular surgeons working in a 'hub' site, acted as a real world example of typical vascular surgery services in the United Kingdom promoting generalisability of the study results. Clinical relevance and research impact were further enhanced through this study incorporating measurements of prognostic value as well as direct head-to-head comparison of frailty assessment tools, enabling clinicians and policy makers to design evidence-based frailty-centric clinical service adaptations. Limitations to this study are acknowledged: although the setting is based in a vascular 'hub' site serving several NHS health boards, this is a single-centre study which excludes patients who lack capacity (e.g., dementia), which may affect the generalisability of results.

Chapter 5 FAVOUR study results: feasibility measures and clinimetric properties

5.1 Chapter summary

Chapter 4 presented the rationale for, and methodological approach to, the FAVOUR study. This chapter presents the preliminary results from the FAVOUR study, specifically participant demographics, feasibility of assessment parameters, and the clinimetric properties of selected frailty assessment instruments, with the view to answering research questions 2a (what is the feasibility of routinely measuring frailty in an outpatient setting) and 2b (how do clinimetric properties of frailty assessment tools compare in prospective frailty assessment).

5.2 Introduction

Despite growing research attention around frailty, there is a described immaturity in the published evidence, which has challenged the translation of research findings into clinical practice and healthcare policy.[263, 264] The work presented in Chapter 3 identified no less than 43 different frailty assessment instruments in vascular surgery related research, with ambiguity on how these instruments are best applied and limited data on how these instruments perform in a clinical setting.[90] Further, despite the abundance of available frailty assessment instruments demonstrating prognostic value, vascular surgeons and health care professionals have demonstrated a preference for relying on subjective means of assessment despite recognising a clinical importance of frailty.[261] This will be expanded upon in Chapter 7.

An evidence gap has been identified and presented in Chapter 4. In this chapter I present data relevant to the feasibility and clinimetric considerations of assessing frailty in a vascular outpatient department.

An appreciation of the accuracy and other properties of frailty tools is of more than academic interest. This data will inform clinicians and policy makers, assisting in considering the suitability of introducing routine frailty screening with the help of standardised tools in clinical environments. This will likely be associated with an improved understanding of the frailty concept, ultimately, enabling services to better meet the needs of the older adult vascular population.[263]

Basing the study in vascular ‘hot clinic’ is an appropriate setting for a study of frailty screening tools. Identification of frailty early in the perioperative pathway should enable risk stratification, joint decision making and, with the support of

appropriate specialist input, syndrome modification, all of which should improve healthcare outcomes in the older adult population.[89]

As discussed in Chapter 2, the prognostic value of frailty has been consistently demonstrated. Therefore, although the FAVOUR study examines prognostic value (see Chapter 6), the focus of this study was primarily on feasibility and comparison of tools rather than prognostic accuracy.

5.2.1 Aim

The aims of the FAVOUR study have been presented in Chapter 4. In brief, the primary aim of this study was to assess the feasibility of implementing routine frailty assessment for vascular patients in an outpatient setting and to compare clinimetric properties of selected frailty assessment instruments. This chapter aims to present the baseline data, including:

- Details of the study population
- Properties of the selected assessments
- Assessing the feasibility of implementing routine frailty assessments into an urgent-referral vascular outpatient clinic setting.

5.3 Methods

Comprehensive methodology has been summarised in Chapter 4 as well as in publication.[260] In brief, the FAVOUR study (NHS R&I reference UGN23CE014/REC reference 23/PR/0062/NCT06040658) is a non-randomised, single-centre observational cohort study with attendance at the acute vascular outpatient clinic 'hot clinic' as inception point. The study has been reported in line with the guidance presented in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, appendix 10.[266]

Due to restrictions in clinic space in the outpatient department patients and their proxy, when present, were required to complete the frailty assessments simultaneously, in the same room. Consequently, patient and proxy collaboration became challenging to consistently avoid, despite informing participants of the need for independent scoring. Often this occurred in the context of patients requesting assistance from their proxy for completing self-assessments. The decision was therefore made to abandon recruitment of proxies in favour of only recruiting patients. Where a patient required assistance (from research team or proxy), this was recorded. The data collected from proxies prior to discontinuing their recruitment, is detailed in section 4.3.12 Statistical methods, with proxy data presented separately in each respective section. This chapter therefore presents:

- Feasibility data
- Interrater reliability
    - Clinician versus patient
    - Clinician versus proxy
    - Patient versus proxy

- Convergent validity
    - Frailty assessment scores compared to clinician CFS
    - Proxy frailty assessment scores compared to clinician CFS
- Assessment of correlation across all tools
- Post-hoc analysis

5.3.1 Statistical analysis

Statistical methods for the data in this chapter have been presented in section 4.3.12. Data were analysed using IBM SPSS Statistics v25. Where SPSS did not have available software for statistical calculation (Delong method: see 4.3.12.3), MedCalc v22.023 was used instead. A p value < 0.05 was considered significant.

5.4 Results

5.4.1 Feasibility parameters

From 30 clinics, over 5 months, there were 326 appointments of which 30 patients did not attend their appointment and 23 were ineligible after application of study inclusion and exclusion criteria. This meant the majority (*n* = 273, 84%) of patients attending clinics were eligible for study participation. From these, 173 (63%) were approached and 150 (87%) were successfully recruited, Figure 5.1. The 100 patients that were not approached was due to inadequate time in the clinic scenario. There were no patient participants that requested discontinuation in study participation during recruitment period.

From 150 recruited patient participants, 46 attended with a proxy and all were eligible for participation. Of these, 25 (54%) were approached for recruitment and 22 (88%) agreed.

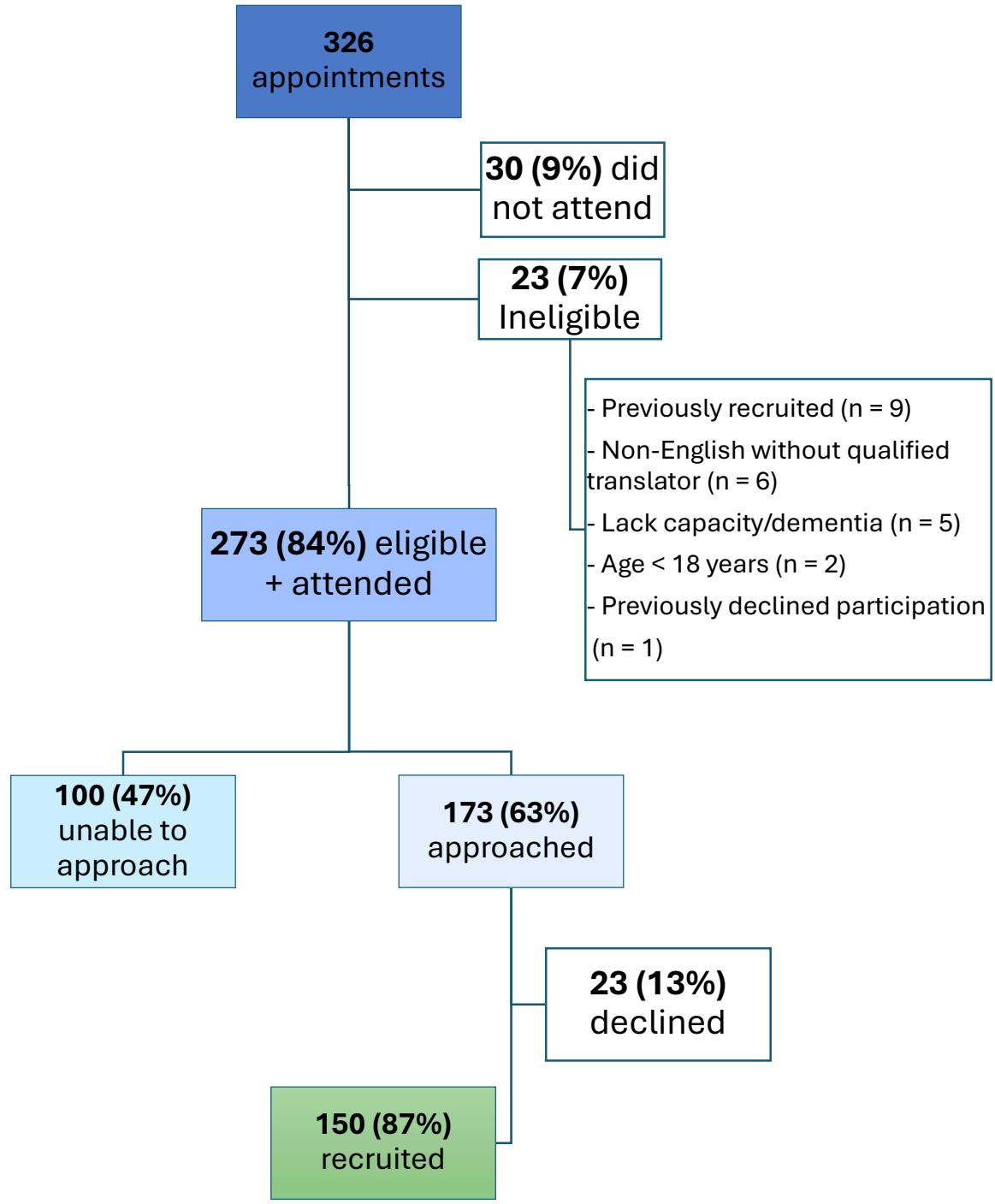


Figure 5.1 - FAVOUR patient participant recruitment flow diagram.

5.4.1.1 Clinician assessments

From 150 participants, 94 (63%) assessments were performed by consultant vascular surgeons and 53 (35%) by vascular trainees. Three (2%) assessments were not completed by clinicians and instead required completion myself as researcher. Reasons for clinician non-completion included: lack of time (n=1), clinician forgot (n=1) or because the patient's appointment was scheduled for vascular nurse specialist review only, with no clinician input required (n=1). Clinician assessments took a mean time of between 2 - 5.5 seconds to complete, with ICE being the quickest form of assessment, Table 5.1.

5.4.1.2 Patient self-assessments

All patient self-assessments were completed in full. The mean time (±SD) taken for patient-CFS (pCFS) and FiND completion was 67 (55.1) and 61 (43) seconds respectively. The majority of patients required assistance for completing the CFS (62%) and FiND (66%) assessments. Where assistance was required, this primarily took the form of hands-on assistance (CFS: 74% and FiND: 77%), Table 5.1. The reasons for requiring assistance were not formally recorded for this study, however typically the reasons included poor task comprehension and sensory impairment (most commonly visual disturbances).

5.4.1.3 Proxy self-assessments

A total of 22 proxies participated in FAVOUR before proxy recruitment was stopped. The mean (±standard deviation, SD) time to complete proxy CFS (prCFS) and FiND (prFiND) was 80 (55.9) and 71 (46.8) seconds respectively, Table 5.1. Although not documented, the longer time to completion typically occurred due to proxies offering assistance to patient participants. All prCFS were completed, one (5%) prFiND was not completed as patient did not notice the questionnaire within the CRF. Two (9%) proxies required verbal assistance with prCFS

completion. This is compared to 4 (18%) of proxies requiring verbal assistance with prFiND completion.

5.4.1.4 Researcher assessment

All mFI-11 assessments were completed, with assessments taking a mean (±SD) time of 46 (42) seconds to gather the relevant data from electronic health records, Table 5.1.

Table 5.1 - Feasibility parameters of frailty instruments in FAVOUR study.

	Clinician assessment			Patient assessment		Researcher assessment	Proxy assessment	
	cCFS	**ICE**	**HIS FRAIL**	**pCFS**	**FiND**	**mFI-11**	**prCFS**	**prFiND**
Mean time (±SD), s	4.5 (3.9)	2.0 (2.8)	5.5 (4.5)	67.0 (55.1)	60.9 (42.6)	45.8 (41.6)	80 (55.9)	71 (46.8)
Non-completion (%)	3* (2%)	3* (2%)	3* (2%)	0	0	0	0	1* (5)
Assistance required	NA	NA	NA	93 (62)	99 (66)	NA	2 (9)	4 (18)
Verbal	-	-	-	24 (26)	23 (23)		2 (9)	4 (18)
Hands-on	-	-	-	69 (74)	76 (77)		0	0

cCFS – Clinician CFS score, pCFS – patient CFS score, ICE – initial clinical evaluation, HIS FRAIL – Healthcare Improvement 'think frailty' FRAIL assessment, FiND – Frail NonDisabled Questionnaire, 11-mFI – 11 item modified frailty index, SD – standard deviation. *Reasons for non-completion: lack of time (n=1), forgot (n =1), patient attended only for vascular nurse specialist review (n=1) and proxy did not notice the questionnaire (n=1). Clinician noncompletion of assessments were instead completed by researcher. NA – not assessed.

5.4.2 Participant baseline demographics

From 150 recruited patient participants, there was a male preponderance (*n* = 93, 62%) and a mean (±SD) age of 68 (±12) years. Most patients (*n* = 105, 70%) had no prior history of treatment for vascular pathology and the most common pathology was critical limb threatening ischaemia (CLTI) (*n* = 90, 61%). The majority of patients (*n* = 92, 61%) came from areas of greatest social deprivation (Scottish Index of Multiple Deprivation, SIMD scores 1 - 4). The patient cohort were comorbid, with mean (SD) CCI score of 5 (2.6), and most had polypharmacy (n = 116, 77%), Table 5.2.

The demographics for participants recruited to FAVOUR were compared to the demographic data for an unselected patient cohort attending hot clinic from a previous internal departmental audit, see section 4.3.12.1. From available comparisons, there were no significant differences between FAVOUR and internal audit demographics for male sex (*n* = 93, 62% vs. 259, 61%, $p > 0.05$), mean age ± SD in years (68±11.9 vs. 69±13.3, $p > 0.05$) or diagnosis code ($p > 0.05$), Table 5.3. The patient cohort selected for the FAVOUR study were therefore felt to be a fair representation of the patient population attending vascular outpatient department services.

Table 5.2 - FAVOUR patient participant demographics.

	Total, *n* = 150
Male (%)	93 (62)
Mean age in years (SD)	68 (±12)
Scottish Index of Multiple Deprivation, *n* (%) (Total *n* = 146)	
1 (most deprived)	36 (24)
2	23 (15)
3	14 (9)
4	19 (13)
5	8 (5)
6	9 (6)
7	8 (5)
8	9 (6)
9	11 (7)
10 (least deprived)	9 (6)
Diagnosis, *n* (%)	
Chronic Limb Threatening Ischaemia	91 (61)
Carotid stenotic disease	18 (12)
Chronic venous insufficiency	12 (8)
Abdominal aortic aneurysm	3 (2)
Acute limb ischaemia (digital)	6 (4)
Mesenteric angina	1 (1)
Miscellaneous vascular	9 (6)
Miscellaneous non-vascular	10 (7)
Number of medications, median (range)	10 (0-24)
Polypharmacy, ≥ 5 repeat medications, *n* (%)	116 (77)
Premorbid Residency Status, *n* (%)	
Independent	80 (53)
Informal care (relatives/friends)	52 (34)
Supported (homecare BD)	6 (4)
Supported (homecare TDS)	2 (1)
Supported (homecare QDS)	5 (3)
Supported (unclear)	4 (3)
Care home	1 (1)
Previous Vascular Treatment, *n* (%)	
None	105 (70)
Treatment > 6 months ago	30 (20)
Treatment < 6 months	15 (10)
Charlson Comorbidity Index, *n* (%)	
0	5 (3)
1	3 (2)
2	13 (9)
3	12 (8)
4	22 (15)
5	22 (15)
6	30 (20)
7	16 (11)

8	10 (7)
9	7 (5)
10+	10 (7)

AAA – Abdominal aortic aneurysm, BD – *bis in die*/twice daily, TDS – *ter die sumendum*/three times daily, QDS – *quarter die sumendum*/four times daily. 'Miscellaneous vascular' includes: neuropathic/stump pain (*n* = 4), Raynaud's (*n* = 3), thrombophlebitis (*n* = 1), Achenbach syndrome (*n* = 1).

Table 5.3 - Comparison of demographics between FAVOUR and internal audit project.

	Demographics		
Variable	FAVOUR study (*n* = 150)	Internal audit (*n* = 428)	Statistics
Male sex, *n* (%)	93 (62)	259 (61)	χ^2 (1, n=578) = 0.103, *p*=0.748
Age (years), *mean* (SD)	68 (11.9)	69 (13.3)	*t* (576) = -0.769, *p=0.442*
SIMD Decile, *mean* (SD)	4 (2.9)	NA	NA
Medication number, *mean* (SD)	7.9 (5.2)	NA	NA
CCI score, *mean* (SD)	4.3 (2.2)	NA	*NA*
Diagnosis			
Chronic limb threatening ischaemia, *n* (%)	91 (61)	276 (65)	χ^2 (1, n=578) = 0.699, *p*=0.403
Carotid stenotic disease, *n* (%)	18 (12)	34 (8)	χ^2 (1, n=578) = 2.232, *p*=0.135
Chronic venous insufficiency, *n* (%)	12 (8)	30 (7)	χ^2 (1, n=578) = 0.162, *p*=0.688
Abdominal aortic aneurysm, *n* (%)	3 (2)	7 (2)	χ^2 (1, n=578) = 0.087, *p*=0.768
Acute limb ischaemia, *n* (%)	6 (4)	11 (3)	χ^2 (1, n=578) = 0.796, *p*=0.372
Mesenteric angina, *n* (%)	1 (1)	4 (1)	χ^2 (1, n=578) = 0.093, *p*=0.760
Miscellaneous vascular, *n* (%)	9 (6)	31 (7)	χ^2 (1, n=578) = 0.266, *p*=0.606
Miscellaneous non-vascular, *n* (%)	10 (7)	35 (8)	χ^2 (1, n=578) = 0.353, *p*=0.552

SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index, NA – Not available. *: p<0.05, **: p<0.001.

5.4.3 Demographics by frailty assessment

This section compares patient participant demographics by frailty status when different frailty assessment tools were applied. There was variation in detected prevalence when applying the different tools when compared to reference standard, Table 5.4. FiND, when performed by both patient and proxy, diagnosed the greatest prevalence of frailty (*n* = 122, 81% and *n* = 19, 90% respectively). Proxy frailty assessments were also associated with a greater diagnosis of frailty compared to patient self-assessment and clinician assessment, as observed by prCFS of 64% (*n* = 14) compared to cCFS of 49% (*n* = 74) and pCFS of 43% (*n* = 65).

Table 5.4 - Prevalence of frailty by instrument

Instrument	Frailty prevalence, *n* (%) [95% confidence interval]	Prevalence compared to reference standard (cCFS)
cCFS	74 (49) [41-57]	-
ICE	85 (57) [49-64]	χ^2 (1, n=150) = 104.830, p<0.001**
HIS FRAIL	64 (43) [35-51]	χ^2 (1, n=150) = 54.838, p<0.001**
pCFS	65 (43) [36-51]	χ^2 (1, n=150) = 21.087, p<0.001**
mFI-11	88 (59) [51-66]	χ^2 (1, n=150) = 12.327, p<0.001**
FiND	122 (81) [74-87]	χ^2 (1, n=150) = 5.937, p=0.015*
prCFS	14 (64) [45-83]	χ^2 (1, n=22) = 1.010, p=0.315
prFiND	19 (90) [71-97]	χ^2 (1, n=21) = 1.360, p=0.243

cCFS – Clinician CFS score, pCFS – patient CFS score, ICE – initial clinical evaluation, HIS FRAIL – Healthcare Improvement 'think frailty' FRAIL assessment, FiND – Frail NonDisabled Questionnaire, 11-mFI – 11 item modified frailty index, *: p<0.05, **: p<0.001

Excepting proxy frailty assessments, all other assessments (five instruments) observed a significant relationship between comorbidity, as defined by CCI, and a frailty positive state. Sections 5.4.3.1-5.4.3.8 expand on observed differences.

5.4.3.1 Demographics by clinician CFS (cCFS) assessment

Clinician assessed CFS (cCFS) score is considered as reference standard assessment tool by this study. Patient characteristics are summarised according to robust and frail status, as defined by cCFS, in Table 5.5. A cCFS assessment diagnosed 74 (49%) of participants as frail, a lower prevalence than ICE, HIS FRAIL and FiND

assessments. Comparing frail patients to robust counterparts, frail patients were significantly more likely to be older (mean age 72 ± 10 vs. 63 ± 12 years, $p < 0.01$), have greater degree of polypharmacy (mean medication number of 11 ± 5 vs. 8 ± 5, $p < 0.01$) and have more comorbidities according to the CCI (6.5 ± 2.4 vs. 4.3 ± 2.2), $p < 0.01$).

5.4.3.2 Demographics by ICE assessment

Patient characteristics are summarised according to robust and frail status, as defined by ICE assessment, in Table 5.6. Clinician ICE assessment diagnosed frailty in 85 (57%) participants. As previously mentioned, frail patients had an increased number of comorbidities compared to robust counterparts, according to CCI (6.3 ± 2.3 vs. 4.1 ± 2.3, $p < 0.001$). Clinicians were more likely to perceive men as robust (30% vs. 32%, $p < 0.05$).

5.4.3.3 Demographics by HIS FRAIL assessment

Patient characteristics are summarised according to robust and frail status, as defined by HIS FRAIL assessment, in Table 5.7. HIS FRAIL assessment diagnosed the lowest prevalence of frailty from all assessments, with 64 (43%) of patients considered frail. As previously mentioned, frail patients had an increased number of comorbidities compared to robust counterparts, according to CCI (6.4±2.5 vs. 4.6±2.4, $p<0.001$).

5.4.3.4 Demographics by patient CFS (pCFS) assessment

Patient characteristics are summarised according to robust and frail status, as defined by pCFS assessment, in Table 5.8. Patient self-assessment with CFS diagnosed a similarly low prevalence of frailty to HIS FRAIL, with 65 (43%) of patients considering themselves frail. As previously mentioned, frail patients had

an increased number of comorbidities compared to robust counterparts, according to CCI (6.3 ± 2.5 vs. 4.7 ± 2.4, p < 0.001).

5.4.3.5 Demographics by mFI-11 assessment

Patient characteristics are summarised according to robust and frail status, as defined by mFI-11 assessment, in Table 5.9. An mFI-11 assessment diagnosed the second greatest prevalence of frailty, with 88 (59%) of participants categorised as frail. Patients diagnosed as frail, as defined by mFI-11, were more likely to be older (mean age ± SD of 70 ± 9.8 vs. 64 ± 13.7, $p < 0.05$) and have a greater number of medications (mean number ± SD of 12 ± 4.5 vs. 5.8 ± 2.8, $p < 0.001$). In contrast, to other frailty assessment tools, the mean (± SD) total CCI score was higher in robust (5.9 ± 2.8) compared to frail counterparts (5.0 ± 2.4), $p < 0.05$.

5.4.3.6 Demographics by FiND assessment

Patient characteristics are summarised according to robust and frail status, as defined by FiND assessment, in Table 5.10. A FiND assessment diagnosed the greatest prevalence of frailty, with 122 (81%) of participants categorised as frail. As previously mentioned, frail patients had an increased number of comorbidities compared to robust counterparts, according to CCI (6.0 ± 2.4 vs. 4.0 ± 2.7, p < 0.05). Further, male patients were more likely to score themselves as frail (n=71, 47%) than robust (n=22, 15%), χ^2 (1, n=150) = 4.013, p=0.045.

5.4.3.7 Demographics by proxy CFS (prCFS) assessment

Patient characteristics are summarised according to robust and frail status, as defined by proxy CFS assessment, in Table 5.11. Twenty-two assessments were completed, no significant differences in demographic data were observed.

5.4.3.8 Demographics by proxy FiND (prFiND) assessment

Patient characteristics are summarised according to robust and frail status, as defined by proxy CFS assessment, Table 5.12. Twenty-one assessments were completed and no significant differences in demographic data were observed.

Table 5.5 - Participant demographics according to cCFS frailty status.

Variable	Frailty status by clinician CFS score		Statistics
	Robust (CFS: 1-4), *n* = 76 (51%)	Frail (CFS: 5+), *n* = 74 (49%)	
Male sex, *n* (%)	46 (31)	47 (31)	χ^2 (1, n=150) = 0.142, *p*=0.706
Age (years), *mean* (SD)	63 (12.3)	72 (9.6)	*t* (141.5) = -5.152, *p*<0.001**
SIMD Decile, *mean* (SD) [$]	4 (2.9)	4 (3.1)	*t* (141.8) = 1.119, *p*=0.265
Medication number, *mean* (SD)	7.9 (5.2)	11.0 (5.0)	*t* (148.0) = -3.757, *p*<0.001**
CCI score, *mean* (SD)	4.3 (2.2)	6.5 (2.4)	*t* (148.0) = -6.045, *p*<0.001**

CFS – Clinical Frailty Scale, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index, *: p<0.05, **: p<0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.6 - Participant demographics according to ICE frailty status.

Variable	Frailty status by ICE score: Robust ('not frail'), *n* = 65 (43%)	Frail ('frail'), *n* = 85 (57%)	Statistics
Male sex, *n* (%)	48 (32)	45 (30)	χ^2 (1, n=150) = 6.832, *p*=0.009*
Age (years), *mean* (SD)	69.4 (11.4)	66.5 (12.3)	*t* (148) = 1.501, *p*=0.136
SIMD Decile, *mean* (SD)[$]	3.9 (2.9)	4.4 (3.0)	*t* (144) = -0.869, *p*=0.386
Medication number, *mean* (SD)	9.7 (5.2)	9.2 (5.4)	*t* (148) = 0.553, *p*=0.581
CCI score, *mean* (SD)	4.1 (2.3)	6.3 (2.3)	*t* (148) = -5.747, *p*<0.001**

ICE – Initial Clinical Evaluation, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.7 - Participant demographics according to HIS FRAIL frailty status.

Variable	Frailty status by HIS FRAIL score		Statistics
	Robust (score≤1), *n* = 86 (57%)	Frail (score≥2), *n* = 64 (43%)	
Male sex, *n* (%)	58 (39)	35 (23)	χ^2 (1, n=150) = 2.534, *p*=0.111
Age (years), *mean* (SD)	68.6 (11.3)	66.5 (12.8)	*t* (148) = 1.503, *p*=0.294
SIMD Decile, *mean* (SD)[$]	4.2 (3.1)	4.2 (2.9)	*t* (144) = -0.131, *p*=0.896
Medication number, *mean* (SD)	9.5 (5.1)	9.3 (5.7)	*t* (148) = 0.271, *p*=0.787
CCI score, *mean* (SD)	4.6 (2.4)	6.4 (2.5)	*t* (148) = -4.304, *p*<0.001**

HIS FRAIL – Healthcare Improvement Scotland FRAIL assessment, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index.
*: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.8 - Participant demographics according to patient CFS frailty status.

Variable	Frailty status by patient CFS score		Statistics
	Robust (CFS: 1-4), *n* = 85 (57%)	Frail (CFS: 5+), *n* = 65 (43%)	
Male sex, *n* (%)	54 (36)	39 (26)	χ^2 (1, n=150) = 0.195, *p*=0.659
Age (years), *mean* (SD)	69 (12.3)	66 (11.3)	*t* (148) = 1.243, *p*=0.216
SIMD Decile, *mean* (SD)[$]	4 (2.9)	4 (3.1)	*t* (144) = 0.168, *p*=0.866
Medication number, *mean* (SD)	9.8 (5.3)	9.0 (5.3)	*t* (148) = 0.968, *p*=0.335
CCI score, *mean* (SD)	4.7 (2.4)	6.3 (2.5)	*t* (148) = -3.967, *p*<0.001**

CFS – Clinical Frailty Scale, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.9 - Participant demographics according to mFI-11 frailty status.

Variable	Frailty status by mFI-11 score		Statistics
	Robust (score≤2), *n* = 62 (41%)	Frail (score≥3), *n* = 88 (59%)	
Male sex, *n* (%)	36 (58)	57 (64)	χ^2 (1, n=150) = 0.695, *p*=0.405
Age (years), *mean* (SD)	64 (13.7)	70 (9.8)	*t* (148) = -3.113, *p*=0.002*
SIMD Decile, *mean* (SD)[$]	4.6 (2.9)	3.9 (3.0)	*t* (144) = 1.445, *p*=0.151
Medication number, *mean* (SD)	5.8 (4.0)	12.0 (4.5)	*t* (148) = -8.852, *p*<0.001**
CCI score, *mean* (SD)	5.9 (2.8)	5.0 (2.4)	*t* (148) = 2.113, *p*=0.037*

mFI-11 – 11-item modified Frailty Index, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001.
[$] - *n* = 146 participants, otherwise no missing data.

Table 5.10 - Participant demographics according to FiND frailty status.

Variable	Frailty status by FiND score		Statistics
	Not frail (C+D+E=0), *n* = 28 (19%)	Frail (C+D+E≥1), *n* = 122 (81%)	
Male sex, *n* (%)	22 (15)	71 (47)	χ^2 (1, n=150) = 4.013, *p*=0.045*
Age (years), *mean* (SD)	71.2 (9.8)	66.9 (12.3)	*t* (148) = 1.730, *p*=0.086
SIMD Decile, *mean* (SD)[$]	3.9 (2.6)	4.3 (3.1)	*t* (144) = -0.566, *p*=0.572
Medication number, *mean* (SD)	9.4 (5.2)	9.5 (5.3)	*t* (148) = -0.084, *p*=0.933
CCI score, *mean* (SD)	4 (2.7)	6 (2.4)	*t* (148) = -3.234, *p*=0.002*

FiND – Patient Frail NonDisabled Questionnaire, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.11 - Participant demographics according to proxy CFS frailty status.

Variable	Frailty status by proxy CFS score		Statistics
	Robust (CFS: 1-4), *n* = 8 (36%)	Frail (CFS: 5+), *n* = 14 (64%)	
Male sex, *n* (%)	7 (32)	10 (45)	χ^2 (1, n=22) = 0.749, *p*=0.387
Age (years), *mean* (SD)	73 (9.4)	72 (9.4)	*t* (20) = 0.381, *p=0.707*
SIMD Decile, *mean* (SD) [$]	7 (3.5)	5 (3.0)	*t* (20) = 1.179, *p*=0.252
Medication number, *mean* (SD)	8.9 (3.3)	11.5 (5.2)	*t* (20) = -1.292, *p=0.211*
CCI score, *mean* (SD)	5.5 (2.3)	5.9 (2.1)	*t* (20) = -0.444, *p=0.662*

CFS – Clinical Frailty Scale, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

Table 5.12 - Participant demographics according to proxy FiND frailty status.

Variable	Frailty status by proxy FiND score		Statistics
	Not frail (C+D+E=0), *n* = 2 (10%)	Frail (C+D+E≥1), *n* = 19 (90%)	
Male sex, *n* (%)	2 (10)	14 (67)	χ^2 (1, n=21) = 0.691, *p*=0.406
Age (years), *mean* (SD)	73 (12.7)	72 (9.4)	*t* (19) = 0.140, *p=0.890*
SIMD Decile, *mean* (SD) [$]	4 (3.5)	6 (3.1)	*t* (19) = -1.046, *p*=0.309
Medication number, *mean* (SD)	9.0 (5.7)	10.4 (4.6)	*t* (19) = -0.397, *p=0.696*
CCI score, *mean* (SD)	6.0 (2.8)	5.7 (2.2)	*t* (19) = 0.158, *p=0.876*

FiND – Frail NonDisabled Questionnaire, SIMD – Scottish Index of Multiple Deprivation, CCI – Charlson comorbidity Index. *: p < 0.05, **: p < 0.001. [$] - *n* = 146 participants, otherwise no missing data.

5.4.4 Interrater reliability between clinician and patient assessment

5.4.4.1 Clinician and patient CFS comparison

In considering CFS scores ≥ 5 as frail, clinicians categorised 74 (49%) patients as frail. In comparison, patients self-assessment diagnosed a lower prevalence of frailty, with 65 (43%) considered frail, Table 5.4. The interrater reliability between patient and clinician CFS scores was poor, Kappa 0.162, $p < 0.001$. Using Bland Altman analysis, the mean difference was -0.11 with a standard deviation of 1.48 indicating similarity in scores, Figure 5.2. However, the 95% limits of agreement were broad (-3.0 to 2.8) and there are outliers, suggesting variability in measurements. Using linear regression, mean difference = -0.282, standard error = 0.80, $p = 0.001$. This indicates proportional bias with greater disagreement between scores toward the higher end of the scale with a negative skew, suggesting patients with greater cCFS scores tended to score themselves as more robust (mode pCFS Score of 4 vs. mode cCFS score of 6).

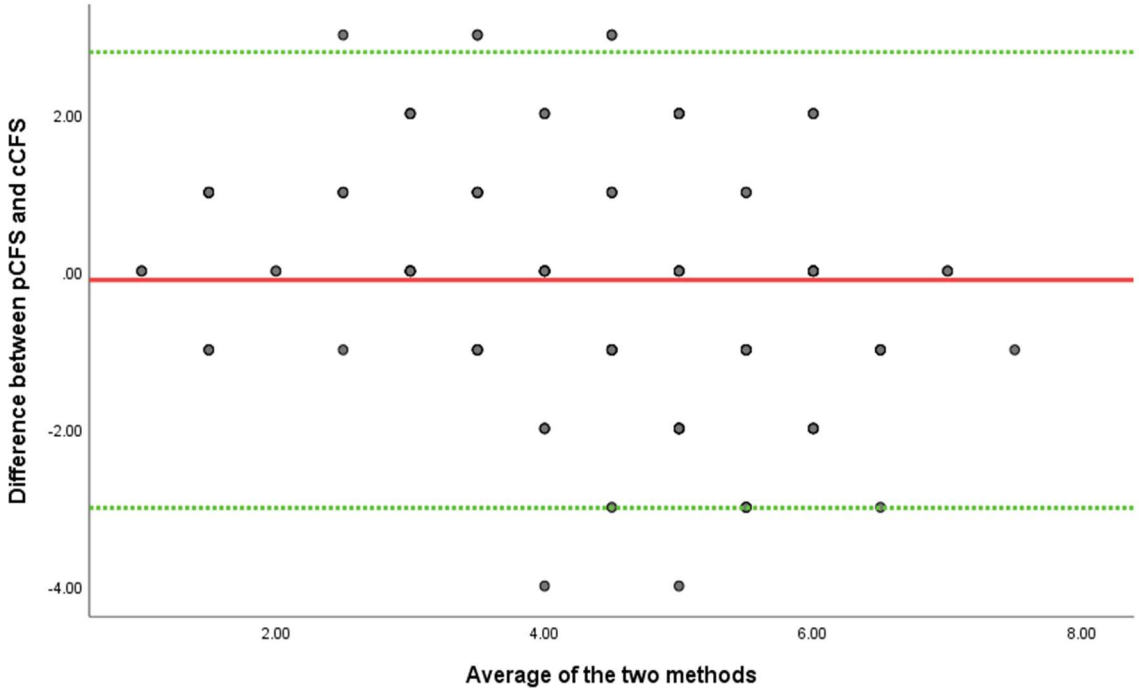


Figure 5.2 - Bland Altman plot representing clinician and patient CFS agreement.

5.4.5 Interrater reliability between proxy assessments

5.4.5.1 Clinician and proxy CFS comparison

The interrater reliability between clinician and proxy CFS score was poor although failed to reach statistical significance in the context of small recruitment numbers, Kappa 0.214, p = 0.315. Bland Altman plot demonstrates no evidence of proportional bias with a degree of variability as observed by broad limits of agreement and some outliers, mean difference -0.273, SD 1.55 and 95% limits of agreement between -3.3 and 2.8, Figure 5.3. Linear regression demonstrated similarity in scores with a mean difference = 0.108, standard error = 0.276, and no proportional bias (p = 0.700).

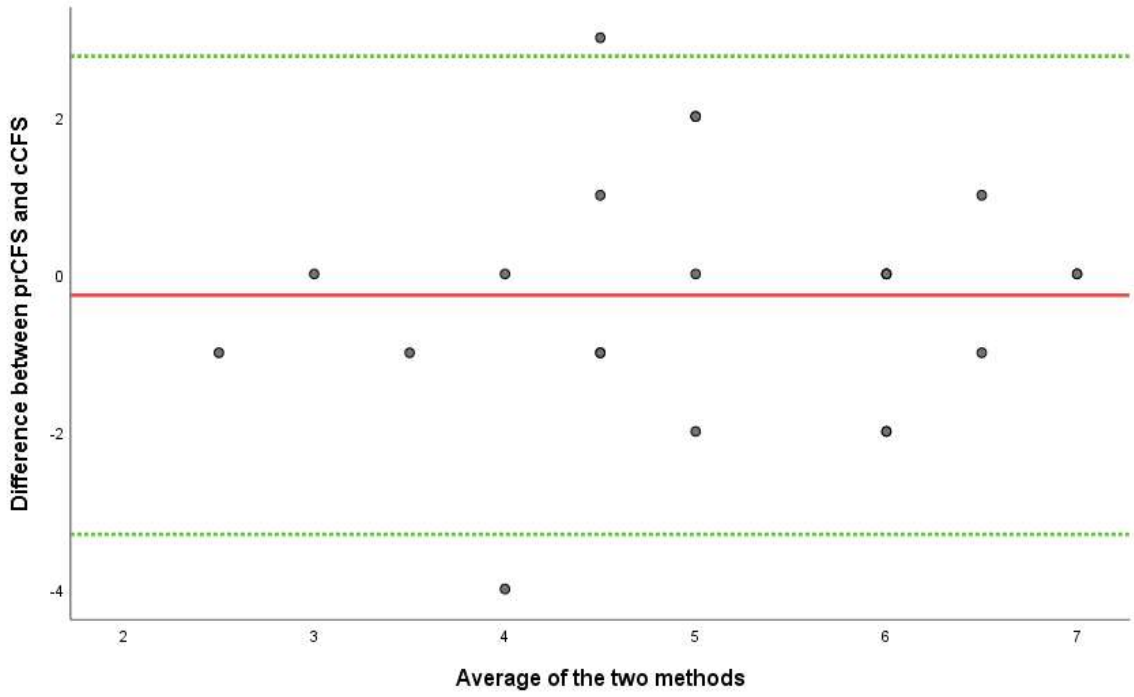


Figure 5.3 - Bland Altman plot representing clinician and proxy CFS agreement.

5.4.5.2 Proxy and patient CFS comparison

Proxy and patient CFS scores demonstrated good interrater reliability, Kappa 0.713, *p* = 0.001. Results must be interpreted with caution in the context of smaller recruited number of proxies. Bland Altman plot demonstrates no evidence of proportional bias with a degree of variability as observed by broad limits of agreement and some outliers, mean difference = -0.500, SD 0.74 and 95% limits of agreement between -1.95 and 0.95, Figure 5.4. Linear regression demonstrated similarity in scores (unstandardised coefficient beta) with a mean difference of -0.047, SE = 0.124 and no proportional bias (p = 0.708).

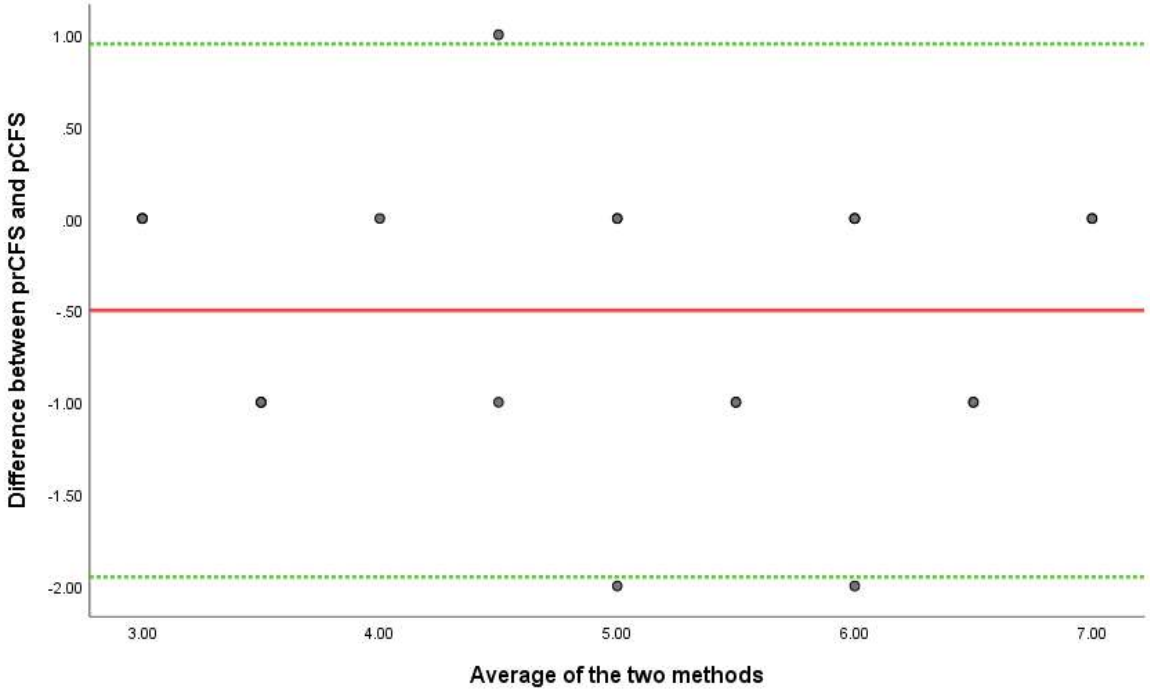


Figure 5.4 - Bland Altman plot representing proxy and patient CFS agreement.

5.4.5.3 Proxy and patient FiND comparison

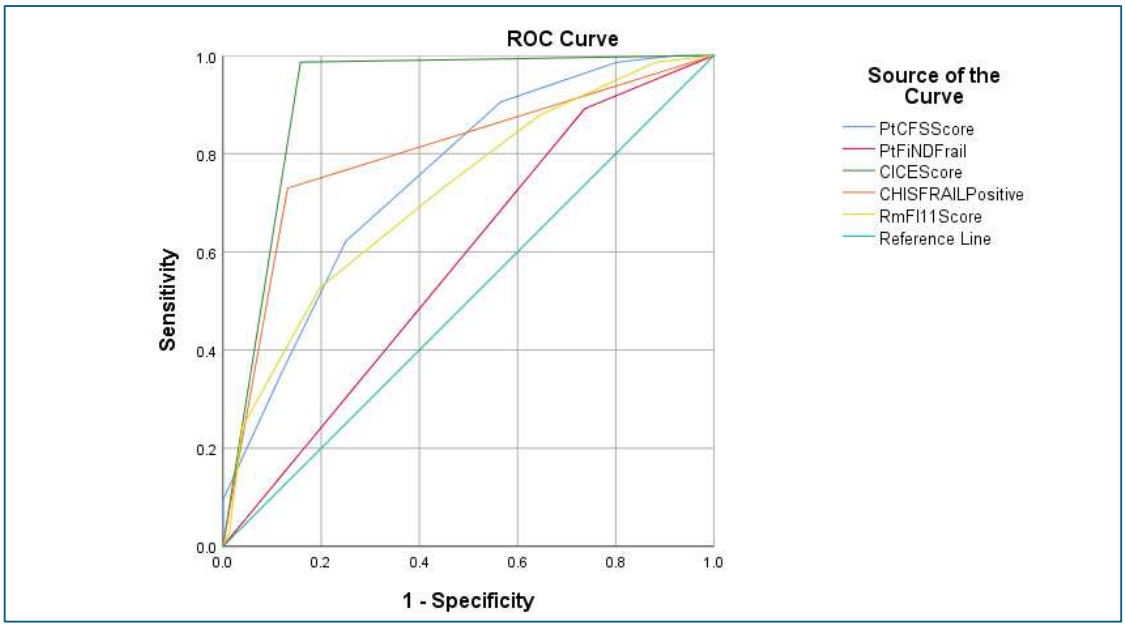
In comparing patient and proxy FiND assessments, the interrater reliability was poor, Kappa 0.173, p = 0.361, as the prevalence of frailty according to proxy assessment was greater than patient self-assessment. Results must be interpreted with caution in the context of smaller recruited number of proxies. Bland Altman analysis has not been performed for dichotomous data.

5.4.6 Convergent validity of frailty assessment instruments compared to clinician CFS

5.4.6.1 Test accuracy compared to clinician CFS (cCFS)

Excluding proxy assessments which are presented later in this section, Figure 5.5 demonstrates test accuracy using ROC analysis and Table 5.13 demonstrates test sensitivity and specificity when comparing selected frailty assessment instruments against the cCFS as reference standard. The clinician reported ICE assessment demonstrated excellent test accuracy on ROC analysis with an AUC = 0.914 (95% CI: 0.863-0.966, p < 0.001) which was associated with excellent sensitivity (99%, 95%CI: 0.942 - 0.999) and good specificity (84%, 95% CI: 0.749 – 0.912). Thereafter, the clinician assessed HIS FRAIL tool was the second most accurate frailty assessment instrument with moderate accuracy (AUC 0.799, 95% CI: 0.725 – 0.873, p < 0.001) arising from good levels of specificity (87%, 95%CI: 0.781 – 0.932) with acceptable levels of sensitivity (73%, 95% CI: 0.622 - 0.822). Patient CFS assessment demonstrated moderate accuracy when compared to cCFS (AUC 0.752, 95% CI: 0.675 – 0.829, p < 0.001). This test had acceptable specificity levels (75%, 95%CI: 0.645 – 0.838) but poor sensitivity levels (62%, 95%CI: 0.508 – 0.727). Comparatively, the mFI-11 demonstrated moderate test accuracy (AUC 0.719, 95% CI: 0.638 – 0.800, p < 0.001) which was associated with moderate sensitivity levels (73%, 95% CI: 0.622 – 0.822) but poor specificity levels (55%, 95% CI: 0.440 – 0.661). Due to poor specificity (26%, 95% CI: 0.173 – 0.369), the test accuracy of FiND assessment did not demonstrate a significant association with cCFS (AUC 0.578, 95% CI: 0.486 – 0.669, p = 0.101).

Thereafter, differences in area under the curve were compared using Delong test, Table 5.14. In comparing the accuracy of frailty assessment tools against the cCFS as reference standard, ICE demonstrated superior accuracy with a significantly greater AUC compared to all other tools. In comparison, FiND appeared to be the least accurate instrument, with the smallest AUC (see Figure 5.5) which was also statistically significantly different when compared to all other instruments. There were no other statistically significant differences when comparing AUC.



Frailty assessment tool	AUC	Std. Error	p value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ICE	0.914	0.026	< 0.001	0.863	0.966
HIS FRAIL	0.799	0.038	< 0.001	0.725	0.873
pCFS	0.752	0.039	< 0.001	0.675	0.829
mFI-11	0.719	0.041	< 0.001	0.638	0.800
FiND	0.578	0.047	0.101	0.486	0.669

Test run under the nonparametric assumption, comparing frailty assessment tool to clinician CFS score as gold standard. ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL assessment, pCFS – patient CFS, mFI-11 – ii-item modified frailty index, FiND – patient Frail NonDisabled Questionnaire.

Figure 5.5 - ROC curve analysis comparing test accuracy against clinician CFS assessment.

Table 5.13 - Sensitivity and specificity of frailty assessments compared to cCFS.

	Sensitivity (%) [95% confidence interval]	Specificity (%) [95% confidence interval]
ICE	99 [0.942-0.999]	84 [0.749-0.912]
HIS FRAIL	73 [0.622-0.822]	87 [0.781-0.932]
pCFS	62 [0.508-0.727]	75 [0.645-0.838]
mFI-11	73 [0.622-0.822]	55 [0.440-0.661]
FiND	89 [0.808-0.949]	26 [0.173-0.369]

ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL, pCFS – patient CFS, mFI-11 – 11-item modified frailty index, FiND – Frail nonDisabled Questionnaire

Table 5.14 - Comparison of AUC for test accuracy.

	ICE	HIS FRAIL	pCFS	mFI-11	FiND
ICE		DBA: 0.115 95% CI: 0.045 - 0.185 z statistic: 3.233 p = 0.001**	DBA: 0.162 95% CI: 0.082 - 0.243 z statistic: 3.952 p < 0.001**	DBA: 0.196 95% CI: 0.110 - 0.281 z statistic: 4.507 p < 0.001**	DBA: 0.337 95% CI: 0.267 - 0.407 z statistic: 9.408 p < 0.001**
HIS FRAIL			DBA: 0.0469 95% CI: -0.037 - 0.131 z statistic: 1.093 p = 0.274	κ DBA: 0.0803 95% CI: -0.014 - 0.174 z statistic: 1.672 p = 0.095	DBA: 0.222 95% CI: 0.138 - 0.305 z statistic: 5.197 p < 0.001**
pCFS				DBA: 0.0333 95% CI: -0.061 – 0.127 z statistic: 0.696 p = 0.486	DBA: 0.175 95% CI: 0.092 – 0.257 z statistic: 4.138 p < 0.001**
mFI-11					DBA: 0.141 95% CI: 0.046 – 0.236 z statistic: 2.290 p = 0.004*
FiND					

cCFS – clinician CFS, ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL, pCFS – patient CFS, mFI-11 – 11-item modified frailty index, FiND – Frail nonDisabled Questionnaire, DBA -Difference between areas. CI = Confidence interval, * : $p < 0.05$, **: $p < 0.001$. Blue indicates statistically significant result.

5.4.6.2 Strength of test agreement and correlation compared to clinician CFS (cCFS)

In comparing agreement and correlation of instruments against cCFS using Cohen's Kappa Coefficient and Spearman's rank test, ICE, HIS FRAIL and pCFS demonstrated a positive correlation, Table 5.15. ICE demonstrated excellent agreement with cFS ($\kappa = 0.827$, $p < 0.001$), with good correlation strength ($r(150) = 0.802$, p 0.001). In comparison, HIS FRAIL demonstrated moderate agreement with cCFS ($\kappa = 0.599$, $p < 0.001$) with moderate correlation strength ($r(150) = 0.664$, $p < 0.001$). As described previously, there was poor agreement with pCFS and cCFS in detecting frailty ($\kappa = 0.162$, $p < 0.001$) with a moderate strength agreement in a positive correlation ($r(150) = 0.570$, $p < 0.001$). There was poor agreement and correlation between cCFS and mFI-11 and FiND.

Table 5.15 - Strength of agreement and correlation with cCFS.

Test value	ICE	HIS FRAIL	pCFS	mFI-11	FiND
Cohen's Kappa Coefficient (κ)	0.827**	0.599**	0.162**	0.282**	0.154*
Spearman's rank correlation, r(150)	0.802**	0.664**	0.570**	0.466**	0.329**

ICE = Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL assessment, pCFS – Patient Clinical Frailty Scale, mFI-11 – 11-item modified frailty index, FiND – patient Frail NonDisabled questionnaire. $p < 0.05$, **: $p < 0.001$. Colour code: Green = excellent agreement/correlation, yellow : good agreement/correlation, blue = moderate agreement/correlation, red: poor agreement/correlation.

5.4.7 Convergent validity of proxy frailty assessment compared to clinician CFS

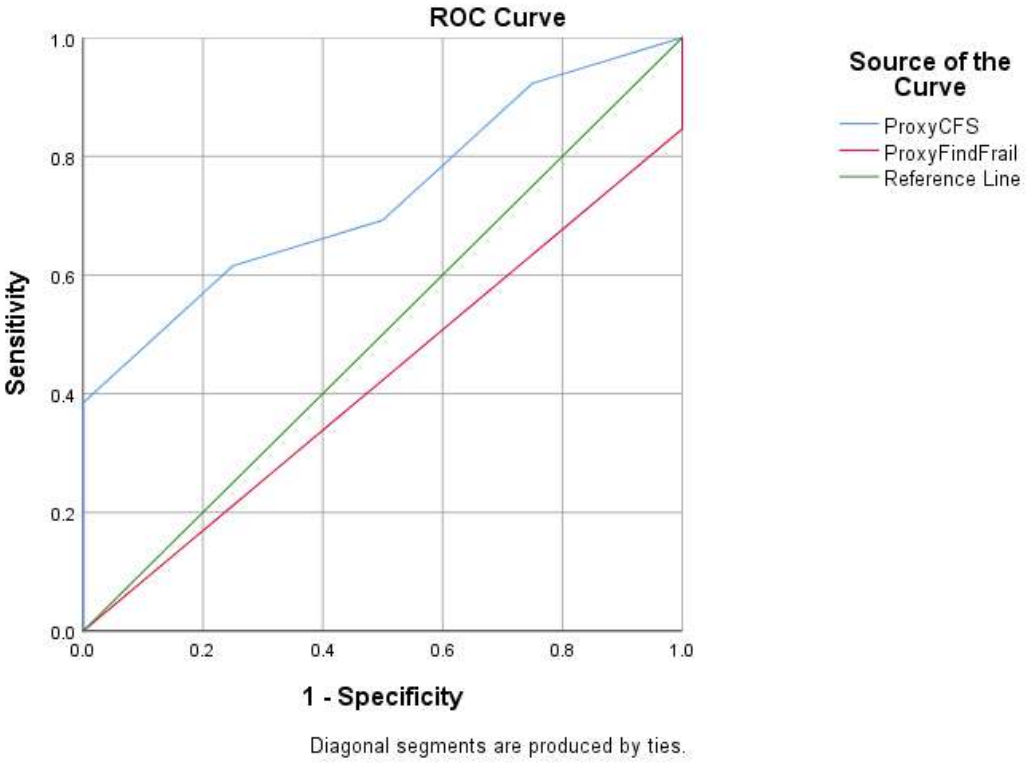
Due to smaller recruitment numbers, proxy assessment data are presented separately, and results are to be interpreted with caution. Statistical significance was not reached for any analysis however there were trends.

5.4.7.1 Proxy test accuracy compared to clinician CFS (cCFS)

Figure 5.6 presents AUC comparisons, and Table 5.16 presents the sensitivity and specificity, between proxy frailty assessment and cCFS as reference standard. Compared to reference standard, proxy CFS demonstrated moderate test accuracy (AUC 0.731, 95% CI: 0.517 – 0.945, p = 0.082). This was associated with an acceptable sensitivity (71%, 95% CI: 0.455-0.901) and poor specificity (50%, 95% CI: 0.191-0.809).

Of note, proxy assessment demonstrates worse specificity compared to reference standard (cCFS) than patient CFS assessment. This was determined by the AUC of prCFS and pCFS being similar when compared to cCFS, however, prCFS demonstrates worse specificity compared to pCFS. Compared to reference standard, proxy FiND assessment demonstrated poor test accuracy (AUC 0.423, 95% CI: 0.174 – 0.672, p = 0.562), associated with good sensitivity (85%) but poor specificity (0%). Due to no true negatives detected with prFiND, 95% confidence intervals could not be calculated.

Thereafter, differences in area under the curve were compared using Delong test which demonstrated a small difference in area under the curve that did not reach statistical significance (Difference between areas: 0.154, 95%CI: -0.0868 – 0.394,z statistic: 1.253, p = 0.210).



Frailty assessment tool	AUC	Std. Error	p value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
prCFS	0.731	0.109	0.082	0.517	0.945
PrFiND	0.423	0.127	0.562	0.174	0.672

Test run under the nonparametric assumption, comparing frailty assessment tool to clinician CFS score as gold standard. prCFS – Proxy clinical frailty scale, prFRAIL - Proxy Healthcare Improvement Scotland FRAIL assessment.

Figure 5.6 - ROC curve analysis comparing proxy test accuracy against clinician CFS assessment.

Table 5.16 - Sensitivity and specificity of proxy frailty assessments compared to cCFS.

	Sensitivity (%) [95% confidence interval]	Specificity (%) [95% confidence interval]
prCFS	71 [0.455-0.901]	50 [0.191-0.809]
prFiND	85 [-]	0

prCFS – Proxy Clinical Frailty Scale, prFiND – proxy Healthcare Improvement Scotland FRAIL assessment.

5.4.7.2 Strength of proxy test agreement and correlation compared to clinician CFS (cCFS)

Compared to reference standard, proxy CFS demonstrated poor agreement (κ = 0.214, p = 0.315) and poor correlation strength (r(22) = 0.449, p 0.036). Similarly, proxy FiND assessment also demonstrated poor test agreement with cCFS (κ = -0.180, p = 0.243) and poor correlation strength (r(21) = -0.109, p = 0.637), Table 5.17.

Table 5.17 - Strength of agreement and correlation of proxy assessments with cCFS.

Test value	**proxy CFS n = 22**	**proxy FiND n = 21**
Cohen's Kappa Coefficient (κ)	0.214	-0.180
Spearman's rank correlation, r(22/21)	0.449*	-0.109

CFS –Clinical Frailty Scale, FiND –Frail NonDisabled questionnaire. p < 0.05, **: p < 0.001. Colour code: Green = excellent agreement/correlation, yellow : good agreement/correlation, blue = moderate agreement/correlation, red: poor agreement/correlation.

5.4.9 Correlation and agreement between all tools

This section presents summary evaluations of relationship strengths and associations between all tools. Table 5.18 summarises the instrument agreement, using Cohens Kappa coefficient. Table 5.19 summarises direction, and strength, of any correlation, using Spearman's rank correlation analysis. In addition to the significant relationships cCFS and tools presented in section 5.4.6.2, positively correlated relationships were observed between another two pairs of frailty assessment instruments: HIS FRAIL and ICE and HIS FRAIL and pCFS. HIS FRAIL and ICE assessments were both performed by clinicians and demonstrated moderate agreement ($\kappa = 0.568$, $p < 0.001$) in ability to detect frailty with moderate correlation strength ($r(150)=0.591$, $p<0.001$). HIS FRAIL and pCFS demonstrated moderate agreement ($\kappa = 0.470$, $p < 0.001$) however the direction and strength of correlation was poor ($r(150)=0.461$, $p<0.001$). FiND and mFI-11 assessments demonstrated poor agreement and correlation with CFS, ICE and HIS FRAIL assessments.

For proxy assessments, in addition to previously discussed relationships in section 5.4.55.4.5, proxy CFS demonstrated moderate agreement (κ 0.545, $p < 0.05$) and a positive correlation of good strength ($r(22)=0.616$, $p < 0.05$) with HIS FRAIL assessment, reflecting the similar trend observed between patient CFS and HIS FRAIL described above. All other tests demonstrated poor interrater reliability scores which did not reach statistical significance. Similarly, the strength of correlation between proxy assessments and remaining frailty assessment tools were poor.

Table 5.18 - Interrater reliability across all frailty instruments

	cCFS	ICE	HIS FRAIL	pCFS	mFI-11	FiND	prCFS	prFiND
cCFS		κ 0.827**	κ 0.599**	κ 0.162**	κ 0.282**	κ 0.154*	κ 0.214	κ -0.180
ICE			κ 0.568**	κ 0.345**	κ 0.304**	κ 0.200*	κ 0.377	κ -0.167
HIS FRAIL				κ 0.470**	κ 0.246*	κ 0.145*	κ 0.545*	κ -0.009
pCFS					κ 0.309*	κ 0.151*	κ 0.713*	κ 0.031
mFI-11						κ 0.162*	κ 0.214	κ -0.180
FiND							κ 0.039	κ 0.173
prCFS								κ 0.056
prFiND								

cCFS – clinician clinical frailty scale, ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL, pCFS – patient clinical frailty scale, mFI-11 – 11-item modified frailty index, FiND – patient Frail nonDisabled Questionnaire. prCFS – Proxy Clinical frailty scale, prFiND – proxy Frail NonDisabled Questionnaire. * : $p < 0.05$, **: $p < 0.001$. Colour code: Green: excellent agreement/correlation, yellow: good agreement/correlation, blue: moderate agreement/correlation, red: poor agreement/correlation using Cohens Kappa coefficient analysis.

Table 5.19 - Correlation strength across all frailty instruments

	cCFS	ICE	HIS Frailty	pCFS	mFI-11	FiND	prCFS	prFiND
cCFS		r(150)=0.802**	r(150)=0.664**	r(150)=0.570**	r(150)=0.466**	r(150)=0.329**	r(22)=0.449*	r(21)=-0.109
ICE			r(150)=0.591**	r(150)=0.452**	r(150)=0.394**	r(150)=0.237*	r(22)=0.470*	r(21)=-0.205
HIS Frailty				r(150)=0.461**	r(150)=0.349**	r(150)=0.206*	r(22)=0.616*	r(21)=-0.015
pCFS					r(150)=0.384**	r(150)=0.321**	r(22)=0.855**	r(21)=-0.041
mFI-11						r(150)=0.195*	r(22)=0.114	r(21)=0.200
FiND							r(22)=-0.088	r(21)=0.200
prCFS								r(21)=-0.082
prFiND								

cCFS – clinician clinical frailty scale, ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL, pCFS – patient clinical frailty scale, mFI-11 – 11-item modified frailty index, FiND – patient Frail nonDisabled Questionnaire. prCFS – Proxy Clinical frailty scale, prFiND – proxy Frail NonDisabled Questionnaire* : $p < 0.05$, **: $p < 0.001$. Colour code: Green: excellent agreement/correlation, yellow: good agreement/correlation, blue: moderate agreement/correlation, red: poor agreement/correlation using Spearman's rank correlation analysis.

5.4.10 Post hoc analysis: Correlation between co-morbidity and frailty index

Due to the observed poor correlation between mFI-11 and FiND with other frailty assessment instruments, post hoc analysis was performed to assess strength of correlation between comorbidity measure, CCI.

The mFI-11 demonstrated a positive correlation of moderate strength with CCI ($r(150) = 0.698$, $p < 0.01$). Remaining instruments demonstrated poor strength of correlation, Table 5.20.

Table 5.20 - Correlation of frailty instruments with comorbdity measurement

	cCFS	ICE	HIS Frailty	pCFS	mFI-11	FiND
CCI	r(150)=0.483**	r(150)=0.415**	r(150)=0.323**	r(150)=0.396**	r(150)=0.698**	r(150)=0.284**

cCFS – clinician CFS, ICE – Initial clinical evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL, pCFS – patient CFS, mFI-11 – 11-item modified frailty index, FiND – Frail nonDisabled Questionnaire. * : $p < 0.05$, **: $p < 0.001$. Colour code: Green: excellent agreement/correlation, yellow: good agreement/correlation, blue: moderate agreement/correlation, red: poor agreement/correlation using Spearman's rank correlation analysis.

5.4.11 Post-hoc analysis: FiND assessment

The FiND questionnaire has five binary-response questions (A - E). At least one positive response to either A or B diagnoses disability. At least one positive response to any of C - E diagnoses frailty. Negative responses to all five questions indicates the patient is robust.

The five questions are:

A. Have you any difficulties at walking 400 metres?

B. Have you any difficulties at climbing up a flight of stairs?

C. During the last year, have you involuntarily lost more than 4.5kg (10 lbs)?

D. How often in the last week did you feel that everything you did was an effort or that you could not get going?

E. Which is your level of physical activity (none or mainly sedentary)?

5.4.11.1 Discrepancies between proxy and patient assessment

Proxy FiND assessment diagnosed a greater prevalence of frailty compared to patient FiND assessment which was associated with poor interrater reliability and poor correlation strength (see section 5.4.9, Table 5.18 and Table 5.19). Subgroup analysis of the three dichotomous questions C - E (of which a positive answer to any one of the three would result in a diagnosis of frailty) was performed using Chi square analysis to explore this discrepancy further. This was performed for all patients, regardless of diagnosed pathology.

There was significant difference in answers to question C ($\chi 2$ (1, n=21) =4.2667, p=0.039), with proxies reporting a greater prevalence of unintentional weight loss. This discrepancy is thought to account for the poor psychometric comparisons between proxy and patient assessment, Figure 5.7. Of note, despite a similar total number of frailty diagnoses, there was significant inconsistencies between patient and proxy answers to question E ($\chi 2$ (1, n=21) =9.4531, p=0.002).

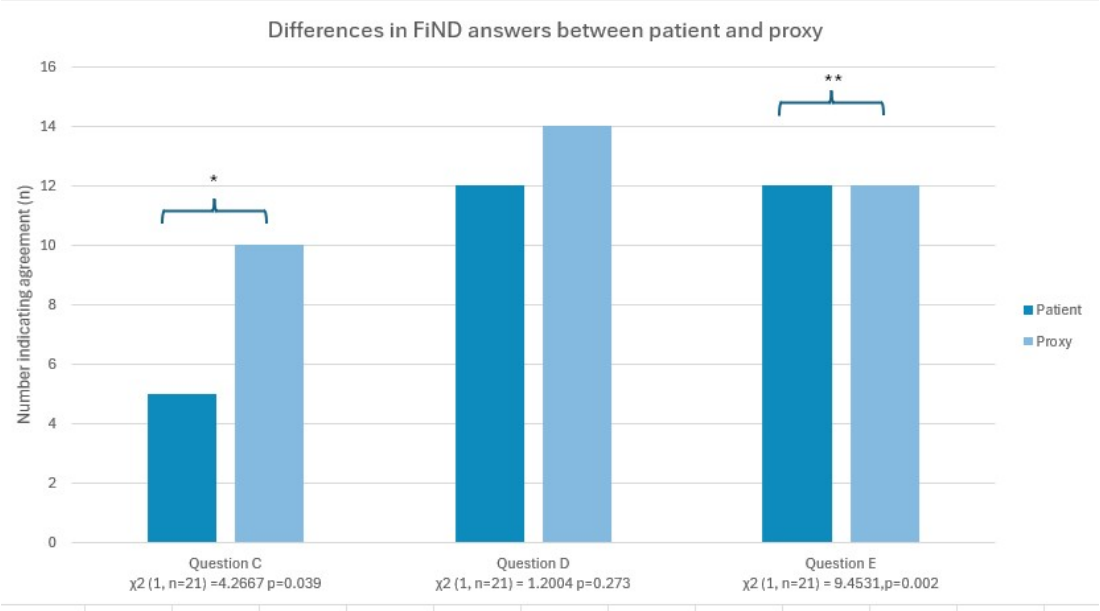


Figure 5.7 - Comparison of patient and proxy responses to FiND questionnaire. FiND – Frail NonDisabled Questionnaire. *: p < 0.05, **: p < 0.001. Questions A + B relate to the presence of disability so are not presented in this figure.

5.4.11.2 FiND and disability in mobility-limiting disease

FiND (when performed by both patient and proxy) assessment diagnosed a substantially greater prevalence of frailty than reference standard. Further, FiND demonstrated poor correlation and agreement with other frailty assessment tools. As most recruited patients were diagnosed with CLTI, and this is a mobility-limiting disease process, post-hoc descriptive analysis was performed to explore whether mobility-limiting pathology may account for the observed discrepancies.

From 91 patients diagnosed with CLTI, 75 (82%) were diagnosed as disabled, according to FiND. In comparison, there was a higher prevalence of self-reported frailty (*n* = 79, 87%), with most of the positive responses observed to arise from question E (*n* = 63, 69%). In comparison, from 11 proxies who performed FiND assessments for patients diagnosed with CLTI there was a very high rate of disability (*n* = 10, 91%). The prevalence of frailty was also greater than patient self-assessment (*n* = 10, 91%) but in contrast to patient self-assessment, this was primarily driven by a greater number of positive responses to question D (*n* = 9, 82%), Table 5.21.

Table 5.21 - Component parts of patient and proxy FiND responses.

	Patient FiND *n* = 91 (%)	Proxy FiND *n* = 11 (%)
Disability questions		
Positive response to A	71 (78)	10 (91)
Positive response to B	58 (64)	8 (73)
Total	75 (82)	10 (91)
Frail questions		
Positive response to C	29 (32)	6 (55)
Positive response to D	58 (64)	9 (82)
Positive response to E	63 (69)	7 (64)
Total	79 (87)	10 (91)

Breakdown in positive responses to FiND questionnaire for patient's, and their proxy where relevant, who were diagnosed with chronic limb threatening ischaemia.

5.5 Discussion

5.5.1 Summary of pertinent results

There have been calls to standardise interdisciplinary approaches to frailty assessment but a lack of head-to-head comparisons, clinimetric properties and uncertainty over prognostic validity has challenged this.[263, 265, 285] The FAVOUR study was designed to speak to the evidence gap. This chapter presented the feasibility parameters and clinimetric properties examined by the FAVOUR study. The prognostic value of selected frailty assessment instruments are presented in Chapter 6.

This data from this study demonstrates that implementing routine frailty assessment in an outpatient department setting is feasible, on the basis of a high recruitment rate, zero drop-out rate, the short time required to complete assessments and high completion rate. It appears the primary limiting step to patient recruitment was the ability of the lead researcher to approach patients, reflecting the fast-paced environment in which this study was conducted. For this reason, the success of rolling out routine frailty assessment for all patients attending a vascular hot clinic will rely on adopting the correct tool and format of application. The clinician assessed instruments do not require additional equipment or training (although it is available for CFS)[286], take only a few seconds to complete and do not require significant information beyond what is routinely collected during a clinical interaction. These qualities make the selected tools accessible, easy to use and minimise disruption to workflow. In comparison, patient self-assessment takes approximately 1 minute. Although this may be an appropriate duration of time for patients to complete self-assessments while awaiting clinical review, the observation that most patients require hands-on assistance suggests implementing self-assessments in this manner are unlikely to result in meaningful compliance. Similarly, the observation that proxy participation was limited by inability not to collaborate with the patient, demonstrates independent proxy assessment is also not feasible. For prospective frailty assessment, clinician assessment is preferred to patient self-assessment.

In the absence of a universally agreed definition, and differing underpinning theories, an abundance of instruments designed to detect and/or quantify frailty exist,[1] with no agreement on a reference standard. In response to COVID outbreak, NICE produced guidelines advising the CFS is used to identify and grade the severity of frailty for patients admitted to hospital.[287] The British Geriatric Society (BGS) also advocate the use of CFS to screen surgical patients who may benefit from a comprehensive geriatric assessment (CGA), delivered by a multidisciplinary team led by a geriatrician.[86] For this reason the CFS was adopted as gold standard in this study. Despite these guidelines, surgeons describe a preference for relying on subjective means of frailty assessment (ICE) due to tool unfamiliarity and uncertainty over tool validity (this will be elaborated on in Chapter 7). The CFS is based on the theory of cumulative deficit and demonstrates excellent agreement with ICE.[270] This demonstrates homogeneity in how clinicians assess frailty and concordance with a formalised assessment criteria, confirming tool validity of the CFS for surgeons.

It has been demonstrated that the CFS can be successfully applied without training due to the tools intuitive nature with illustrations and descriptions.[288] The observed consistency in its use between different healthcare professionals supports this, as some evidence demonstrates excellent interrater agreement between vascular surgeons and medical assistants[152] as well as staff nurses.[106] Excellent agreement has also been observed between less clinically experienced medical students and critical care doctors.[289]

The data presented in this chapter has uncovered a potential unconscious bias in clinicians assessment, with men more likely to be deemed robust compared to women according to ICE. This was not replicated in objective assessment instruments and in fact contradicts patient self-assessment where male patients were more likely to score themselves as frail according to the FiND questionnaire. The adoption of standardised, objective frailty assessment tools will help

overcome such bias in assessment and should be considered a favourable alternative to ICE. In comparison, the remaining tools did not perform as well against the reference standard due to variation in sensitivity and specificity levels. The importance of these parameters when selecting a diagnostic instrument will depend on the intended benefit of instrument application.

A high degree of sensitivity (proportion of patients with the disease who test positive) should be prioritised where the consequences of a missed diagnosis/false negative are great. Conversely, a high degree of specificity (correctly identifying those who do not have the variable being tested for) may be prioritised where the implications of inappropriately treating someone for a condition that is not present, or not offering treatment due to misdiagnosis, are severe.[290] These are important considerations for surgeons and vascular healthcare professionals (HCPs) when trying to avoid over or under-treating patients. On balance it would seem reasonable to prioritise greater sensitivity levels over specificity in selecting a proposed frailty screening tool due to the intended benefits. Such benefits may include guiding operative decision making, informing discussion between HCPs and patients/relatives, unifying language between HCPs as well as help in identifying patients who may benefit from more-resource-intensive CGA assessments perioperatively. A standardised tool will also overcome the demonstrated unconscious bias in assessment observed by this study. For these reasons, and due to the acceptable feasibility and clinimetric properties, this study recommends the CFS be considered the gold standard tool for the purpose of standardising a multidisciplinary approach to frailty diagnosis.

The recruitment of proxies was discontinued when it was realised that the environment in which assessments were being completed challenged the ability of patients and proxies to work independently. The observed relationship between pCFS and prCFS is probably reflective of such collaboration. In contrast, there was discrepancy between patient and proxy FiND assessments. This appears to be due to proxies reporting a greater presence of unintentional weight loss. Although the frailty instrument queries the presence or absence of weight loss, it might be that

the observed discrepancy between patient and proxy stems from a relatives perception of weight loss, rather than being able to objectively evidence it. Certainly there are inherent flaws in requesting proxies to report subjective experiences on behalf of patients. This is exemplified in the differences between patient and proxy responses to how often a patient "felt that everything was an effort" (Question D in FiND). In a study exploring weight loss, appetite and concerns around weight in patients with advanced malignancy, there was significantly greater reports of concern around weight loss when questionnaires were completed with the assistance of relatives, compared to self-reported or nurse-assisted completion.[291] It would be desirable to corroborate reported weight loss with objective evidence, however this was out with the scope of this study. The influence of concerned relatives in patients who require assistance to respond to questionnaires about subjective experiences should be considered in future research.

The mFI-11 and FiND demonstrated poor agreement and correlation with the remaining frailty assessment instruments which suggests these tools measure different constructs. Similar to the CFS, the mFI-11[192] is based on the cumulative deficit theory, however it has been criticised in the past for being heavily reliant on comorbidities, such that comorbidity alone can produce a frailty positive score.[90] It was therefore unexpected to observe that patients defined as robust according to mFI-11 had a greater number of comorbidities than their frail counterparts, particularly as this was not replicated by any other tool. The relationship between mFI-11 and CCI demonstrated moderate correlation too. This directly contradicts the mFI-11's main criticism. However, this finding could be presentative of a bias in the weighting of the variables in the CCI. The explanation behind this observed inconsistency warrants further investigation. In considering this, and the observed poor agreement between mFI-11 with reference standard CFS, the role of the mFI-11 as a frailty assessment tool in clinical practice is disputed. This is of particular relevance for vascular surgery patients where the presence of peripheral arterial disease constitutes one of the 11 'frailty' variables, and indeed demonstrated significant findings in this respect. Selecting the most

appropriate variables for an abbreviated frailty index is challenging as component parts are not weighted by relevance. As described in previous my previous chapter, one of the expected standards of frailty indexes being a requirement for at least 30 variables, this might overcome some of these issues.[74] However, such comprehensive frailty indexes might prove too cumbersome and not lend themselves to application in clinical practice. Nevertheless, a role for comprehensive electronic frailty indices when applied to large research datasets remains.

Conversely, the FiND assessment sets out to differentiate disability from frailty and is the only tool in this study that is based on the Fried phenotypic frailty theory.[17] FiND assessment diagnosed the greatest prevalence of frailty (81%), and when compared to cCFS had the second highest sensitivity (89%) with lowest specificity (26%). Our data mirrors that from a previous study comparing FiND to CFS assessment in vascular population (sensitivity 89%, specificity 26% and AUC 0.57).[136] However, there are particular considerations around the appropriateness of utilising phenotypic measures of frailty in vascular populations. This study demonstrates most patients present with mobility-limiting disease, chronic limb threatening ischaemia. This is recognised by the high prevalence of disability in FiND assessments. In exploring phenotypic measures of frailty, the most common reasons for being diagnosed as frail, was a self-reported sedentary lifestyle, or perceiving significant effort in conducting activities of daily living. It is not inconceivable that the resultant lifestyle limitations occur as a consequence of the aforementioned disability born from their vascular pathology. There is concern that relying solely on phenotypic measures of frailty in a population with such a high prevalence of mobility-limiting disease may sooner act as a measure of function, rather than frailty. For this reason, it is felt more could be done to elucidate the relationship between frailty and disability in patients with mobility-limiting disease.

5.5.2 Comparisons with published literature

The prevalence of frailty will vary between populations and with the use of different frailty assessment instruments. Nevertheless, the observed prevalence of frailty in this study is consistent with observations of frailty within vascular surgery populations.[90] Using the CFS, a prevalence of frailty approximately four times that estimated for the general population was identified by this study, highlighting the critical relevance of frailty in vascular patients.[51] Elective patients being considered for abdominal aortic aneurysm repair may be considered one of the fittest vascular subgroups and even this cohort has demonstrated a frailty prevalence of between 14 and 29% according to the CFS.[97, 123] Frailty is more common in women and with increasing age.[292-294] However, this study had a relatively young mean age of 68 years and a significant male preponderance, as expected with male sex being associated with increased risk of cardiovascular disease.[295] This is testament to the multifactorial nature of frailty. Our population demonstrated significant comorbidity, polypharmacy and socioeconomic deprivation which is felt to contribute toward the observed early-onset frailty. This mirrors data that has demonstrated the most disadvantaged patients are more than twice as likely to develop frailty than most advantaged patients.[296]

The presence of comorbidity and socioeconomic deprivation are suspected confounding factors in the development of frailty.[297] Lower socioeconomic status is associated with comorbidity, poorer health outcomes and reduced access to care whereas multimorbidity is associated with disability, social isolation and poor self-rated physical and mental health with a greater need for acute care services.[298] A larger prospective study would be helpful to enable analysis to control for such variables with the view to clarifying any confounding relationships. As populations continue to age, frailty will continue to become a growing public health crisis and the importance of driving equity in healthcare and social service provision for this vulnerable patient cohort is self-evident.

Despite concordance between healthcare professionals, our study demonstrated poor interrater reliability between patient and clinicians. In comparison, studies examining the interrater reliability of the CFS between healthcare practitioners and patients attending emergency departments have demonstrated moderate agreement (kappa 0.43 – 0.59).[299, 300] However, these studies include a comparatively more robust patient cohort (CFS score 1 - 4: 63-74%), with a self-identified potential patient selection bias, avoiding approaching unwell patients for recruitment. There were no data on presenting complaints, comorbidity or socioeconomic status which challenges further comparison of data. Socioeconomic deprivation and associated low healthcare literacy in our patient demographic may be contributing toward the observed discrepancy between patient and clinician assessments.[301, 302] It is likely this discrepancy will result in a misalignment of patient expectations with the healthcare outcomes felt reasonably achievable by HCPs. This is of particular importance when considering patients attach a high level of importance, and satisfaction, to the feeling of being kept appropriately informed of their care.[303] This study therefore proposes that adopting and referencing a standardised frailty assessment tool may be a useful adjunct to aligning patient/proxy expectations and enhancing clinical discussion.

The CFS is not recommended for use in patients under 65 years of age due to concerns around lack of validation in younger populations.[287] However, this study demonstrates that, using CFS criteria, frailty is prevalent in a younger vascular clinic population. As discussed in Chapter 2 and Chapter 3, beneficial clinical and financial outcomes have been demonstrated when targeting and managing frailty for vascular patients. Employing a binary age cut-off when implementing/adapting clinical services fails to recognise the unique demographic of vascular patients and will exacerbate the healthcare inequalities, obstructing attempts at improving health outcomes for frail patients. Concerted efforts should be made to explore the validity of CFS use across younger patient populations as some of these patients likely stand to benefit from accessing frailty related healthcare pathways.

5.5.3 Strengths and limitations

This study has selected only five frailty tools, but these were chosen based on either common use in clinical practice, endorsement by (inter)national healthcare policy and representation of different theories of frailty. Given the 'real world' nature of the study and included patients, the data from the feasibility parameters relating to researcher and clinician frailty assessments could plausibly be extrapolated to other outpatient department settings. Despite this being a single-centre study, the hub-and-spoke design of vascular services and broad inclusion criteria, generates a large catchment area which does enhance applicability of results to a broader population.

There are limitations identified in this study. The exclusion of patients lacking capacity, as although this represented a small proportion of excluded patients (*n* = 6, due to dementia), it is likely that patients with dementia display higher levels of frailty, which may have contributed to recruitment bias. However, the relatively low number of patients who could not be recruited on this basis is low, demonstrating favourable feasibility for implementing frailty screening in the studied environment. The FiND questionnaire is subject to recall bias and the significant proportion of patients observed to require assistance raises the question of unintended influence by involvement of proxy and/or researcher. However, this challenge is an important feasibility metric and demonstrates well some of the difficulties that will be encountered when using patient self-assessments.

5.5.4 Conclusion

The FAVOUR study responds to calls to standardise frailty assessment. Our data confirms feasibility of implementing routine frailty assessment in a vascular outpatient setting when performed by clinicians. Further, the data from this demonstrates favourable clinimetric properties when comparing clinician preferred subjective measures of assessment (ICE) to Rockwood Clinical Frailty Scale. This should give HCPs confidence in adopting the CFS, overcoming areas of unconscious bias in assessment, and bringing the speciality in line with current healthcare policy recommendations. This will contribute toward unifying healthcare services in their approach to managing frail patients. The prognostic value of frailty assessment instruments is explored in Chapter 6.

Chapter 6 FAVOUR study results: 30-day outcomes

6.1 Chapter summary

Chapter 4 outlines FAVOUR study methodology and Chapter 5 summarises the feasibility and clinimetric data. This chapter aims to answer research question 2c (how do the prognostic properties of frailty assessment compare in prospective frailty assessment). The 30-day home-time and mortality for all participants from the date of recruitment is presented. Further, post-operative 30-day outcomes are also presented for those patients who proceeded to surgical and/or endovascular treatment. A comparison of the prognostic values of the five different frailty assessment instruments is made. While participants recruited to the FAVOUR study will undergo an additional 1-year follow-up, these data are not yet complete and will not be presented in this thesis.

6.2 Introduction

Despite the described abundance and heterogeneity in frailty assessment tools, frailty as a construct has consistently demonstrated correlations with poor health outcomes compared to robust counterparts in surgical patients.[60, 61, 63, 304, 305] It is likely that the application of various assessment instruments to different surgical, or medical, patient populations in different clinical situations (e.g., elective versus emergent) will demonstrate different prognostic accuracy.[90] As presented in Chapter 3, there is a relative lack of evidence to support clinicians in selecting a desirable frailty-assessment instrument in vascular surgery services. To improve this, a call has been made for direct comparisons of various instruments.[306] This will aid clinicians and policy makers in identifying instruments suitable for their patient cohort. This is of particular interest given the increasing age and medical complexity observed in surgical populations.

As previously discussed, the Frailty Assessment in Vascular OUtpatients Review (FAVOUR) study speaks to this evidence gap.[260] This study included all eligible urgent-referral vascular clinic attendees regardless of diagnosis or clinical management plan. The methodology has been reported in Chapter 4. The feasibility and clinimetric results are presented in Chapter 5. This chapter presents a comparison of the predictive value of the five frailty assessment tools at 30-day follow-up. Additional 1-year post study recruitment and 1-year post-operation, where applicable, follow-up period will take place for this study.

6.2.1 Aim

This chapter aims to present data relevant to the secondary outcomes described in Chapter 4. These include assessment of the relationship between frailty status measured by differing tools and:

1. 30 day all-cause mortality
2. 30-day home-time
3. Post-operative 30-day surgical outcomes, including:
    a. Mortality
    b. Morbidity (as defined by Clavien-Dindo classification)
    c. Length of hospital stay
    d. Readmission rate
    e. Nonhome discharge
    f. Discharge with greater social care requirements

6.3 Methods

Comprehensive methodology is presented in Chapter 4. In brief, this is a single-centre prospective observational cohort study (NHS R&I reference UGN23CE014/REC reference 23/PR/0062/NCT06040658).

I performed all aspects of follow-up data collection. All recruited participants had electronic follow-up at 30-days from recruitment to assess mortality and home-time.[271]

A secondary post-operative 30-day follow-up was applied for those patients who proceeded to surgical and/or endovascular treatment following their attendance at the clinic. This is in line with current practice for reporting post-operative outcomes according to the number of days that have passed since the index intervention. A comprehensive summary of outcome measures, with definitions, has been presented in Chapter 4, section 4.3.5: Secondary outcomes (follow-up). In brief, these include: surgical procedure, mortality, post-operative morbidity, length of hospital stay, readmission rates, non-home discharge and discharge with a higher level of social care requirements.

Of note, where patients underwent serial interventions as an inpatient, this was documented as a complication (Clavien-Dindo 4), unless the patient was planned for staged intervention (e.g., angioplasty followed by digital amputation). In this instance, both operations were considered part of the ‘index procedure’ with ‘time to procedure’ calculated from date of clinic to first procedure and the 30-day post-operative follow-up period beginning following completion of the planned secondary procedure. In the instance where the second procedure was not performed (due to cancellation for any reason, including patient mortality), the primary procedure only was documented as the index procedure.

In the instance where patients were assessed and treated for arterial disease of one limb, but developed symptomatic disease of the contralateral limb during inpatient admission, this was not documented as a complication. Rather, it was documented as a primary presentation of contralateral limb disease. In this circumstance patients were not entered into the database.

6.3.1 Sample size

The primary aim of the FAVOUR study was to assess feasibility of introducing frailty assessment in a vascular 'hot' clinic, so rather than set a desired sample size, describing the number of assessments possible in a fixed time period was one of the primary outcomes. As this prognostic analysis made use of the primary FAVOUR cohort, the sample size was pre-determined.

6.3.2 Statistical analysis

Statistical methods for the data in this chapter have been presented in Chapter 4, section 4.3.12 Statistical methods. Data were analysed using IBM SPSS Statistics v25. A p value < 0.05 was considered significant.

6.4 Results

6.4.1 Participant demographics

Participant demographics have been detailed in Chapter 5. Section 5.4.2 according to frailty status as defined by the different instruments and their mode of application. These have not been duplicated in this chapter.

As discussed in Chapter 5, the decision was made to abandon proxy recruitment due to difficulties in preventing proxy and patient collaboration. The feasibility and clinimetric properties are discussed in the previous chapter. However, due to small recruitment numbers, the observed correlation between pCFS and prCFS, as well as the substantial prevalence of frailty according to prFiND, prognostic value of proxy assessment is not presented in favour of presenting patient self-assessment only.

6.4.2 30-day outcomes for all participants

6.4.2.1 30-day mortality

During the follow-up period there were 3 (2%) participant deaths. One patient had a cCFS score of 3 who was admitted for medical management of critical limb threatening ischaemia (CLTI) with infection but deteriorated and died from bacteraemia and sepsis before receiving surgical treatment. Two patients had cCFS scores of 5, both proceeded to treatment for CLTI, one open and one endovascular, both dying from lower respiratory tract infections within 30 days of index treatment. With this small number of events, no frailty assessment instrument demonstrated significance in predicting 30-day mortality, Table 6.1.

Table 6.1 - 30-day mortality following study recruitment.

Frailty instrument	Survived (total *n* = 147) *n* (%)	Death (total *n* = 3) *n* (%)	Statistics
cCFS			χ^2 (1, n=150) = 0.368, *p*=0.544
Robust (*n* = 76)	75 (50)	1 (1)	
Frail (*n* = 74)	72 (48)	2 (1)	
ICE			χ^2 (1, n=150) = 0.125, *p*=0.724
Robust (*n* = 65)	64 (43)	1 (1)	
Frail (*n* = 85)	83 (55)	2 (1)	
HIS FRAIL			χ^2 (1, n=150) = 0.109, *p*=0.741
Robust (*n* = 86)	84 (56)	2 (1)	
Frail (*n* = 64)	63 (42)	1 (1)	
pCFS			χ^2 (1, n=150) = 0.679, *p*=0.410
Robust (*n* = 52)	84 (56)	1 (1)	
Frail (*n* = 65)	63 (42)	2 (1)	
mFI-11			χ^2 (1, n=150) = 0.081, *p*=0.776
Robust (*n* = 62)	61 (41)	1 (1)	
Frail (*n* = 88)	86 (57)	2 (1)	
FiND			χ^2 (1, n=150) = 0.703, *p*=0.402
Robust (*n* = 28)	28 (19)	0 (0)	
Frail (*n* = 122)	119 (79)	3 (2)	

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire

6.4.2.2 30-day home-time

Most patients did not have any hospital inpatient episodes in the 30-day follow-up period following study recruitment (*n* = 96, 64%). The median (interquartile range, IQR) and mean (±standard deviation, SD) were 30 (2.25) and 27 (±7.3) respectively, with a skewness of -2.6 (standard error 0.198), Figure 6.1

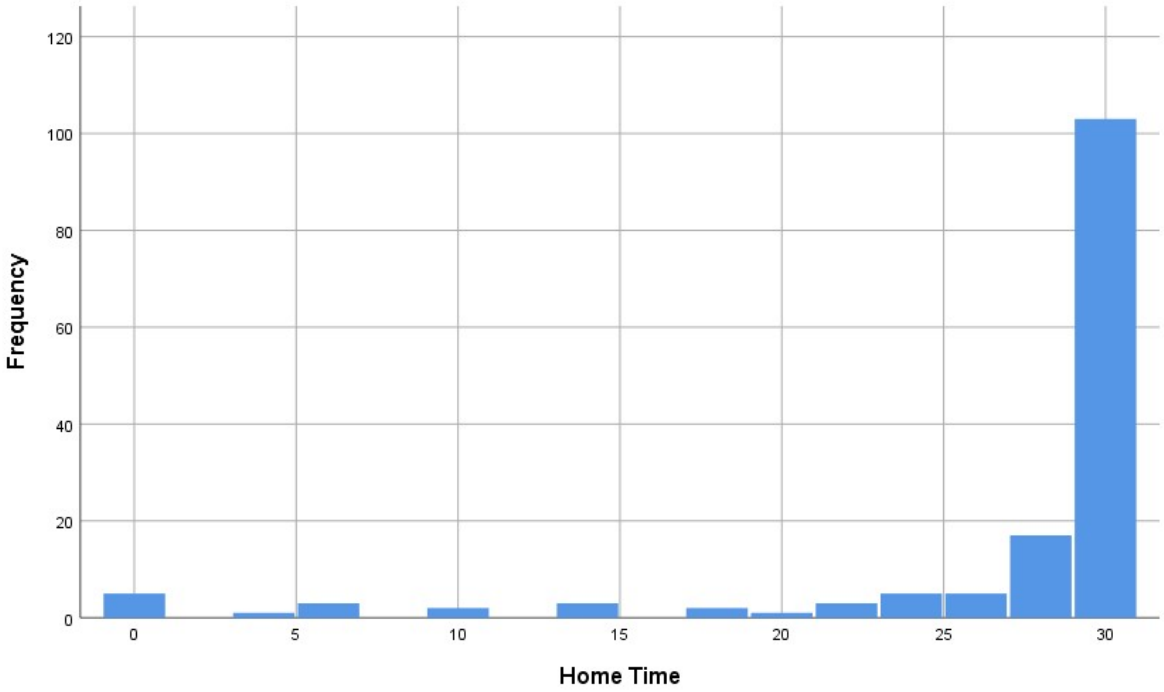


Figure 6.1 - Histogram of 30-day home time.

There was no significant difference in home-time between robust and frail groups as defined by any of the selected frailty assessment instruments, although home-time was consistently lower in the frail group, Table 6.2

Table 6.2 – Home-time according to frailty assessment instruments.

Frailty instrument	30-day home-time in days, median (IQR) / Mean (±SD)	Statistics
pCFS		Z = -0.267, *p*=0.789
Robust (*n* = 52)	30 (2.5) / 27 (±6.4)	
Frail (*n* = 65)	30 (3) / 26 (±8.4)	
ICE		Z = -0.742, *p*=0.458
Robust (*n* = 65)	30 (2) / 28 (±4.6)	
Frail (*n* = 85)	30 (3.5) / 25 (±8.8)	
cCFS		Z = -0.700, *p*=0.484
Robust (*n* = 76)	30 (2) / 28 (±5.0)	
Frail (*n* = 74)	30 (2.8) / 25 (±9.0)	
HIS FRAIL		Z = -0.697, *p*=0.486
Robust (*n* = 86)	30 (2) / 28 (±5.6)	
Frail (*n* = 64)	30 (3) / 25 (±9.1))	
mFI-11		Z = -1.088, *p*=0.277
Robust (*n* = 62)	30 (2) / 27 (±7.2)	
Frail (*n* = 88)	30 (3) / 26 (±7.5)	
FiND		Z = -1.028, *p*=0.304
Robust (*n* = 28)	30 (1.8) / 29 (±2.6)	
Frail (*n* = 122)	30 (3) / 26 (±8.0)	

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire

6.4.3 Operatively managed patients

6.4.3.1 Participant demographics

From 150 recruited patients, 54 (36%) proceeded to operative management of vascular pathology including both surgical and/or endovascular treatment. Baseline participant demographics for patients managed operatively compared to those managed non-operatively (this includes discharge from clinic), are summarised in Table 6.3.

There were no differences in age or sex between those who were managed operatively (mean age of 69 years and male preponderance, 69%) compared to non-operatively managed group. Most (*n* = 43, 80%) patients proceeding to operative management were diagnosed with CLTI. Statistically significant differences were observed in operatively managed patients being more likely to present with polypharmacy (mean medication number ± SD: 11 ± 5 vs. 9 ± 5, $p < 0.05$) and significant comorbidity as defined by CCI (mean CCI ± SD: 6 ± 2 vs. 5 ± 3, $p = 0.001$) compared to non-operatively managed patients.

A positive frailty score, as defined by mFI-11, was associated with a greater likelihood of proceeding to operative treatment (39 of 45, 72%, of operatively managed patients were frail vs. 51 of 96, 53%, of non-operatively managed patients were frail, $p < 0.05$). No other frailty assessment instrument demonstrated significant differences between the two groups.

Table 6.3 – Comparison of baseline demographics between operatively and non-operatively managed patients.

	Operatively managed *n* = 54 (%)	Non-operatively managed *n* = 96 (%)	Statistics
Male, *n* (%)	37 (69)	56 (58)	χ^2 (1, n=150) = 1.522, *p*=0.217
Mean age in years (±SD)	69 (±9)	67 (±13)	*t* (148) = -1.322, *p*=0.188
Scottish Index of Multiple Deprivation, mean (±SD)	4 (±3)	4 (±3)	Z = -0.707, *p*=0.479
Breakdown in SIMD groups, *n (%)*:			
1	12 (22)	24 (25)	
2	6 (11)	17 (18)	
3	5 (9)	9 (9)	
4	10 (19)	9 (9)	
5	4 (7)	4 (4)	
6	1 (2)	8 (8)	
7	1 (2)	7 (7)	
8	5 (9)	4 (4)	
9	3 (6)	8 (8)	
10	5 (9)	4 (4)	
Diagnosis, *n* (%)			Z = -4.649, *p*<0.001**
Critical Limb Threatening Ischaemia	44 (81)	47(49)	
Carotid stenotic disease	9 (17)	9 (9)	
Chronic venous insufficiency	-	12 (13)	
Abdominal aortic aneurysm	-	3 (3)	
Acute limb ischaemia (digital)	-	6 (6)	
Mesenteric angina	1 (2)	-	
Miscellaneous vascular	-	9 (9)	
Miscellaneous non-vascular	-	10 (10)	

Number of medications, mean (±SD)	11 (±5)	9 (±5)	*t* (148) = -2.513, *p*=0.014*
Premorbid Residency Status, *n* (%)			Z = -0.011, *p*=0.991
Independent	29 (54)	51 (53)	
Informal care (relatives/friends)	18 (33)	34 (35)	
Supported (homecare BD)	3 (6)	3 (3)	
Supported (homecare TDS)	-	2 (2)	
Supported (homecare QDS)	3 (6)	2 (2)	
Supported (unclear)	1 (2)	3 (3)	
Care home	-	1 (1)	
Previous Vascular Treatment, *n* (%)			Z = -0.219, p=0.827
None	37 (69)	68 (71)	
Treatment > 6 months ago	12 (22)	18 (19)	
Treatment < 6 months	5 (9)	10 (10)	
Charlson Comorbidity Index, mean (±SD)	6 (±2)	5 (±3)	*t* (148) = -3.414, *p*=0.001*
Breakdown in CCI groups, *n (%)*:			
0	-	5 (5)	
1	-	3 (3)	
2	1 (2)	12 (13)	
3	4 (7)	8 (8)	
4	6 (11)	16 (17)	
5	9 (17)	13 (14)	
6	15 (28)	15 (16)	
7	6 (11)	10 (10)	
8	4 (7)	6 (6)	
9	4 (7)	3 (3)	
10+	5 (9)	5 (5)	
Frailty positive status, *n (%)*			
cCFS	28 (52)	46 (48)	χ^2 (1, n=150) = 0.214, *p*=0.644

ICE	33 (61)	52 (54)	χ^2 (1, n=150) = 0.679, *p*=0.410
HIS FRAIL	27 (50)	37 (39)	χ^2 (1, n=150) = 1.855, *p*=0.173
pCFS	23 (43)	42 (44)	χ^2 (1, n=150) = 0.019, *p*=0.891
mFI-11	39 (72)	49 (51)	χ^2 (1, n=150) = 6.394, *p*=0.011*
FiND	48 (89)	74 (77)	χ^2 (1, n=150) = 3.173, *p*=0.075

AAA – Abdominal aortic aneurysm, BD – *bis in die*/twice daily, TDS – *ter die sumendum*/three times daily, QDS – *quarter die sumendum*/four times daily, cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. * $p < 0.05$.

6.4.3.2 Surgical details

Table 6.4 summarises operative demographics. Briefly, from 54 patients planned to proceed to operative management during hot clinic attendance, most (*n* = 53, 98%) were treated by inpatient admission. Two of these patients (3.7%) underwent outpatient angioplasty procedures prior to admission for hallux amputation as part of a planned staged procedure. Only one patient (1.9%) was managed entirely on an outpatient basis with angioplasty procedure. From 53 inpatient episodes, 43 (8.1%) were urgent scheduled, eight (15.1%) were emergent and two (3.8%) were scheduled admissions. The most commonly performed open surgical procedure was digital amputation (*n* = 11, 21%) followed by carotid endarterectomy (*n* = 9, 17%). The most commonly performed endovascular procedure was infrainguinal angioplasty ± stent (*n* = 15, 28%) followed by iliac procedures (*n* = 6, 11%).

Hybrid cases (combined surgical and endovascular approaches) are presented within 'open surgery' cases, Table 6.4. From ten hybrid cases three (30%) were common femoral artery endarterectomy (CFAE) with endovascular treatment of iliac segments alone, one (10%) underwent CFAE with combined iliac and infrainguinal endovascular treatment and one (10%) underwent CFAE with infrainguinal endovascular treatment. There were two (20%) infrainguinal bypass procedures with iliac endovascular treatment and two (20%) combined digital amputations with infrainguinal endovascular treatment. One case (10%) underwent open iliofemoral bypass procedure with on table angiogram of infrainguinal segment without demonstrable endovascular targets.

To examine if patients with CLTI represent a discrete patient population with separate outcomes when compared to all operatively managed patients, subgroup analysis for all outcomes described in section 6.4.4 was performed. As no significant differences were observed these results have not been presented in respective sections and are instead included in tabular form in appendix 9.

Table 6.4 - Baseline surgical demographics

	n, (%)
Outpatient treatment (*n* = 3)	
Infrainguinal angioplasty ± stent, *n* (%)	3 (100)
Days from clinic to treatment, median (range)	21 (7 – 83)
Inpatient treatment (*n* = 53)	
Admission type	
Urgent scheduled	43 (81)
Emergent	8 (16)
Scheduled	2 (4)
Inpatient treatment type	
Open surgery	27 (51)
Endovascular procedure	16 (30)
Hybrid	10 (19)
Days from clinic to inpatient treatment, median (interquartile range, IQR)	13 (32)
Open surgery	7 (21)
Endovascular procedure	30 (39)
Hybrid	39 (27)
Inpatient surgery type (including hybrid)	
Minor amputation (i.e., hallux, toe(s), fingers)	11 (21)
Carotid endarterectomy (CEA)	9 (17)
Infrainguinal bypass (±CFAE)	9 (17)
Common femoral artery endarterectomy (CFAE)	6 (11)
Iliofemoral bypass	1 (2)
Major limb amputation	1 (2)
Inpatient endovascular type (including hybrid)	
Infrainguinal angioplasty ± stent	15 (28)
Iliac angioplasty ± stent	6 (11)
Combined iliac and infrainguinal procedure	1 (2)
Coeliac artery stent	1 (2)
Upper limb angioplasty	1 (2)
Lower limb angiogram (no target)	2 (4)

6.4.3.3 Frailty in the context of operative management

The presence of frailty did not appear to prejudice operative approach as there was no statistically significant difference in the prevalence of frailty in patients managed by endovascular treatment alone compared to those who underwent open surgical treatment with or without hybrid approach, Table 6.5

Table 6.5 - The prevalence of frailty according to operative approach.

	Endovascular only (n = 17) n (%)	Open surgery ± endovascular (n =37) n (%)	Statistics
Frailty positive status by mode of assessment			
cCFS (*n*=28)	10 (59)	18 (49)	$\chi 2$ (1, n=54) = 0.483, *p*=0.487
ICE (*n*=33)	11 (65)	22 (60)	$\chi 2$ (1, n=54) = 0.135, *p*=0.713
HIS FRAIL (*n*=27)	10 (59)	17 (46)	$\chi 2$ (1, n=54) = 0.773, *p*=0.379
pCFS (*n*=23)	10 (59)	13 (35)	$\chi 2$ (1, n=54) = 2.673, *p*=0.102
mFI-11 (*n*=39)	12 (71)	27 (73)	$\chi 2$ (1, n=54) = 0.033, *p*=0.856
FiND (*n*=48)	15 (88)	33 (89)	$\chi 2$ (1, n=54) = 0.011, *p*=0.917

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

6.4.4 Operatively managed patients: short-term outcomes

6.4.4.1 Post-operative 30-day mortality

As mentioned in section '6.4.2.1 30-day mortality', from 54 patients there were two (3.7%) deaths within 30-days of index procedure. Care must be taken in interpreting data with a small number of outcome events. Although there is an apparent trend with frailty being associated with a higher risk of 30-day mortality, there was no significant difference between frailty status and mortality risk according to the different modes of frailty assessment, Table 6.6

Table 6.6 - Post-operative day 30 mortality rate.

Frailty instrument (*n*=frailty positive)	Frail + mortality, n (%)	Robust + mortality, n (%)	Statistics
cCFS (*n*=28)	2 (7)	0	$\chi 2$ (1, n=54) = 1.929, *p*=0.165
ICE (*n*=33)	2 (6)	0	$\chi 2$ (1, n=54) = 1.322, *p*=0.250
HIS FRAIL (*n*=27)	1 (4)	1 (4)	$\chi 2$ (1, n=54) = 0.000, *p*=1.000
pCFS (*n*=23)	2 (9)	0	$\chi 2$ (1, n=54) = 2.799, *p*=0.094
mFI-11 (*n*=39)	2 (5)	0	$\chi 2$ (1, n=54) = 0.799, *p*=0.371
FiND (*n*=48)	2 (4)	0	$\chi 2$ (1, n=54) = 0.260, *p*=0.610

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

6.4.4.2 Post-operative 30-day morbidity

From 54 patients managed operatively, 23 (43%) suffered 30-day morbidity. According to the Clavien-Dindo (CD) classification[273], most complications were grade 1 (*n* = 11, 48%). This means 12 (22%) patients suffered treatment-altering post-operative morbidity, with two (9%) grade 3a and eight (35%) grade 3B complications, Table 6.7. No patient required unplanned admission to high dependency or intensive care units perioperatively.

Table 6.7 – Clavien-Dindo grading of postoperative morbidity.

Clavien-Dindo Grade	Total, *n*=23 (%)
I	11 (48)
II	0
IIIa	2 (9)
IIIb	8 (35)
IV	0
V	2 (9)

Summary of postoperative morbidity according to Clavien-Dindo grading system. Definitions of each grading severity are previously summarised in **Table 4.2 - Summary of Clavien-Dindo grading of post-operative morbidity.**

Frailty was not associated with increased risk of postoperative morbidity, Table 6.8, however, there were trends. With the exception of the mFI-11 instrument, a diagnosis of frailty was associated with an increasing risk of 30-day morbidity. Frail patients were between 1.1 to 4.2 times more likely to suffer perioperative morbidity, however this did not reach statistical significance. Adjusting for age and sex saw patients diagnosed as frail according to CFS self-assessment (pCFS) 1.6 times more likely to suffer perioperative morbidity than robust counterparts, tending toward significance, p = 0.061, Table 6.9.

The frailty instruments demonstrated poor ability to discriminate those likely to suffer postoperative morbidity from those who did not, as demonstrated by an AUC for all instruments between 0.439 – 0.600, $p > 0.05$, Figure 6.2.

Table 6.8 - Risk of 30-day post-operative morbidity according to frailty assessment

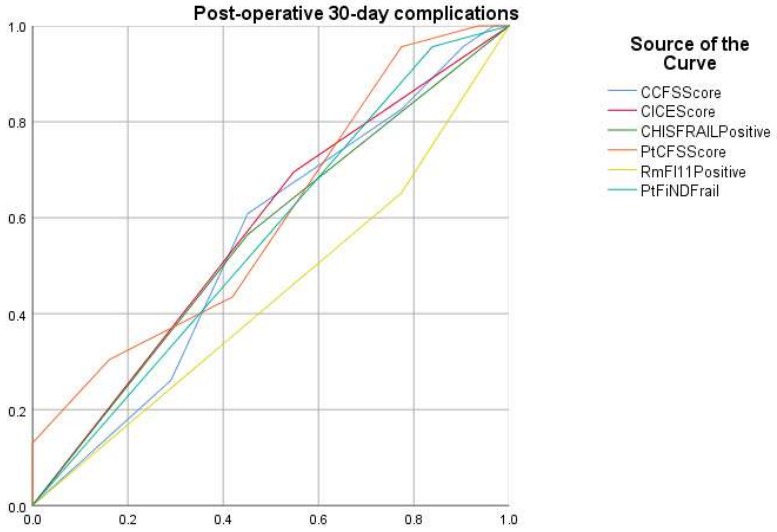
Frailty instrument (*n*=frailty positive)	Frail + morbidity, n (%)	Robust + morbidity, n (%)	Statistics
cCFS (*n*=28)	14 (50)	9 (35)	$\chi 2$ (1, n=54) = 1.305, *p*=0.253
ICE (*n*=33)	16 (48)	7 (33)	$\chi 2$ (1, n=54) = 1.205, *p*=0.272
HIS FRAIL (*n*=27)	13 (48)	10 (37)	$\chi 2$ (1, n=54) = 0.682, *p*=0.409
pCFS (*n*=23)	10 (43)	13 (42)	$\chi 2$ (1, n=54) = 0.013, *p*=0.910
mFI-11 (*n*=39)	15 (38)	8 (53)	$\chi 2$ (1, n=54) = 0.980, *p*=0.322
FiND (*n*=48)	22 (46)	1 (17)	$\chi 2$ (1, n=54) = 1.856, *p*=0.173

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

Table 6.9 - Risk of 30-day post-operative morbidity according to frailty assessment (Odds ratio).

	Unadjusted				Adjusted			
		95% confidence interval				95% confidence interval		
	Odds ratio (OR)	Lower	Upper	*p* Value	Odds ratio (OR)	Lower	Upper	*p* Value
cCFS	1.14	0.772	1.679	0.512	1.12	0.801	1.794	0.378
ICE	1.88	0.605	5.859	0.275	2.70	0.764	9.526	0.123
HIS FRAIL	1.58	0.533	4.678	0.410	1.82	0.587	5666	0.299
pCFS	1.51	0.928	2.444	0.098	1.61	0.978	2.654	0.061
mFI-11	0.55	0.164	1.820	0.325	0.56	0.164	1.916	0.356
FiND	4.23	0.459	38.987	0.203	5.08	0.512	50.457	0.165

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. The data has been adjusted for patient age and sex.



	AUC	Std. Error	p value	95% Confidence Interval Lower Bound	Upper Bound
cCFS	.550	.079	.535	.395	.705
ICE	.574	.079	.358	.419	.728
HIS FRAIL	.557	.080	.479	.401	.713
pCFS	.600	.078	.214	.447	.753
mFI-11	.439	.080	.447	.282	.596
FiND Frail	.559	.079	.463	.405	.713

Test run under the nonparametric assumption, comparing the discriminative capacity of frailty assessment instruments. cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

Figure 6.2 - Frailty assessment instruments ability to discriminate post-operative 30-day morbidity.

6.4.4.3 Post-operative length of hospital admission

From 53 operatively managed patients admitted to hospital for treatment, the overall median (IQR) and mean (±SD) length of hospital admission were 3.0 (8) and 11.6 (±23.4) days respectively, with a skewness of 3.7 (standard error 0.327), Figure 6.3.

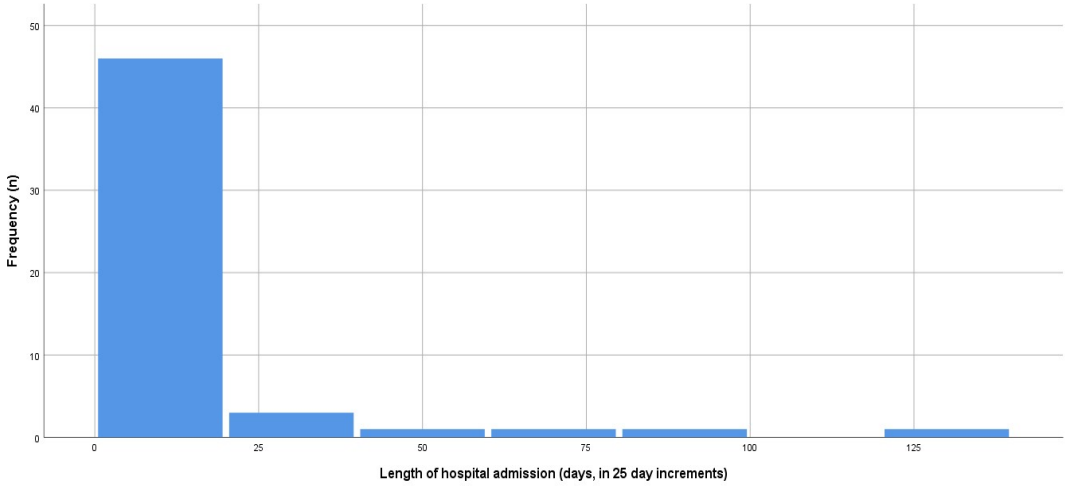


Figure 6.3 - Length of hospital admission for operatively managed patients.

The median and mean length of hospital admission tended to be longer for frail patients than robust patients, Table 6.10. However, this only reached significance when defining frailty by the clinician ICE assessment with median (IQR) length of hospital admissions of 5 (17) days for frail patients compared to 2 (3) for robust, $p < 0.05$.

Table 6.10 - Postoperative length of hospital admission according to frailty assessment.

Frailty instrument	Length of hospital admission in days, median(IQR) / mean (±SD)	Statistics
cCFS		Z = -1.478, *p*=0.140
Robust (*n* = 25)	3 (2.5) / 8 (±26.1)	
Frail (*n* = 28)	6 (17) / 15 (±20.8)	
ICE		Z = -2.097, *p*=0.036*
Robust (*n* = 21)	2 (3) / 3 (±2.7)	
Frail (*n* = 32)	5 (17) / 17 (±28.9)	
HIS FRAIL		Z = -1.889, *p*=0.059
Robust (*n* = 26)	2 (4.5) / 4 (±4.9)	
Frail (*n* = 27)	4 (18) / 19 (±31.2)	
pCFS		Z = -1.880, *p*=0.060
Robust (*n* = 31)	2 (5) / 10 (±25.3)	
Frail (*n* = 22)	5 (17) / 14 (±20.8)	
mFI-11		Z = -0.709, *p*=0.478
Robust (*n* = 15)	6 (11) / 10 (±14.7)	
Frail (*n* = 38)	3 (6) / 12 (±26.2)	
FiND		Z = -0.639, *p*=0.523
Robust (*n* = 6)	2 (13.5) / 7 (±10.7)	
Frail (*n* = 47)	3 (7) / 12 (±24.6)	

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. * $p<0.05$.

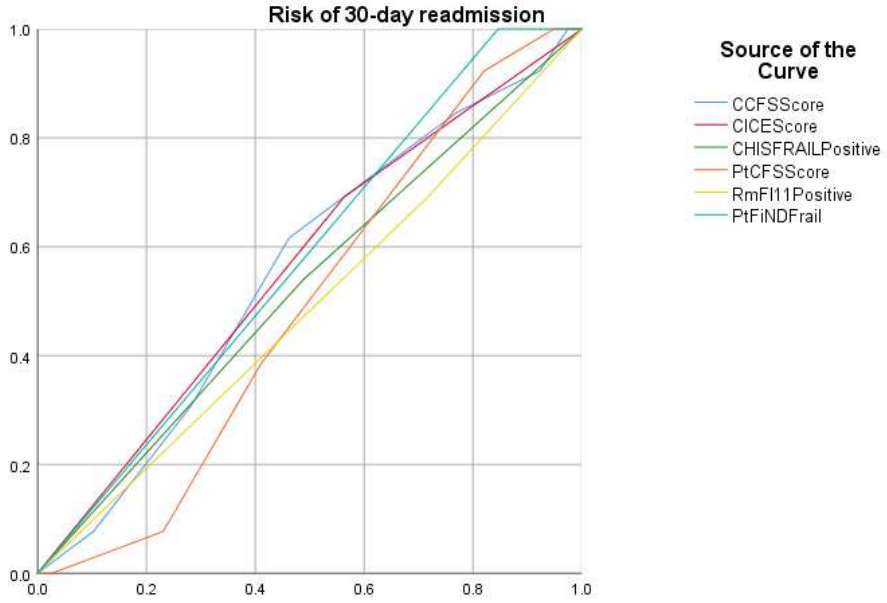
6.4.4.4 Post-operative readmission rates

Excluding two 30-day post-operative mortalities from 52 operatively managed patients, a total of 13 patients were readmitted within 30-days of index procedure. Ten (77%) were re-admitted to vascular surgery, two (15%) two general surgery and one (7%) to renal medicine. Frailty was not associated with increased risk of readmission post discharge, Table 6.11. Further, the frailty instruments demonstrated poor ability to discriminate those likely to be readmitted to hospital postoperatively, as demonstrated by an AUC for all instruments between 0.492 – 0.577 ($p > 0.05$), Figure 6.4.

Table 6.11 - Risk of postoperative readmission according to frailty status.

Frailty instrument (*n*=frailty positive)	Frail+ readmission n (%)	Robust + readmission n (%)	Statistics
cCFS (*n*=26)	8 (31)	5 (19)	$\chi 2$ (1, n=52) = 0.923, *p*=0.3376
ICE (*n*=31)	9 (29)	4 (19)	$\chi 2$ (1, n=52) = 0.666, *p*=0.415
HIS FRAIL (*n*=26)	7 (27)	6 (23)	$\chi 2$ (1, n=52) = 0.103, *p*=0.749
pCFS (*n*=21)	5 (24)	8 (26)	$\chi 2$ (1, n=52) = 0.027, *p*=0.870
mFI-11 (*n*=37)	9 (24)	4 (27)	$\chi 2$ (1, n=52) = 0.031, *p*=0.860
FiND (*n*=46)	13 (28)	0	$\chi 2$ (1, n=52) = 2.261, *p*=0.133

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.



	AUC	Std. Error[a]	p Value	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
cCFS	.557	.090	.540	.381	.733
ICE	.564	.091	.492	.386	.743
HIS FRAIL	.526	.093	.784	.343	.708
pCFS	.492	.084	.933	.328	.656
mFI-11	.487	.094	.891	.303	.671
FiNDl	.577	.086	.410	.408	.745

Test run under the nonparametric assumption, comparing the discriminative capacity of frailty instruments in predicting post-operative readmission. cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

Figure 6.4 - Frailty assessment instruments ability to discriminate post-operative 30-day readmission.

A diagnosis of frailty by any frailty assessment instrument was not significantly associated with an increase in the risk of post-operative readmission and this remained true when adjusting for age and sex, Table 6.12. However, patients who suffered perioperative morbidity were more likely to be readmitted than those who did not (OR 8.485, 95% CI: 1.957-36.779, p = 0.004.). Secondary analysis, adjusting for perioperative morbidity, was not associated with frailty diagnoses predicting risk of readmission, Table 6.13.

Table 6.12 - Risk of 30-day readmission according to frailty assessment.

	Unadjusted				Adjusted			
		95% confidence interval				95% confidence interval		
	Odds ratio (OR)	Lower	Upper	p Value	Odds ratio (OR)	Lower	Upper	p Value
cCFS	0.98	0.563	1.706	0.944	0.97	0.554	1.691	0.910
ICE	1.74	0.457	6.621	0.417	2.38	0.548	10.329	0.247
HIS FRAIL	1.23	0.349	4.322	0.749	1.53	0.406	5.761	0.530
pCFS	0.98	0.563	1.706	0.944	0.97	0.554	1.691	0.910
mFI-11	0.88	0.225	3.474	0.860	0.99	0.237	4.141	0.990
FiND	636399381	0.000	-	0.999	585659883.3	0.000	-	0.999

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. The data has been adjusted for patient age and sex.

Table 6.13 - Risk of 30-day readmission according to frailty assessment adjusted for perioperative morbidity.

	Adjusted for perioperative morbidity			
		95% confidence interval		
	Odds ratio (OR)	Lower	Upper	p Value
cCFS	1.10	0.661	1.824	0.718
ICE	1.46	0.336	6.360	0.612
HIS FRAIL	0.97	0.237	3.925	0.961
pCFS	0.81	0.423	1.541	0.516
mFI-11	1.34	0.289	6.196	0.710
FiND	402029414.0	0.000	-	0.999

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. The data has been adjusted for patient age and sex.

6.4.4.5 Post-operative non-home discharge

From 53 patients admitted for operative treatment, one (2%) patient experienced a nonhome discharge. This patient was admitted with a diagnosis of CLTI for primary major limb amputation. The patient developed a wound infection (CD grade 1) and had a prolonged admission due to rehabilitative requirements and delays in social care due to the need for rehousing to accommodate wheelchair access. Frailty assessment was not predictive of nonhome discharge, although care must be taken in interpretation of data in the context of low number of outcome events, Table 6.14.

Table 6.14 - Post-operative non-home discharge.

Frailty instrument (*n*=frailty positive)	Frail + non-home discharge n (%)	Robust + non-home discharge n (%)	Statistics
cCFS (*n*=28)	0	1 (4)	$\chi 2$ (1, n=53) = 1.142, *p*=0.285
ICE (*n*=32)	1 (3)	0	$\chi 2$ (1, n=53) = 0.669, *p*=0.413
HIS FRAIL (*n*=27)	1 (4)	0	$\chi 2$ (1, n=53) = 0.981, *p*=0.322
pCFS (*n*=22)	0	1 (3)	$\chi 2$ (1, n=53) = 0.723, *p*=0.395
mFI-11 (*n*=38)	1 (3)	0	$\chi 2$ (1, n=53) = 0.402, *p*=0.526
FiND (*n*=47)	1 (2)	0	$\chi 2$ (1, n=53) = 0.130, *p*=0.718

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

6.4.4.6 Post-operative discharge with greater social care requirements

From 53 patients admitted for operative management, two (4%) were discharged with greater care requirements. Frailty assessment was not predictive of discharge with greater social care requirements, although care must be taken in interpretation of data in the context of low number of outcome events, Table 6.15.

Table 6.15 - Operatively managed patients discharged with greater social care requirements.

Frailty instrument (*n*=frailty positive)	Frail + increased social care requirement, n (%)	Robust + increased social care requirement, n (%)	Statistics
cCFS (*n*=28)	1 (4)	1 (4)	$\chi 2$ (1, n=53) = 0.007, *p*=0.935
ICE (*n*=32)	2 (6)	0	$\chi 2$ (1, n=53) = 1.364, *p*=0.243
HIS FRAIL (*n*=27)	1 (4)	1 (4)	$\chi 2$ (1, n=53) = 0.001, *p*=0.978
pCFS (*n*=22)	0	2 (6)	$\chi 2$ (1, n=53) = 1.475, *p*=0.225
mFI-11 (*n*=38)	1 (3)	1 (7)	$\chi 2$ (1, n=53) = 0.482, *p*=0.487
FiND (*n*=47)	2 (4)	0	$\chi 2$ (1, n=53) = 0.265, *p*=0.606

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire.

6.5 Discussion

6.5.1 Summary of pertinent results

The results presented in this study intended to speak to research question 2c (how do the prognostic properties of frailty assessment compare in prospective frailty assessment), exploring the clinical utility of various frailty assessments in predicting short-term outcomes in an urgent-referral outpatient vascular ('hot') clinic setting.

For all frailty assessment instruments applied in this study, short-term mortality and home-time for all patients recruited to this study did not differ significantly between frail and robust patients. Similarly, in operatively managed patients, there was a general trend toward increased risk of morbidity, longer length of hospital stay and a greater readmission risk for frail patients, although this failed to reach statistical significance. There was no observed correlation between frailty status and risk of perioperative mortality, non-home discharge or discharge with greater care requirements. However, the prognostic validity of the selected frailty assessment tools observed in this study are limited by a small sample size and relatively small number of outcome events. Post hoc sample size calculation was performed to confirm underpowered sample size. According to the 2024 National Vascular Registry patients undergoing lower limb revascularisation had a 30-day mortality of 2.1%.[1] As discussed in Chapter 2, frail patients when compared to robust patients have upwards of up to 4.8 times greater chance of 30-day mortality. To detect this difference with 80% confidence, no attrition and $p < 0.05$ would dictate a sample size of 322 operatively managed patients; 161 per group (frail and robust).

The primary pathology presenting to the Vascular 'hot' clinic is CLTI, reflecting the clinic's purpose: enabling senior clinical review of urgent, but not emergent, vascular pathology for expedited investigation and management.[4] The

observation that frailty does not influence management plan or mode of treatment, despite the availability of minimally invasive treatment which proposes less morbidity[63], might imply clinical management plans prioritise pathophysiological and anatomical considerations over host factors. This differs to similar units which have demonstrated differences in approach to management of their frail patients, where frail patients are more likely to be managed conservatively despite presenting with a greater degree of limb threat.[307] There are key considerations around these differences in local practices. Firstly, the primary aim in treating critically ischaemic limbs is to preserve limb function.[308] However, a proposed role for aggressive revascularisation exists (and is briefly explored on in Chapter 7), where what may be considered aggressive treatment is done with the aim of preserving quality of life. Provided the morbidity of the required procedure is considered appropriate.

Secondly, typically arterial imaging identifies surgical targets and will propose preferential mode of treatment with the key consideration being to restore in-line flow, where possible. This will be guided by the availability of surgical and endovascular techniques. However, surgical technique is not all-or-nothing, in addition to the differing modes of treatment, surgeons can also tailor the burden of the proposed treatment by altering the extent to which surgical targets are treated. Where a robust patient may be reasonably expected to withstand multi-level revascularisation, a vulnerable patient with similar disease pattern may sooner benefit from targeted treatment of selected lesions, which may be adequate to achieve clinical improvement without subjecting patients to the morbidity of more extensive treatment.

These considerations may account for the pattern of treatment observed in this study and reflect nuanced surgical decision-making, which will be challenging to capture in prospective studies. However, as part of aiming to clarify these considerations, a recommendation is made for future relevant studies to consider

stratifying patients with CLTI according to recognised classification systems, such as Rutherford[309], Fontaine[310] or the Wound Ischaemia Foot Infection score.[311] An additional possible benefit to stratifying CLTI by disease severity is clarifying the discrepancy between the number of days from clinic to receiving operative treatment, with patients undergoing endovascular treatment (in isolation or as hybrid case) waiting significantly longer than those proceeding to open surgical repair. At present, it is unclear if this apparent discrepancy is driven by these patients presenting with less advanced disease, or perhaps more likely, the practical challenges associated with organising multi-disciplinary care combined with how the availability of endovascular versus surgical skillsets may influence management plans.

Similar to the data presented in Chapter 5, the data from mFI-11 assessments demonstrated discrepancies from other modes of frailty assessment. A frailty positive state as defined by mFI-11, was associated with a greater likelihood of operative treatment where remaining frailty assessment tools were not. This may suggest that it is not an accurate measure of frailty as surgeons are unlikely to preferentially operate on a frail group. Further, mFI-11 frailty positive patients were also less likely to experience morbidity and had shorter admissions, albeit this failed to reach statistical significance. This discrepancy between mFI-11 and the other frailty tools supports the theory that mFI-11 in fact measures comorbidity, rather than frailty, albeit the two are not independent constructs, as discussed in Chapter 5. Further adequately powered studies are required to confirm this.

6.5.2 Comparisons with published literature

The non-significant trend for increased 30-day post-operative mortality in patients living with frailty observed in this study mirrors current literature. A meta-analysis examining mortality outcomes in patients operatively treated for peripheral arterial disease found frailty was associated with a non-significant 2.11-fold greater risk of 30-day mortality compared to robust patients and significant association with a 1.86-fold increased risk of long-term mortality, ($p < 0.05$).[312] The study reported a major limitation in the published literature of heterogeneity in mode of frailty assessment. This is reflected in the challenges in frailty assessment that have been previously discussed in Chapter 3. Further, the work presented in Chapter 3 identifies only one prospective study comparing the prognostic value of different frailty assessment tools in CLTI patients undergoing operative treatment. The instruments included in that study were Edmonton Frail Scale (EFS), Groningen Frailty Indicator (GFI), modified Essential Frailty Toolset (mEFT), 11-item modified Frailty Index (mFI-11), Multidimensional Prognostic Index (MPI) and the Risk Analysis Index-C (RAI-C). A similarly low 30-day mortality rate (1%) was observed. The primary end point of this study was mortality at 1-year which was predicted by the GFI and mEFT instrument.[124] FAVOUR complements the data from this study, as it will enable comparison of frailty tools in different patient cohorts, over differing time scales, as well as introducing additional frailty tools to compare prognostic utility.

Patients reviewed in vascular 'hot' clinic can be considered 'high risk' and pose a public health dilemma, the reasons being two-fold: firstly, the prevalence of frailty is high (as demonstrated in Chapter 5), and secondly, the primary presenting pathology is CLTI. Although not definitively demonstrated in this study, frailty in undifferentiated hospitalised older adults, and vascular surgery populations specifically, confers a greater risk of mortality (in-hospital, medium- and long-term), post-operative morbidity, longer length of hospital stay as well as functional decline at discharge.[60, 61, 63, 313] CLTI is an aggressive disease with a 1-year mortality rate between 20 – 25%.[314, 315] American population statistics have demonstrated CLTI has a worse survival rate than the majority of common

terminal malignancies.[316] In addition to substantial morbidity, CLTI is common and growing in prevalence due to population demographic changes of increasing age and rising incidence of diabetes mellitus.[317] CLTI already has a greater global prevalence than cerebrovascular disease, heart failure and cancer.[318] Considering the growing prevalence and morbidity of this disease, CLTI can be considered an underappreciated public health threat, with increasing health and healthcare cost implications.[319] The 30-day follow-up in FAVOUR may be an inadequate timeframe to capture the sequelae of the disease and its intervention, emphasising the clinical relevance of the planned 1-year follow-up. Improving health care outcomes and mitigating the financial burden through deliberate and proactive secondary care service restructuring for this population must be declared a priority.

6.5.3 Strengths and limitations

Strengths and limitations of the FAVOUR study have been discussed in Chapter 5, section 5.5.3. The role of comparing unadjusted and adjusted data for 30-day outcomes is considered. Comparing unadjusted analysis will be clinically relevant for clinicians in considering the role of applying frailty assessment to all-comers in clinical practice, informing discussions around predicted outcomes if offered operative or conservative management. Specific to the results presented in this chapter, for 30-day outcomes this study is underpowered to support a meaningful comparative analysis of the tools. Adjusted analysis is of research interest, exploring the role of frailty independent from concomitant factors, such as age, sex and multimorbidity. However, the small number of outcome events limits the number of variables that can reasonably be adjusted for in this data. The planned longer follow-up should allow for more events to accrue which could improve power. It is reiterated a power calculation for sample size was not performed for this study due to the ability to recruit patients being an important feasibility metric.

6.5.4 Future directions

No patients diagnosed as robust according to FiND required readmission to hospital but this was not replicated by any other frailty assessment instrument. FiND was also associated with a greater risk of morbidity compared to other frailty assessment instruments (albeit not significant in this small study). Of the tools assessed in this study, FiND is the only tool that is derived from the frailty phenotype theory. It is unclear to what extent FiND diagnoses frailty or disability (or both). This is exemplified in the observed high sensitivity but poor specificity for diagnosing frailty, as discussed in Chapter 5. There is a risk that, as most operatively managed patients were diagnosed with CLTI, which inherently impairs mobility, phenotypic measures of frailty are confounded by disability resulting in bias in assessment. For this reason, a role for comparing the prognostic value of different phenotypic measurements of frailty, such as gait speed, timed-up-and-go or grip strength is proposed. This might help elucidate whether phenotypic measures of frailty, in a vascular population known for presenting with mobility-limiting pathology, is a bias in assessment or in fact a true estimation of frailty prevalence and severity, as discussed in Chapter 3. A significant proportion of patients presenting to the vascular hot clinic are diagnosed with clinically urgent CLTI warranting operative management. While the presence of frailty, as defined by five different assessment instruments, did not appear to influence decision to offer operative treatment, nor guide operative strategy, this may reflect unmeasured nuanced surgical decision making. A role for exploring how frailty influences surgical decision-making, in particular the extent of operative management, is identified. This is explored in the upcoming Chapter 7.

6.5.5 Conclusion

Frailty, when assessed by ICE, CFS and HIS FRAIL is associated with a greater risk of morbidity, length of stay and risk of morbidity, although a moderate participant size means the results did not reach significance, likely due to being under powered. The 1-year follow-up results will be helpful in defining, and comparing, a proposed prognostic role for frailty assessment for patients reviewed in a vascular hot clinic. Further, discrepancies in outcomes between phenotypic measures of frailty (FiND) and remaining tools identifies a challenge in differentiating frailty from disability in the context of mobility-limiting pathology.

Chapter 7 Assessing stakeholder's perception and utilisation of frailty assessment in a Vascular Surgery setting – A mixed methods study.

7.1 Chapter summary

This chapter sets out to answer research question 3 (what are stakeholder's perception and utilisation of frailty assessments in a vascular surgery setting). A mixed-methods study explores vascular surgery stakeholders' perception and utilisation of frailty assessment techniques in clinical practice. The work presented in this chapter will inform clinicians and policy makers in their efforts to modify service-wide approaches to frailty with the view to improving health outcomes for this vulnerable cohort.

7.2 Introduction

The adoption of realistic medicine as a Scottish health police agenda encourages clinicians to consider personalised approaches to care, manage risks better and reduce patient harm.[320] It also aims to empower patients to discuss their treatment with clinicians as part of holistic patient-centred care, prioritising patient wishes and quality of life considerations. The heterogeneity of the frailty assessment may challenge health care professionals ability to comfortably deliver realistic medicine in the midst of such a multifactorial and far-reaching construct.

The burden frailty places on healthcare infrastructure has been explored in earlier chapters presenting the adverse health outcomes associated alongside its financial implications. Despite growing academic interest and national guidance, it has been demonstrated that frailty is inconsistently assessed and considered in clinical practice by vascular surgeons in the United Kingdom.[261] Relatively little is known about stakeholders' perceptions of frailty assessment, how they use frailty tools in decision making, and how services incorporate frailty assessment.[87, 261, 321, 322]

This study aims to speak to this evidence gap as improved understanding is critical to develop approaches to encourage the up-take and roll-out of collaborative frailty-centric pathways in busy clinical services in line with national guidance.

7.2.1 Aims and objectives

The purpose of this study is to explore healthcare professionals' (HCPs) familiarity with, and understanding of, the frailty concept and frailty identification tools within vascular surgery and identify barriers to implementing frailty screening into clinical practice.

7.3 Methods

7.3.1 Study design

This is a mixed-methods study based on a phenomenological approach. Data were gathered using both questionnaires and semi-structured interviews/focus-groups. Questionnaires were selected to gather data from a large number of participants whereas the use of follow-up semi-structured focus groups and interviews acted as a complement to the questionnaires. This allowed for a more nuanced understanding of complex issues and enabled the exploration of these from all angles thus providing e a complete and well-rounded summary of stakeholders perceptions. For the questionnaires, this study was conducted and reported in line with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES), appendix 11.[323] The conduct and reporting of interviews and focus-groups follows the Consolidated criteria for Reporting Qualitative studies (COREQ) guidelines, appendix 12.[324]

7.3.2 Research team and reflexivity

I conducted the interview/focus-groups. Through previous clinical experience and attendance at relevant scientific events, I have professional relationships with some participants. Prior to participation, participants were informed of the research goals which were that this study was conducted as part of a clinical research fellowship exploring frailty in vascular disease, with the view to obtaining an MD.

The second author assisting in thematic analysis is female with a background in academic medicine (Geriatric speciality trainee) with a specialist interest in organisation of care services and pathways and published experience in qualitative research methods. Involving a second author with no surgical background was felt

useful to ensure rigour and reduce risk of unintentional bias in data analysis processes.

7.3.3 Participant selection

Any health care worker in Scotland with professional experience (current or previous) of working in a vascular surgery service was eligible to participate. Questionnaires were distributed by email. Initial purposive sampling was complemented by a snowball approach. The email list was created through contacting the clinical lead for all vascular surgery services across Scottish regional health boards. The clinical lead was invited to provide a list of clinicians and allied healthcare workers representative of all stakeholders in their regional service, including vascular nurse specialists, clinical scientists, interventional radiologists, staff nurses, consultant anaesthetists and British Association of Chartered Physiotherapists in Limb Absence Rehabilitation (BACPAR)-registered physiotherapists. The Scottish training programme director for vascular surgery trainees was also contacted to provide an email list for trainees. Non-rotational allied healthcare professionals working in vascular services, such as physiotherapists, occupational therapists and podiatrists were eligible for participation and their recruitment was permitted through snowballing.

Participants were invited to in-depth interview/focus group sessions through an optional question in the questionnaire. This was done by inviting participants to leave contact details in order for the sessions to be arranged. This could be email or telephone numbers. Where participants declined follow-up interviews, the relevant part of the questionnaire was left blank. To encourage interview/focus group recruitment, attendees were allowed to invite colleagues who expressed an interest in participating, irrespective of questionnaire completion.

7.3.4 Sample size

No sample size calculation was performed for questionnaire recruitment. Rather, questionnaires were distributed with long response deadlines to encourage uptake. Focus group/interview sample size was determined by reaching data saturation, defined as the point in which additional data did not produce new themes.[325]

7.3.5 Setting

The first questionnaire was distributed by email in November 2022 with a response deadline of April 2023. This allowed for paper versions of the questionnaire to be distributed at the Scottish Vascular Meeting 2023. This is a multidisciplinary meeting for all health care workers involved in the delivery of vascular services across Scotland.

Interviews and focus groups were primarily conducted virtually (Microsoft Teams, Version 1.0) but some in-person sessions were offered depending on participant preference. Focus groups were designed to host no more than six participants as this was felt to represent a group size that enables contribution by each attendee gaining a variety of perspectives, whilst being small enough to avoid disorderly or fragmented discussions.[326] Participants of similar professional backgrounds were grouped to reduce any perceived hierarchical structure to the meeting and encourage participation. Interviews and focus groups were conducted between September 2023 – January 2024.

7.3.6 Ethical considerations

Questionnaire participation was voluntary, and consent was implied through the completion and return of questionnaire. Those expressing interest in participating

in interviews were contacted electronically with participant information sheets and consent forms which were sought, including for audiovisual recording, prior to agreeing an interview date. Research data storage is compliant with the University of Glasgow's data retention policy. The study was given favourable ethical opinion from the University of Glasgow, College of Medical, Veterinary & Life Sciences Ethical Committee, Project No: 200220006, 16th September 2022.

7.3.7 Data collection

7.3.7.1 Questionnaire administration

The 18-item questionnaire was developed in conjunction with a consultant geriatrician and piloted on two vascular consultants. It consisted of four parts (participant demographics, perception of frailty significance, frailty assessment methods and implementing frailty assessment into clinical practice), appendix 11. Responses were provided through a combination of tick-box answers, Likert scales and free text options. The document was locked so that the participants could only interact/amend the response fields to the document. Demographic data answers were categorical to promote anonymisation in data analysis. The responses were open for amendment should participants want to alter their answers during completion. Completion of the questionnaire was voluntary, and no incentives were offered. Questionnaires were returned to myself as lead researcher by email or in-person at the vascular meeting. Hard copies of questionnaires were scanned to create electronic copies for storage before original versions were securely destroyed. Completed questionnaires were electronically stored by participant initials, preventing multiple entries from the same participant, and enabling linkage of data with follow-up interviews. Upon completion of interviews, responses (and paired interview data, where relevant) were transformed to anonymous participant numbers prior to data analysis.

7.3.7.2 Interviews/focus groups

A semi-structured interview guide was developed and piloted on a consultant geriatrician, appendix 12. In brief, the topics set out to be covered included: exploring participant understanding of the frailty concept, how it might influence clinical practice, methods for assessing and justification for described mode of assessment as well as exploring the perceived role for treating frailty and how best this can be achieved. Interviews were planned to take approximately 30 - 45 minutes. Participant demographics were taken from previously completed questionnaire and confirmed in the interview. Virtual interviews were subject to automated transcribing with paired video recording, where consented, to enable quality control of the transcriptions. In-person interviews were conducted in a venue of the participant's choice and used audio recording and researcher field notes. I performed all aspects of quality control of automated transcription processes as well as creating verbatim transcriptions of audio recordings from in-person sessions. Transcription processes were conducted, stored and analysed on Microsoft Word, Version 2310. Participants were not invited to comment on final transcriptions.

7.3.8 Analysis

I manually transcribed all data from questionnaires into a data extraction template using Microsoft Excel, Version 2310. Analysis was preformed using IBM SPSS Statistics, Version 25.Questionnaires with incomplete responses had areas of missing data coded so that the questionnaire could be included in analysis, excluding only missing data points. Demographic and categorical data were analysed descriptively, and comparisons of categorical data were performed by Chi Square analysis with a p value < 0.05 considered statistically significant. Data visualisations were created using both Microsoft Excel, Version 2310 and IBM SPSS Statistics, Version 25. Free text answers were combined with the interview transcripts and assessed in aggregate.

Data analysis for interviews and focus groups followed Braun and Clarke's' six phases of thematic analysis, deducing themes from the data.[327]. This was performed manually using the transcripts stored in Microsoft Word, Version 2310. Transcripts were critically appraised by aforementioned authors working independently to code quotes. Quotes were then reviewed and collated into specific themes and subthemes. Identified themes were not returned to participants for comment. Anonymised exemplar quotes representing these themes are presented in the results section of this chapter. Where relevant, themes and subthemes were collated to produce visual summaries and acronyms with Microsoft Word, Version 2310.

7.4 Results

7.4.1 Questionnaire results

A total of 160 HCPs were contacted by email with 60 (38% response rate) returned questionnaires. Responses were elicited from ten of fourteen Scottish regional NHS health boards, including all six health boards that provide a vascular surgery 'hub' service, Figure 7.1. There was excellent compliance with 1181 (99.4%) responses to a total of 1188 questions. Six of seven blank responses were for free-text answer questions.

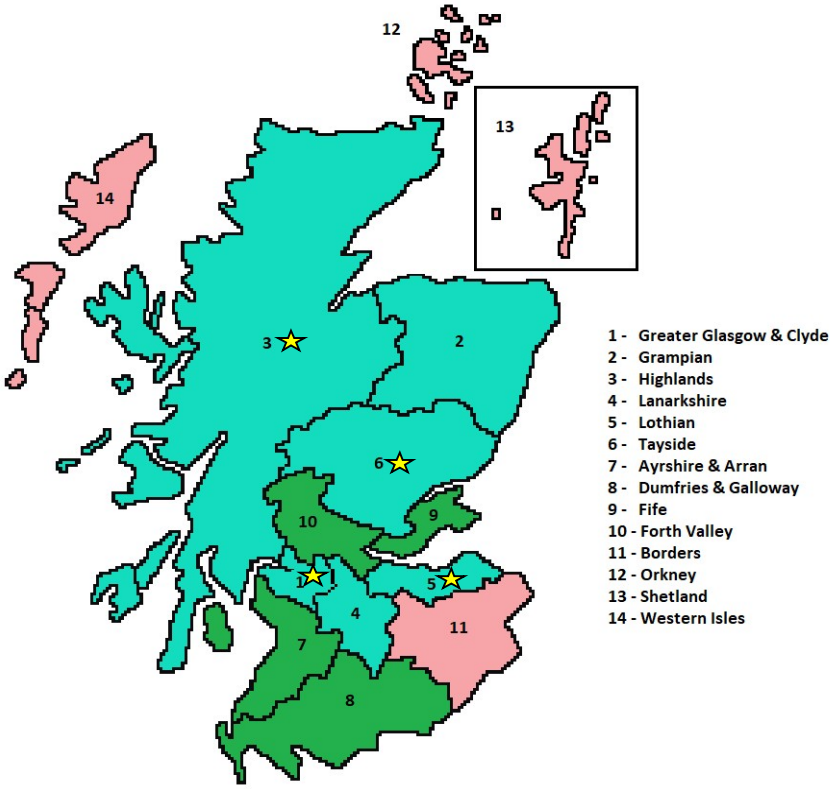


Figure 7.1 - Participating Scottish health boards This map depicts the 14 regional NHS health boards in Scotland. Green (1 – 10) indicate health boards that responded to the questionnaire. Red (11 - 14) indicate health boards where responses to the questionnaire were not received. Light green health boards (1 – 6) represent health boards that have a hospital providing a Vascular Surgery 'Hub' service. The remaining health boards (7 – 14) act as vascular surgery 'spoke' sites. A gold star indicates health boards that participated in follow-up interviews and focus groups.

7.4.1.1 Respondent demographics

Most respondents were male (n = 50, 83%), aged 40 - 49 years (n = 19, 32%) and were consultant vascular surgeons (n = 24, 40%) or vascular surgical trainees (n = 17, 28%). The largest proportion worked in NHS Greater Glasgow & Clyde (n = 24, 37%), Table 7.1.

Table 7.1 - Questionnaire respondent demographics.

Sex	**Male**	**50 (83%)**
Age (years)	20-29	11 (18%)
	30-39	13 (22%)
	40-49	19 (32%)
	50-59	17 (28%)
	60+	0 (0%)
Years worked in NHS	0-9	21 (35%)
	10-19	13 (22%)
	20-29	15 (25%)
	30-39	11 (18%)
	40+	0 (0%)
Profession	Consultant Vascular Surgeon	24 (40%)
	Surgical Trainees (vascular)	17 (28%)
	Consultant Interventionalist	5 (8%)
	Nurse practitioner	5 (8%)
	Vascular Nurse Specialist	3 (5%)
	BACPAR Physio	2 (3%)
	Podiatrist	1 (2%)
	Consultant Anaesthetist	1 (2%)
	Clinical Scientist	1 (2%)
	Scottish Ambulance Service	1 (2%)
Scottish regional health board	Greater Glasgow & Clyde (‘Hub’)	22 (37%)
	Tayside (‘Hub’)	10 (17%)
	Lanarkshire (‘Hub’)	9 (15%)
	Lothian (‘Hub’)	6 (10%)
	Grampian (‘Hub’)	5 (8%)
	Highlands (‘Hub’)	2 (3%)
	Forth Valley Royal Hospital (‘Spoke’)	2 (3%)
	Dumfries & Galloway (‘Spoke’)	1 (2%)
	Ayrshire & Arran (‘Spoke’)	1 (2%)
	Fife (‘Spoke’)	1 (2%)

7.4.1.2 Mode of frailty assessment

Frailty is usually assessed on a daily basis (n = 37, 62%). Multiple choice answers were used to explore typical locations where frailty assessment takes place, and who usually performs the assessment. Sixty respondents provided 192 responses to location of assessment, with the most common location being in outpatient departments (n = 43, 22%) or during the acute inpatient admission process (n = 43, 22%), Table 7.2. Where respondents described 'other' points of assessment in the patient journey (n = 4, 2%), this included: each patient contact (n=2), at some point during an inpatient stay (n = 1, 1%) and 'not sure' (n = 1, 1%). Sixty respondents provided 173 responses to who usually performs frailty assessments in their department. It was felt consultant vascular surgeons (n = 35, 20%) and consultant anaesthetists (n = 26, 15%) most commonly assessed vascular patients for frailty. Five (3%) respondents from NHS Tayside reported the presence of a surgical frailty team who performed frailty assessments in their unit.

Table 7.2 - Response to multiple choice questions on mode of frailty assessment

Frequency of assessment (n=60)	Daily	37 (62%)
	Weekly	9 (15%)
	Monthly	2 (3%)
	Rarely	6 (10%)
	Never	6 (10%)
Location of assessment (n=192)	Outpatient department	43 (22%)
	Acute inpatient admission process	43 (22%)
	Preoperatively	33 (17%)
	Postoperatively	31 (16%)
	In community	16 (8%)
	On the day of surgery	12 (6%)
	Not assessed	10 (5%)
	Other	4 (2%)
Who assesses frailty (n=173)	Consultant Vascular Surgeon	35 (20%)
	Consultant Anaesthetist	26 (15%)
	Junior Doctor	23 (13%)
	Geriatric physician	22 (13%)
	Ward staff nurse	19 (11%)
	Physiotherapist	18 (10%)
	Occupational therapist	12 (7%)
	Not performed	10 (6%)
	Dedicated surgical frailty team	5 (3%)
	Medical registrar	3 (2%)

Where frailty was reported as assessed (n = 53, 88%), most respondents do not use a formal tool, instead relying on a subjective 'End of Bed' assessment (n = 44, 83%). The 'End of Bed' assessment is considered synonymous with 'initial clinical evaluation'[159] described in Chapters 4-6. If a frailty tool was used, the most popular tool was the Rockwood Clinical Frailty Scale[94] (n = 15, 28%), with other tools displayed in Figure 7.2. Of the three 'other' modes of assessment, this included: anaesthetic pre-operative assessment (n = 1, 2%), nursing care assessment such as pressure ulcer risk and nutritional assessment (n = 1, 2%) and the use of Eastern Cooperative Oncology Group[328] (ECOG) performance status (n = 1, 2%). The seven (12%) respondents who reported not assessing frailty, included: nurse practitioners (n = 2, 29%), BACPAR-physiotherapists (n = 2, 29%), a clinical vascular scientist (n = 1, 14%), a consultant interventional radiologist (n = 1, 14%) and a consultant vascular surgeon (n = 1, 14%).

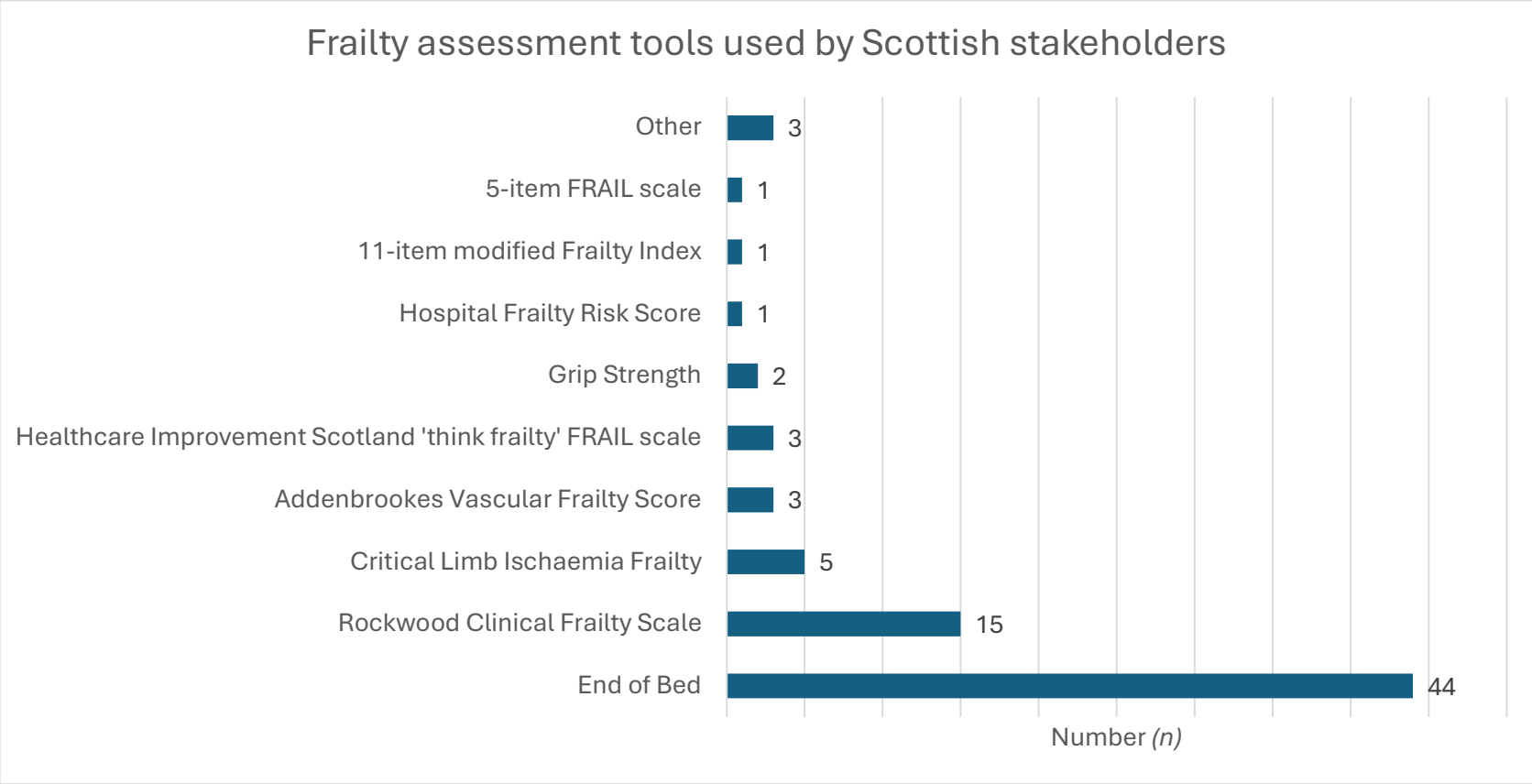


Figure 7.2 - Frailty assessment tools used by Scottish stakeholders. A visual representative of all frailty assessment tools reported as used in clinical practice by vascular surgery healthcare professionals. This includes: End of Bed/Initial clinical evaluation[159], Clinical Frailty Scale[94], Critical Limb Ischaemia Frailty[155], Addenbrookes Vascular Frailty Score[100], Healthcare Improvement Scotland (HIS) 'think frailty' FRAIL scale[269], Grip strength[70], Hospital Frailty Risk Score[133], 11-item modified Frailty Index[192] and the 5-item FRAIL Scale[329] instruments.

7.4.1.3 Significance of frailty

The majority of respondents (n = 53, 88%) described being 'comfortable' or 'very comfortable' with the frailty concept with agreement to some extent that there was added value to assessing frailty over and above comorbidity (n = 46, 77%) and disability (n = 49, 82%). A lesser proportion described using frailty assessments to help guide management plans (n = 30, 50%) or for joint decision-making (n = 33, 55%), Figure 7.3. Of eighteen (30%) respondents who described not using frailty assessment to guide management plans, most (n = 14, 78%) were not consultant or trainee surgeons: nurse practitioners (n = 3, 17%), clinical vascular scientists (n = 3, 17%), vascular nurse specialists (n = 2, 11%), consultant interventional radiologists (n = 2, 11%), BACPAR-physiotherapists (n = 2, 11%), a physician associate (n = 1, 6%) and a podiatrist (n = 1, 6%). Similarly, of seventeen (28%) respondents describing not using frailty assessment for joint decision-making, most (n = 11, 65%) were not consultant or trainee surgeons: nurse practitioner (n = 3, 18%), consultant interventionalist (n = 2, 12%), vascular nurse specialist (n = 2, 12%), BACPAR-physiotherapists (n = 2, 12%), clinical vascular scientist (n = 1, 6%) and physician associate (n = 1, 6%).

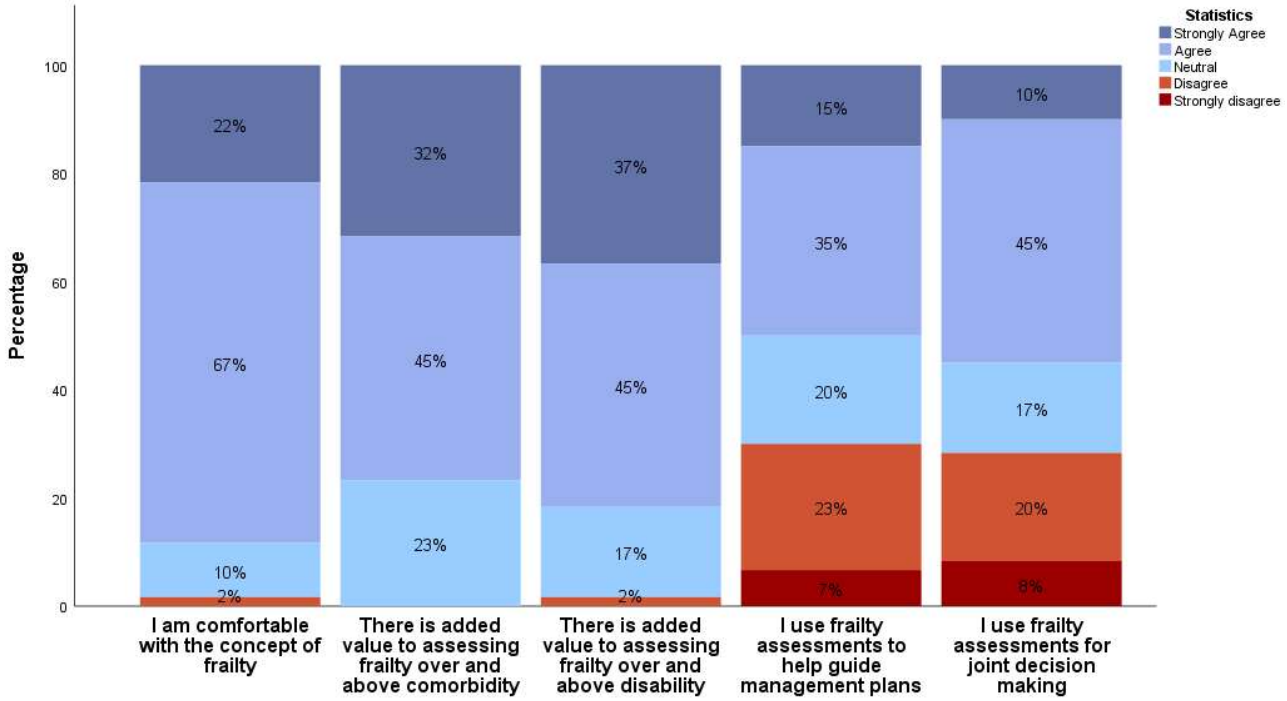


Figure 7.3 - Healthcare providers' familiarity and utilisation of frailty assessment in clinical practice.

7.4.1.4 Interprofessional differences in opinion

There were demonstrable differences between surgeons (consultant vascular surgeon and junior surgical doctors) and non-surgical healthcare professionals. Surgeons were more likely to report being comfortable with the frailty concept (*n* = 40, 98%) compared to non-surgeons (*n* = 13, 68%), $p < 0.05$. Further, surgeons were more likely to use frailty as part of designating management plans (*n* = 26, 63%) compared to non-surgeons (*n* = 4, 21%), $p < 0.05$. Within surgical respondents, there were no observed differences between consultants and junior doctors, Table 7.3.

Table 7.3 - Interprofessional differences in practice.

	Surgeons (consultant and junior doctors) *n*=41 (%)	Non-surgeons *n*=19 (%)	Statistics	Consultant vascular surgeons *n*=24 (%)	Surgical trainees *n*=17 (%)	Statistics
Comfortable with the frailty concept (scores 4+/5)	40 (98)	13 (68)	χ^2 (1, n=60) = 10.698 *p*=0.001*	24 (100)	16 (94)	χ^2 (1, n=41) = 1.447 *p*=0.229
Agree added value to assessing frailty over comorbidity (scores 4+/5)	32 (78)	14 (74)	χ^2 (1, n=60) = 0.138 *p*=0.710	20 (83)	12 (71)	χ^2 (1, n=41) = 0.943 *p*=0.331
Agree added value to assessing frailty over disability (scores 4+/5)	34 (83)	15 (79)	χ^2 (1, n=60) = 0.137 *p*=0.711	21 (88)	13 (77)	χ^2 (1, n=41) = 0.855 *p*=0.355
Use frailty to guide management plans (scores 4+/5)	26 (63)	4 (21)	χ^2 (1, n=60) = 9.320 *p*=0.002*	17 (71)	9 (53)	χ^2 (1, n=41) = 1.373 *p*=0.241
Use frailty for joint decision making (scores 4+/5)	26 (63)	7 (37)	χ^2 (1, n=60) = 3.704 *p*=0.054	18 (75)	8 (47)	χ^2 (1, n=41) = 3.349 *p*=0.067

7.4.2 Interviews/focus groups

A total of seven individual interviews and four focus groups (three groups of three and one group of four) were conducted, recruiting 20 participants. There were no interviews terminated early or cancelled. This included twelve consultant vascular surgeons, three surgical trainees, three vascular nurse specialists, one BACPAR-physiotherapist and one nurse practitioner across four regional NHS health boards with vascular 'hub' service provision. Mean interview duration was 44 minutes (35 – 60 minutes) with a total of 8 hours and 4 minutes of interview time recorded.

Four themes were identified with several subthemes. These were: **(i) conceptualising frailty through a vascular lens**, identifying **(ii) drivers for change** in approach to frailty. **(iii) Challenges and opportunities** were identified in exploring methods for doing this. Lastly, HCPs identified potential risks and benefits to **(iv) operationalising frailty for vascular services** to benefit patients, clinicians and services by directing collaborative, frailty-centric pathways in service provision, Figure 7.4.

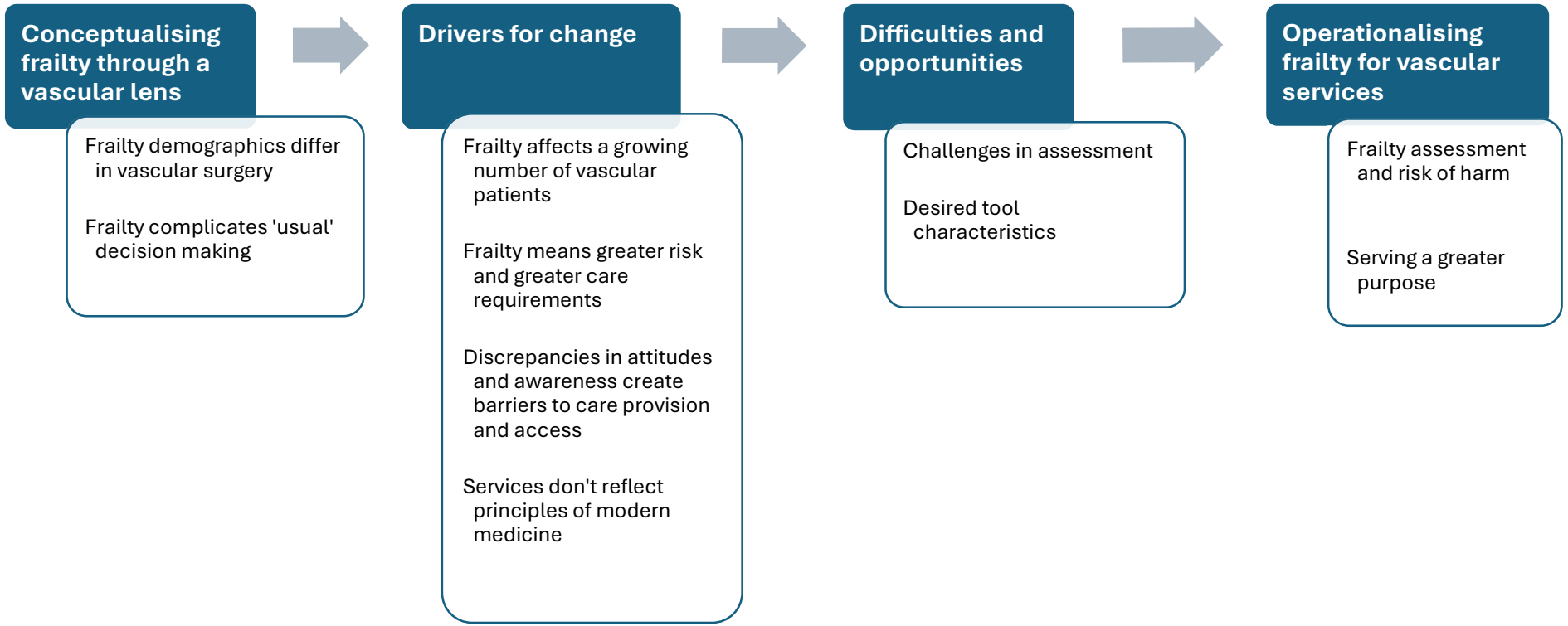


Figure 7.4 - Themes and subthemes. Flow diagram representing the themes and subthemes derived from thematic analysis of structured interview and focus groups.

7.4.2.1 **Theme 1:** Conceptualising frailty through a vascular lens

There was agreement around frailty existing as a complex, multidimensional construct, producing a degree of vulnerability and/or dependence which can exist independently from age, comorbidity and physical fitness:

> "Frailty covers a huge spectrum of situations where patients have become less physiologically robust and that might be due to specific comorbidity, and I accept that comorbidity and frailty might be different, or it might just be that they're getting old and therefore don't have the same reserve that they used to have. So, it's a multifactorial thing which is slightly difficult to define and certainly slightly difficult to quantify as well" (Consultant vascular surgeon, CVS1).

Subtheme 1.1: Frailty demographics differ in vascular surgery

Frailty was felt to be common in the vascular population. It was appreciated that typically increasing age is associated with a greater risk of frailty. However, there was a clear feeling that in a vascular population, there was a disproportionately greater number of younger patients presenting with advanced frailty compared to the general population. In these circumstances some alluded to a relationship between frailty, socioeconomic factors and medical comorbidity:

> "The amount of high quality life that people have varies far more by socioeconomic status than by age. I think working in Scotland and with the [Vascular] population that we have, it's so obvious" (Junior doctor, JD1).

Subtheme 1.2: Frailty complicates 'usual' decision-making

Frailty was recognised as having important prognostic value, mainly that of increased vulnerability to surgical stress which can influence surgical decision making and expected clinical course. Vascular surgery was described as a speciality where a substantial proportion of treatment is offered on a time-sensitive basis to patients with high disease burden and with a variety of treatment options, each affording a different burden of stress. Clinical decision-making was

felt to be intricate and nuanced, and HCPs recognised an additional complexity that frailty introduces to this process:

> "You can recognise it but it's quite hard to pin down as to what it means, what its implications are and what the severity is. So, I think the whole concept is very nebulous to start with…It's hard because you're going to assess someone when they're sick and unwell and it's not always straight forward to know what's recoverable and what they can get better from." (CVS2).

7.4.2.2 Theme 2: Drivers for change

Subtheme 2.1: Frailty affects a growing number of vascular patients

There was unanimous agreement that frailty is becoming an increasingly common problem, compared to historic clinical interactions. The primary reasons for this were felt to be arising from increasing life expectancy as well as progress in surgical technique that has enabled successful active treatment beyond what was historically possible, specifically endovascular treatments. Frailty was commonly described as a result of living longer due to medical treatment enabling comorbid survival but, perhaps for younger frail patients, social factors were recognised as important contributors to poor health quality and early onset frailty:

> "It's a modern epidemic to some extent. We're living longer and we're not living better. We're increasingly complex, more comorbid and a more disengaged society so there's all sorts of problems that probably weren't there or weren't so exposed in the past". (CVS2).

Subtheme 2.2: Frailty means greater risk and greater care requirements

It was universally felt that caring for frail patients introduced particular considerations and challenges whether describing surgical or non-surgical treatment. The primary implication recognised by all HCPs was that frail patients are vulnerable, their ability to tolerate physiological stress, big or small, is limited and consequentially there was recognition that frail patients are more likely to suffer adverse health outcomes. Typically this was illustrated by a description of adverse health outcomes occurring as a multistep sequence of patients unravelling, often initiated by a seemingly innocuous insult:

> "You know, not letting somebody get constipated so they end up with a [discharge] delay from confusion, falls and stump dehiscence for example." (Physiotherapist).

Surgeons primarily considered the implications of frailty in the context of their ability to safely offer surgical or endovascular treatment. Typically, a

conservative, or non-operative, approach was preferred in order to mitigate the risk of systemic harm, even in instances where more aggressive treatment may be preferable for the pathology. Some surgeons reflected on the opportunity frailty can offer in delivering realistic medicine, aligning patients' priorities with clinical management plans. This could mean subjecting patients to more invasive treatment and possibly a more tumultuous perioperative course, in order to prioritise patient-centred care goals, provided a positive outcome was felt achievable:

> "By salvaging *[arterial reconstruction]* him as he is just now, I think we will be able to maintain functional independence for him in his own home. Whereas, if we were to subject someone with the level of frailty which he currently has to a major limb amputation, I think he would struggle to rehabilitate. So, I think the question as to how frailty influences clinical practice will actually be quite variable depending on who you're talking to". (CVS3).

Nonmedical HCPs also recognised additional considerations for providing care for frail patients compared to robust counterparts. Frail patients were typically felt to have greater nursing care requirements, primarily in personal care and nutrition which can be challenging to meet in a fast-paced surgical ward. Having to prioritise medically urgent care commonly meant softer aspects of nursing care might not be met which was felt to have a detrimental effect on the general health and rehabilitative capacity of frail patients.

> "There are more people that have more needs now, like incontinence, or 2-hourly turns to prevent skin damage. Vascular is crazy, it's a continuous flow of patients and then if patients are coming back from theatre, you're with them a long time and it's maybe not meeting everybody else on the floors needs. So, if your band two's and three's *[care support workers]* aren't on the ball, then people can slip through the net. Like somebody sitting with them just to help…it's things like not being able to cut up their own food or they're maybe needing a plate guard just to assist them, and prompting with their eating..." (Staff nurse, SN).

A loss of independence and reliance on (in)formal support was identified as a key part in the frailty pathway. There was recognition that a patient's ability to access and/or comply with (even the least invasive form of) care plans could be entirely reliant on the components of community delivered social care packages. There

was an understanding by HCPs that successfully delivering care to frail patients relied on clear, bidirectional lines of communication within a multidisciplinary approach. It was felt critical for HCPs to elucidate and understand the degree of support each patient requires, and clearly communicate care instructions to variable support networks:

> "So, with regards to compression you have different types of stockings, different grades and classes. Giving anyone a decent class of stocking, if they're frail, they're not going to manage so you need to bear that in mind in terms of how they're going to be supported, either by community nurses or by family or carers or whatever else. Or indeed if they're going to manage at all with it." (Vascular nurse specialist, VNS).

A differentiation between physical frailty and psychological frailty was explored by some, recognising the multidomain nature of frailty and the more comprehensive support these patients may require. There was an impression that psychological frailty, described by some as '*not having a zest for life*' was an important factor in some patients failing to tolerate physiological stress and return to premorbid levels of function. Some felt there was overlap between psychological frailty and social vulnerability where patients were less likely to engage in treatment in the absence of a self-perceived satisfactory social role. The ability to care for this need in a hospital setting was difficult in the absence of staff with adequate time to provide emotional support or practical considerations like nightingale-style wards:

> "I think when they're taken out of their environment, they think they're not going to make it. Some people just turn their head to the wall and just think that, like, maybe that's their time." (SN).

Subtheme 2.3: Discrepancies in attitudes and awareness create barriers to care provision and access

While interviewees felt they had a good understanding of frailty and its implications, there was a general impression this was not reflected on a wider service level:

> "I still think the big problem is acknowledging frailty and how many of our patients are frail and sometimes we 'burry our head in the sand'.

> Patients are living longer; we've got more treatments we can offer, and this will only become a bigger problem." (JD2).

There were important questions raised around meeting the care needs of this patient cohort in the absence of education and awareness, recognising the clinical utility of frailty and how the service may target this to improve patient care:

> "It's a lack of awareness of being able to do anything about [frailty]. Or, that you can improve outcomes for these patients or even, you know, it can help you to guide management rather than just saying, oh well, they're frail. Not having an awareness of the ability to do something about it means that mobilising the resource then becomes more of a barrier because it's not seen as something that is a valid construct." (JD3).

Some expressed concerns that a misunderstanding about the ability to positively influence the medical course of an unwell frail patient meant this had precluded some patients in accessing appropriate care:

> "I think frailty is a really important problem within vascular surgery particularly because I think vascular patients are the ones that become frail the fastest. I have worked in units or specialities where clinicians have identified frailty as a reason to disengage or not accept referrals. Their concern about the patient's anticipated poor clinical outcomes means there is a reluctance to get involved in the first place as surgeons worry about causing harm when trying to treat surgical pathology". (JD2)

Further, HCPs felt there were inconsistencies in the general population's understanding of the frailty concept which could challenge clinical communication due to patients and/or relatives presenting with unrealistic expectations and negatively influence perceptions of individualised healthcare journeys:

> "The biggest challenge perhaps is not just with us healthcare practitioners, whatever brand of medicine or surgery you do, it's with patients. Because, well [I know that] some people don't recognise their own frailty. So, maybe a more important thing is to try and introduce the concept of frailty to a general population. During COVID there were lots of people who's grandads were really, really fit and well until they went into that nursing home and died. But they weren't that fit and well when they go to that nursing home really, they were frail." (CVS3).

Subtheme 2.4: Services not reflecting principles of modern medicine

A key driver for changing the approach to managing frailty is perhaps the recognition by vascular surgeons that many were attracted to the speciality because of a sense of professional responsibility and personal fulfilment that came with pursuing a career in a speciality which is felt to recognise the importance of both surgical and medical management of patients. Yet increasingly complex patients and a rapidly evolving evidenced-based health care system can make it challenging to deliver such holistic care:

> "I also think that when you have really complexly comorbid patients, when you're surgical, it's difficult to keep on top of all the changes in medicine and what the current best practice is…there's a lot of stuff where I think we don't manage optimally and we could probably be doing better in surgical wards to minimise the hit from operating and to try and minimise the perioperative medical damage…I think it's unrealistic somehow to expect us as surgeons to keep on top of all that" (JD1).

This is complicated by the busy nature of the speciality of which part of the success in service delivery relies on rapid patient turnover. HCPs recognised that both the comprehensive and, at times, complex nature of care requirements demand a multifaceted approach which is challenging to deliver in a streamlined way, limited by a lack of resources. Yet there was an appreciation that the service could perhaps be redesigned to better meet the needs of patients and optimise staff utilisation:

> "We're going back to the health economics thing, what's the best use of us as vascular surgeons? It's probably dealing with the outpatient waiting lists, the emergencies that come in, the theatre waiting lists. It's getting time to revascularisation sorted…sorting these things that are kind of urgent. So, if we could be freed up by getting help with [medical management of patients], that might be within our remit, but not quite, that would be useful". (CVS4.)

The challenges introduced by additional care needs were particularly noticeable in discussing rehabilitation and discharge planning to support a safe transition between hospital and community care. Clear communication and continuity in care between inpatient and outpatient care was felt crucial in this process, as a

breakdown in this could affect treatment compliance and negatively impact patient care. Growing pressures on community and social care were felt to commonly result in delays in meeting discharge care requirements, long hospital admissions and complex periods of convalescence.

> “People have high demands for getting home, or they need to move to accommodate a wheelchair and different things, some patients get stuck quite readily [in hospital], so beds aren’t always available”. (SN).

7.4.2.3 Theme 3: Difficulties and opportunities

All interviewed surgeons reported assessing frailty as part of clinical interactions with patients. While such an assessment was unanimously described simplistically ('end of bed' assessment), the component parts of this process reflect the complex and multidomain nature of the construct. Clinicians described a variable constellation of screening questions, as well as an in-person visual assessment, developed through clinical experience, to establish a combination of functional (in)dependence, medical co-morbidity, cognitive function and psychosocial parameters which were used to ascertain the presence, and severity, of frailty:

> "I suspect a lot of my colleagues make a subjective assessment of frailty, looking at physiological reserve, multiorgan dysfunction, physical capability, ability to mobilise, potential to rehabilitate, higher level of function, their independence, need for carers, meal prep…it's a combination of these things." (CVS5)

Surgeons unanimously described professional pride and confidence in their clinical acumen, acknowledging subjectivity in assessment without a loss of 'test' sensitivity or accuracy:

> "I think we don't routinely use a formal frailty score, but I don't think that means we notice less frailty." (CVS6)

Conversely, non-medical HCPs tended to describe a lack of confidence in perceived ability to assess frailty due to an lack of education and structured guidance on how to do so:

> "I don't think I do a good job; I don't think I properly assess it. I think it's a lack of confidence, that's for sure. Just, I have never properly looked at it [assessing frailty], but you know, it's crossed my mind before. Because I have thought about it, we should probably all look at this in a bit more detail." (Physiotherapist).

Subtheme 3.1: Challenges in assessment

HCPs felt there was merit in standardisation in the approach to frailty assessment, even beyond the confines of vascular surgery as a speciality. It was felt utilisation of one standardised tool would endorse universal understanding of the frailty construct, as well as the proposed assessment format, which would be key to setting up and delivering frailty-centric care:

> "There'll always be limitations to any tool, so it's better to stick to one and use it well." (CVS7).

However, the ability to identify a preferred frailty assessment tool proved difficult with HCPs citing several challenges to this process, including an abundance of tools resulting in tool unfamiliarity, a lack of evidence and a lack of confidence in tool selection. There was also felt to be a system-wide lack of awareness and understanding of the frailty concept, with an abundance of frailty tools felt to be complicating an already underappreciated and confused construct:

> "The problem is also you never know what other people's understanding is. And I think the reality is that when it comes to frailty, people respond much better to, and this is a housebound man who has four times a day package of care, who can't walk up the flight of stairs rather than, oh, they've got a score of something or other, you know?" (JD2).

There were also concerns about tool validity and the ability to conceptualise the complex decision making process that underpins a surgeon's end of bed assessment. Further, surgeons appreciated a heterogeneity in clinical manifestation of frailty and variability in how it interplays with pathophysiological and treatment stress burden. There was an impression that the prognostic validity of a tool, with any degree of statistical accuracy, would be questionable when utilising population based tools for stochastic patient interactions:

> "It's the complexity of the disease. I see frailty not just as a single domain, it's multiple biological systems failing to produce that common pathway of frailty. I wonder how the complexity of frailty can be standardized. One person's frailty is different. So, it's a case of standardising/quantifying that, I'm not sure I could." (CVS4).

Counterintuitive to the expressed interest in utilising frailty assessment to help guide accurate decision making, most surgeons reported they felt it unrealistic to

expect widespread uptake of different disease- and treatment-specific frailty tools and were willing to compromise on this as part of an acceptance that frailty assessment likely plays a bigger role than solely acting as a predictive test:

> "Having a single standardised frailty assessment tool across NHS Scotland in clinical practice would be helpful, even if the prognostic accuracy is less in certain circumstances." (JD2).

Subtheme 3.2: Desired tool characteristics

Five categories were identified that HCPs felt would give them confidence in adopting a standardised frailty assessment tool: Relevant, Accessible, Validated, Evidenced and Standardised (RAVES), Figure 7.5.

Relevant/Accessible: the tool must be quick, user friendly and not require additional information surplus to that routinely collected during a clinical interaction.

Valid: The tool must demonstrate content validity, distinguishing it from an excess of tools with perceived questionable accuracy. Questions were raised around the ability to accurately conceptualise the intricate process clinicians conduct in subjective frailty assessments however.

Evidenced: There were comprehensive discussions around the need for evidence to support the promotion of a tool. Surgeons expressed a desire to observe positive predictive and prognostic values as well non-inferiority/superiority evidence comparing tool sensitivity to the established subjective measures of assessment performed by clinicians. However some clinicians felt that variation in the quality of evidence supporting evidence-based practice can be significant. Some drew parallels with other tools described as measures of fitness with a perceived low quality evidence base, with the impression such tools held no role in replacing clinical assessment, but performed well as an adjunct in complimenting complex decision making around challenging clinical cases:

> "You've seen the role that [cardiopulmonary exercise testing] plays in our AAA decisions. I think that it is part of a jigsaw and you know, for some patients it undoubtedly changes the direction we're going. So I think frailty could be used in the same way." (CVS8).

Standardised: The tool must be used consistently across all areas of clinical work and medical specialities to ensure users develop tool/construct familiarity, improved awareness of its implications and accurate use of the proposed tool.

- Relevant
- Accessible
- Valid
- Evidenced
- Standardised

Relevant	The tool should not require additional information surplus to what is routinely collected as part of clinical interactions with patients: *"It has to be simple to use and match your practice, use the same information we extract as surgeons." (CVS10).*
Accessible	The tool must be simple, quick and easy to use in a clinical setting otherwise engagement would be poor. It was also felt a simple tool would act favourably in complimenting informed discussions with patients, as well as with professionals: *"If it's not simple and pretty much instant, folk just won't use it." (CVS1).*
Valid	Accuracy in a tools assessment of frailty as a multidomain construct was pertinent to some prospective users, acknowledging an abundance of tools which may only consider one aspect of frailty (e.g., comorbidity) and therefore lack construct validity: *"If you've got a tool that measures one domain, that's only one element of frailty and my worry would be that using this too, you would end up excluding people that you might have otherwise treated, or vice versa." (CVS4).*
Evidenced	There was a desire for evidence confirming a health and economic benefit to using a frailty score and within this there was a desire for confirmation that such a tool was able to replicate clinical acumen: *"I would need to be convinced that [a tool] is better, that it's picking things up that I'm not intuitively". (CVS8).*
Standardised	Using one tool consistently and repetitively throughout all areas of clinical communication (i.e., part of MDT meetings, verbal/written clinical handovers and reinforced on software systems) was felt critical to improve communication, endorse a better understanding and make it easier to learn and use accurately: *"You wanna use the same thing over and over again, because then you learn." (CVS7).*

Figure 7.5 - Desired frailty assessment tool characteristics.

7.4.2.4 Theme 4: Operationalising frailty for vascular services

There were conflicted opinions when exploring the role for formalisation in frailty assessment processes. There were concerns around the functional utility and a risk of unintended harm to patient outcomes, professional interactions and patient communication. Conversely there was an impression that formalising an established process represented an opportunity for improving awareness and creating a standard against which health care infrastructure and patient care can be developed against.

Subtheme 4.1: Frailty assessment and risk of harm

The primary role for frailty assessment identified by surgeons lay in patient selection and the ability to identify patients who are at greatest risk of coming to harm from surgical intervention and who may best be served by palliative/symptom-based management. Its presence commonly formed part of professional discussion and informed discussion with patients/relatives to rationalise treatment options. However, concerns were expressed by some around a perceived lack of clinical utility in introducing a standardised formal frailty assessment tool to this process. Two key areas of concern were expressed: (a) the feasibility of conceptualising a tool that replicates intricate clinical assessments of frailty status, and (b) the ability of a population-based risk assessment tool to consider the uniqueness of stochastic patient interactions and/or replicate the burden of decision surgeons navigate during clinical decision making processes. An inability to replicate these processes in an objective tool were felt to introduce a risk of patient harm:

> "So, I think we make a complex, multifaceted decision that we probably don't give ourselves enough credit for. So that, that's the complexity I need replicated [in an assessment tool] because clearly, I don't want to overtreat people, but I also don't want to undertreat people." (CVS4).

Further concern was raised about unintended negative patient interactions if such a tool were to be used in isolation or as substitution for clinical assessment:

> "It could have legal ramifications as well, where patients challenge your decision making." (CVS9).

It was also felt a frailty tool might confuse multidisciplinary processes and could be used to inappropriately influence clinical decision making:

> "The risk is that non-surgical specialists start using these tools to inappropriately make decisions on whether or not to operate on patients. I don't think they should be doing that." (CVS2).

Some felt the decision to formalise a frailty assessment would only act as a surrogate for a process that has already taken place, introducing unnecessary additional paperwork to time-limited clinical situations. Ultimately, there was a perception that a score derived from an assessment tool could not replace clinical acumen, and at most it could serve a role as an adjunct in enhancing the multifaceted approach to constructing clinically appropriate, individualised management plans for patients:

> "The sense I'm getting is that frailty is going to be an adjunct at the moment. I think the reason we have MDT meetings, the reason we have a group of consultants is so we can bounce ideas off each other and regulate ourselves…it would be nice to show something validated that will help us in that decision making." (CVS4).

Subtheme 4.2: Serving a greater purpose

A positive role for formalising frailty assessment was more clearly defined when discussing its value more generally, considering frailty assessment as more than the score it produces. HCPs felt more could be done to overcome the additional medical, nursing and community care challenges inherent to the frailty syndrome. This would require a multifaceted, multidisciplinary approach centring around early problem identification and efficient collaboration. There was an impression that introducing standardisation in the approach to its assessment might be used to guide such development with three major positive

themes proposed: improving patient outcomes, unifying services through unified language and enhancing job satisfaction, Figure 7.6.

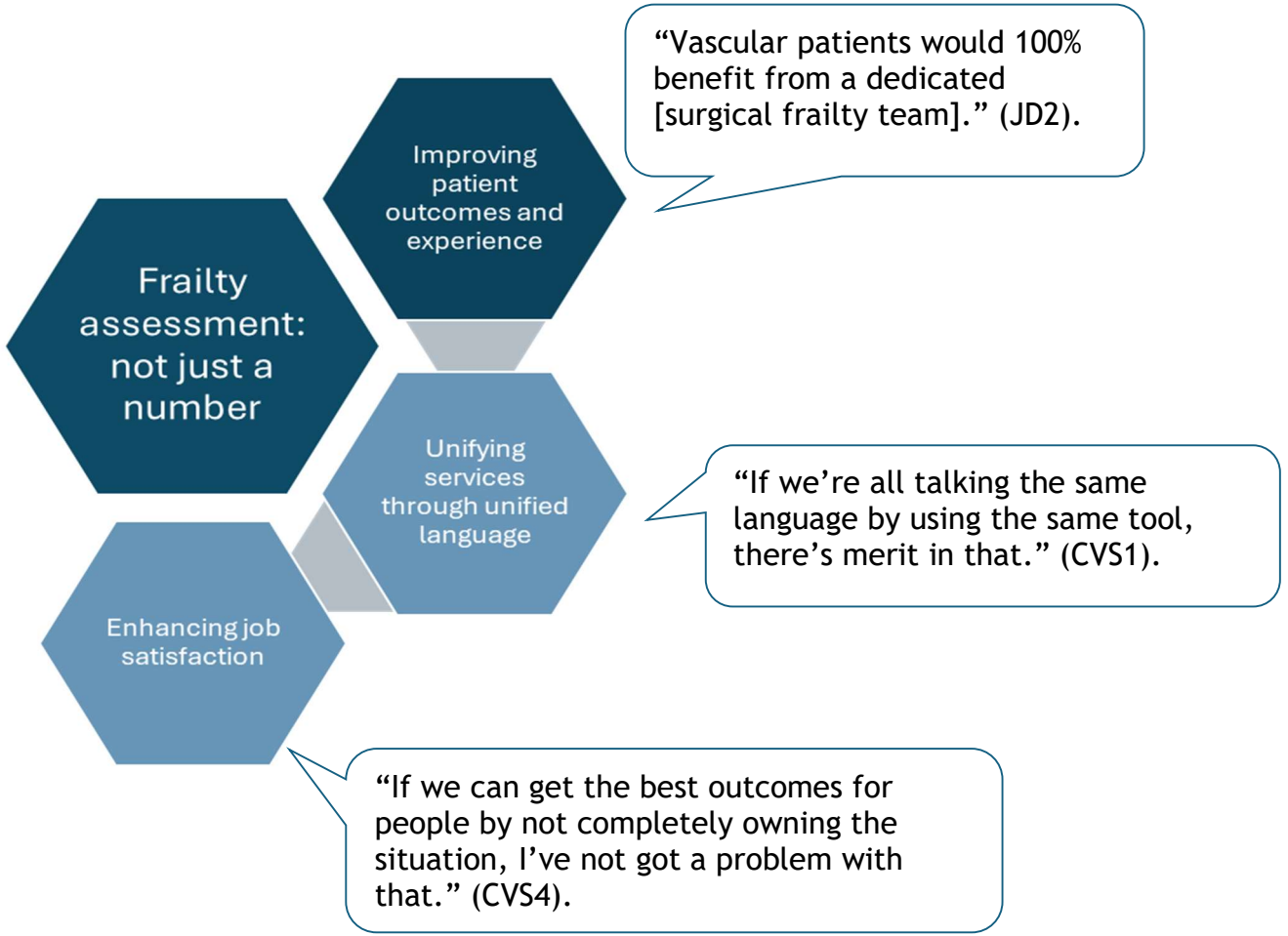


Figure 7.6 - Frailty assessment serving a greater purpose.

Improving patient outcomes and experience

HCPs generally appreciated a role for utilising frailty scoring as a means of early identification of those who need additional input and may benefit from a frailty-shared-care model/pathway, running from admission to discharge. This would involve identifying and quantifying the needs of vulnerable patients to build a framework against which aspects of multidisciplinary medical, nursing and social care can be redirected toward, with expectations this would improve health outcomes. This might include defining areas of medical care, not immediately relevant to the surgical presentation, that are amenable to optimisation with the view to mitigating physiological stress of surgery, enhance rehabilitative potential and improve health outcomes. This was usually discussed in the context of peri- or post-operative health care for acute admissions. Some queried a role for pre-operative optimisation of elective/prophylactic patients, targeting 'reversible' areas of frailty, but felt additional evidence would be valuable to observe financial and health benefit to this prior to accepting a role for this clinical approach:

> "I think that is an interesting area and I think there isn't enough evidence around the reversibility of frailty, it is poorly understood. I think a lot of people feel once a patient is labelled as frail, that's it. However optimising frailty deficits would be good for a select group, in theory." (JD3).

A standardised frailty assessment was felt to represent an opportunity to structure a multidisciplinary approach to a successful '**proactive instead of reactive**' approach to treating frail patients. This was perceived as likely to mitigate the recognised morbidity and mortality associated with frailty:

> "If you were a member of the public, you'd be like, yes, I want my surgeon doing more surgical things. And yes, I want my geriatrician looking after geriatric things. You know, we need to have the right person dealing with the right stuff at the right time." (JD2).

HCPs felt the use of a standardised frailty assessment tool could be applied as part of a screening process to identify patients that are likely to benefit from a multifaceted, frailty-centric approach to their care:

> "I think to really benefit you would need to be almost prospectively identifying these patients. Because again, I think one of the things we do less well on a surgical ward is that we get medical help quite late for these patients. We wait until everything has properly fallen to pieces…and I guess a frailty score could be part of that." (JD1).

Further, there was an impression that patient, and relative, expectation management and healthcare experience could be improved by adopting a simple and objective measure of frailty to help navigate challenging conversations by bridging discrepancies in understanding, rationalise treatment options and guide informed discussions around intended benefits and risks of treatments as well as informing consent processes:

> "Frailty assessment [by a surgical frailty team] is also helpful for informed decision making with the patient, where we can inform them of the expected impact of the surgery on them in terms of return of function, or not." (CVS7).

Unifying services through unified language

Despite a recognition of frailty requiring a multidisciplinary approach to treatment, the care delivered to these patients was perceived to be suffering from a lack of joined up thinking. Enforcing a standardised frailty assessment tool was felt critical for enabling cohesion in care delivery on a service wide level through generating a unified language around a complex, heterogeneous construct. It was felt this would improve awareness and understanding of its ramifications, as well as benefiting (inter)-professional communication. Ultimately this would benefit healthcare outcomes by enabling greater sensitivity and consistency in the delivery of realistic medicine:

> "There's merit in extending this beyond just the vascular world and even patients that are being referred into the vascular world, you know, it might just encourage a bit more realistic medicine. If we're all talking

> the same language by using the same tool, there's merit in that." (CVS1).

Vascular surgeons take pride in the comprehensive surgical and medical care they provide for their patients. However, there was a growing feeling that the rising complexity of patients and advances in modern medicine made it unrealistic to continue to deliver comprehensive care without seeking advice from appropriate subspecialities. Standardisation in the approach to frailty assessment was felt salient to the ability to consistently identify patients and communicate anticipated multidimensional needs with appropriate members of a multidisciplinary team. Geriatricians were considered to be frailty-experts with surgeons commonly recognising a role for their involvement in elements of inpatient vascular patient care, including: proactively managing nuanced medical care, providing a medical opinion on likely post-operative trajectory, bringing close links with related medical specialities and improving efficiency in complex discharge planning process through familiarity with relevant in-hospital allied healthcare professionals and relevant spoke and community services:

> "I think it would be very good to have a team with more dedicated medical input for sure, because [our patients] are all old and frail, geriatricians are probably the right people." (CVS6).

In addition to perceived improvements in patient care, such a service was felt to improve service productivity due to the introduction of responsibility attribution, improving access to appropriate services, allowing deduplication in workload and improving efficiency in workload and time management. This was highlighted as a particular benefit to vascular surgery after the centralisation of services has meant a substantial proportion of inpatients rely on safe expatriation to local services for rehabilitation and discharge planning, as part of safeguarding limited tertiary speciality bed availability for emergency and planned admissions.

> "[The surgical frailty team are] helpful for organising best medical treatment and linking in with palliative care, where required, to ensure best symptomatic management. This has created really good links between in-hospital medical management and community care which helps expedite discharge planning. (CVS7).

A formal frailty score was also proposed as a novel and succinct approach for medical staff to highlight newly admitted patients to nursing staff who are vulnerable and at risk of requiring greater medical/nursing care, in order to direct limited nursing resources in an attempt to mitigate avoidable patient harm:

> "And it doesn't need to be lengthy, but it just means, I think it would be good if it was just one sheet of paper, like a frailty overview…and then it would maybe highlight to the nurses that they are one to watch, one to look out for." (SN).

Surgeons reflected on the ever increasing pressures on the NHS, both in-hospital and in community services. A loss of continuity in primary care from workforce challenges and difficulties in accessing services, as well as the introduction of non-medical HCP referral pathways designed to mitigate these challenges, has altered the style of referrals. A perceived loss of historically intricate and long-standing relationships between a patient and their family doctor has meant referrals can lack important personal information that was helpful to the triage process. Surgeons expressed a positive opinion on the utility of a standardised frailty assessment score being able to bridge this gap, with some wondering if an assessment could be made as part of a patient's annual health check-up. Surgeons explicitly stated it would be inappropriate to use a frailty score to decline a referral. There was an impression a frailty assessment would be mutually beneficial, enhancing community awareness of the construct and increasing opportunities for delivering realistic medicine. An important aspect of this was the opportunity this could afford patient counselling in the community:

> "GP's have a different way of working now where they don't see the same patient or have continuity the same so, absolutely, having a frailty assessment in the GP letter would be helpful to increase the amount of detail on the referral. Part of the problem is that primary care referrals are coming from different health care professionals, like nurse specialists or podiatrists, who are skilled at their job but may not be able to assess a patient holistically the way a doctor can, so a community frailty score would help overcome this." (CVS10).

However, there were feelings of futility when discussing service restructuring due increasing pressures on NHS services from a growing disparity in resource requirement and the availability of time, staff and finances. Some expressed concerns that attempting to organise and deliver any new, collaborative, frailty-centric service would only burden a limited resource pool further.

> "There aren't enough geriatricians to just be geriatricians, so for someone to say well we'd now like to be involved in surgical patients…there's not a push from the organisation, if you'd like, to say, yeh, we see this as a useful place to employ geriatrician time." (CVS1).

The success in introducing and sustaining a collaborative frailty-centric service was felt to be reliant on the demonstration of concurrent benefits to health outcomes and service efficiency balanced against competing financial priorities of a vascular department, such as surgical/endovascular equipment, training and the supplementation of established health care professional roles. A perceived lack of formal evidence was felt to be clouding buy-in from senior stakeholders and on a directorate level, obstructing the ability to implement change despite a perceived benefit:

> "So we used to have a Perioperative care for Older People undergoing Surgery service…they would go around and look at their medical comorbidities and try and optimize their medical condition but it has been withdrawn because it was not seen to be cost effective. We liked it, we thought it was quite good but I think they struggled to show a significant change in length of stay and bed days saved versus consultant and nursing salary." (CVS11).

Enhancing job satisfaction

Most surgeons looked favourably upon involving a geriatrician as a frailty-expert to improve the delivery of comprehensive and realistic medicine. Where such a service had successfully been implemented, there was a feeling of professional development with improved clinical knowledge as well as greater confidence in patient care:

> "It's a positive working environment. Both teams feel valued and feel that the service benefits patients. Vascular surgery really respects and sees the value of the surgical frailty team's opinions/assessments and advice. Equally the surgical frailty team feel really appreciated by the vascular surgery department because we really involve them in the decision making and planning." (CVS7).

The integration of medical physicians with vascular surgical teams was felt to empower surgeons and non-medical HCPs to take ownership of frail and complex surgical patients. There was a sense of satisfaction as HCPs felt patients were better cared for through opening access to proactive care that previously would have been challenging to deliver:

> "Having a surgical frailty team is useful as this helps to act as a point of contact to escalate medical concerns to, which may not be immediately relevant to surgical team. It gives me confidence in escalating concerns about patients…I think the outcomes for patients are better with their different background and different skillset, now that we have that service, and we have access to that team. Before the existence of the surgical frailty team, medical reviews were possible, but it wasn't easy, it was more of a fight." (Physiotherapist).

This notion was complimented by an anticipated bidirectional relationship of learning between vascular surgeons and geriatricians, which was favourably considered as it spoke to the pride surgeons take in being involved in patient care. It came naturally therefore that some surgeons expressed concerns around how introducing regular medical help may result in surgeon deskilling. This was typically interpreted as a consequence of surgeons losing ownership over aspects of clinical decision making. Some felt a proposed loss of ownership could complicate patient admissions and result in additional delays to discharge. This was coupled with a sense of dissatisfaction around inadequately optimised theatre utilisation and a concern that a loss of involvement in medical care would not be

complimented by improved technical skill consolidation nor an ability to positively tackle theatre waiting lists:

> "My worry is that the healthcare service isn't set up for efficient theatre utilisation so if we are not involved in patient care outside of theatre, then job satisfaction may drop substantially. We will just be sitting around as surgeons…" (JD3).

Acknowledging these issues, the common priority expressed by surgeons was ensuring appropriate, tailored and patient-centred care in order to reduce harm, improve health outcomes and patient satisfaction. For most, the understanding was that these goals were more likely to be successfully met through a comprehensive approach, which includes introducing a collaborative multidisciplinary approach where appropriate. Key to this process, however, is the notion of collaboration:

> "I think that we've moved on, on the area of owning patients. I would value a geriatrician's opinion. I think the key thing is not about ownership but it's about collaboration. If we can get the best outcomes for people by not completely owning the situation, I've not got a problem with that." (CVS4).

Several drew direct examples from specialities that already deliver integrated medical and surgical care as standard practice. There was a feeling that such a setup had not only positively affected the care provided to patients with complex needs, but also demonstrated efficient resource utilisation and resulted in professional development, improving the surgical team's confidence in independently managing some aspects of care where medical advice may previously have been sought:

> "Yeh, I mean, it works in transplant, doesn't it. You know, joint surgical and medical ward rounds. And I suppose, if one day, one of them isn't there, it doesn't fall to bits!" (CVS8).

7.5 Discussion

This study set out to address an evidence gap, assessing the perception and utilisation of frailty assessment by Scottish vascular surgery stakeholders. Frailty is recognised by most HCPs as an important construct due to its association with complex care needs and poor health outcomes. However, the questionnaires demonstrate a discrepancy between appreciation of frailty as a clinically relevant construct and the frequency to which frailty assessment is utilised in clinical decision-making. Further, the observation that vascular surgeons, compared to allied health care professionals, are more comfortable with the frailty concept and are more likely to consider it when formulating clinical management plans may well reflect differences in experiences and perceptions of professional responsibility and job roles between occupations within vascular surgery services. Follow up interviews and focus groups expanded on this difference with nonsurgical professionals tending toward considering frailty more holistically. Value is seen in early frailty identification to assist in managing aspects of the patient journey as a whole, identifying those with greater care and discharge planning requirements. However, there is an apparent lack of confidence around frailty assessment and an appetite for more formalised training to assist in recognising, and communicating, its presence. Alongside this is a view that standardising a service-wide approach, targeted toward complex frailty-related care needs, would facilitate non-surgical HCPs in their ability to seek help where patient needs were identified that fall outside the perceived remit of a vascular surgeons expertise.

In comparison, surgeons tend to consider frailty primarily in the context of patient selection for operative or non-operative management. An awareness of the multifaceted nature of the syndrome was reflected in the intricate and sensitive processes clinicians reported when elaborating on their subjective (“end-of-bed”) measures of assessment. Concerns around the ability of a tool to conceptualise complex clinical assessment meant surgeons were tentative in perceiving a role for adopting a standardised frailty tool for this purpose. This expands on previously

reported discrepancies between growing progress in frailty-research and a relative lesser appetite for adopting these tools into clinical practice. In keeping with current literature, care providers report a surplus of validated tools cause unfamiliarity, confusion and a concern over tool validity.[261] In looking beyond this however, surgeons did recognise that evolving patient demographics and restricted resources increasingly challenged holistic, patient-centred care for frail patients: a growing role for integrated multidisciplinary team input for these patients was identified.

Increasingly it is recognised that vascular care is delivered by the whole vascular team, with the sum of the product only being as good as its component parts. With HCPs recognising that more can be done to improve outcomes for frail patients, introducing a standardised frailty assessment may be the first step in achieving this. Where historic research efforts primarily propose the role of frailty assessment for prognostication purposes[90], perhaps the greatest benefit may sooner be observed in unifying language, improving awareness and creating shared goals in frailty management. This will help overcome barriers to improving outcomes by guiding the restructuring of disjointed and resource-limited healthcare services, ultimately enabling infrastructure to better reflect the principles of modern healthcare which HCPs strive toward. Unifying health and social care services' approach to caring for vascular patients with frailty is of critical value following the centralisation of vascular services where the successful delivery of medical and nursing care relies on clear, concise communication between all members of the multidisciplinary team caring for vascular patients, across community care, primary, secondary health care centres and between hub and spoke services.[330] Key to this is the proposed continuous collaborative efforts between geriatricians and care providers with a specialist interest in care of the older patient with surgical directorates.[331]

The benefits in unifying language speak to the needs expressed by frail patients in surgical wards. Patients prioritise feeling informed, being involved in decision-making and take greater comfort in feeling nurtured for, than considering the type of intervention they received.[303] Feelings of nurtured care have been exampled by frail patients in social support and practical assistance with aspects of daily activities. Allied HCP in this study recognised these needs but felt it difficult to always identify and provide them. Training and improved awareness could help focus attention toward identifying and managing patients care priorities, promoting realistic medicine principles.

7.5.1 Consistency with frailty assessment in current literature

Geriatricians are similarly incentivised by a collaborative approach which is primarily motivated by their recognition that surgical patients, particularly vascular patients, often have considerable care needs that could most suitably be met by skillsets offered by geriatricians.[332, 333] The recognition of shared priorities is observed in the growing momentum of integrated perioperative services internationally.[334] The British Geriatrics Society has recognised the need to standardise geriatric medicine input for the care of older surgical patients and have produced guidelines setting out key clinical, governance and educational/training principles for service models to refer to when setting up collaborative pathways: Peri-operative Care for Older Patients Undergoing Surgery (POPS).[87] Examples of successful alignment of services has produced a strong business case for involving geriatricians in the care of surgical patients.[1, 89, 334, 335] Demonstrable improvement in health outcomes across vascular surgery and non-vascular surgical specialities alike have been observed, which improve as models evolve over time.[89, 336]

The data from this study is consistent with current literature. In addition to the UK study described earlier in the introduction to this chapter, an Italian nation-wide cross-sectional study of vascular surgeons' perception and utilisation of

frailty assessment demonstrated concordance with a high level of appreciation of the importance of frailty as a construct (93%). Despite this, most surgeons do not use a formal frailty assessment instrument, meaning frailty was felt to be underassessed, and likely undertreated. This was felt to be due to insufficient guidance on available instruments as well as a relative knowledge gap around perioperative management of frailty, and a lack of staff or time.[337] Of note, when frailty assessment tools were used, the Rockwood Clinical Frailty Scale (CFS)[94] was preferred by clinicians in studies.

7.5.2 Implications for future work

The findings in this study resonates with current literature, re-iterating the call for reaching a consensus on a common approach to frailty assessment.[265, 285] This study identifies a role for further research to be targeted at comparing clinimetric properties of subjective means of frailty assessment ("end-of-bed" test) with validated tools that comply with the RAVES criteria set out in this study. This may be complimented by incorporating MoSCoW prioritisation principles, a framework which the requirements identified by stakeholders can be matched against an abundance of frailty tools. It consists of four categories: 'Must have', 'Should have', 'Could have' and 'Won't have'.[338-340]

This study identifies a role for exploring proposed benefits of a collaborative frailty-centric service delivery models through outcome measures that might historically be less commonly considered by surgical directorates. These may include patient (and family member) reported outcome measures and incidence of frailty-associated morbidity. There is also a role for promoting continued qualitative exploration of the departments providing or working toward such collaborative efforts. This has already been declared a priority by some (colorectal) surgical guidelines, as presented in Chapter 2 section 2.10. Governing bodies, like British Geriatrics Society and Centre of Perioperative care[87], Getting It Right First Time[341] and the American College of Surgeons publication

of ‘Optimal Resources for Geriatric Surgery’[342] have set out clear clinical guidelines and care pathways in the management of frail surgical patients. There is a call for these to be utilised in the development of geriatric-specific quality control and outcome indicators to then be made available for institutional registration with audit processes to allow benchmarking and continued development of existing programmes.[343, 344]

7.5.3 Strengths and limitations

This was a multi-centre mixed methods qualitative study with excellent recruitment from the majority of Scottish health boards, including all that provide a vascular surgery ‘hub’ service. Including all members of the clinical team caring for a vascular patient was a deliberate effort to capture frailty and its implications on a vascular service in the broadest sense. The broad inclusion and data collection method enables this study to recognise the far-reaching effects of frailty for all relevant care providers within vascular services. This may better inform policy makers and any subsequent implementation of frailty care programs for vascular patients in secondary care.

There was a large contribution from vascular surgeons, with data saturation felt to have been satisfactorily achieved. A role for expanding on the views of allied HCPs is identified, to accurately reflect the multidisciplinary care team that is required to provide holistic care for frail surgical patients. Where allied HCPs did take part, there was a self-described lack of confidence on the topic, reported to be due to inadequate training provision, which may have negatively impacted recruitment. The professional relationship that I had with some of the interviewees means some participants may have presumed a degree of shared knowledge, influencing the content of discussion. The effect of this was minimised through the use of the same standardised interview guide. Further, any subsequent unintentional bias in thematic analysis was mitigated through

independent coding and joint thematic analysis with an expert in qualitative methodology with no surgical background.

7.5.4 Conclusion

Vascular surgery HCPs recognise the importance of frailty in clinical practice. Assessment of frailty is primarily performed through subjective clinical assessment as part of any clinical interaction. A call was made for standardising the assessment of frailty primarily due to a multitude of positive implications this would bring to unifying disjointed services into the multidisciplinary collaborative approach frail patients require from health care services. Improved health outcomes, refining patient education/counselling and enhanced job satisfaction were implicated in this movement. The utility of a standardised frailty assessment in prognostication is disputed by surgeons due to concerns around how a population-based tool can replicate nuanced surgical decision-making. This study highlights the need for future research to be directed at identifying a standardised tool for service wide adoption, delineating the opinions stakeholders have on desired characteristics for such a tool as well as the need to validate this against the commonly utilised ‘end of bed’ test to infer test validity and encourage uptake in clinical practice.

Chapter 8 Discussion

8.1 Chapter summary

This chapter presents and discusses a summary of the findings of the work presented in this thesis. The findings for each research question are presented first, followed by a discussion of the strengths and limitations to this body of work. Thereafter, this chapter will discuss where the work in this thesis sits relative to current literature with implications for clinical practice. Following on from this will be a discussion on proposed areas for future research.

8.2 Summary of findings

With the work presented in this thesis I set out to explore the implications of frailty in vascular surgery patients, specifically examining methodological approaches to frailty assessment in research and clinical settings. I conducted a study to examine the feasibility of routine frailty assessment in a vascular outpatient setting. Additionally, my mixed-methods study was conducted to develop an understanding of observed discrepancies between the role of frailty assessment in research and clinical practice. It is reiterated that as the prognostic value of frailty assessment has been demonstrated previously, it was felt there would be no additional benefit to repeating this work in this thesis.

8.2.1 Research question 1: What are the methodological approaches to frailty assessment in vascular surgery related research.

Research question one was addressed through a two-part systematic review presented in Chapter 3. In the first systematic review (111 studies), I identified significant issues with heterogeneity in instrument selection, mode of data analysis and poor methodological description of tool application. This has generated disparate data which challenges data pooling for meta-analysis and weakens the evidence base for translation of research findings into clinical practice. To minimise data wastage and enhance research impact, I have made recommendations for standardising the application and reporting of frailty assessment both in research and clinical practice.

The second systematic review (11 studies) explored psychometric and clinimetric properties of commonly adopted frailty assessment instruments in surgical populations with the view to informing clinicians and policy makers. The most notable finding was the stark paucity of evidence in the vascular field. For this reason, I broadened the search syntax to encompass COSMIN assessment of frailty instruments used across any surgical population, not just vascular surgery. When

assessed, the majority of instruments (both frailty index and cumulative deficit model/person assessed) demonstrated acceptable psychometric and clinimetric properties when applied to surgical populations. However, due to the relative paucity in studies, and the included populations, I believe there is a role for further psychometric assessment of frailty instruments, particularly in middle-aged patients who may be living with early-onset frailty.

8.2.2 Research question 2: Can frailty assessment be implemented as part of routine care in clinical practice

There were three parts to this research question, expanded upon below, which the FAVOUR study addresses. The methodological approach to this study was presented in Chapter 4, and describes an approach to routine, prospective frailty assessment in a vascular urgent-referral ('hot') clinic using five different frailty assessment instruments: Clinical Frailty Scale (CFS, clinician- and patient-assessed), Initial Clinical Evaluation (ICE), Healthcare Improvement Scotland 'think frailty' FRAIL scale (HIS FRAIL), Frail nonDisabled questionnaire (FiND) and 11-item modified frailty index (mFI-11). In Chapter 5 and Chapter 6 I summarise clinimetric results as well as early (30-day and post-operative day 30) follow-up results respectively, evaluating and comparing each tool's prognostic value. An additional 1-year follow-up is planned for the FAVOUR study, however, the results are not available for inclusion in this thesis at the time of writing, and will instead be analysed and amalgamated with early results for journal publication at a later date.

8.2.2.1 Research question 2a: What is the feasibility of routinely measuring frailty in an outpatient setting.

The results presented in Chapter 5 address research question 2a. My results show that implementing routine frailty assessment in a vascular surgery outpatient setting is possible. Vascular surgery clinicians (consultant and trainees) can independently complete subjective and objective measures of frailty assessment

within seconds. In comparison, both researcher-applied and patient self-assessment take substantially longer. Further, most patients require assistance to complete self-assessments and would typically request help from their proxy if present (so proxy recruitment was discontinued). For this reason, frailty assessment when applied by vascular surgery clinicians is felt to be the superior mode of application in this setting. A key observation in this study was that patients were inclined to consider themselves more robust than clinician assessment would suggest. This has important implications when considering informed decision-making and realistic patient expectations. Introducing a standardised frailty assessment represents an opportunity to bridge discrepancies in patient/clinician expectations and improve patient's subjective experience of their healthcare journey.

8.2.2.2 Research question 2b: How do clinimetric properties of frailty assessment tools compare in prospective frailty assessment.

The results presented in Chapter 5 address research question 2b, a response to the identified paucity in psychometric and clinimetric evaluation of frailty assessment tools which I presented in Chapter 3. Compared to reference standard (clinician applied CFS), vascular surgeons initial clinical evaluation (ICE) demonstrated superior convergent validity, strength of agreement and correlation compared to the other frailty screening tools that were examined. An unconscious bias in clinician assessment was demonstrated in the observation that clinicians were more likely to consider female patients to be frail, which was not replicated in objective measures of assessment. Important psychometric and clinimetric considerations are also made. Firstly, the observation that mFI-11 correlated better with comorbidity measure CCI than the selected frailty assessment tools, supports the proposition that it is sooner a measure of comorbidity than frailty. The appropriateness of the mFI-11 being the most commonly used tool for assessing frailty in vascular research (as demonstrated in Chapter 3) is therefore questioned. Secondly, FiND did not correlate with well with frailty assessment instruments. The instrument is designed to identify and distinguish frailty from disability. However, the poor specificity and correlation with other frailty tools

raises the question if this might sooner be considered a measure of function only. The role of relying on phenotypic measures of frailty in a population with such a high prevalence of disability-inducing pathology, remains to be clarified (as discussed in Chapter 5 and Chapter 6). For this reason, based on the data presented in this thesis, and in acknowledging satisfactory psychometric and clinimetric properties, an argument is made to adopt the CFS assessment for prospective frailty screening vascular patients in an outpatient setting when applied by clinicians.

8.2.2.3 Research question 2c: How do the prognostic properties of frailty assessment compare in prospective frailty assessment.

The results presented in Chapter 6 address research question 2c. In prioritising studying the feasibility measures in FAVOUR, the results were limited by a moderate sample size and it is likely the study was underpowered for observing short-term outcomes. For this reason, no single frailty assessment tool was observed to hold greater prognostic value than another. However, the prevalence of frailty was observed to be high and although no statistical significance was observed, the presence of frailty assessment by clinician-assessed CFS, ICE and Healthcare Improvement Scotland (HIS) FRAIL instruments trended toward associations with increased risk of morbidity, mortality and longer hospital admissions. These results are in keeping with the well-recognised increased risk of morbidity and mortality that has consistently been demonstrated in vascular surgery patients living with frailty, as discussed in Chapter 2. Patients proceeding to surgical management of vascular pathology were more comorbid but the presence of frailty did not affect the mode of operative treatment (endovascular vs. open surgery). While this observation may suggest technical considerations for the treatment of vascular pathology takes precedence over 'host' factors, I discuss a proposed role for aggressive 'palliative' revascularisation (elaborated upon in Chapter 7) and how the availability of surgical versus endovascular skillset may have influenced these data in Chapter 6. This study therefore demonstrates the need to recognise frailty as a condition that has previously demonstrated clear

associations with worse perioperative outcomes (although not replicated in this study's early results) and tailor clinical care to mitigate these risks.

8.2.3 Research question 3: What are stakeholder's perception and utilisation of frailty assessments in a vascular surgery setting.

The work presented in Chapter 7 is designed to address research question 3. I conducted a mixed methods study to understand the perception and utilisation of frailty assessment in clinical practice by both vascular surgeons and allied healthcare professionals serving vascular patients. The study demonstrated that vascular surgeons acknowledged the clinical relevance of frailty in patient selection due to associations with worse health outcomes. However, an unfamiliarity and uncertainty over tool validity, born out of the abundance of heterogeneous instruments, has meant surgeons tend to prefer subjective measures of assessment. Further there was concern around the ability of population based tools to accurately replicate nuanced clinical decision-making. Ultimately, the introduction of a standardised frailty assessment was felt likely to have imprecise prognostic value, sooner identifying patients more generally as 'high risk' operative candidates. Conversely, non-surgical healthcare professionals considered frailty more holistically, considering nursing care requirements, functional needs and multifactorial discharge considerations. The critical finding in this study was the common recognition that frail vascular patients were at increased risk of morbidity and mortality and more could be done to mitigate these risks and improve outcomes. Key to this process is the universal call for standardising the approach to frailty assessment, less so for prognostic value, and primarily due to a multitude of positive implications this would bring to unifying disjointed services into the multidisciplinary collaborative approach frail patients require from health care services. There was an acknowledgement that standardisation in frailty assessment would preferably take the form of adopting a single instrument across all healthcare professionals and on an interdisciplinary level across adult specialities, accepting this would be associated with lower

levels of prognostic accuracy for the variety of pathologies and treatment options relevant to vascular surgery patients.

8.3 Strengths and limitations

Several strengths and limitations to the body of work presented in this thesis have been identified and have been presented in the discussion sections for each respective chapter. This section discusses general points across the body of work presented in this thesis.

Firstly, all original work presented in this thesis (including systematic review, prospective observational study and mixed-methods study) was conducted according to a pre-registered and/or published protocol which ensures transparency and credibility of the conducted work (see appendices). Further, pre-registration and/or publication of study protocols also enhances the reproducibility and integrity of all original work. This is further complimented by the inclusion of complete search syntax's for the systematic/literature reviews, comprehensive display of frailty assessment instruments and complete structured interview guide, where relevant. This will enable researchers to accurately replicate studies, thereby demonstrating research concordance, or more accurate comparisons between differing populations, where desired. Overall this will facilitate data pooling, increasing the strength of evidence that can be taken from generated data.

The adoption of binary age cut-offs (e.g., typically > 65 years) for diagnosing frailty may be considered a contentious issue. Authors of certain frailty assessment instruments commonly describe an instrument as validated only in an older population (including Clinical Frailty Scale, Edmonton Frail NonDisabled questionnaire, Critical Limb Ischaemia Frailty, Addenbrookes Vascular Frailty Score, FiND and Hospital Frailty Risk Score).[195-198, 345-347] The evidence produced by such age cut-offs will guide frailty-specific treatment pathways and therefore has implications for the general population accessing medical treatment. By discounting arbitrary age cut-offs, the work presented in this thesis demonstrates the prevalence of frailty across older as well as middle-aged patient

groups, producing evidence relevant to a vascular population. This should act positively in reducing inequity in healthcare access and provision. For academic rigour, it is important these tools are validated in middle-aged populations to confirm the validity of results and their interpretations/conclusions (elaborated upon in section 8.4.1).

There are limitations to the work that has been presented in this thesis. Firstly, I accepted broad and varying definitions of frailty when including studies in the systematic review with the view to summarise comprehensively current research and clinical practices. However, I noted a repeated area of discrepancy in authors' definitions of the relationship between frailty and sarcopenia. To ensure methodological consistency, the decision was made to exclude studies describing sarcopenia measurements as surrogate markers of frailty. As discussed in Chapter 2, sarcopenia and frailty are not mutually exclusive constructs, particularly in considering the phenotypic theory of frailty. For this reason, it may be argued that this exclusion criterion means the methodological approaches to frailty in research practice is incompletely summarised. A review comparing the clinical utility of frailty and sarcopenia in vascular patients demonstrated that radiologically diagnosed sarcopenia, in isolation, was not clinically useful. Whereas frailty demonstrated clear associations with worse outcomes.[83] The findings were limited by poor quality studies and few included studies using validated assessment tools (for frailty and sarcopenia alike). An updated review of this literature would be of clinical and academic interest.

The prospective observational study included participants attending a single-centre vascular 'hub' site which serves a catchment area that incorporates approximately 1.7 million patients, constituting one third of the Scottish population. Although the catchment area is comprehensive, the data from this study would benefit from corroboration through the recruitment of further hub site(s). Firstly, there are differences in the ethnic background of the Scottish

population with a smaller proportion of black and ethnic minorities compared to English or Welsh populations.[348, 349] Further, adjusted indices of multiple deprivation have also demonstrated differences in UK populations with greater levels of deprivation in Ireland and Wales but higher mortality rates in deprived areas in Scotland compared to English populations of similar deprivation index. Complementing the data generated from this study through study replication across additional tertiary centres caring for different patient demographics would enhance generalisability of the data, and research impact. A further limitation identified in the prospective observational study is the moderate sample size of recruited participants which negatively influences the confidence in statistical analysis of the data. Although recruitment of participants was good, the recruitment period was relatively short in order to achieve the primary aims of the study within the timescale of my research fellowship. Corroborating the findings by replicating the study in alternate vascular 'hub' centres would be of value.

Lastly, despite excellent recruitment to the mixed-methods study, a degree of selection bias may be observed in the disproportionately lower numbers of non-surgical health care professionals that were recruited. The observation that non-surgical HCPs report a self-described lack of confidence in their understanding, and utilisation, of frailty assessment, supports this argument.

8.4 Implications of findings

The implications of the individual components of work presented in this thesis have been discussed in each relevant chapter. This section will draw on key points made in this thesis and discuss them within the context of broader literature.

Progress has been made in the understanding of frailty as a heterogeneous, multifactorial and complex construct which has demonstrated clear associations with morbidity and mortality. Research advances in frailty have been compared to those made in oncological fields, creating defined categories toward its approach: 1) defining disease features for measurement, 2) understanding of pathophysiological mechanisms, and 3) developing disease-modifying interventions.[350] The work in this thesis addresses considerations relevant to the first point, namely developing an understanding of frailty measurement, with the view to better informing approaches to the latter points. A key message is defining the role of frailty assessment in vascular surgery practice. From the body of work presented in this thesis I propose migrating away from attempts to define prognostic accuracy for predicting surgical outcomes, as is favoured by clinicians and evidenced in frailty-related vascular research.[60, 61, 63] Instead, the primary role of frailty assessment may well lie in improving understanding and awareness of frailty and its implications. This will help to develop a framework against which patients can experience improved access to redirected multidisciplinary services with the view to ameliorate the well-recognised poor health outcomes.

The work presented in this thesis demonstrates the growth in frailty-related research interest has resulted in a growing number of frailty assessment instruments as well as increased variability in methodological application of such tools. A discordance between frailty theories (cumulative deficit model and phenotypic model), and the derivative assessment instruments, has also been demonstrated.[351, 352] In fact, an argument has been made that the phenotypic

model of frailty in fact represents only one avenue ('physical frailty'[353, 354]) of the multidomain nature of frailty and fails to consider similar frailty syndromes such as cognitive frailty[355], social frailty[356] and organ-specific frailty.[357] With most vascular patients presenting with mobility-limiting pathology (CLTI), this may represent a bias in assessment. Further, many instruments have been purposefully designed to meet the research interest of specific studies and have not been operationalised on larger populations.[358] Nevertheless, the ability of instruments based on either frailty theory to risk stratify frail populations in a general way is accepted, and has been explored and discussed within a vascular surgery population context earlier in this thesis. With this, some may argue the adaptation of a tool derived from either theory is suitable for population screening purposes.[353] However, different models of frailty, and associated assessment instruments, are likely to capture different groups of adults experiencing variable frailty pathways.[351, 352] Critics would therefore argue caution in adopting different assessment instruments in varying population subgroups where the clinical significance of such differences are typically poorly understood.[359] In a vascular surgery population, two specific considerations are identified which may affect frailty assessments: 1) the high prevalence of early-onset frailty in a middle-aged population, and 2) common vascular pathology is associated with impaired physical function.

Historically frailty would be considered a syndrome of old age. However, the observation of frailty in middle aged populations suggests that there may be pathological ageing mechanisms that takes place independently from chronological ageing. People living with early-onset and late-onset frailty have demonstrated significant differences in health deficit and demographic data. Multi-national population based studies demonstrate patients living with early-onset frailty are more likely to score worse in mental well-being, pain scores and immunological domains. This is compared to patients living with late-life frailty, who score worse in sensory, cardiometabolic, musculoskeletal and cancer health domains.[360] A link with socioeconomic deprivation in early-onset frailty has also been demonstrated, with significant associations with low education and

occupation levels in young people living with frailty which was not replicated in older patients with frailty. In general surgery populations, early-onset frailty is associated with comorbidity, polypharmacy, cognitive impairment and social deprivation, whereas late-onset frailty is only significantly associated with increasing age.[361, 362] The observed differences between patients living with early-onset compared to late-onset frailty may imply different underlying pathological mechanisms that culminate in similarly reduced homeostatic reserves and poor health outcomes from heterogeneous aetiological risk factors. Despite these differences, frailty retains its value as a marker of poor prognosis irrespective of age. Improved understanding of these proposed different pathological mechanisms observed in different demographic groups is likely to benefit approaches to its assessment, which will similarly guide tailored approaches to syndrome modification. It is unlikely that a blanket approach to its prevention and/or treatment will be successful, emphasising the need for dedicated specialist input to provide patient-centred personalised care plans. With this in mind, the role of arbitrary age cut-offs in frailty screening to access relevant services should be reconsidered. Current British Geriatrics Society's (BGS) "Fit for Frailty" (2015) recommendations state only older adults (aged > 75 years) should be assessed for the presence of frailty during all clinical encounters.[363] It is also common practice that established liaison geriatric services describe an arbitrary minimum age cut-off (typically > 65 years) which patients must achieve prior to accessing services.[364] This may, in part, be due to a relative paucity in research practice where no tool has been validated exclusively in younger (aged < 60 years) populations.[346] In considering the observed early-onset frailty in this patient population, and the 5-year all-cause mortality for patients diagnosed with CLTI being 50%, a substantial proportion of vascular patients will never reach the minimum age requirements to benefit from much needed care.[365] Therefore, a role for formally validating frailty assessment tools in middle aged populations (for all medical specialities) is identified.

Secondly, the work presented in this thesis demonstrates that a significant proportion of the clinical workload for vascular surgeons is made up of patients presenting with signs and symptoms of end stage peripheral arterial disease of the lower limb. This is typically chronic limb threatening ischaemia but the growing obesity epidemic and secondary diabetes mellitus is driving a rise in microvascular complications and diabetic foot emergencies.[366] Incidentally, it has also been observed that diabetic related morbidity is associated with an accelerated ageing process and increased risk of frailty.[367-369] Both pathologies are associated with significant impairment in physical function which presents inherent considerations in frailty assessments if intending on relying solely on phenotypic measurements, producing a high prevalence of frailty. This differs from population studies. When comparing frailty assessment instruments based on phenotypic measurements of frailty with cumulative deficit models, differences in correlation have been observed when applied to different populations. The greatest agreement between mode of assessment is observed when applying assessments to older patients (aged > 80 years) with high prevalences of comorbidity and functional impairment.[359] Conversely, discordance is greatest in middle-aged patients with significant comorbidity. This confounds the age-associated health deficit and demographic differences discussed previously. Patients with early-onset frailty are more likely to be diagnosed as frail when applying a frailty index, but not phenotypic measurement, of frailty. This suggests young frail patients typically experience multimorbidity but retain physical resilience and independence. The degree to which the functional impairment observed in common vascular pathology correlates to or influences the onset and/or progression of frailty, may prove difficult to differentiate and indeed more could be done to elucidate this relationship. This is particularly relevant when considering the aforementioned “Fit for Frailty” guidelines which recommend phenotypic measures of frailty for screening older adults (aged > 75 years) during any clinical encounter, including: ‘gait speed’[370], ‘timed-up-and-go’[371] or the ‘Program of Research to Integrate Services for the Maintenance of Autonomy (PRISMA-7)’[372] questionnaire.[363]

Frailty should not be considered an inevitable part of the ageing process, as measures can be taken to deter, delay, or reverse, its onset.[373] Geroscience, describes a scientific field designed to enhance understanding of the intersection between health, the biology of ageing and chronic disease.[374] This is with the view to inform methods for prevention and/or treatment of health deficits. Complimenting this is the salutogenic promotion of healthy ageing for improved health quality and independent living in older age.[375] Salutogenic models have demonstrated intrinsic and extrinsic factors supporting human well-being and health, such as being part of a supportive social networks, high levels of education and socioeconomic demographics and engaging with leisure activities.[376] Developing an understanding of the interaction between salutogenic factors and methods for optimising health domain deficits stands to produce substantial advances in frailty management on a population level. This should be a public health priority as part of promoting healthy living for both chronologically and biologically older adults as the primary consumers of health and social care services.[377] Defining an agreed approach to frailty identification represents a key component of this process.

Frailty is multifactorial and multifaceted and so any approach to identification and/or treatment should be multimodal to reflect this. It feels appropriate to suggest that within a vascular ecosystem patients living with frailty are identified and subjected to a structured, multi-step service model beginning with a standardised approach to case identification. This would feed into comprehensive evaluation by an appropriately trained individual to identify and quantify frailty-related domains. After quantification, measures would then be taken to optimise identified deficits through the recruitment of relevant HCPs through formalised service pathways with interested HCPs working a job plan with sessions dedicated toward frailty-service care provision. For patients managed operatively this would include peri- and post-operative management plans which may or not be protocolised to encourage understanding and adherence. This could be likened to the Enhanced Recovery After Surgery (ERAS) which describes a care pathway including evidence-based items designed to reduce perioperative stress, maintain

perioperative physiological function and accelerate recovery from surgery.[378] As part of facilitating an expedited and supportive discharge process, such a frailty pathway would ideally benefit from direct links with community medical and social services with continued follow-up, ensuring continual optimisation and promotion of healthy ageing. To reflect the nature of vascular surgery services, both elective and unplanned patients must be able to access such a services as exposure to frailty-sensitive care pathways has demonstrated benefits in both circumstances, as discussed earlier in this thesis. The application of a standardised frailty screening tool could in theory be applied during any patient contact (e.g., routine outpatient clinic or post emergency surgery), and by any HCP. Identified patients would then be enrolled in the frailty care pathway at any point relevant to their care. Frailty services should run in parallel, complimenting surgical care and reflect a collaborative ethos. For inpatients this may consist of joint-care exhibited in weekly multidisciplinary ward rounds for selected patients and/or multidisciplinary team meetings. Outpatient care may be best served by the development of geriatrician-led outpatient surgical clinic for frail patients to attend, to plan perioperative optimisation, or for continued patient-centred care where surgical management may not be deemed appropriate. A graphical representation of such a proposed service model is presented in Figure 8.1.

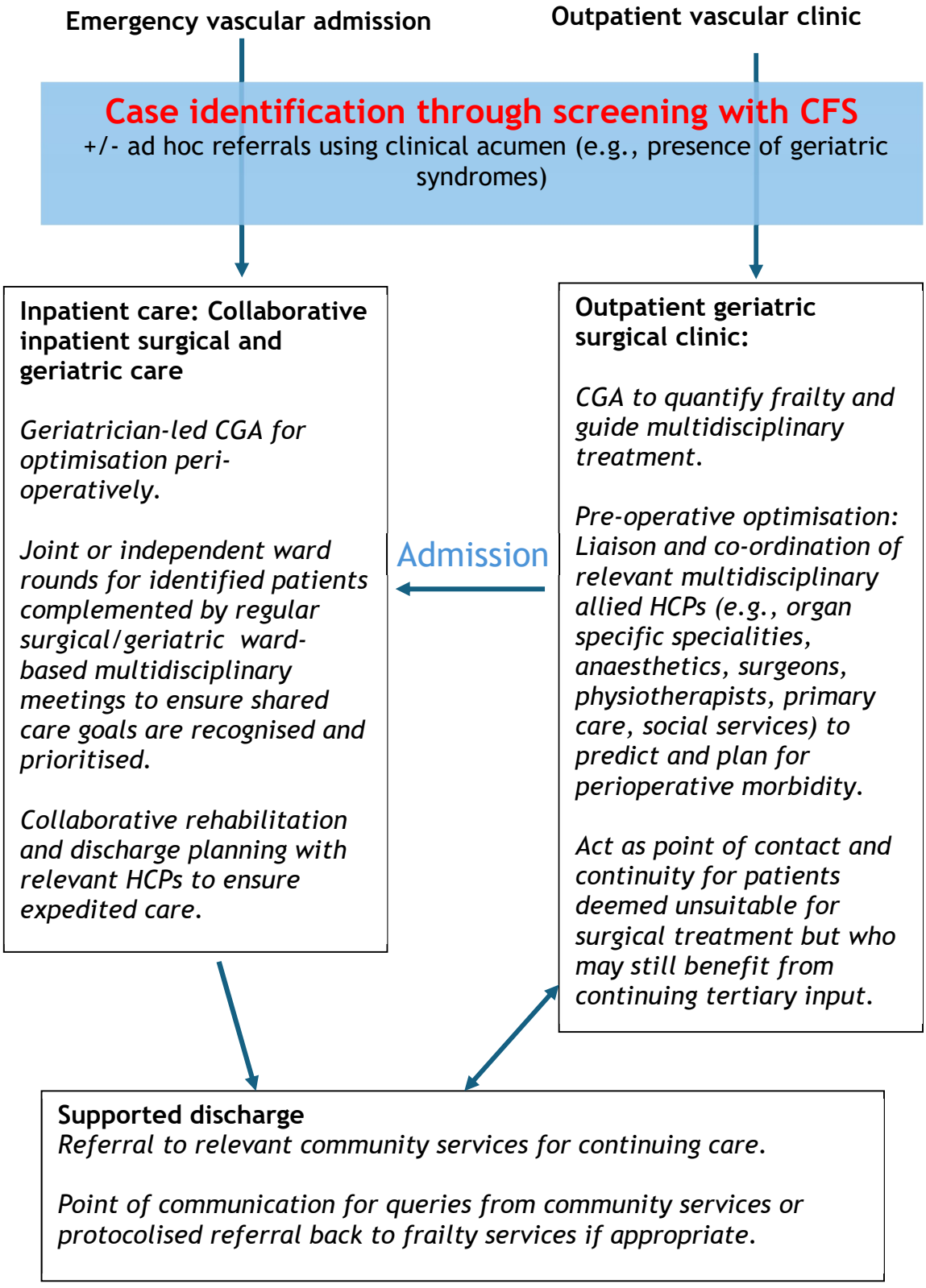


Figure 8.1 - A theoretical model of a collaborative vascular-geriatric frailty service model. Modified from www.popsolderpeople.org/about.[379]

Although not specific to vascular surgery, a service similar to the aforementioned model has been successfully set-up and delivered in the Guys and St Thomas NHS Trust, coined the "Perioperative Care for Older People undergoing Surgery Network (POPS).[380] This is a geriatrician-led service aimed at improving outcomes for surgical patients through the application of the comprehensive geriatric assessment (CGA) to identify areas for improvement from which a multidisciplinary care team can be coordinated to deliver patient-centred, frailty-centric care.

In contrast to the rapidly applied tools preferred by surgeons in this study, the comprehensive geriatric assessment (CGA) is the cornerstone to modern geriatric care and consists of a multidimensional and holistic framework against which geriatricians assess patients and address frailty issues.[381] The comprehensive nature of such an assessment is time consuming, taking upward of two hours, and for maximal benefit should be applied by appropriately trained individuals.[86, 382] Attempts have been made to introduce a shorter CGA-toolkit for application by surgeons in secondary care. Unfortunately, despite initial enthusiasm, the aims of the toolkit were not achieved due to divergent views on professional domains and a desire by surgeons for continued geriatrician support as part of service improvement which was complicated by competing professional priorities.[331] This reiterates the importance of continued interdisciplinary collaboration as part of respecting professional duties and continued job role satisfaction.

To safeguard a resource intensive service as part of service development, a two-stage system is proposed: a] early frailty-screening using a standardised assessment tool for HCPs to easily and consistently identify frail patients followed by b] escalation to collaborative multidisciplinary services spearheaded by a geriatrician for CGA. Examples of successful models have been presented in Chapter 2, Figure 2.7. Despite the growth in geriatric-surgical care models, there remains considerable variation in access across the UK.[383] The structure of

various collaborative approaches will differ between healthcare establishments and so the accumulation of dedicated cost-efficiency data as well as the dissemination of experiential knowledge and collaboration with commissioners is sought after to support the continued growth of such services. Where collaborative services have been established, it is worth noting that a minority receive funding from a surgical directorate, suggesting more could be done to improve awareness of the role for geriatric input across surgical boards.[262, 384]

Chapter 2 has explored challenges in achieving perioperative optimisation for vascular patients, primarily born out of time-sensitive pathology and time-restricted guidelines.[4] Despite these challenges, examples of successful alignment of services exist, producing a strong business case for involving geriatricians in the care of vascular and surgical patients in a formalised and structured manner.[16, 18-20] However, the roll-out of such a service across NHS trusts has been challenging.[337] In an attempt to mitigate challenges, a trimodal approach to rolling out POPS services across the UK has been made available, which includes: 1) POPS toolkit, a free-to-access compilation of useful resources to help set up a service, 2) Expert coaching, and 3) Assisting services with the identification of measurements for improvement.[385] In practice, the constituent parts and daily functioning of frailty services will differ between health care services depending on available resources and established practices. However, standardising the diagnostic tool, and language, around frailty will help bring clarity to clinicians and policymakers, helping to unify fragmented services and improve outcomes for frail patients.

An abundance of frailty tools and variable guidelines may generate clinician uncertainty when exploring frailty assessment instruments and considering implementing them in practice. However, the number, and variability, in available instruments also acts as a representation of the heterogeneity of the syndrome and a testament to the versatility of assessment instruments. Ultimately, the

decision to adopt one tool over another should be based on a thorough understanding of the intended benefit of the assessment, population requirements and an understanding of what differing frailty assessment instruments offer. The proposed clinical and managerial benefits to standardising frailty assessments in vascular surgery have been discussed in Chapter 7. Based on available literature, current policy, psychometric and clinimetric evaluation and primary studies presented in this thesis, I recommend the CFS is considered for adoption by vascular surgery services for screening purposes to identify vulnerable patients who are felt to potentially benefit from collaborative frailty services. In this vein, formal validation of the psychometric properties of the CFS when applied to younger populations (aged < 65 years) is of clinical and research interest.[347]

8.4.1 Directions for future work

Areas for further work have been identified and discussed throughout each chapters in this thesis. Some of which have been addressed by parts of the work conducted in this thesis. This section summarises three outstanding areas that I have identified for future research.

Firstly, improving the understanding of aetiological risk factors and pathological mechanisms observed in early-onset compared to late-onset frailty. This is likely achieved through large epidemiological observational studies exploring intrinsic and extrinsic mechanisms such as genetic predisposition, social and environmental exposures as well as behavioural risk factors. An improved understanding of underlying mechanisms will inform approaches to case identification and syndrome modification.

Secondly, there is a key requirement for validating frailty assessment tools in middle aged populations through large scale psychometric studies. A direct comparison of psychometric properties when applied to middle-aged (i.e., age < 65 years) compared to older adults (i.e., aged > 65 years) will be particularly relevant for updating healthcare policies. This work should include comparisons of tools that are designed based on differing theories of frailty (cumulative deficit and frailty phenotype). To maximise applicability of results, such studies should ideally be applied to large populations. Where this cannot be achieved, the publication of detailed methodological processes should be encouraged to enable study replication and enhance research impact. This will contribute toward updating policies and guidelines, encouraging access to appropriately designed health services.

Lastly, the degree to which the functional impairment observed in common vascular pathology correlates to or influences the onset and/or progression of frailty remains uncertain. A role is identified for direct comparisons of tools designed to assess disability to tools used to assess frailty (particularly according to phenotypic measurements), as part of exploring this relationship in patients with mobility-limiting pathology. This should be complimented with long-term observational studies with pre-specified outcome measures to understand the clinical significance of measured constructs.

8.5 Conclusion

Frailty is a complex, multifactorial syndrome associated with significant morbidity and mortality and appears to be over-represented in the vascular surgery population, particularly in middle-aged adults. There is substantial heterogeneity in approaches to frailty assessment in clinical and research practice which may be associated with variable diagnostic and prognostic accuracy which introduces considerable implications to clinical and service planning. The prognostic accuracy of a considerable number of frailty assessment tools have been demonstrated in research fields, and have been accepted by vascular surgery healthcare professionals. However, vascular HCPs identify a greater purpose for frailty assessment in clinical practice. This includes the implementation of standardised frailty assessments in clinical practice to guide unification of language, awareness of a growing problem and to redirect the attention and priorities of multidisciplinary services toward a common purpose with the view to improving health care delivery and improving outcomes for this vulnerable patient group. As part of achieving shared care goals, a deepened understanding of early-onset frailty and the interplay with mobility-limiting pathology, particularly in considering frailty phenotypically, is recommended.

Chapter 9 References

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Supplementary materials

Appendix 1: Supplementary material for Chapter 2 and 3: Search syntaxes for literature and systematic review.

PubMed syntax, performed 11/08/22

Search number	Query	Filters	Results
1	(frail*) OR (pre-frail) OR (prefrail) OR (sarcopenia) OR (Rockwood) OR (geriatric syndrome) OR (Fried) OR (geriatric assessment) OR (Clinical frailty scale)		109,549
2	(Vascular Surgical procedures) OR (axillofemoral bypass grafting) OR (embolectomy) OR (thrombectomy) OR (vascular surg*) OR (bypass graft*) OR (Vascular graft*) OR (stent*) OR (atherectomy*) OR (lower limb amputation*) OR (lower extremity amputation*) OR (leg amputation*) OR (embolectomy*) OR (thrombectomy*) OR (revasculariz*) OR (revascularis*) OR (peripheral vascular intervention*) OR (aorto-femoral bypass*) OR (aortofemoral bypass*) OR (aorto-iliac bypass*) OR (aortoiliac bypass*) OR (axillo-femoral bypass*) OR (axillofemoral bypass*) OR (femoro-femoral bypass*) OR (femorofemoral bypass*) OR (femoral bypass*) OR (femoro-popliteal bypass*) OR (femoropopliteal bypass*) OR (femoro-popliteal-tibial bypass*) OR (femoro-tibial bypass*) OR (crural bypass*)		814,587
3	femorotibial bypass* or distal bypass* or infrainguinal bypass* or profundoplast* or obturator bypass* or percutaneous transluminal angioplasty or PTA or angioplast* or percutaneous vascular intervention* or endovasc*		185,587
4	carotid endarterectomy or carotid artery endarterectomy or carotid artery stent* or transcarotid*		23,283
5	abdominal aortic aneurysm* or aorto-bifemoral bypass graft or aortobifemoral bypass graft or aorto-bifemoral bypass or aortobifemoral bypass or EVAR or tEVAR or fEVAR or endovascular aneurysm repair* or thoracic endovascular aneursym repair or fenestrated endovascular aneurysm repair		
6	Mesenteric or SMA or mesenteric isch*		43,248
7	#2 OR #3 OR #4 OR #5 OR #6		934,186
8	#1 AND #7		2,626
9	#1 AND #7 Filters: English, Humans		2,085

Embase syntax <1996 to 2022 Week 31>

#	Query	Results
1	frail elderly/ or Edmonton Frail Scale/ or frail*.mp	52435
2	prefrail.mp. or frailty/	20946
3	pre-frail.mp	1702
4	sarcopenia/	16687
5	geriatric disorder/	5264
6	geriatric assessment/	18823
7	geriatric syndrome.mp	1310
8	rockwood.mp	1137
9	Clinical Frailty Scale/	837
10	(frail* adj3 (index* or phenotype* or assess* or instrument* or measure* or scale* indice* or score*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	12289
11	(fried* adj4 (frail* or index* or phenotype*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	2188
12	(Vascular Surgical procedures or axillofemoral bypass grafting or embolectomy or thrombectomy or vascular surg* or bypass graft* or vascular graft* or stent* or atherectomy* or lower limb amputation* or lower extremity amputation* or leg amputation* or embolectomy* or thrombectomy* or revascular iz* or revascularis* or peripheral vascular intervention* or aorto-femoral bypass* or aortofemoral bypass* or aorto-iliac bypass* or aortoiliac bypass* or axillo-femoral bypass* or axillofemoral bypass* or femoro-femoral bypass* or femorofemoral bypass* or femoral bypass* or femoro-popliteal bypass* or femoropopliteal bypass* or femoro-popliteal-tibial bypass* or femoro-tibial bypass* or crural bypass*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	453067
13	(femorotibial bypass* or distal bypass* or infrainguinal bypass* or profundoplast* or obturator bypass* or percutaneous transluminal angioplasty or PTA or angioplast* or percutaneous vascular intervention* or endovasc*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	190260
14	(carotid endarterectomy or carotid artery endarterectomy or carotid artery stent* or transcarotid*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword	25311

	heading word, floating subheading word, candidate term word]	
15	(abdominal aortic aneurysm* or aorto-bifemoral bypass graft or aortobifemoral bypass graft or aorto-bifemoral bypass or aortobifemoral bypass or EVAR or tEVAR or fEVAR or endovascular aneurysm repair* or thoracic endovascular aneursym repair or fenestrated endovascular aneurysm repair).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	40854
16	(mesenteric or SMA or mesenteric isch*).mp	100619
17	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	85224
18	12 or 13 or 14 or 15 or 16	651924
19	17 and 18	2157
20	limit 18 to (human and english language)	2046

CINAHL syntax - Monday, August 15, 2022

#	Query	Limiters/Expanders	Last Run Via	Results
S9	S1 AND S7	Expanders - Apply equivalent subjects Narrow by Language: - english Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	379
S8	S1 AND S7	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	385
S7	S2 OR S3 OR S4 OR S5 OR S6	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	111,443
S6	Mesenteric or SMA or mesenteric isch*	Expanders - Apply equivalent subjects	Interface - EBSCOhost	8,612

		Search modes - Boolean/Phrase	Research Databases Search Screen - Advanced Search Database - CINAHL	
S5	abdominal aortic aneurysm* or aorto-bifemoral bypass graft or aortobifemoral bypass graft or aorto-bifemoral bypass or aortobifemoral bypass or EVAR or tEVAR or fEVAR or endovascular aneurysm repair* or thoracic endovascular aneursym repair or fenestrated endovascular aneurysm repair	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	6,303
S4	carotid endarterectomy or carotid artery endarterectomy or carotid artery stent* or transcarotid*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,877
S3	femorotibial bypass* or distal bypass* or infrainguinal bypass* or profundoplast* or obturator bypass* or percutaneous transluminal angioplasty or PTA or angioplast* or percutaneous vascular intervention* or endovasc*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	34,702
S2	(Vascular Surgical procedures) OR (axillofemoral bypass grafting) OR (embolectomy) OR (thrombectomy) OR (vascular surg*) OR (bypass graft*) OR (Vascular graft*) OR (stent*) OR (atherectomy*) OR (lower limb amputation*) OR (lower extremity amputation*) OR (leg	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	81,757

	amputation*) OR (embolectomy*) OR (thrombectomy*) OR (revascular iz*) OR (revascularis*) OR (peripheral vascular intervention*) OR (aorto-femoral bypass*) OR (aortofemoral bypass*) OR (aorto-iliac bypass*) OR (aortoiliac bypass*) OR (axillo-femoral bypass*) OR (axillofemoral bypass*) OR (femoro-femoral bypass*) OR (femorofemoral bypass*) OR (femoral bypass*) OR (femoro-popliteal bypass*) OR (femoropopliteal bypass*) OR (femoro-popliteal-tibial bypass*) OR (femoro-tibial bypass*) OR (crural bypass*)			
S1	(frail*) OR (pre-frail) OR (prefrail) OR (sarcopenia) OR (Rockwood) OR (geriatric syndrome) OR (Fried) OR (geriatric assessment) OR (Clinical frailty scale)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	45,117

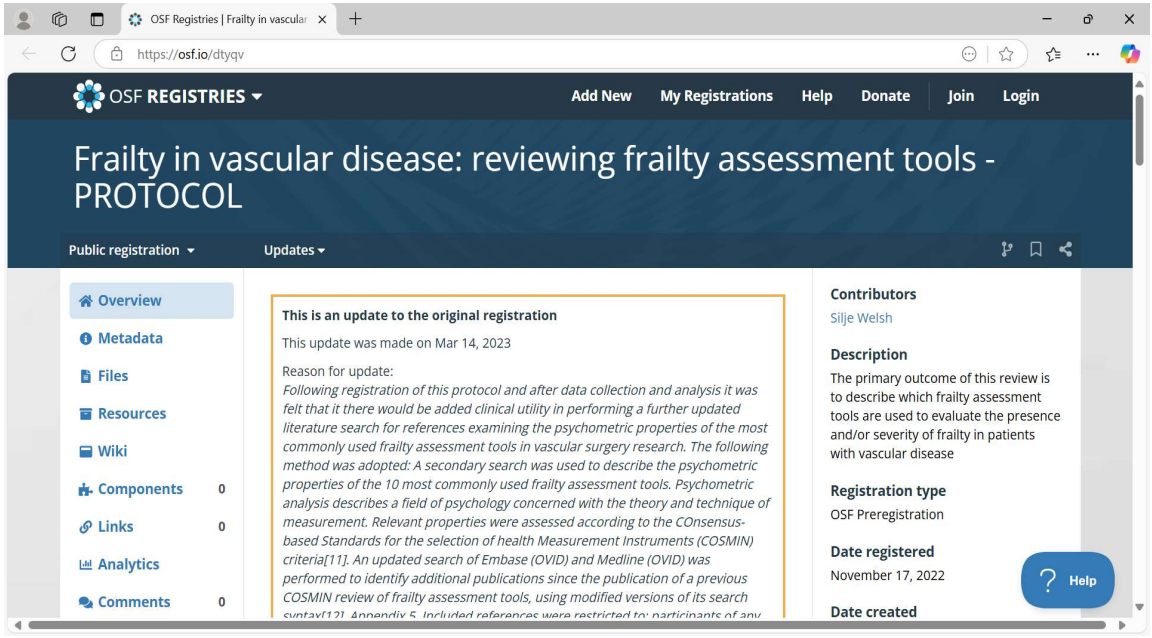
Ovid MEDLINE(R) <1946 to August Week 1 2022>

1	Frail Elderly/ or Frailty/ or Geriatric Assessment/ or frail*.mp	56333
2	prefrail.mp	562
3	pre-frail.mp	829
4	Sarcopenia/	7821
5	geriatric syndrome.mp	673
6	rockwood.mp	515
7	(frail* adj3 (index* or phenotype* or assess* or instrument* or measure* or scale* indice* or score*)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	6024
8	(fried* adj4 (frail* or index* or phenotype*)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading	1050

	word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	
9	(Vascular Surgical procedures or axillofemoral bypass grafting or embolectomy or thrombectomy or vascular surg* or bypass graft* or vascular graft* or stent* or atherectomy* or lower limb amputation* or lower extremity amputation* or leg amputation* or embolectomy* or thrombectomy* or revascular iz* or revascularis* or peripheral vascular intervention* or aorto-femoral bypass* or aortofemoral bypass* or aorto-iliac bypass* or aortoiliac bypass* or axillo-femoral bypass* or axillofemoral bypass* or femoro-femoral bypass* or femorofemoral bypass* or femoral bypass* or femoro-popliteal bypass* or femoropopliteal bypass* or femoro-popliteal-tibial bypass* or femoro-tibial bypass* or crural bypass*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	258186
10	(femorotibial bypass* or distal bypass* or infrainguinal bypass* or profundoplast* or obturator bypass* or percutaneous transluminal angioplasty or PTA or angioplast* or percutaneous vascular intervention* or endovasc*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	134536
11	(carotid endarterectomy or carotid artery endarterectomy or carotid artery stent* or transcarotid*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	12552
12	(abdominal aortic aneurysm* or aorto-bifemoral bypass graft or aortobifemoral bypass graft or aorto-bifemoral bypass or aortobifemoral bypass or EVAR or tEVAR or fEVAR or endovascular aneurysm repair* or thoracic endovascular aneursym repair or fenestrated endovascular aneurysm repair).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	23284
13	(mesenteric or SMA or mesenteric isch*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	77276
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	63089

15	9 or 10 or 11 or 12 or 13	413349
16	14 and 15	898
17	limit 16 to (english language and humans)	847

Appendix 2: Supplementary material for Chapter 3: Systematic review protocol registration (OSF Registries | Frailty in vascular disease: reviewing frailty assessment tools - PROTOCOL).



Evidence of pre-registered protocol with time-stamped amendment. Please follow URL to view the entire document.

Appendix 3: Supplementary material for Chapter 3: Comprehensive taxonomy of COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) definitions. Table as presented in www.cosmin.nl, date accessed: 14/03/2035.

COSMIN definitions of domains, measurement properties, and aspects of measurement properties

Term			Definition
Domain	Measurement property	Aspect of a measurement property	
Reliability			The degree to which the measurement is free from measurement error
Reliability (extended definition)			The extent to which scores for patients who have not changed are the same for repeated measurement under several conditions: e.g. using different sets of items from the same health related-patient reported outcomes (HR-PRO) (internal consistency); over time (test-retest); by different persons on the same occasion (inter-rater); or by the same persons (i.e. raters or responders) on different occasions (intra-rater)
	Internal consistency		The degree of the interrelatedness among the items
	Reliability		The proportion of the total variance in the measurements which is due to 'true'† differences between patients
	Measurement error		The systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured
Validity			The degree to which an HR-PRO instrument measures the construct(s) it purports to measure
	Content validity		The degree to which the content of an HR-PRO instrument is an adequate reflection of the construct to be measured
		Face validity	The degree to which (the items of) an HR-PRO instrument indeed looks as though they are an adequate reflection of the construct to be measured
	Construct validity		The degree to which the scores of an HR-PRO instrument are consistent with hypotheses *(for instance with regard to internal relationships, relationships to scores of other instruments, or differences between relevant groups)* based on the assumption that the HR-PRO instrument validly measures the construct to be measured
		Structural validity	The degree to which the scores of an HR-PRO instrument are an adequate reflection of the dimensionality of the construct to be measured
		Hypotheses testing	Idem construct validity
		Cross-cultural validity	The degree to which the performance of the items on a translated or culturally adapted HR-PRO instrument are an adequate reflection of the performance of the items of the original version of the HR-PRO instrument
	Criterion validity		The degree to which the scores of an HR-PRO instrument are an adequate reflection of a 'gold standard'
Responsiveness			The ability of an HR-PRO instrument to detect change over time in the construct to be measured
	Responsiveness		Idem responsiveness
Interpretability*			Interpretability is the degree to which one can assign qualitative meaning - that is, clinical or commonly understood connotations – to an instrument's quantitative scores or change in scores

† *The word 'true' must be seen in the context of the CTT, which states that any observation is composed of two components – a true score and error associated with the observation. 'True' is the average score that would be obtained if the scale were given an infinite number of times. It refers only to the consistency of the score, and not to its accuracy (ref Streiner & Norman)*
* *Interpretability is not considered a measurement property, but an important characteristic of a measurement instrument*

Appendix 4: Supplementary material for Chapter 3: Search syntax for second (COSMIN) systematic review. Search performed on 21/02/2023 on OVID (medline + embase).

1	(psychometric* or "validation studies" or clinimetric* or "internal consistency" or "predictive value" or sensitivity or questionnaire or assessment or evaluation or "self-reported" or "self-report" or validity).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	12121226
2	(frail* adj3 (index or scale or score or questionnaire)).m_titl.	2769
3	"Risk analysis index".m_titl.	56
4	2 or 3	2796
5	1 and 4	2124
6	Limit 5 to (English language and humans and year="2019-Current")	1307
7	Deduplicate	870

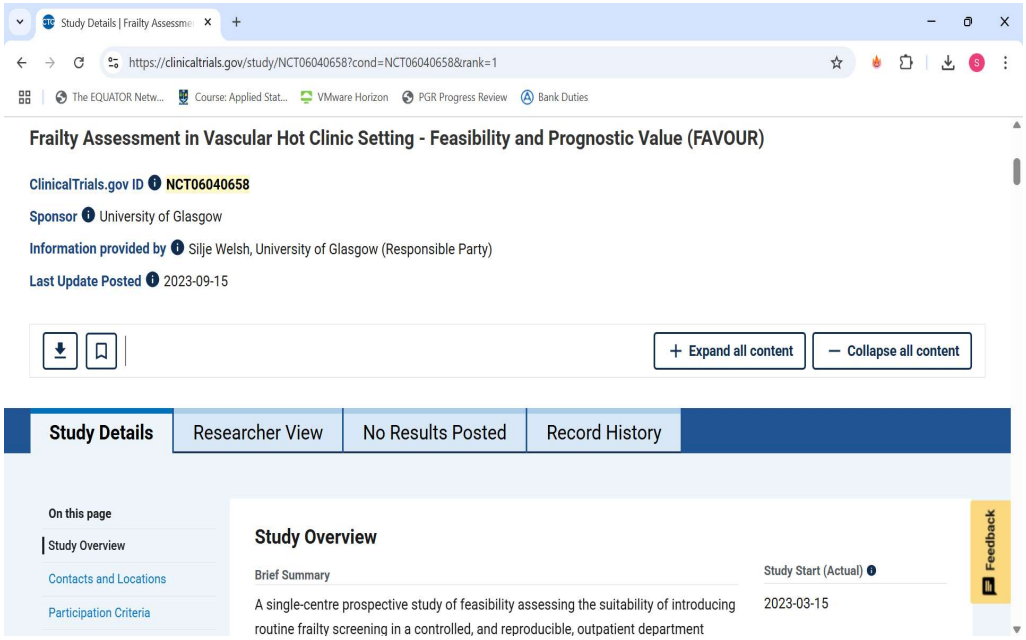
Appendix 5: Supplementary material for Chapter 3: Complete list of all Risk Analysis Index tools (RAI) identified in the first systematic review

Tool used to assess frailty	Number of assessments	Number using standard tool	Modified version	Not described
RAI Risk Analysis Index (RAI-C)*	1	1		
RAI Risk Analysis Index (RAI-A)[$]	5	5		
RAI Revised Risk Analysis Index (RAI-Rev) (includes RAI-P/RAI-PC)[£]	6	2	4	
RAI VQI-derived Risk Analysis Index (VQI-RAI)[#]	3	3		
RAI Risk Analysis Index (unspecified)	2	0		2
TOTAL RAI	17	11	4	2

*RAI-C: 14 point prospective patient-completed questionnaire. 11 variables and 2 statistical interactions, scoring from 0 - 81. Set up on a veteran population database (92% male). Predicts 30-, 180- and 365- day mortality. [$]RAI-A: 11-point variable retrospective collection of data in Veterans Affairs Surgical Quality Improvement Program (VASQIP) designed in a way to mirror the RAI-C, scored 0 - 81. [£]RAI-Rev: Recalibrated RAI-A to American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database which includes females with improved predictive values, scored 0 – 81. [#]VQI-RAI: Adjusted RAI-A to suit the Society of Vascular Surgery Patient Safety Organization Vascular Quality Initiative (SVS-PSO VQI), by amending some defined variables, including changing 'shortness of breath' to 'chronic obstructive pulmonary disease' and excluding cancer status as the VQI database was reported not to record this.

.

Appendix 6: Supplementary material for Chapter 4: Frailty Assessment in Vascular Outpatient Review (FAVOUR) study registration.



Evidence of FAVOUR study registration on ClinicTrials.gov. For full document, please refer to URL: https://clinicaltrials.gov/study/NCT06040658?cond=NCT06040658&rank=1

London - Riverside Research Ethics Committee
Ground Floor
Temple Quay House
2 The Square
Bristol
BS1 6PN

Telephone: 020 7104 8150

23 February 2023

Dr Terry Quinn
2nd Floor, Lister Building
Glasgow Royal Infirmary
84 Castle Street
G4 0SF

Dear Dr Quinn

Study title:	**Frailty Assessment in Vascular OUtpatients Review (FAVOUR Trial) – comparing feasibility and prognostic value of commonly used assessments.**
REC reference:	**23/PR/0062**
Protocol number:	**n/a**
IRAS project ID:	**322086**

Thank you for your letter of 22 February 2023, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved on behalf of the PR sub-committee.

Confirmation of ethical opinion
On behalf of the Research Ethics Committee (REC), I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Good practice principles and responsibilities
The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants

4. sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as:

- clinical trial of an investigational medicinal product
- clinical investigation or other study of a medical device
- combined trial of an investigational medicinal product and an investigational medical device
- other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.

Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by the HRA (for more information on registration and requesting a deferral see: Research registration and research project identifiers).

If you have not already included registration details in your IRAS application form you should notify the REC of the registration details as soon as possible.

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-sum maries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements
The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites
The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents
The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Covering letter on headed paper [REC cover letter]	1	13 February 2023
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance]	1	20 July 2022
IRAS Application Form [IRAS_Form_22022023]		22 February 2023
IRAS Application Form XML file [IRAS_Form_22022023]		22 February 2023
IRAS Checklist XML [Checklist_22022023]		22 February 2023
Non-validated questionnaire [Patient CRF]	1.1	16 December 2022
Non-validated questionnaire [Proxy CRF]	1.1	16 December 2022
Non-validated questionnaire [Clinician CRF]	1.1	21 December 2022
Non-validated questionnaire [Researcher CRF]	1.1	21 December 2022
Other [REC response letter]	1	13 February 2023
Participant consent form [Patient consent form]	1.2	10 January 2023
Participant consent form [Proxy consent form]	1.2	10 January 2023
Participant consent form [Clinician consent form]	1.2	10 January 2023
Participant information sheet (PIS) [Patient PIS clean]	1.3	13 February 2023
Participant information sheet (PIS) [Patient PIS tracked]	1.3	13 February 2023
Participant information sheet (PIS) [Proxy PIS Clean]	1.3	13 February 2023
Participant information sheet (PIS) [Proxy PIS Tracked]	1.3	13 February 2023
Participant information sheet (PIS) [Clinician PIS clean]	1.3	13 February 2023
Participant information sheet (PIS) [Clinician PIS tracked]	1.3	13 February 2023
Research protocol or project proposal [Protocol]	1.3	16 February 2023
Summary CV for Chief Investigator (CI) [CV template TJ Quinn2022]	1	04 January 2023
Summary CV for student [Student CV]	1.0	25 October 2022
Summary CV for supervisor (student research) [Supervisor CV]	1	04 January 2023
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Gantt Chart]	1.1	21 December 2022

Validated questionnaire [Clavien-Dindo Classification]	1.0	21 December 2022
Validated questionnaire [11-mFI]	1.0	21 December 2022
Validated questionnaire [HIS Frailty questionnaire]	1.0	21 December 2022
Validated questionnaire [Rockwood's CFS Questionnaire]	1.0	21 December 2022
Validated questionnaire [FiND questionnaire]	1.0	21 December 2022

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:
https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 322086	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Matthew Hyde Chair

PP Dan Pygall Approvals Specialist

Email: riverside.rec@hra.nhs.uk

Enclosures: **After ethical review guidance for sponsors and investigators – Non CTIMP Standard Conditions of Approval]**

Copy to: Dr Colette Montgomery Sardar

Appendix 7: Supplementary material for Chapter 4: Example of FAVOUR 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.** ☐
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. ☐

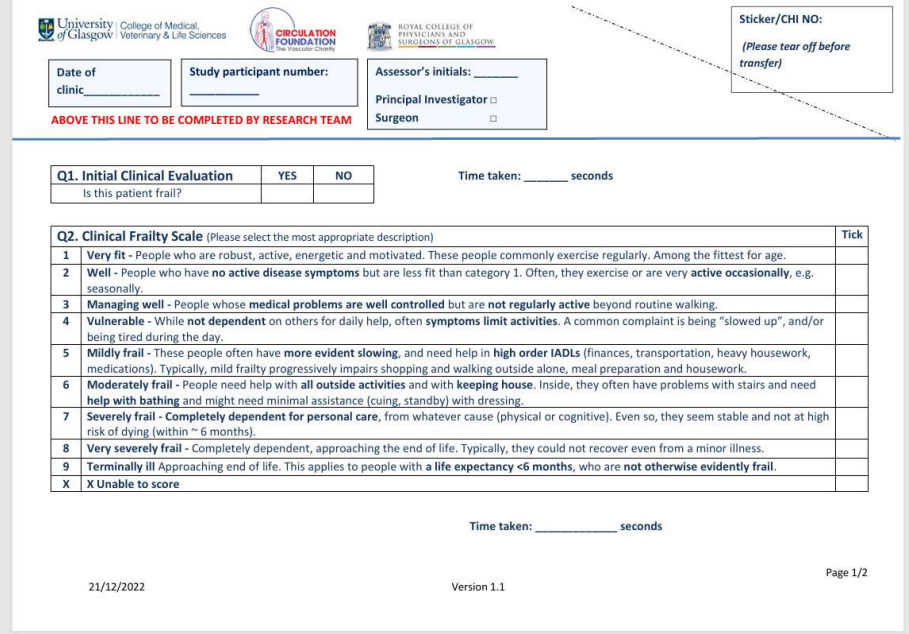
OR

(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 8: Supplementary material for Chapter 4: List of case report forms (CRFs) completed by clinicians, patients/proxies and researcher in FAVOUR study.



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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?		

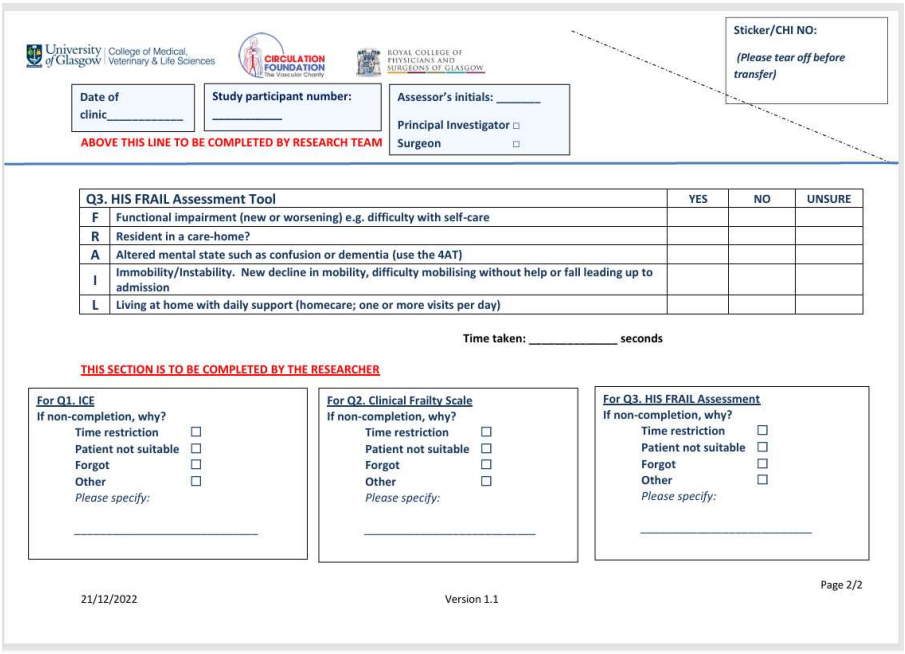
Time taken: _____ seconds

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

Page 1/2

21/12/2022 Version 1.1



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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:
_____

Page 2/2

21/12/2022 Version 1.1

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* _____

Version 1.1
Date 16/12/2022

PLEASE TURN OVER

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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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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Sticker/CHI NO:
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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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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:* _____

Appendix 9: Supplementary material for Chapter 4: Short term outcome results - subgroup analysis of patients diagnosed and treated for critical limb threatening ischaemia (CLTI), presented in tabular form.

The following 30-day outcomes were analysed:

1. **30-day mortality**
2. **30-day morbidity**
3. **Post-operative length of hospital stay**
4. **Post-operative readmission rates (to any speciality)**
5. **Post-operative non-home discharge**
6. **Post-operative discharge with greater social care requirements**

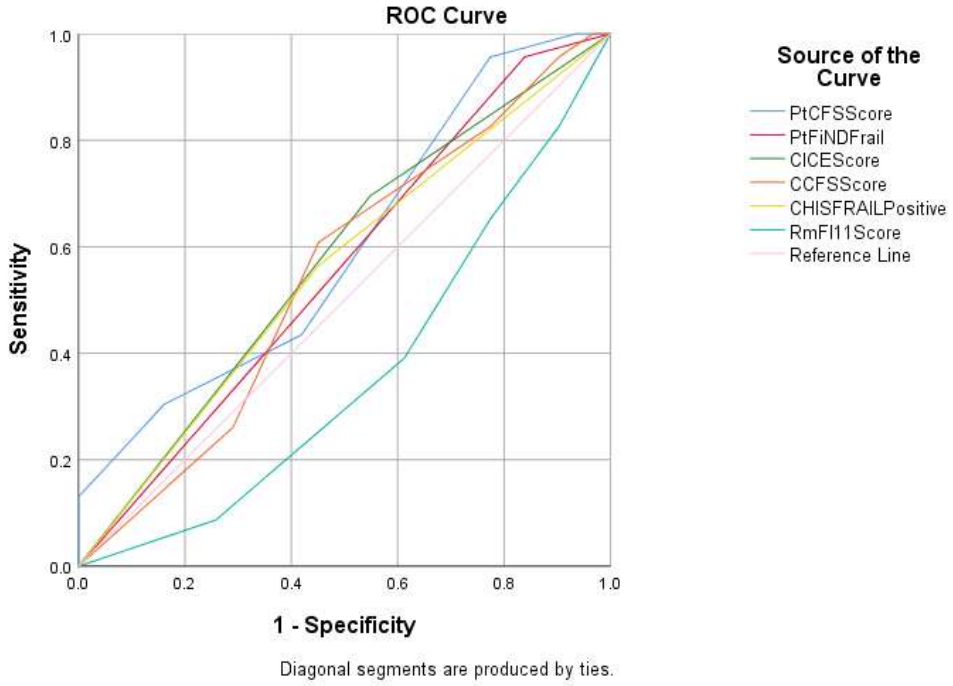
Subgroup analysis – Postoperative 30-day mortality for CLTI patients only			
Frailty instrument (*n*=frailty positive)	**Frail + mortality, n (%)**	**Robust + mortality, n (%)**	**Statistics**
cCFS (*n*=27)	2 (7)	0	$\chi 2$ (1, n=45) = 1.395, *p*=0.238
ICE (*n*=32)	2 (6)	0	$\chi 2$ (1, n=45) = 0.850, *p*=0.356
HIS FRAIL (*n*=25)	1 (4)	1 (5)	$\chi 2$ (1, n=45) = 0.026, *p*=0.872
pCFS (*n*=21)	2 (10)	0	$\chi 2$ (1, n=45) = 2.392, *p*=0.122
mFI-11 (*n*=34)	2 (6)	0	$\chi 2$ (1, n=45) = 0.677, *p*=0.411
FiND (*n*=41)	2 (5)	0	$\chi 2$ (1, n=45) = 0.204, *p*=0.651

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Subgroup analysis – Postoperative 30-day morbidity for CLTI patients only			
Frailty instrument (*n*=frailty positive)	**Frail + mortality, n (%)**	**Robust + mortality, n (%)**	**Statistics**
cCFS (*n*=27)	14 (52)	6 (33)	$\chi 2$ (1, n=45) = 1.500, *p*=0.221
ICE (*n*=32)	16 (50)	4 (31)	$\chi 2$ (1, n=45) = 1.385, *p*=0.239
HIS FRAIL (*n*=25)	12 (48)	8 (40)	$\chi 2$ (1, n=45) = 0.288, *p*=0.592
pCFS (*n*=21)	9 (43)	11 (46)	$\chi 2$ (1, n=45) = 0.040, *p*=0.841
mFI-11 (*n*=34)	13 (38)	7 (6)	$\chi 2$ (1, n=45) = 2.172, *p*=0.141
FiND (*n*=41)	19 (46)	1 (25)	$\chi 2$ (1, n=45) = 0.672, *p*=0.412

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Postoperative 30-day morbidity for CLTI only patients AUC analysis



Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval Lower Bound	Upper Bound
PtCFSScore	.600	.078	.214	.447	.753
PtFiNDFrail	.559	.079	.463	.405	.713
CICEScore	.574	.079	.358	.419	.728
CCFSScore	.550	.079	.535	.395	.705
CHISFRAILPositive	.557	.080	.479	.401	.713
RmFI11Score	.364	.076	.090	.215	.513

The test result variable(s): PtCFSScore, PtFiNDFrail, CICEScore, CCFSScore, CHISFRAILPositive, RmFI11Score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

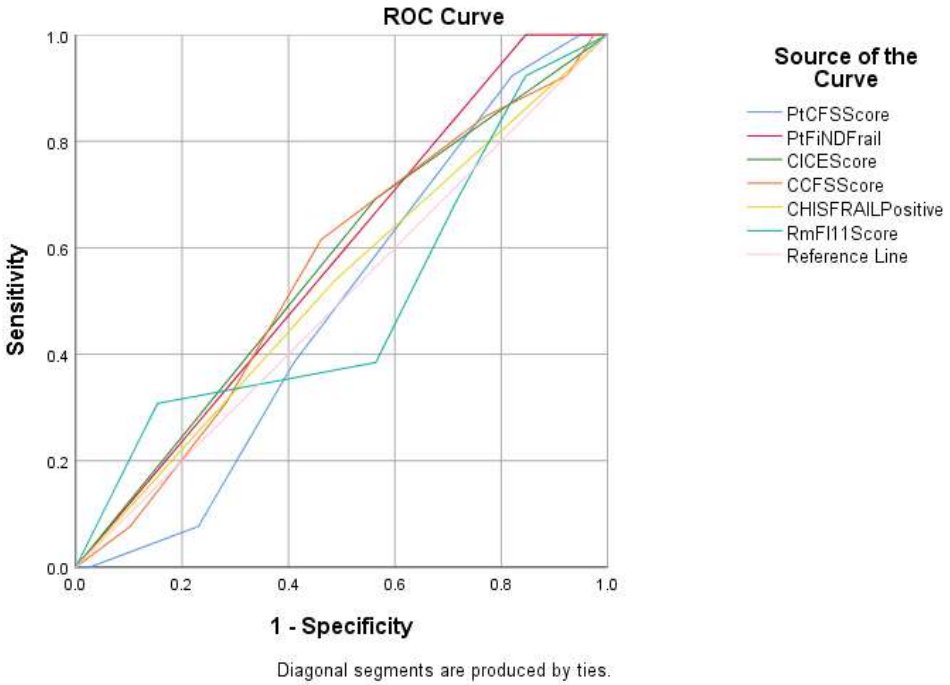
Subgroup analysis - postoperative length of hospital stay for CLTI patients only		
Frailty instrument	**Length of hospital admission in days, median(IQR) / mean (±SD)**	**Statistics**
cCFS		Z = -1.300, *p*=0.194
Robust (*n* = 17)	3 (4.5) / 11 (±31.5)	
Frail (*n* = 27)	6 (17) / 15 (±21.0)	
ICE		Z = -1.880, *p*=0.060
Robust (*n* = 13)	2 (5) / 4 (±3.3)	
Frail (*n* = 31)	6 (17) / 18 (±29.2)	
HIS FRAIL		Z = -1.696, *p*=0.090
Robust (*n* = 19)	2 (9) / 5 (±5.6)	
Frail (*n* = 25)	6 (22) / 20 (±32.0)	
pCFS		Z = -1.402, *p*=0.161
Robust (*n* = 24)	3 (6) / 12 (±28.4)	
Frail (*n* = 20)	7 (17) / 15 (±21.6)	
mFI-11		Z = -1.352, *p*=0.176
Robust (*n* = 11)	7 (12) / 14 (±16.2)	
Frail (*n* = 33)	3 (12) / 13 (±27.9)	
FiND		Z = -0.309, *p*=0.758
Robust (*n* = 4)	6 (23) / 10 (±12.7)	
Frail (*n* = 40)	4 (11) / 14 (±26.3)	

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. * $p<0.05$. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Subgroup analysis – Postoperative 30-day readmission for CLTI patients only			
Frailty instrument (*n*=frailty positive)	**Frail + mortality, n (%)**	**Robust + mortality, n (%)**	**Statistics**
cCFS (*n*=25)	8 (32)	4 (22)	$\chi 2$ (1, n=43) = 0.497, *p*=0.481
ICE (*n*=30)	9 (30)	3 (23)	$\chi 2$ (1, n=43) = 0.216, *p*=0.642
HIS FRAIL (*n*=24)	7 (29)	5 (26)	$\chi 2$ (1, n=43) = 0.043, *p*=0.836
pCFS (*n*=19)	5 (26)	7 (29)	$\chi 2$ (1, n=43) = 0.043, *p*=0.836
mFI-11 (*n*=32)	9 (28)	3 (27)	$\chi 2$ (1, n=43) = 0.003, *p*=0.957
FiND (*n*=39)	12 (31)	0	$\chi 2$ (1, n=43) = 1.707, *p*=0.191

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Postoperative 30-day readmission for CLTI patients only AUC analysis



Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptoti Confidence Inter Lower Bound	Bou
PtCFSScore	.492	.084	.933	.328	
PtFiNDFrail	.577	.086	.410	.408	
CICEScore	.564	.091	.492	.386	
CCFSScore	.557	.090	.540	.381	
CHISFRAILPositive	.526	.093	.784	.343	
RmFI11Score	.500	.098	1.000	.308	

The test result variable(s): PtCFSScore, PtFiNDFrail, CICEScore, CCFSScore, CHISFRAILPositive, RmFI11Score has at least one tie between the positive actual sta and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Subgroup analysis – Postoperative nonhome discharge for CLTI patients only			
Frailty instrument (*n*=frailty positive)	**Frail + mortality, n (%)**	**Robust + mortality, n (%)**	**Statistics**
cCFS (*n*=27)	0	1 (6)	$\chi 2$ (1, n=44) = 1.625, *p*=0.202
ICE (*n*=31)	1 (3)	0	$\chi 2$ (1, n=44) = 0.429, *p*=0.512
HIS FRAIL (*n*=25)	1 (4)	0	$\chi 2$ (1, n=44) = 0.778, *p*=0.378
pCFS (*n*=20)	0	1 (4)	$\chi 2$ (1, n=44) = 0.853, *p*=0.356
mFI-11 (*n*=33)	1 (3)	0	$\chi 2$ (1, n=44) = 0.341, *p*=0.559
FiND (*n*=40)	1 (3)	0	$\chi 2$ (1, n=44) = 0.102, *p*=0.749

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Subgroup analysis – Postoperative discharge with greater social care requirements for CLTI patients only			
Frailty instrument (*n*=frailty positive)	**Frail + mortality, n (%)**	**Robust + mortality, n (%)**	**Statistics**
cCFS (*n*=27)	1 (4)	1 (6)	$\chi 2$ (1, n=44) = 0.114, *p*=0.736
ICE (*n*=31)	2 (6)	0	$\chi 2$ (1, n=44) = 0.879, *p*=0.349
HIS FRAIL (*n*=25)	1 (4)	1 (5)	$\chi 2$ (1, n=44) = 0.040, *p*=0.842
pCFS (*n*=20)	0	2 (8)	$\chi 2$ (1, n=44) = 1.746, *p*=0.186
mFI-11 (*n*=33)	1 (3)	1 (9)	$\chi 2$ (1, n=44) = 0.698, *p*=0.403
FiND (*n*=40)	2 (5)	0	$\chi 2$ (1, n=44) = 0.210, *p*=0.647

cCFS – clinician-assessed Clinical Frailty Scale, ICE – Initial Clinical Evaluation, HIS FRAIL – Healthcare Improvement Scotland FRAIL tool, pCFS – patient-assessed Clinical Frailty Scale, mFI-11 – 11-item modified frailty index. FiND – Frail NonDisabled Questionnaire. This patient cohort consists of 44 patients diagnosed with CLTI and 1 patient diagnosed with CLTI and mesenteric angina who underwent treatment for CLTI.

Appendix 10: Supplementary material for Chapter 5: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Table from STROBE (2025) STROBE Checklists, STROBE. Available at: https://www.strobe-statement.org/checklists/ (Accessed: 07 April 2025).

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage

		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 11: Supplementary material for Chapter 7: Checklist for Reporting Results of Internet E-Surveys (CHERRIES) checklist.

Table from Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res. 2004 Sep 29;6(3):e34. doi: 10.2196/jmir.6.3.e34. Erratum in: doi:10.2196/jmir.2042. PMID: 15471760; PMCID: PMC1550605.

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
Design		
	Describe survey design	Describe target population, sample frame. Is the sample a convenience sample? (In "open" surveys this is most likely.)
IRB (Institutional Review Board) approval and informed consent process		
	IRB approval	Mention whether the study has been approved by an IRB.
	Informed consent	Describe the informed consent process. Where were the participants told the length of time of the survey, which data were stored and where and for how long, who the investigator was, and the purpose of the study?
	Data protection	If any personal information was collected or stored, describe what mechanisms were used to protect unauthorized access.
Development and pre-testing		
	Development and testing	State how the survey was developed, including whether the usability and technical functionality of the electronic questionnaire had been tested before fielding the questionnaire.

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
Recruitment process and description of the sample having access to the questionnaire		
	Open survey versus closed survey	An “open survey” is a survey open for each visitor of a site, while a closed survey is only open to a sample which the investigator knows (password-protected survey).
	Contact mode	Indicate whether or not the initial contact with the potential participants was made on the Internet. (Investigators may also send out questionnaires by mail and allow for Web-based data entry.)
	Advertising the survey	How/where was the survey announced or advertised? Some examples are offline media (newspapers), or online (mailing lists – If yes, which ones?) or banner ads (Where were these banner ads posted and what did they look like?). It is important to know the wording of the announcement as it will heavily influence who chooses to participate. Ideally the survey announcement should be published as an appendix.
Survey administration		
	Web/E-mail	State the type of e-survey (eg, one posted on a Web site, or one sent out through e-mail). If it is an e-mail survey, were the responses entered manually into a database, or was there an automatic method for capturing responses?
	Context	Describe the Web site (for mailing list/newsgroup) in which the survey was posted. What is the Web site about, who is visiting it, what are visitors normally looking for? Discuss to

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
		what degree the content of the Web site could pre-select the sample or influence the results. For example, a survey about vaccination on a anti-immunization Web site will have different results from a Web survey conducted on a government Web site
	Mandatory/voluntary	Was it a mandatory survey to be filled in by every visitor who wanted to enter the Web site, or was it a voluntary survey?
	Incentives	Were any incentives offered (eg, monetary, prizes, or non-monetary incentives such as an offer to provide the survey results)?
	Time/Date	In what timeframe were the data collected?
	Randomization of items or questionnaires	To prevent biases items can be randomized or alternated.
	Adaptive questioning	Use adaptive questioning (certain items, or only conditionally displayed based on responses to other items) to reduce number and complexity of the questions.
	Number of Items	What was the number of questionnaire items per page? The number of items is an important factor for the completion rate.
	Number of screens (pages)	Over how many pages was the questionnaire distributed? The number of items is an important factor for the completion rate.
	Completeness check	It is technically possible to do consistency or completeness checks before the questionnaire is submitted. Was this done, and if “yes”, how (usually JAVAScript)? An alternative is to check for completeness after the questionnaire has been submitted (and highlight mandatory items). If this has

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
		been done, it should be reported. All items should provide a non-response option such as “not applicable” or “rather not say”, and selection of one response option should be enforced.
	Review step	State whether respondents were able to review and change their answers (eg, through a Back button or a Review step which displays a summary of the responses and asks the respondents if they are correct).
Response rates		
	Unique site visitor	If you provide view rates or participation rates, you need to define how you determined a unique visitor. There are different techniques available, based on IP addresses or cookies or both.
	View rate (Ratio of unique survey visitors/unique site visitors)	Requires counting unique visitors to the first page of the survey, divided by the number of unique site visitors (not page views!). It is not unusual to have view rates of less than 0.1 % if the survey is voluntary.
	Participation rate (Ratio of unique visitors who agreed to participate/unique first survey page visitors)	Count the unique number of people who filled in the first survey page (or agreed to participate, for example by checking a checkbox), divided by visitors who visit the first page of the survey (or the informed consents page, if present). This can also be called “recruitment” rate.
	Completion rate (Ratio of users who finished the survey/users who agreed to participate)	The number of people submitting the last questionnaire page, divided by the number of people who agreed to participate (or submitted the first survey page). This is only relevant if there is a separate “informed consent” page or if the survey goes over several pages. This is a measure for attrition.

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
		Note that “completion” can involve leaving questionnaire items blank. This is not a measure for how completely questionnaires were filled in. (If you need a measure for this, use the word “completeness rate”.)
Preventing multiple entries from the same individual		
	Cookies used	Indicate whether cookies were used to assign a unique user identifier to each client computer. If so, mention the page on which the cookie was set and read, and how long the cookie was valid. Were duplicate entries avoided by preventing users access to the survey twice; or were duplicate database entries having the same user ID eliminated before analysis? In the latter case, which entries were kept for analysis (eg, the first entry or the most recent)?
	IP check	Indicate whether the IP address of the client computer was used to identify potential duplicate entries from the same user. If so, mention the period of time for which no two entries from the same IP address were allowed (eg, 24 hours). Were duplicate entries avoided by preventing users with the same IP address access to the survey twice; or were duplicate database entries having the same IP address within a given period of time eliminated before analysis? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?
	Log file analysis	Indicate whether other techniques to analyze the log file for identification of multiple entries were used. If so, please describe.

	Checklist for Reporting Results of Internet E-Surveys (CHERRIES)	
Item Category	**Checklist Item**	**Explanation**
	Registration	In “closed” (non-open) surveys, users need to login first and it is easier to prevent duplicate entries from the same user. Describe how this was done. For example, was the survey never displayed a second time once the user had filled it in, or was the username stored together with the survey results and later eliminated? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?
Analysis		
	Handling of incomplete questionnaires	Were only completed questionnaires analyzed? Were questionnaires which terminated early (where, for example, users did not go through all questionnaire pages) also analyzed?
	Questionnaires submitted with an atypical timestamp	Some investigators may measure the time people needed to fill in a questionnaire and exclude questionnaires that were submitted too soon. Specify the timeframe that was used as a cut-off point, and describe how this point was determined.
	Statistical correction	Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for the non-representative sample; if so, please describe the methods.

Appendix 12: Supplementary material for Chapter 7: the Consolidated criteria for Reporting Qualitative studies (COREQ): 32-item checklist.

Table form Allison Tong, Peter Sainsbury, Jonathan Craig, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups, *International Journal for Quality in Health Care*, Volume 19, Issue 6, December 2007, Pages 349–357, https://doi-org.knowledge.idm.oclc.org/10.1093/intqhc/mzm042

No	Item	Guide questions/description
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*
3.	Occupation	What was their occupation at the time of the study?
4.	Gender	Was the researcher male or female?
5.	Experience and training	What experience or training did the researcher have?
Relationship with participants		
6.	Relationship established	Was a relationship established prior to study commencement?
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.*g. personal goals, reasons for doing the research*
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic*
Domain 2: study design		

Theoretical framework		
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis*
Participant selection		
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball*
11.	Method of approach	How were participants approached? e.*g. face-to-face, telephone, mail, email*
12.	Sample size	How many participants were in the study?
13.	Non-participation	How many people refused to participate or dropped out? Reasons?
Setting		
14.	Setting of data collection	Where was the data collected? e.*g. home, clinic, workplace*
15.	Presence of non-participants	Was anyone else present besides the participants and researchers?
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date*
Data collection		
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many?
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?
20.	Field notes	Were field notes made during and/or after the interview or focus group?
21.	Duration	What was the duration of the interviews or focus group?
22.	Data saturation	Was data saturation discussed?

23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?
Domain 3: analysis and findings		
Data analysis		
24.	Number of data coders	How many data coders coded the data?
25.	Description of the coding tree	Did authors provide a description of the coding tree?
26.	Derivation of themes	Were themes identified in advance or derived from the data?
27.	Software	What software, if applicable, was used to manage the data?
28.	Participant checking	Did participants provide feedback on the findings?
Reporting		
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.*g. participant number*
30.	Data and findings consistent	Was there consistency between the data presented and the findings?
31.	Clarity of major themes	Were major themes clearly presented in the findings?
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?

ADDITIONAL CONSIDERATIONS

Domain 1: research team and reflexivity

1) Personal characteristics
2) Relationship with participants

Domain 2: Study design

1) Theoretical framework – ethnography (to understand the culture of groups with shared characteristics)
2) Participant selection – Purposive sampling by contacting vascular surgeons through professional memberships. Snowball effect permitted to encourage the wider healthcare team to join

3) Setting – Teams/Hospital/university facilities. Include presence of nonparticipants and basic demographics

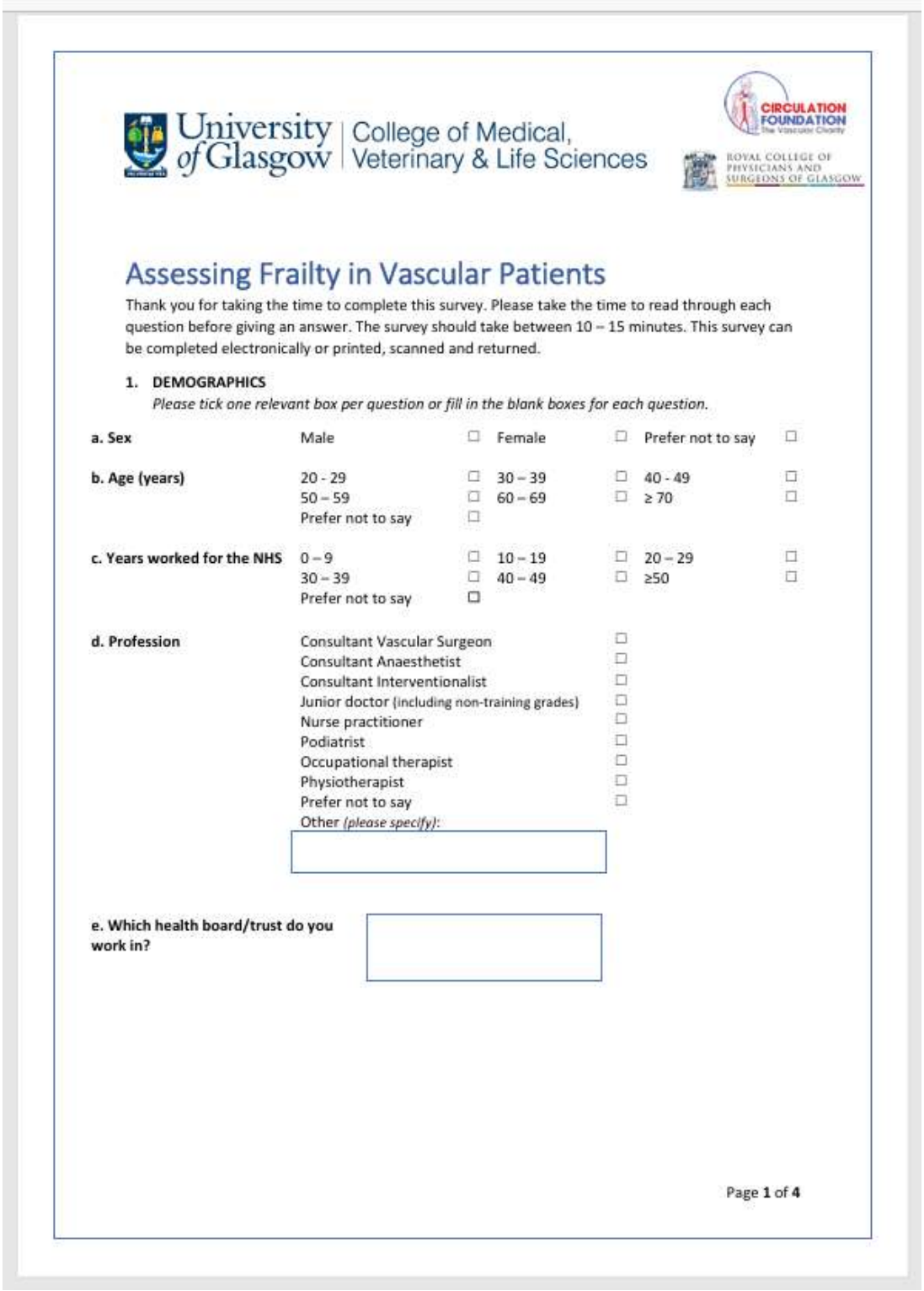
4) Data collection – Audio recording and transcription. ?? Participants not invited to perform transcript checking for authenticity. Field notes – maintain contextual detail and document nonverbal communication. Participants were not re-interviewed by focus group, instead they will be invited to leave contact details for re-contact through repeat survey at a later date. Duration anticipated 30-45 minutes for groups of up to six participants. Mention that data saturation was not considered as the greater the sample size, the greater the results would reflect population opinion and also, the greater the chance of recruiting participants from non-surgical (but relevant) specialities. I.e., nursing, physio, anaesthetics)

Domain 3: Analysis and findings

1) Data analysis – The credibility of the findings can be assessed if the process of coding (selecting significant sections from participant statements), and the derivation and identification of themes are made explicit.

2) Reporting - If supporting quotations are provided, researchers should include quotations from different participants to add transparency and trustworthiness to their findings and interpretations of the data. Summary findings, interpretations and theories generated should be clearly presented in qualitative research publications.

Appendix 13 : Supplementary material for Chapter 7: 18-item questionnaire used in the study.



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

CIRCULATION FOUNDATION The Vascular Charity

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

Assessing Frailty in Vascular Patients

Thank you for taking the time to complete this survey. Please take the time to read through each question before giving an answer. The survey should take between 10 – 15 minutes. This survey can be completed electronically or printed, scanned and returned.

1. **DEMOGRAPHICS**

Please tick one relevant box per question or fill in the blank boxes for each question.

a. Sex
Male ☐ Female ☐ Prefer not to say ☐

b. Age (years)
20 - 29 ☐ 30 – 39 ☐ 40 - 49 ☐
50 – 59 ☐ 60 – 69 ☐ ≥ 70 ☐
Prefer not to say ☐

c. Years worked for the NHS
0 – 9 ☐ 10 – 19 ☐ 20 – 29 ☐
30 – 39 ☐ 40 – 49 ☐ ≥50 ☐
Prefer not to say ☐

d. Profession
Consultant Vascular Surgeon ☐
Consultant Anaesthetist ☐
Consultant Interventionalist ☐
Junior doctor (including non-training grades) ☐
Nurse practitioner ☐
Podiatrist ☐
Occupational therapist ☐
Physiotherapist ☐
Prefer not to say ☐
Other *(please specify)*:

e. Which health board/trust do you work in?

Page **1** of **4**

2. SIGNIFICANCE OF FRAILTY

Please tick one relevant box for each question.

	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree
a. I am comfortable with the concept of frailty	1☐	2☐	3☐	4☐	5☐
b. I use frailty assessments to help guide management plans	1☐	2☐	3☐	4☐	5☐
c. I use frailty assessments for joint decision making	1☐	2☐	3☐	4☐	5☐
d. There is added value to assessing frailty over and above disability	1☐	2☐	3☐	4☐	5☐
e. There is added value to assessing frailty over and above multi-morbidity	1☐	2☐	3☐	4☐	5☐

3. FRAILTY ASSESSMENT

Please tick the relevant box as appropriate. More than one box may be ticked.

a. When patient-facing, I assess frailty…

- Daily ☐
- Weekly ☐
- Monthly ☐
- Rarely ☐
- Never ☐

b. When in the patient journey is frailty assessed

- In community prior to referral ☐
- In outpatient department ☐
- Pre-operative assessment clinic ☐
- On acute admission ☐
- On the day of surgery ☐
- Post-operatively ☐
- Frailty is not assessed ☐
- Other (*please specify*): ☐

c. Which frailty assessment tools do you use, if any?

Rockwood Clinical Frailty Scale	☐	Groningen Frailty Index	☐
11-item Modified Frailty Index	☐	Ruptured Aneurysm Frailty Score	☐
5-item modified Frailty Index	☐	FRAIL Scale	☐
Risk Analysis Index	☐	Electronic frailty index	☐
Edmonton Frail Scale	☐	Hospital Frailty Risk Score	☐
Critical Limb Ischaemia Frailty (CLI Frailty)	☐	Geriatric Nutritional Risk Index (GNRI)	☐
Addenbrookes Vascular Frailty Score	☐	'End of bed test'	☐
Healthcare Improvement Scotland Frailty Tool	☐	Grip strength	☐
I do not assess frailty	☐		

Other, or if you do not routinely assess frailty currently, which tool would you use? (*Please specify)*:

d. In your unit, who (also) performs a frailty assessment

Consultant Vascular Surgeon	☐	Geriatric/MOE team	☐
Anaesthetic team	☐	Physiotherapist	☐
Junior doctors (any grade)	☐	Medical registrar	☐
Ward staff nurses	☐	Occupational therapist	☐
Dedicated surgical comprehensive geriatric team	☐	No frailty assessment performed	☐

Other (*please specify, or if no frailty assessment is performed, who do you think should perform it?*):

4. IMPLEMENTING FRAILTY ASSESSMENT INTO CLINICAL PRACTICE

'The Provision of Vascular Services for People with Vascular Disease (2021)' identified the vascular patient population as having a high proportion of frail patients. The following questions pertain to these guidelines. *Please give a short summary for each question. If not applicable, please indicate with: N/A and give a short explanation.*

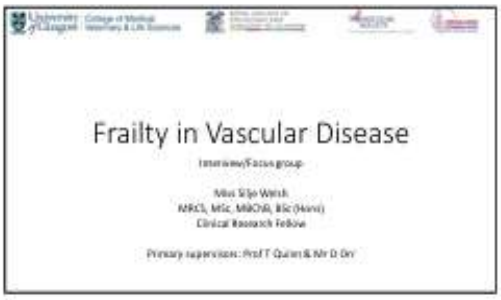
a. Does identifying frailty influence your practice? If so, how?
b. Do vascular patients in your unit have access to a comprehensive geriatric assessment (CGA) by a suitably trained specialist to address issues of frailty and multi-morbidity peri-operatively?
c. Do Care of the Elderly and Frailty members participate in your vascular MDT?
d. Do you think there are barriers to implementing frailty assessment into your clinical practice, if so, what are they?

This is the end of the questionnaire, thank you for taking the time to complete!

Please return the completed questionnaire to: Silje.welsh3@nhs.scot

If you are interested in participating in a focus group to further discuss frailty and its assessment, please indicate so by leaving contact details in the box below so that we can be in touch with further details in due course (e.g., e-mail/telephone number).

Appendix 14: Supplementary material for Chapter 7: The semi structured interview guide used during interview and focus group sessions.



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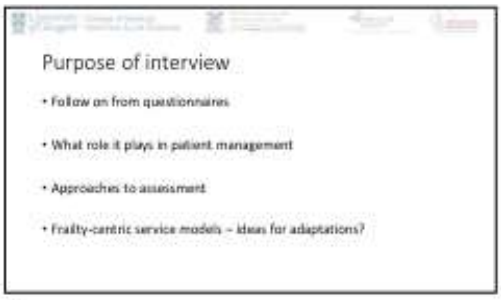

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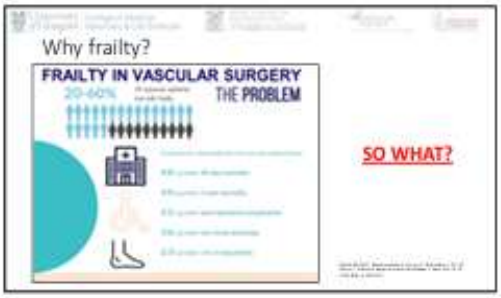

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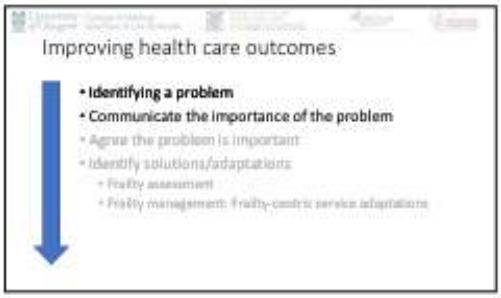

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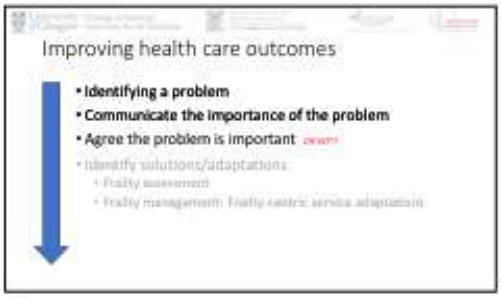


6

How important is frailty to your practice/within your department?

Is there recognition of frailty in your unit / how? (Existence of a frailty service)

Do you think there are ways to improve awareness of frailty? (barriers)

What would be the perceived benefits of detecting frailty?

Does the recognition of frailty translate into change in clinical practice/patient management?

What factors guides decision making for suitability for surgery, how big a role does frailty play and why?

7

Improving health care outcomes

- **Identifying a problem**
- **Communicate the importance of the problem**
- **Agree the problem is important**
- **Identify solutions/adaptations**
  - **Frailty assessment**
  - Frailty management: Frailty-centric service adaptations

8

Frailty assessment (1)

Is there a structured/standardised approach to assessing frailty in your unit?

Positives v negatives of mode of frailty assessment?

Why do you assess frailty in the way that you do? How did you come across selected tools?

Do you know of any others? Reasons for not adopting alternate tools?

9

Frailty assessment (2)

Would you use different tools for outpatient/elective v inpatient/urgent?

Opinion on disease/treatment-specific tools v generic ones?

Do you commonly assess other prognostic markers ?P-Possum or ASA?

Do you think it would be useful to incorporate frailty into anaesthetic risk stratification tools?

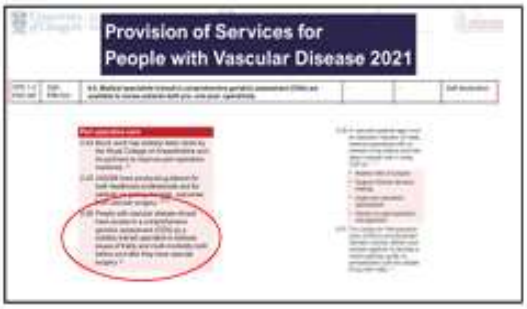
10

Improving health care outcomes

- **Identifying a problem**
- **Communicate the importance of the problem**
- **Agree the problem is important**
- **Identify solutions/adaptations**
  - **Frailty assessment**
  - Frailty management: Frailty-centric service adaptations

11

12



13

Frailty management

Does your service offer something similar this?

- If not, why?
- If yes, how was it set up?

Do you think there has been a notable improvement in care following implementation?

Is the service used optimally? Can it be improved? Barriers to implementation?

14

Designing a frailty-centric service

If you were to design a frailty-related clinical service models, or adapt established models, for this growing cohort of patients, what would it look like?

15

Round up

Unexplored areas?

Questions?

16

University of Glasgow

16th September 2022

MVLS College Ethics Committee

Project Title: Assessing the familiarity and utilisation of frailty assessment tools within a vascular surgery service
Project No: 200220006

Dear Dr Quinn,

The College Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study. It is happy therefore to approve the project.

- Project end date: As stated in application.
- The data should be held securely for a period of ten years after the completion of the research project, or for longer if specified by the research funder or sponsor, in accordance with the University's Code of Good Practice in Research:
- https://www.gla.ac.uk/media/media_490311_en.pdf
- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.
- For projects requiring the use of an online questionnaire, the University has an Online Surveys account for research. To request access, see the University's application procedure at https://www.gla.ac.uk/research/strategy/ourpolicies/useofonlinesurveystoolforresearch/.

Yours sincerely,

Jesse Dawson
MD, BSc (Hons), FRCP, FESO
Professor of Stroke Medicine
Consultant Physician
Clinical Lead Scottish Stroke Research Network / NRS Stroke Research Champion
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