Pre-frailty and frailty in hospitalised older adults: Prevalence, identification, and development of a self-managed exercise and nutrition program

by

Chad Yixian Han

BNutDiet (Hons), APD

Thesis

Submitted to Flinders University

for the degree of

Doctor of Philosophy

College of Nursing and Health Sciences

26th October 2022

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ACG	Attention Control Group
ADL	Activities of Daily Living
AMU	Acute Medical Unit
ANZCTR	Australia New Zealand Clinical Trials Register
ANOVA	One-way Analysis of Variance
AUC	Area Under Curve
AQoL	Assessment of Quality of Life
BMI	Body Mass Index
CBT	Cognitive Behavioral Therapy
CCI	Charlson Comorbidity Index
CGA	Comprehensive Geriatric Assessment
CHF	Chronic Heart Failure
CI	Confidence Intervals
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COREQ	Consolidated Criteria for Reporting Qualitative Research
CONSORT	Consolidated Standards of Reporting Trials
DVD	Digital Versatile Disc
EFS	Edmonton Frail Scale
EQ-5D-5L UI	EuroQol-5-Dimension-5-Level Utility Index
EQ-5D VAS	EuroQol-5-Dimension Visual Analog Scale
ESPEN	European Society for Clinical Nutrition and Metabolism
EWGSOP	European Working Group on Sarcopenia in Older People
FMC	Flinders Medical Centre
FOCUS	Frailty Management Optimisation through European Innovation Partnership on Active and Healthy Ageing Commitments and Utilisation of Stakeholder Input
GDS	Geriatric Depression Scale
GFI	Groningen Frailty Indicator
HARP	Hospital Admission Risk Profile
HR	Heart Rate
HREC	Human Research Ethics Committee
IADL	Instrumental Activities of Daily living
IG	Intervention Group
INDEPENDENCE	Individualised Therapy for Elderly Patients using Exercise and Nutrition to Reduce dependence post discharge
INTERACTIVE	Individual Nutrition Therapy and Exercise Regime: A Controlled Trial of

	Injured, Vulnerable Elderly
ITT	Intention-To-Treat
LL	Lower Limb
LOS	Length of Stay
M	Months
MMSE	Mini Mental State Examination
MNA	Mini Nutrition Assessment
MNA-SF	Mini Nutrition Assessment Short Form
MNT	Medical Nutrition Therapy
MoBERG	Modified Berg Balance Scale
MUST	Malnutrition Universal Screening Tool
NICE	National Institute for Health and Clinical Excellence
NPV	Negative Predictive Value
NR	Not Reported
ONS	Oral Nutrition Supplements
OR	Odds Ratio
PADL	Physical Activities of Daily Living
PEDro	Physiotherapy Evidence Database
PG-SGA	Patient Generated Subjective Global Assessment
Ph	Physical
PNNS	Programme National Nutrition Santé
PP	Per Protocol
PPT	Physical Performance Test
PPV	Positive Predictive Value
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register on Systematic Reviews
Ps	Psychological
QoL	Quality of Life
RCT	Randomised Controlled Trial
RM	Repetition Max
RoB-2	Risk of Bias Tool version 2
ROC	Receiver Operator Curve
S	Social
SALHN	Southern Adelaide Local Health Network
SD	Standard Deviation

SHARE-FI	Survey of Health, Ageing, and Retirement in Europe
SPPB	Short Physical Performance Battery
SPSS	Statistical Package for Social Sciences
STAND-Cph	Sit-To-Stand Exercise Copenhagen
STATA	Statistical Software for Data Science
TDF	Theoretical Domain Framework
TIDieR	Template for Intervention Description and Replication
T2DM	Type 2 Diabetes Mellitus
UCG	Usual care group
UL	Upper Limb
USD	United States Dollars
VAS	Visual Analog Scale
VO_2 Max	Maximal Oxygen Uptake
W	Weeks
WEBB	Weight-Bearing for Better Balance Exercise Program
Y	Years
YI	Youden Index

THESIS SUMMARY

Pre-frailty and frailty, as age-associated conditions, are increasing as more adults are surviving into old age. The hallmark symptoms of pre-frailty and frailty are emphasised when vulnerable older adults are hospitalised, putting them at higher risk of further decline, functional loss, and malnutrition. Within multimodal therapies for pre-frailty and frailty, combined exercise and nutrition interventions are suggested to be amongst the most effective to treat and prevent aspects of pre-frailty and frailty. However, the understanding of such pre-frailty and frailty interventions in hospitalised older adults is still poor. The involvement of dietitians in such interventions also lacks understanding. The identification of pre-frailty and frailty can also pose a challenge in the time-pressured hospital environment. This thesis aims to identify new knowledge to address these challenges to improve pre-frailty and frailty detection and care in hospitalised older adults.

Comprehensive literature reviews of combined exercise and nutrition interventions in hospitalised older adults and the involvement of dietitians in nutrition interventions were conducted in Chapter 1. The first systematic review and meta-analysis found weak evidence that combined exercise and nutrition interventions are effective in improving pre-frailty and frailty and their related indicators in hospitalised older adults. However, there was a lack of self-management component in such interventions. The roles of dietitians in conception or delivery of components within such multimodal therapies are also understood less than exercise professionals. Also, pre-frailty and frailty were not commonly assessed with validated tools. The second systematic review in Chapter 1 describing involvement of dietitians in nutritional components of pre-frailty and frailty interventions found five characteristics of nutrition interventions that involved dietitians in planning and/or delivery – Nutrition counselling; Supplements; Customised dishware; Motivational cards; Therapeutic meals.

An observational study was conducted in an acute medical unit (AMU) to (1) investigate the prevalence, associated factors and clinical outcomes of pre-frailty and frailty using validated tools in Chapter 2 and (2) determine whether a nutritional assessment tool could also identify pre-frailty and frailty status in Chapter 3. This study found a high prevalence of pre-frailty and frailty combined (57%) in hospitalised older adults admitted to an AMU. Pre-frailty was associated with a number of factors such as higher number of medications and a lower education level, compared to non-frail participants. Length of hospital stay was significantly higher in frail older adults, compared to non-frail participants. The nutritional assessment tool, Scored Patient-Generated Subjective Global Assessment, was found to have good sensitivity (0.711) and specificity (0.746) in identifying pre-frailty and frailty and can be useful in identifying these conditions concurrently.

To help inform the development of a self-managed, hospital-to-home, combined exercise and nutrition

program for pre-frailty and frailty (INDEPENDENCE), two studies were conducted. First, a secondary analysis of a previously completed randomised controlled trial of an individualised combined exercise and nutrition intervention in older post-operative orthopaedic patients who might also be pre-frail and frail was undertaken in Chapter 4. This study highlighted the need for formal assessment of pre-frailty and frailty over surrogate measures (i.e., frailty tool as opposed to gait speed) in future studies. The data from the secondary analysis was also pooled in a meta-analysis with the studies found in first systematic review, to reveal that exercise and nutrition can improve gait speed in hospitalised older adults who might also be pre-frail or frail. Other learnings from the secondary analysis that informed this thesis, and the design of the INDEPENDENCE program were the lack of a self-management component as part of the combined exercise and nutrition intervention, and lack of methods for measuring adherence to individualised therapies with a standardised measure.

Second, a qualitative study, using principles from grounded theory, was conducted in 22 pre-frail and frail hospitalised older adults to investigate what they wanted out of pre-frailty and frailty interventions, in Chapter 5. The study found that hospitalised older adults desired education on the condition, and preferred physical and telephone contacts over video-calls in a hospital-to-home program. They also hoped that combined exercise and nutrition interventions were individualised to meet their needs and delivered by one consistent healthcare worker.

The next study (pilot RCT) was informed by the aforementioned qualitative study, such that modifications were made to a structured intervention program, INDEPENDENCE, developed based on current guidelines and literature review. Chapter 6 describes the pilot RCT of 32 pre-frail and frail older medical patients of the INDEPENDENCE program found good levels of participation, low voluntary drop-out rates, and preliminary evidence that it significantly improved pre-frailty and frailty and physical performance post intervention, and at 6-month follow-up.

An evaluation of barriers and enablers to the INDEPENDENCE program using an embedded qualitative study with 11 program participants, was analysed using the theoretical domain framework, in Chapter 7. Barriers and enablers to adherence of the INDEPENDENCE program were identified. Example of domains (*themes*) are knowledge (*increased awareness about lifestyle behaviours*), reinforcement (*physical/health benefits*) and environmental context/resource (*education resource booklet)*.

Overall, this thesis augmented knowledge in pre-frailty and frailty to better their detection and treatment in hospitalised older adults through investigation of prevalence, identification of a pre-existing tool to screen pre-frailty and frailty, and development of a novel self-managed exercise and nutrition intervention.

SUMMARY OF PUBLICATIONS AND CONFERENCE ABSTRACTS DURING CANDIDATURE

Table 1a: Summary of publications contributing to thesis

Chapter	Full Citation	Status	Impact factor 2021	SCImago quartile ranking 2021
Journal Publications				
1	**Han CY**, Miller M, Yaxley A, Baldwin C, Woodman R, Sharma Y. Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a systematic review and meta-analysis. BMJ open. 2020 Dec 1;10(12):e040146.	Published	2.692	Q1
2	**Han CY**, Sharma Y, Yaxley A, Baldwin C, Miller M. Prevalence, factors and clinical outcomes associated with nutritional status and frailty in hospitalised older adult patients: a cross sectional observational study. International Journal of Older People Nursing	Under review	2.115	Q2
3	**Han CY**, Sharma Y, Yaxley A, Baldwin C, Miller M. Use of the Patient-Generated Subjective Global Assessment to Identify Pre-Frailty and Frailty in Hospitalised Older Adults. The Journal of Nutrition, Health & Aging. 2021 Dec;25(10):1229-34.	Published	4.075	Q1
4	**Han CY**, Crotty M, Thomas S, Cameron ID, Whitehead C, Kurrle S, Mackintosh S, Miller M. Effect of Individual Nutrition Therapy and Exercise Regime on Gait Speed, Physical Function, Strength and Balance, Body Composition, Energy and Protein, in Injured, Vulnerable Elderly: A Multisite Randomised Controlled Trial (INTERACTIVE). Nutrients. 2021 Sep;13(9):3182.	Published	5.429	Q1

Table 1b: Conference abstracts and presentations from thesis

Authors, title	Conference (year)	Delivery mode
Han CY, Yaxley A, Baldwin C, Sharma Y, Miller M, Barriers and enablers to diet and exercise in self-managed support program for pre-frailty and frailty	Dietitians Australia National Conference (2022)	Oral
Han CY, Yaxley A, Baldwin C, Sharma Y, Miller M, Perspectives of diet and exercise in frail and pre-frail hospitalised older adults: a qualitative report describing patterns before, during and after hospitalisation	International Society of Behavioural Nutrition and Physical Activity Conference virtual (2022)	Poster
Han CY, Sharma Y, Yaxley A, Baldwin C, Miller M, Individualised therapy for elderly patients using exercise and nutrition to reduce dependence post discharge (INDEPENDENCE): a randomised controlled pilot trial	International Conference on Frailty and Sarcopenia Research virtual (2022)	Oral
Han CY Miller M, Yaxley A, Sharma Y, Baldwin C, Frailty, and malnutrition in hospitalised older adults: a cross-sectional analysis of patient characteristics	Dietitians Australia National Conference, virtual (2021)	Poster
Han CY, Yaxley A, Miller M, Sharma Y, Ho R, Dietetic interventions for pre-frail or frail older adults: a systematic review and meta- analysis, Dietitians Australia National Conference	Dietitians Australia National Conference, abstract only (2020)	Poster

Table 1c: 3-Minute Thesis® competition presentation

Author, title	Competition round	Outcome
Han CY, Stay at home: Breaking the vicious cycle of hospital readmissions	Asia-pacific finals	Finalist – Top 9 of 54
Han CY, Stay at home: Breaking the vicious cycle of hospital readmissions	University finals	Winner and people's choice

Table 1d: Grants and funding during candidature

Date	Name of grant/fund
Jun 2019-2022	Australian Government Research Training Program Scholarship (International) AUD$75,600 with Research Student Maintenance AUD$6,000
Oct 2021	ERA Australian Association of Gerontology Conference Bursary AUD$100
Aug 2020	Flinders University Student Association Development Grant AUD$381
May 2020	repliCATS virtual workshop grant by University of Melbourne USD$500
Sept 2019	Travel Grant by University of Melbourne for AIMOS 2019 conference USD $500

DECLARATION

I, Chad Yixian Han, certify that this thesis does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university, and that to the best of my knowledge and belief, it does not contain any material previously published or written by another person except where due reference is made in the text.

No editor was used in the creation of this thesis.

Signed by Chad Yixian Han on 22nd June 2022

ACKNOWLEDGEMENTS

I would first like to thank Mdm (Dr) Kalpana and Dr (A/Prof) Mary that believed in me and recommended me for this PhD application. I will pay it forward and one day pass the baton to the next generation of healthcare professionals/researchers.

I would like to thank my four supervisors: Professor Michelle Miller (Principal Supervisor); Dr Alison Yaxley (Associate Supervisor); A/Prof Yogesh Sharma (Associate Supervisor); Dr Claire Baldwin (Associate Supervisor).

To Michelle, thank you for trusting me and supporting my ambitious endeavours. I really appreciate your generosity in sharing your wisdom, resources, and connections for which allowed my creativity reign free. I never once felt that there were issues that I couldn't approach you for. I have learnt a great deal just watching how you juggle work and life. Thank you for taking a chance on this dark horse. I will remember to stay classy :D To Alison, my teacher/psychologist/social worker, what more can I say. You are part of many of my core pleasant memories at Flinders starting with that tofu brownie. Thank you for your patience and reminders of what is real and important. To Claire, you are meant to be in academia and any students would be so fortunate to have you as their teacher. Thank you for being genuine and ethical, you have been such a great role model for me. To Dr Yogesh, thank you for paving the way for our projects. It is not easy to navigate around hospital politics and I am grateful for your fighting spirit and guidance. Also, thank you very much for working through some of the weekends with me!

To Prof Richard Woodman and Dr Pawel Skuza, thank you for your statistical expertise, for which I would not have honed my analysis skills. I would also like to express my gratitude to Leila Mohammadi, from the research library for her help in my reviews, and A/Prof Di Chamberlain and A/Prof Maayken Van Den Berg, in their capacity as HDR coordinators, and supporting me throughout the PhD journey.

I would like to acknowledge the generosity of the Australian Government Research Training Program Scholarship (International) and Flinders University for the Research Student Maintenance Funds to enable the completion of this thesis.

I want to thank the support from my psychologist during my darkest time living independently in a foreign place amidst a global pandemic. I want to thank God for sending his angels to me in times of great need. I also want to thank James, Andrea, Gary, all the RCs/RTs at Flinders Living for the most amazing support you can ever give to any international student. You have shaped my "second adolescence".

To my dear PhD fighters Mitali, Clare, Georgia, and Shabnam, thank you all for making me feel at home, especially to Mitali who saw me through my darkest days. Thank you, Jenni, for supporting me both in and outside of research. I owe you both a lifetime of coffees. I would also like to thank my amazing friends and my #heartstopper.

To my family especially Bobo and Boleh, I will use the rest of my days to express my gratitude. To my dear niece Jersyn, thank you for support and I hope seeing my journey will inspire you to pursue a career in healthcare.

Most importantly, I would like to thank all of the patients who participated in my studies in this thesis. Particular thanks to the patients taking part in this amidst a global pandemic though we were very lucky in Adelaide to be in a covid-safe bubble during crucial points in the studies. To Barbs, thank you for making my project so fun! For those that have left, I wish that you have found peace in heaven. To J and P, it's okay that we never had the chance to have that promised lunch at your places, I am grateful to have supported you during your final days. I continue to be inspired by your stories and promise that I will continue to use research to improve our healthcare systems.

CHAPTER 1: PRE-FRAILTY AND FRAILTY – BACKGROUND, LITERATURE REVIEW AND GAPS

The following section contains materials from a co-authored publication accepted in 2020. Please refer to Appendix 1 for the co-signed author statement and contribution.

Han CY, Miller M, Yaxley A, Baldwin C, Woodman R, Sharma Y. Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a systematic review and meta-analysis. BMJ open. 2020 Dec 1;10(12):e040146.

1.1 Concepts and definitions of pre-frailty and frailty

Frailty is not a disease or disability, rather it is a clinical syndrome. Frailty has been defined by Fried et al as a clinical syndrome having a combination of three or more of the following symptoms present: unintentional weight loss, weakness, exhaustion, slowness and reduced physical activity.[1] Although there is no consensus on a gold standard for measurement of frailty, consensus from experts have suggested that an operational definition of frailty should include components from the domains of cognition.[2] In Rockwood's frailty model of cumulative deficits, the importance for poor cognition to be included as one of the possible deficits is emphasised; poor cognition can lead to physical frailty while physical frailty is a predictor of future incidence of cognitive impairment.[3] Hubbard et al have also recently highlighted frailty as a continuum as opposed to a dichotomous syndrome.[4] The Frailty Operative Definition Consensus Conference Project implemented a Delphi consensus building process and experts agreed that it is important to have a more comprehensive definition of frailty.[5] The six domains include physical performance, gait speed, mobility, nutritional status, cognition and mental health.[5] As the definition of frailty is based on specific set of criteria that can be inconsistent, biomarkers have also been explored in attempt to provide a more definitive approach in the clinical setting. However, the usefulness of inflammatory markers such as the C-Reactive Protein (CRP) and Interleukin-6 to define frailty in clinical settings has been shown to be limited.[6]

As a stage prior to frailty, pre-frailty is defined as having any one or two of these above mentioned criteria defined by Fried et al.[1] Recently, a systematic review of definitions of pre-frailty in scientific literature was conducted to clarify its definition.[7] The results from the review helped define pre-frailty as a multi-factorial and multi-dimensional syndrome; a transitional state away from non-frail and towards frailty.[7] As suggested by the authors of the review, a consensus of the definition of pre-frailty was established through an international Delphi consensus.[8] Pre-frailty is now further understood as "*an aged-associated, multi-factorial, multi-dimensional, and non-linear prodromal risk-state associated with one or more of physical impairment, cognitive decline, nutritional deficiencies, and*

socioeconomic inequalities, predisposing to the development of frailty".[8(p.1)]

Pre-frailty and frailty are multi-factorial syndromes involving biopsychosocial aspects of health. As such, individual domains (sub-types) within these concepts are being further explored today. For example, nutritional frailty and social frailty are concepts that have garnered much research attention in recent years.[9, 10] Similarly to frailty, types of pre-frailty have also been classified in literature e.g., physical, social, cognitive, and nutritional.[7] Therefore, it is recommended by experts to address multiple domains rather than individual domains when screening and assessing for both pre-frailty and frailty in older adults.[11]

The definitions of pre-frailty and frailty are still evolving and will solidify as discussions among geriatric experts progresses.[8, 12] Regardless of definitions and classification criteria, pre-frailty and frailty are recognised as transitional states between a wider dynamic process from robustness to functional decline. Notwithstanding variations in definitions and criteria, there appears to be a gradual decrease in total physiological reserves and ultimately a state of insufficiency for maintenance and repair of the physical body of an ageing person.[13] In this thesis, pre-frailty and frailty were defined as dynamic states impacting a person's function within the physical, nutritional, psychological, and social domains.

1.2 Prevalence of pre-frailty and frailty

An updated systematic review and meta-analysis of the prevalence of pre-frailty and frailty across 62 countries was conducted.[14] Based on the two earliest definitions i.e., physical frailty measures, deficit accumulation model, the reported pooled prevalence of these two syndromes were different. The global prevalence for pre-frailty and frailty was estimated to be 46% to 49% and 12% to 24%, respectively.[14] In Australia, the prevalence of pre-frailty and frailty using the Fried Frailty criteria (physical frailty measure)[1] from a pooled dataset of four national cohort, was 48% and 21%, respectively.[15] Population-level prevalence for pre-frailty and frailty varied based on methodological approaches to data collection.[14] This is unsurprising since the criteria to define pre-frailty and frailty can be inconsistent across literature. A step towards defining pre-frailty and frailty using a multidimensional approach that encompassed the physical, nutritional, psychological, and social domains, can more holistically represent the multiple domains within these two syndromes.

Although the pooled data from 240 studies suggest a high prevalence of pre-frailty and frailty, a majority of these studies consisted of older adults in the community and most used physical frailty measures.[14] Another review on pre-frailty and frailty used a multidimensional approach that encompasses the physical, nutrition, cognition, co-morbidity, and social domains.[16] The authors found that the prevalence

of pre-frailty and frailty vary across settings i.e., community (ambulatory and population-based), nursing home, and hospital (Figure 1.) The prevalence of pre-frailty was highest in hospitals.[16] In both hospitals and nursing homes, the prevalence of frailty was also higher than in the community i.e., ambulatory, population-based studies.[16] A systematic review of prevalence of frailty among hospitalised geriatric patients is underway but more primary studies are needed to allow for a more accurate representation.[17]

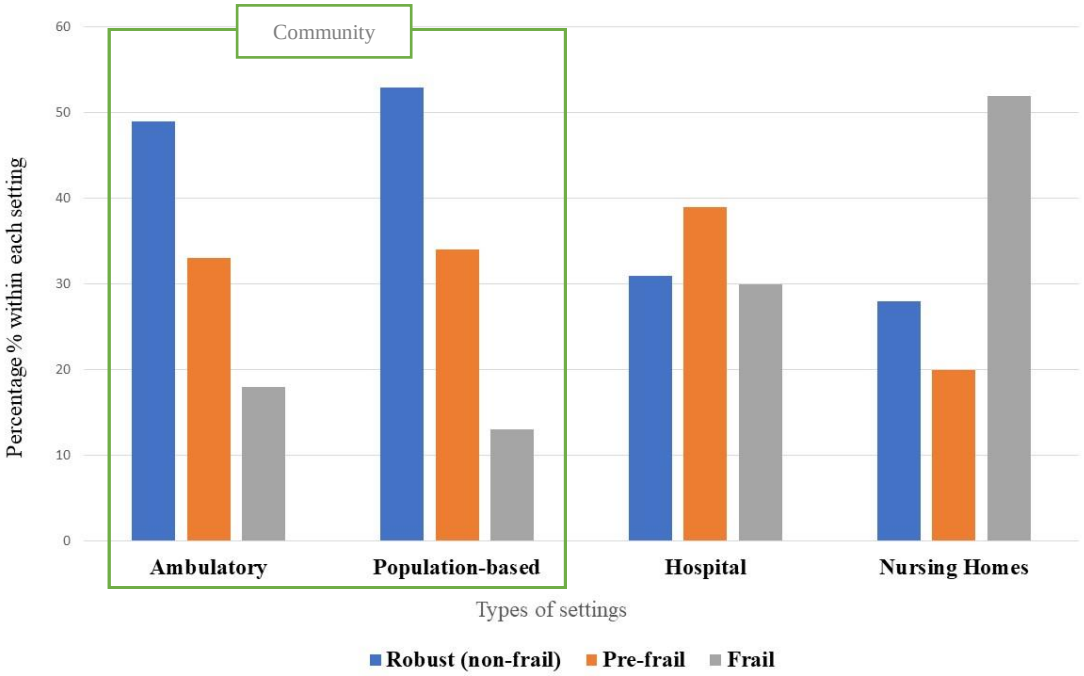


Figure 1. Prevalence of pre-frailty and frailty across settings using a multidimensional approach (adapted from Veronese et al 2021[16])

There are limited studies on pre-frailty and frailty conducted in hospitalised older adults in the context of general medical patients in Australian health care settings. Of the 35 studies included in the systematic review of prevalence of pre-frailty and frailty in hospitals using a multidimensional approach,[16] only one study used data from Australia.[18] A study in the hospitalised older adults that might be pre-frail and frail may help increase the awareness of this issue among general physicians and health care professionals in acute care settings in Australia.

1.3 Factors associated with pre-frailty and frailty

Ageing presents many biopsychosocial changes affecting pre-frailty and frailty. Anorexia of ageing can affect appetite/oral intake and contribute to under-nutrition, reduced muscle mass and strength in older adults.[19] Social factors such as isolation are associated with frailty.[20] The presence of depression has also been suggested to increase the risk for frailty in older adults.[21] A systematic review of frailty and polypharmacy in older adults suggested that polypharmacy might have a bidirectional relationship with frailty.[22] In a later large cohort study comparing polypharmacy between non-frail, pre-frail and frail

older adults, Midao et al found that the prevalence of polypharmacy (defined as taking five or more medications per day) was two and three times higher in pre-frail and frail older adults, respectively.[23] However, these data were derived from a population of community-dwelling older adults, and more data from hospital settings are needed. Several biomarkers have also been identified by the International Conference for Frailty and Sarcopenia Research Task Force in 2019,[24] to be linked to the development of frailty, e.g. inflammatory markers, altered glucose dynamics. However, the level of evidence is still insufficient to implement routine screening and assessment of pre-frailty or frailty using biomarkers. Furthermore, studies that reported factors associated with or clinical outcomes of frailty may not always include pre-frailty. Future studies on frailty, should also include pre-frailty, preferably with measured with a multi-dimensional assessment tool.[8] A study on pre-frailty and frailty in the hospitalised older adults may help improve the identification of at-risk populations in acute care settings in Australia.

1.3.1 Malnutrition in pre-frailty and frailty

Pre-frailty and frailty should be differentiated from malnutrition. Malnutrition is a condition that refers to all abnormalities of optimal nutritional status, including undernutrition and overnutrition in older adults.[25] In this thesis, malnutrition refers to the aspect of undernutrition.[26] As mentioned earlier, pre-frailty and frailty are defined as vulnerable and non-resilient states with short supply of reserve capacity in major physiological systems. On the other hand, malnutrition is defined as a state of nutrient insufficiency, as a result of inadequate nutrient intake or inability to absorb or use ingested nutrients.[27] Malnutrition is also regarded as a chronic state that consequently can lead to poor health outcomes and is associated with a higher risk for pre-frailty and frailty, as part of the syndromes' pathogenesis. Like pre-frailty and frailty, malnutrition is common in hospitalised older adults with a prevalence as high as 50%.[28, 29] The following table (Table 2) adapted from Gingrich et al,[30] provides an overview of the diagnostic criteria of pre-frailty, frailty and malnutrition, and provides an overview of the different areas as described.

Table 2. Diagnostic criteria for pre-frailty, frailty and malnutrition (adapted from Gingrich et al)[30]

	Pre-frailty and Frailty (Fried et al)[1]	Malnutrition (ESPEN)[31]
Weight loss	≥4.5kg unintended in previous year	>10% unintended in previous year
BMI [kg/m^2]	-	<18.5 / <22
FFMI [kg/m^2]	-	<15 (female) / <17 (male)
Grip strength [kg]	≤17–21 (female) / ≤29–32 (male)	-
Usual gait speed [m/s]	<0.65 or <0.762	-
Fatigue / exhaustion	positive answer to ≥1 of 2 questions	-
Physical activity [kcal/week]	<270 (female) / <383 (male)	-

Abbreviations: BMI, Body Mass Index; FFMI, fat-free mass index; ESPEN, European Society for Clinical Nutrition and

Pre-frailty and frailty have intersectional and interdependent relationships with malnutrition (Figure 2), especially in older adults.[32] In their review highlighting the overlap of pre-frailty, frailty and malnutrition, Laur et al identified several gaps and directions for future research addressing pre-frailty, frailty and malnutrition related to this thesis: (1) screening tools to identify pre-frailty and nutrition risk, and interventions are needed; (2) research on the overlapping prevalence rates of pre-frailty and frailty, and malnutrition in hospitalised populations; and (3) develop interventions e.g., nutritional supplements and physical activity, that address pre-frailty, frailty and malnutrition for hospital and community sectors.

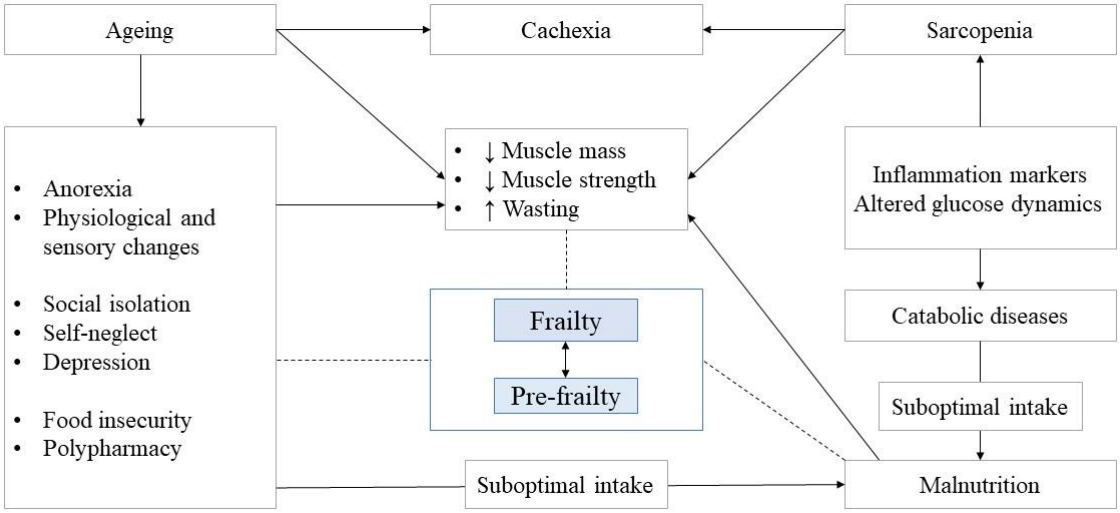


Figure 2. Risk factors for pre-frailty and frailty (adapted from Roy, Gaudreau and Payette 2016)[35]

Pre-frailty and frailty screening and assessment tools often include components that overlap with tools used to identify malnutrition.[33, 34] Therefore, it would be useful to identify a tool that is sensitive and specific enough to detect these conditions simultaneously. The factors related to pre-frailty and frailty (including malnutrition) identified in the literature review as part of this thesis are presented in Figure 2.

1.4 Pre-frailty and frailty in hospitalised older adults: a major public health issue

Pre-frailty and frailty are recognised as increased states of vulnerability such that the ability to cope with acute or daily stressors is compromised.[36] Illness or stressors can cause disability in frail older people but not in the non-frail, highlighting why frail older adults are more vulnerable.[37] Pre-frailty and frailty are also risk factors for functional decline.[38] In a review, Clegg et al demonstrated that those who were non-frail achieved complete recovery after an acute stressor while in frail older adults, functional ability remain impaired such that they are dependent.[37] The time required for recovery was also shorter

in non-frail individual as compared to those deemed as frail.[37] Pre-frailty and frailty are major contributors to late-life disability as they lead to loss of independence,[39] and are associated with poor health outcomes and increased health-care costs and service use.[39]

Hospitalisation further stresses older adults in the presence of pre-frailty and frailty. It can put them at higher risk of functional loss,[40] malnutrition,[28, 41] and further decline in pre-frailty and frailty statuses. In hospital settings, frailty is recognised as a common geriatric syndrome that increases the risk of adverse health outcomes (e.g., longer hospital length of stay, increased mortality) in older adults.[37, 42] Older adults (aged ≥65 years) that have been classified as frail and hospitalised, have a three-fold higher risk of hospital readmission or death, as compared to the younger and non-frail population.[43] However, more evidence on pre-frailty and its impact on the risk of adverse health outcomes are needed.

The clinical management of older adults who are frail has an incremental effect on health expenditures – an estimated additional equivalent of AUD$2400 per frail patient per year.[44] The 3-month healthcare cost (defined by use of inpatient/outpatient treatments, pharmacotherapy, and nursing care) increases with the severity of frailty.[45] Bock et al found such cost to have incremental patterns with increasing frailty symptoms – no symptom (AUD$945), three symptoms (AUD$2390), four or five symptoms (AUD$5412).[45] However, pre-frailty (one or two symptoms) was not considered in that study.[45] Since pre-frailty and frailty represent a spectrum of the same condition, the cost for pre-frailty though yet to be determined, would likely follow a similar trajectory. With 48% of the population over 65 years estimated to be pre-frail and 21% estimated to be frail, concerns of economic impact would be further compounded by the ageing population.[15] Due to its dynamic nature and potentially dire clinical and societal consequences to both the patient and public health system, pre-frailty and frailty are growing public health concerns.[46]

1.5 Screening and assessment in the hospital: challenges and available tools for pre-frailty and frailty

To tackle these growing concerns, screening (i.e., improved detection) and providing early treatment are important, especially in hospital settings, to limit the burden that pre-frailty and frailty can have on the public health system.[47] A standardised screening for pre-frailty and frailty during hospital admissions could facilitate the implementation of early interventions. Ambagtsheer et al have proposed the concept of an electronic index to identify pre-frail and frail patients using data from electronic health records in South Australia.[48] However, there is insufficient robust evidence at present that can link pre-frailty and frailty screening with improved clinical care and cost-effectiveness to warrant public health systems to mandate pre-frailty and frailty screening in hospitalised older adults.[49] Thus, pre-frailty and frailty screening has yet to be made routine in hospitalised older adults. One of the reasons is the lack

of resources and manpower in the time-pressured clinical setting. A proposed solution could be validation of a pre-existing tool commonly used in the hospital that can have a secondary function to detect pre-frailty and frailty to improve identification rates without the need for an additional process of screening.

Although there is currently no international standardised measure for pre-frailty and frailty, there are a multitude of tools to evaluate them.[50] A recent survey study of 388 clinicians from 44 countries showed a wide variety of tools to assess pre-frailty and frailty in hospital settings.[51] Faller et al have summarised a list of 27 tools in a recent systematic review to detect pre-frailty and frailty.[50] Table 3 was adapted from that review to show 11 tools suitable for hospital settings for pre-frailty and frailty assessment.[50]

Table 3. List of tools in English to identify pre-frailty and frailty detection instruments in hospitalised older adults (adapted from Faller et al)[50]

Instrument	No. of items	Domains	Country	Scale type	Measure pre-frailty?
11-point Frailty Index[52]	11	Ph	USA	Dichotomous (frail—not frail) Range: 0–11	No
5-item modified Frailty Index[53]	5	Ph	USA	Dichotomous (frail—not frail) Range: 0–5	No
Brief Frailty Index[54]	5	Ph, Ps, S	Canada	Dichotomous Frail—Not Frail ≥3 frail	No
Care Partners Frailty Index Comprehensive Geriatric Assessment[55]	62	Ph, Ps, S	Canada	Dichotomous (frail—not frail)	No
Clinical Frailty Scale[56]	70	Ph, Ps	Canada, Australia	Ordinal: 1–7 7 levels (from non-frail to complete dependence)	Yes
Edmonton Frail Scale[57]	11	Ph, Ps, S	Canada, Brazil, Colombia	Ordinal: 0–17 5 levels (not frail, apparently vulnerable, mild, moderate, and severe frailty)	Yes
Reported Edmonton Frail Scale[58]	8	Ph, Ps, S	Australia	Ordinal: 0–18. 5 levels (not frail, apparently vulnerable, mild, moderate and severe frailty). Adapted version of the Edmonton Frail Scale	Yes
Gronigen Frailty Indicator[59]	15	Ph, Ps, S	Nether-lands, Romania, Brazil, Germany	Dichotomous (frail—not frail). Range: 0–15. ≥4 frail	No
Trauma-Specific Frailty Index[60]	15	Ph	USA	Dichotomous (frail—not frail), >0.27 frail	No
Upper Extremity Frailty[61]	8	Ph	USA	Ordinal: 3 levels (not frail, prefrail, frail)	Yes
Tilburg Frailty Indicator[62]	15	Ph, Ps, S	Nether-lands, Denmark, Poland, Portugal, Germany, Brazil, Italy, China, Spain	Dichotomous (frail—not frail). Range: 0–15, ≥5 frail	No

Abbreviations: Ph, Physical; Ps, Psychological; S, Social; USA, United States of America

Out of 11 tools identified, four (*Clinical Frailty Scale; Edmonton Frail Scale; Reported Edmonton Frail Scale; Upper Extremity Frailty*) can detect pre-frailty.

1.5.1 Edmonton Frail Scale

The Edmonton Frail Scale (EFS) is one of the most commonly used pre-frailty and frailty assessment

tools for hospitalised older adults.[57] The EFS assesses nine domains contributing to pre-frailty and frailty – cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance.[57] The EFS score ranges from 0-17 points with higher scores indicative of a greater severity of frailty.[57] The total score categorises a patient into one of the following three main categories: non-frail; pre-frail; frail (mild frail, moderate frail, severe frail). The EFS, was first validated in the community but has since been validated in tertiary hospital settings across countries and patient populations e.g., in Canada for elderly patients with acute coronary syndrome,[63] in Ireland for cancer patients undergoing radiotherapy[64] and general medical patients in New Zealand.[65] The EFS evaluates the highest number of clinical domains (a total of nine including cognition, functional performance, general health status, functional independence, social support, pharmacological condition, nutritional aspect, mental condition and continence), which makes it the most comprehensive assessment tool covering all physical, psychological and social aspects of pre-frailty and frailty. It is one of only two tools identified in that review that can assess both pre-frailty and predict mortality.[50]

1.6 Multifaceted interventions combining exercise and nutrition in hospitalised older adults: a systematic review

Exercise and nutrition are inextricably linked, in particular strength training can address component issues of the frail phenotype.[66] Yet much evidence supporting the effectiveness of combined exercise and nutrition interventions for reversal of frailty is limited to community-dwelling older adults.[67] In a study of community participants, a 3-month combined exercise and nutrition intervention resulted in a significant reversal of frailty at 6-months, compared to the control group.[68] The combination of exercise and nutrition intervention in older adults who are frail, has also been reported to increase muscle strength[69] and improve nutritional status.[70] A recent meta-analysis suggested that exercise combined with nutrition was not more effective in treating frailty than exercise alone.[71] However, the majority of included studies were conducted in a community setting, with only 15% of older adults either hospitalised or recruited from acute care settings. The Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR) expert working group now recommends multifaceted interventions combining exercise and nutrition as part of management strategies for pre-frail and frail hospitalised older adults.[72] However, the authors from this workgroup also reported that there were some inconsistencies from the results of the studies cited for their recommendations.[72]

Since many domains of pre-frailty and frailty can be attributed to malnutrition, as described in Section 1.3,[32] the effect of nutrition intervention when combined with exercise, may be more significant in the hospitalised population.[32] Also, a recent review on the effectiveness of multidisciplinary nutritional support in hospitalised older adults suggests that nutritional support, provided by a multidisciplinary

team, may have a positive impact on mortality and quality of life (QoL).[73] The authors suggest that multidisciplinary therapeutic approaches beyond those nutritional are needed because the cause of malnutrition in the hospital is multifactorial.[73] Nutrition interventions also extend beyond protein and nutrition supplementation as reported in previous studies, and may be more effective as part of individualised medical nutrition therapies (MNT) involving dietitians to improve diet adequacy.[74]

This following section presents a systematic review to determine the effectiveness of combined exercise and nutrition interventions on (1) pre-frailty and frailty, (2) pre-frailty- and frailty-related indicators, falls, QoL and (3) cost effectiveness in hospitalised older adults.

1.6.1 Methods

Protocol and registration

The protocol for this review was compliant with Cochrane systematic review guidelines,[75] and registered with the International Prospective Register of Systematic Reviews (PROSPERO), CRD42020153934. The methods reported in this section of thesis were in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[76]

Search methods

Systematic searches of electronic databases (MEDLINE, Emcare, CINAHL, Ageline, Scopus, Cochrane and PEDro) were conducted by the PhD candidate from inception until 10th October 2019 using search strategies reviewed by an academic librarian (search queries available in Appendix 2). Additionally, related citations to eligible items were identified using the suggested related citation function in Pubmed. Reference lists of eligible items were also screened.

Inclusion and exclusion criteria

The inclusion criteria were: 1) randomised controlled trial (RCT); 2) inclusion of pre-frail or frail participants (as defined by study authors); 3) recruitment of older adult inpatients and/or those hospitalised within the past 30 days of recruitment; 4) interventions that started while patients were admitted and continued in the community/post-hospitalisation, or, commenced within 30 days of hospital discharge; 5) interventions that involved both physical exercises and nutritional interventions (dietary modifications/education/training alone or combined with oral nutrition supplementation); 6) measured frailty with an assessment tool or at least one indicator relevant to frailty (nutritional status, physical function, cognitive function and mood, physical activity level or biomarkers, falls and QoL and/or economic analysis of interventions. Studies were excluded if they described protocols with no pilot outcomes, interventions delivered as a part of a palliative care program, or interventions solely

designed to facilitate discharge planning (e.g., telephone support services, providing no pre-frailty or frailty intervention element), recruited participants admitted following a mental health episode.

Study selection and data extraction

Covidence software was used to manage citations for title and abstract, and full-text screening.[77] Screening was performed independently by the PhD candidate and another member of the research team. Any disagreement in screening/selection of studies between the PhD candidate and another member of the research team was resolved through discussion or consensus opinion with a third member. A data extraction form was developed a priori by the PhD candidate and members of the research team. The PhD candidate and a member of the research team performed data extraction independently, on eligible full-text articles. Where available, the continuous data were extracted as (i) mean change with standard deviation (SD), standard error of mean (SE) or 95% confidence interval (CI), or (ii) mean or median values with SD, SE, or interquartile range post intervention. If the required data were not reported within a publication (including change in means for outcomes of interest), the PhD candidate emailed the authors of the articles to request them.

Quality of the studies

The risk of bias in the individual studies was assessed by the Revised Cochrane risk-of-bias tool for randomised trials (RoB-2) by the PhD candidate and another member of the research team independently.[78] Any disagreements were resolved by discussion or if required with consensus of a third member of the research team. The Cochrane risk-of-bias tool is widely used to assess RCTs for best practice.[79] Studies were given an overall risk-of-bias judgement of low, some concerns or high. Overall risk-of-bias was determined as having "some concerns" if any one of the risks of bias domains was rated as having "some concerns". Likewise, studies were deemed to have an overall high risk of bias if any one domain had a high risk of bias.

Data synthesis and statistical analyses

Where possible, a meta-analysis was performed; continuous outcome data were pooled and reported as either the difference of means (MD) if the same outcome assessment tools were used or the standardised mean difference (SMD) if different outcome assessment tools were used, and the 95% CI, if there were two or more studies. The SMD is the mean difference when the outcome for each study is standardised to have mean zero and SD=1. Studies presenting SE were converted to SD via the conversion formula.[75] The fixed-effect meta-analyses were carried out with Cochrane Review Manager (RevMan) 5.3.[80] A P-value of <0.05 was considered statistically significant. The variability between studies (heterogeneity) was assessed by I^2 and its 95% CI.[81] For studies with unobtainable, missing, or incomparable data, results were qualitatively synthesised.

1.6.2 Results

Study selection

The flow of studies through the review process was summarised in Figure 3. For data synthesis and analysis, 20 articles reporting on 11 studies were eligible. A total of three of 11 studies presented results from their cohort across separate publications. First, Villareal et al[82] reported on physical functioning outcomes with biomarker results in the publication of Armamento-Villareal et al.[83] Second, Cameron et al[84] reported on frailty and some physical function outcomes, with other physical function outcomes in a secondary publication[85] fall rates[86] and cost-analysis in another.[87] Third, Luger et al[88] reported on pre-frailty, frailty and nutritional status, with physical functioning outcomes across two other publications,[89, 90] fall efficacy[91] and QoL.[92] For clarity, the primary articles that report pre-frailty and frailty or physical function outcomes are cited for descriptive data in Table 4 and Table 5 while individual articles are cited for synthesis of outcome results.

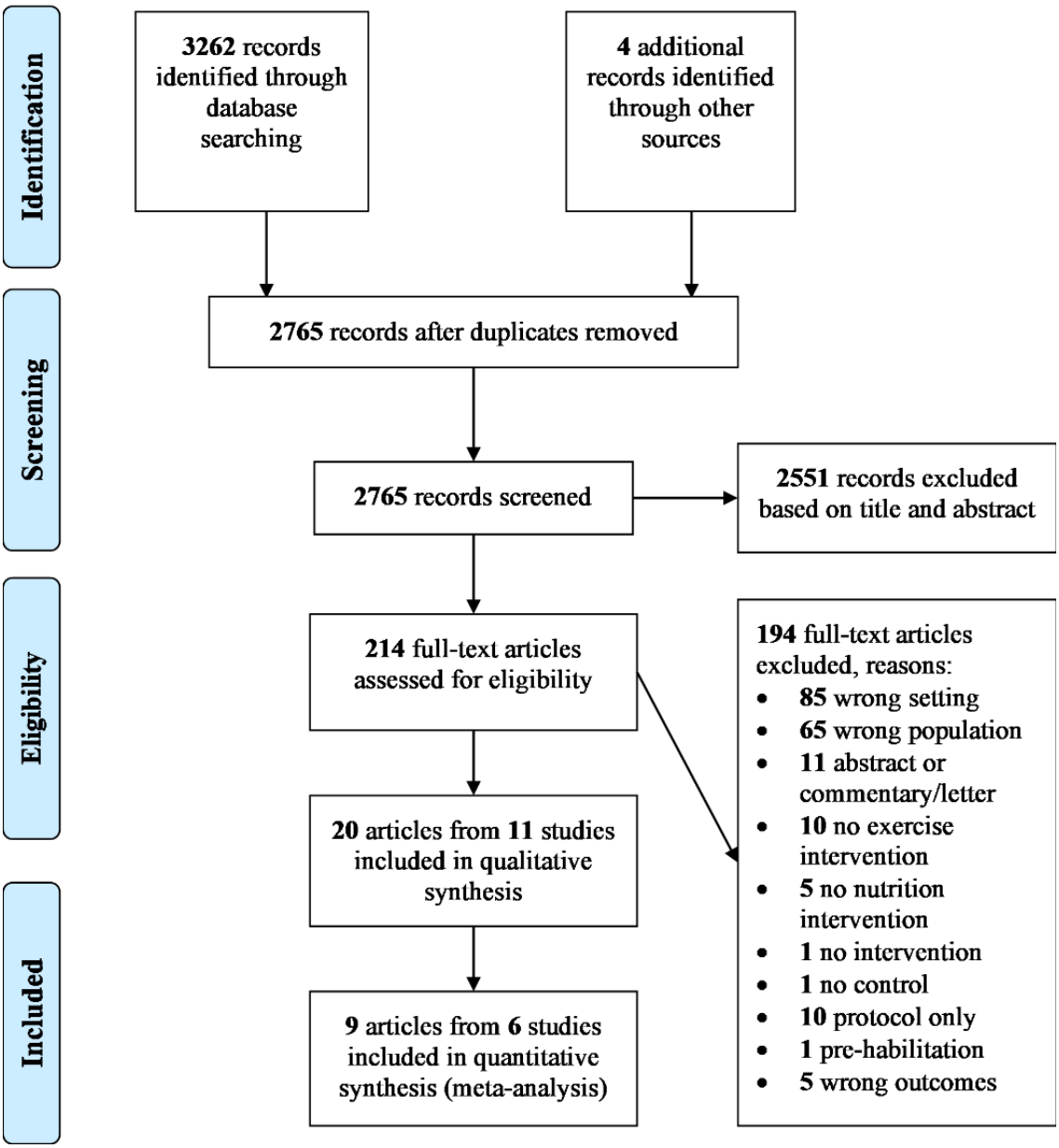


Figure 3. Flow diagram illustrating results of the search and study selection process as described in the PRISMA statement of first systematic review (Section 1.6)

Details of study characteristics are available in Table 4. Across all studies, a total of 2307 participants were investigated. Most studies reported that patients were recruited from hospital wards (n=7)[84, 93-98] while the other four studies[82, 88, 99, 100] included patients that were recruited from hospital wards and the community. Seven studies included only frail participants,[82, 84, 95-98, 100] and the remaining four studies[88, 93, 94, 99] included pre-frail, frail and non-frail participants. The Fried frailty phenotype criteria[1] was used most frequently to classify pre-frailty and frailty (n=4).[84, 93, 94, 99] Luger et al used the Frailty Instrument for Primary Care of the Survey of Health, Ageing, and Retirement in Europe (SHARE-FI)[88] which integrates components of exhaustion, appetite, grip strength, walking difficulties and physical activity.[101] Five studies did not report any assessment method using validated assessment tools to define

pre-frailty and frailty.[95-98, 100] One study used a combination of three tools – modified Physical Performance Test, the measurement of Maximal Oxygen Uptake (VO_2 peak), and the Functional Status Questionnaire.[82] Table 5 shows characteristics of exercise and nutrition interventions of studies reviewed from systematic search.

Table 4. Characteristics of included studies examining pre-frail and frail hospitalised older adults in first systematic review

Study	Country	n	Mean age	Study participants, characteristics	Recruitment site	Duration of intervention	Follow-up period	Pre-frailty and Frailty diagnostic tool/criteria used	Reported % of prefrail, frail
Arrieta et al, 2019[93]	France	302	76.7 ±5.0	Frail, onco-geriatric, older men & women; BMI: 26.1 ±4.6 kg/m^2 (UCG); 26.2 ±4.4 kg/m^2 (IG)	Acute hospital	1y	1y, 2y	Fried frailty phenotype criteria	Non-frail: 73.6% Frail: 26.4%
Rodriguez-Manas et al, 2019[99]	Spain	964	78.0 ±5.4	Pre-frail and frail older men and women with T2DM; BMI: 29.6 ±5.0 kg/m^2	Acute hospitals or primary care sites	4.5m (exercise), 3.5-4w (nutrition)	1y	Fried frailty phenotype criteria	Pre-frail: 62.2% Frail: 37.8%
Niccoli et al, 2017[94]	Canada	47	81.3 ±1.0	Pre-frail and frail older men and women hospitalised patients; BMI: 26.4 ±6.6 kg/m^2 (UCG), 24.2 ±5.2 kg/m^2 (IG)	Acute hospital	Average LOS (days): 20.9 (UCG), 26.5 (IG)	Upon discharge	Fried frailty phenotype criteria	Pre-frail: at least 87.8% Frail: NR
Luger et al, 2016[a,88]	Austria	80	82.8 ±8.0	Frail older men and women; BMI: 27.2 ±4.3 kg/m^2	Acute hospital and community	3m	3m	SHARE-FI (female>0.315; male: >1.212 points)	Non-frail: 1% pre-frail: 35%, frail: 64%
Milte et al, 2016[95]	Australia	175	83.0 ±6.2 (UCG), 82.4 ±5.7 (IG)	Frail older men and women post hip fracture, BMI: NR	Acute hospital	6m	6m	NR	Frail: 100% as determined by study authors
Cameron et al, 2013[b,84]	Australia	241	83.3 ±5.9	Frail older men and women, BMI: 26.4 ±6.0 kg/m^2 (UCG) 26.1 ±5.9 kg/m^2 (IG)	Acute hospital	1y	3m, 1y	Fried frailty phenotype criteria	Frail: 100% as determined by study authors
Singh et al, 2012[96]	Australia	124	79.3 ± 9.6	Frail older men and women; BMI: NR	Acute hospital	1y	4m, 1y	NR	Frail: 100% as determined by study authors

Villareal et al, 2011[c,82]	United States	107	69.3 ±4.1	Frail obese older men; BMI: 36.8 ±4.6 kg/m^2	Acute hospital and community	1y	6m, 1y	≥2 criteria: Modified PPT score 18–32; VO^2 peak of 11–18 ml ml/kg; difficulty in performing 2 IADL or 1 basic ADL	Mild-moderate frailty: 100%
Azad et al, 2008[100]	Canada	91	74.2 and 75.8	Frail CHF older women; BMI: NR	Acute hospital and community	6 weeks	6w, 6m	Screened by a CHF coordinator, frailty assessment undefined	Frail: 100% as determined by study authors
Blanc-Bisson et al, 2008[97]	France	76	85.4 ±6.6	Frail older men and women; BMI: 24.0 ±5.1 kg/m^2	Acute hospital	Until clinical stability	Clinically stable, 1m	NR	Frail: 100% as determined by study authors
Miller et al, 2006[98]	Australia	100	83.5 ±2.8	Frail older men and women with LL fracture; BMI: 22.1 ±4.3 kg/m^2 (ACG), 23.2 ± kg/m^2 (IG)	Acute hospital	3m	3m	NR	Frail: 100% as determined by study authors

Abbreviations: BMI, Body Mass Index; w, Weeks; m, Months; y, Years; VO^2 max, maximal oxygen uptake; PPT, physical performance test; IADL, Instrumental Activities of Daily Living; ADL, Activities of Daily Living; SHARE-FI, Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; T2DM, Type 2 Diabetes Mellitus; CHF, Chronic Heart Failure; LL, Lower Limb, LOS, length of stay; IG, Intervention group; UCG, Usual care group; ACG, Attention control group; NR, not reported; BMI presented in Mean ±standard deviation
Multiple articles reported from same study, study chosen to represent other reports from the same study: [a]Luger et al[88] – Haider et al 2017[89], Winzer et al 2019[90], Kapan et al 2017[91], Kapan et al 2017[92]; [b]Cameron et al 2013[84] – Fairhall et al 2012[85], Fairhall et al 2014[86], Fairhall et al 2015[87]; [c]Villareal et al 2011[82] – Armamento-Villareal et al 2016[83]

Table 5. Characteristics of exercise and nutrition intervention and controls of included studies of first systematic review

Study	Exercise intervention	Nutrition intervention	Control
Arrieta et al, 2019[93]	**Type:** *Strength* **–** Intensity ranged from low to high, starting at 10 repetition per exercise **(UL, LL)** with option of progressive loading *Aerobic, Flexibility, Balance* **–** intensity individualised **Frequency:** 2 sessions/week, duration per session NR + home exercises duration NR **Setting:** Inpatient (supervised, individual) + post-discharge (unsupervised, individual) **Additional support reported:** Phone consults (by trainer 2x/month for first 6 months then monthly for 1 year); Education resource	**Self-guided education resource:** Provided with French National Nutrition Health Program education booklet – *Programme National Nutrition Santé* (PNNS)	**Usual care:** NR, variable between study sites **Self-guided education resource:** Provided with French National Nutrition Health Program education booklet – *Programme National Nutrition Santé* (PNNS)
Rodriguez-Manas et al, 2019[99]	**Type:** *Strength* – 40-80% of estimated 1RM, 8–10 repetitions **(LL)** **Frequency:** 2-weeks pretraining followed by 16-week program of 2 days/week; 20-30 minutes/sessions **Setting:** Inpatient (supervised, individual)	**Nutrition consultation/education:** 7 educational sessions, each 45 minutes, delivered by a trained researcher or nutritional therapist, twice a week over 3.5-4 weeks. Therapy focused on behavioural change, nutrition optimisation and diabetes.	**Usual care:** usual health care from local health system and/or general practitioner
Niccoli et al, 2017[94]	**Type:** *Strength, Aerobic, Flexibility, Balance* – intensity and target muscle group individualised based on patient's baseline assessment **Frequency:** individualised based on patient's baseline assessment **Setting:** Inpatient (supervised, individual)	**Supplements:** Daily ONS with 24g whey protein per day (*9g breakfast, 7.5g at lunch and dinner*) in addition to usual diet	**Usual care:** usual medical care, no whey protein supplementation. **Individual supervised exercise**: Individualised exercises as per intervention.
Luger et al, 2016[a,88]	**Type:** *Strength* –2 sets of 15 repetitions **(UL, LL)** until muscular exhaustion, **Frequency:** 2x/week, >30 minutes each session	**Nutrition consultation/education** Trained lay volunteers visit twice/week for dietary discussions aimed at achieving adequate energy, protein and other nutrients. Taught how to enrich	**Usual care with attention control:** Trained lay "buddies" visit twice a week but doing a portfolio of possible activities (go out, have a chat, and sharing

	Setting: Post-discharge (supervised, individual) **Additional support reported:** Physical education (2-3 times/week, 30 minutes each session); Exercise education resource (demonstration DVD); Motivational interviewing.	food with protein, recipes, healthy for life plate which consists of food-cards and a play board. **Motivational interviewing**: Techniques utilised with nutrition goal setting and tools to reinforce self-efficacy.	interest), especially cognitive training
Milte et al, 2016[95]	**Type:** *Strength, Balance (Otago exercise program)* – Intensity and repetitions NR, at the discretion of the treating physiotherapist **(LL)** **Frequency:** 3 times/week, 20-30minutes/session for 12 weeks **Setting:** Inpatient (supervised, individual) + post-discharge (supervised, individual)	**Nutrition consultation/education:** **I**ndividualised nutrition therapy aimed at improving energy and protein intake to meet requirements by dietitian who visits fortnightly. **Meal program:** ordered as deemed necessary by dietitian. **Supplements:** commercial ONS recommended if needed by dietitian	**Usual care:** Usual rehabilitation program recommended during hospitalisation, social visits weekly from trial staff and generic nutrition, exercise and falls prevention information
Cameron et al, 2013[b,102]	**Type:** *Strength, Balance, Aerobic + WEBB program* – intensity and target muscle groups NR **Frequency:** Exercises prescribed 3-5x/week (with 2 sessions for mobility training) for 1 year, supported by up to 10 home visits **Setting:** Post-discharge (supervised, individual) + (unsupervised, individual)	**Nutrition consultation/education:** Clinical evaluation of nutritional intake at home. A series of diet intervention as needed by dietitian. **Meal program:** ordered as deemed necessary by dietitian. **Supplements:** commercial ONS recommended if needed by dietitian	**Usual care:** usual health care during hospitalisation and from their general practitioner and community services after discharge
Singh et al, 2012[96]	**Type:** *Strength* **–** 80% of most recent 1RM or RPE <15, 3 sets of 8 repetitions **(UL, LL)** **Frequency:** 2 sessions/week, session duration NR, over average of 80 sessions in 1 year, start as early as post assessment in hospital or at home. **Setting:** Inpatient (supervised, individual) + (supervised, group-based) **Additional support reported:** Monthly phone consults	**Nutrition consultation/education:** Counselling on increase in diet quality, frequency NR **Supplements:** ONS +/- dietary advice to increase daily energy (400-600 kcal) and protein (20 g/day) intake. For those calcium or vit-D deficient (52%), 12 months of vit-D orally (1000 IU/day) or calcium (1200 mg/d) and vit-D combination supplement **Self-guided nutrition resource:** Food sources of calcium, vitamin D and sun exposure	**Usual care:** standard service offered for hip fracture in the area health service, including orthogeriatric care, rehabilitation service, other medical and allied health consultation as required, and physiotherapy.

Villareal et al, 2011[c,82]	**Type:** *Strength* **–** 65% of 1RM; 8-12 repetitions of each exercise **(UL, LL)** with options for progression *Aerobic*, ~65% of peak HR with gradual progression to 70-85% *Flexibility, Balance* **Frequency:** 90 minutes, 3 sessions/week **Setting:** Inpatient (supervised, group-based)	**Nutrition consultation/education:** prescribed a balanced diet with energy deficit of 500-750 kcal/d from daily energy requirement, 1 g of high-quality protein/kgbw/d. Weekly group consultation with dietitian for adjustments of their caloric intake, goals and behavioral therapy. **Supplements:** 1500 mg of calcium/d day and ~1000 IU vitamin D/d	**Usual care:** General healthy lifestyle advice **Supplements:** 1500 mg of calcium/d day and ~1000 IU vitamin D/d
Azad et al, 2008[100]	**Type:** 'Comprehensive exercise program'; type, intensity and target muscle groups NR **Frequency:** 11 sessions over 6 weeks + NR home exercises **Setting:** Inpatient (supervised, group-based), post-discharge (unsupervised, individual)	**Nutrition consultation/education:** 3 sessions of individualised counselling about diet and nutrition in the management of CHF by dietitian	**Usual care:** Optimal medical care
Blanc-Bisson et al, 2008[97]	**Type:** *Strength* **–** intensity (RM) NR, 10 x repetitions each exercise **(LB)** **Frequency:** 30 minutes, twice/day, five days/week **Setting:** Inpatient **(**supervised, individual)	**Meal program:** Geriatric hospital meals of 1800-2000 kcal/d **Supplements:** 1 daily ONS of 200 kcal and 15g protein	**Usual care:** From day 3 to 6, patients started to walk with human help with or without technical assistance in the physiotherapy room for three sessions per week until discharge. **Individual supervised exercise:** Physiotherapy continued at home for one month.
Miller et al, 2006[98]	**Type:** *Strength* – intensity (RM) NR, 2 sets of 8 repetitions (**LL**) with progressive loading, at the discretion of the treating physiotherapist **Frequency:** 3 times/week, 20-30minutes/session for 12 weeks	**Nutrition consultation/education:** Individualised nutrition therapy by dietitian. **Supplements:** single type of ONS to cover the shortfall between individual estimated energy and	**Usual care with attention control group** – received tri-weekly visits weeks 1-6, then weekly visits 7-12 to account for the possibility of the attention effect.

	Setting: Inpatient (supervised, individual) + post-discharge (supervised, individual)	protein requirements and actual intake over 42 days.

Abbreviations: UL, Upper Limb; LL, Lower Limb; NR, not reported; HR, Heart Rate; CHF, Chronic Heart Failure; ONS, Oral Nutrition Supplements, RM, Repetition Max; DVD, Digital Versatile Disc; WEBB, Weight-Bearing for Better Balance exercise program is designed to improve mobility, increase physical activity and prevent falls; Otago exercise program – series of 17 strength and balance at-home exercises for fall prevention program in frail older adults.

Multiple articles reported from same study, study chosen to represent other reports from the same study: [a]Luger et al[88] – Haider et al 2017[89], Winzer et al 2019[90], Kapan et al 2017[91], Kapan et al 2017[92]; [b]Cameron et al 2013[84] – Fairhall et al 2012[85], Fairhall et al 2014[86], Fairhall et al 2015[87]; [c]Villareal et al 2011[82] – Armamento-Villareal et al 2016[83]

Characteristics of exercise intervention component

Characteristics of the exercise interventions used in studies are outlined in Table 5, and included combinations of the following: supervised individual exercises (n=10),[82, 84, 93-100] group exercises (n=3),[82, 96, 100] education including support with resources (digital versatile disc (DVD) or visual aid instruction booklet, n=2),[88, 93] and motivational interviewing using a standardised protocol (n=1).[88] A total of three studies[94, 97, 99] had inpatient-only interventions, five[93, 95, 96, 98, 100] had interventions that extended from inpatient to post-discharge, two[84, 88] studies offered the intervention post-discharge only and one[82] did not report. In the majority of studies (n=9), the exercise component was delivered by a physiotherapist.[82, 93-100] Two studies used trained fitness instructors,[93, 96] and another engaged lay volunteers who received training for the study.[88] All studies included strength exercises as part of their interventions. Only three studies described guidance on training intensity based on repetition maximum's (RM) between 40-80%.[82, 96, 99] Other components of exercise programs included aerobic fitness,[82, 84, 93, 94] flexibility,[82, 93, 94] and/or balance.[82, 84, 93, 94] The frequency of interventions ranged from two[88, 93, 96, 99, 100] to five[84, 97] sessions a week, lasting between 20[95, 98, 99] to 90 minutes[82] each. The duration of exercise intervention varied from six weeks[100] to one year.[82, 84, 93, 96]

Characteristics of nutrition intervention component

Characteristics of the nutrition interventions used in studies, is outlined in Table 5, and included combinations of the following: nutrition consultation/education (n=8),[82, 84, 88, 95-98, 100] oral nutrition and/or multivitamin/mineral supplements (n=7),[82, 84, 94-98] meal programs (n=3),[84, 95, 97] self-guided education materials (n=2),[93, 96] and motivational interviewing (n=1).[88] The most common combination of nutrition intervention was consultation/education with oral nutrition and/or multivitamin/mineral supplements (n=5).[82, 95, 98, 100] Five of nine nutrition consultation/education interventions were performed by dietitians.[82, 95, 98, 100] Other studies used trained lay volunteers,[88] a researcher/nutrition therapist or did not specify a skill set for who delivered the consultation/education.[99] All counselling/education-based interventions aimed to achieve adequate dietary targets for energy, protein and other nutrients. One study on obese frail participants aimed for calorie deficit but ensured that all achieved 1g/kg/day of protein in the intervention group.[82] The reported frequency of consultations ranged from twice a week[88, 99] to fortnightly.[95, 98] Oral nutrition supplements (ONS) were the most common supplements prescribed to intervention group participants (n=7),[82, 94, 95, 97, 98, 100] typically providing 200-300kcal and 12-24g protein per serve with a frequency of consumption up to seven times a week[94, 97] or as prescribed by dietitians[82, 95, 98, 100] to cover any identified deficits between individually estimated energy and protein requirements and actual intake. Calcium and vitamin D were the two most commonly supplemented micronutrients [82, 96] at doses in the range of 1200-1500mg/d and 1000IU/d, respectively. Meal programs were either delivered as inpatient specialised geriatric meals providing 1800-2000kcal/d or home-delivered meal programs.[84, 95, 97]

Risk of bias within individual studies

Table 6 outlines the risk of bias in individual studies. One study[82] had a low risk of bias and one study had a high risk of bias (including unblinded secondary outcome assessment and insufficient detail on standard care in control groups across recruitment sites). The other nine studies[84, 88, 93-95, 97-100] were rated as having some concerns overall, of which five could have been improved in ≥1 domain. The remaining four studies[27, 31, 39, 41] that were rated as having "some concerns" overall, had risk in only one domain with the most common reason being failure to blind intervention/allocated group to participants. Examples of other concerns about risk of bias included: assessors being aware of the group allocation[88] (measurement of outcomes domain); or a lack of information about participants/researcher blinding to group allocation.[82, 84, 99]

Table 6. Assessment of methodology quality of included studies using Cochrane Risk of Rias 2.0 tool in first systematic review

Study	Cochrane Risk of Bias 2.0 tool assessment domains					
	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Arrieta et al, 2019[93]	+	?	?	?	+	?
Rodriguez-Manas et al, 2019[99]	+	?	+	?	+	?
Niccoli et al, 2017[94]	?	?	+	?	+	?
Luger et al, 2016[a88]	+	+	+	?	+	?
Milte et al, 2016[95]	+	?	+	+	+	?
Cameron et al, 2013[b84]	+	?	+	+	+	?
Singh et al, 2012[96]	+	?	+	—	+	—
Villareal et al, 2011[c82]	+	+	+	+	+	+
Azad et al, 2008[100]	+	?	+	?	+	?
Blanc-Bisson et al, 2008[97]	+	?	+	?	+	?
Miller et al, 2006[98]	+	?	+	+	+	?

Key: + = Low risk of bias; ? = Some concerns of risk of bias; — = High risk of bias

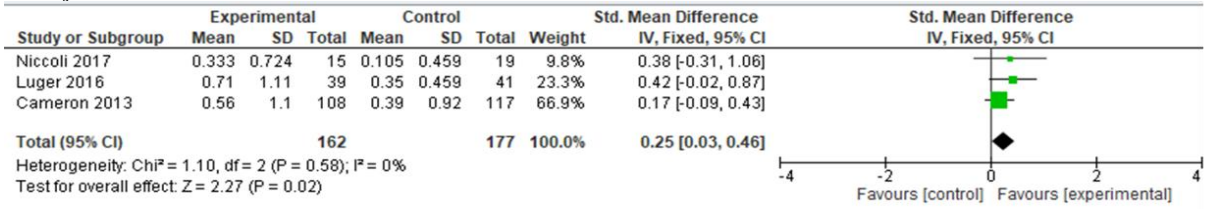
[a]Deviations from intended interventions (effect starting and adhering to intervention)

Multiple articles reported from same study, study chosen to represent other reports from the same study: [a]Luger et al[88] – Haider et al 2017[89], Winzer et al 2019[90], Kapan et al 2017[91], Kapan et al 2017[92]; [b]Cameron et al 2013[84] – Fairhall et al 2012[85], Fairhall et al 2014[86], Fairhall et al 2015[87]; [c]Villareal et al 2011[82] – Armamento-Villareal et al 2016[83]

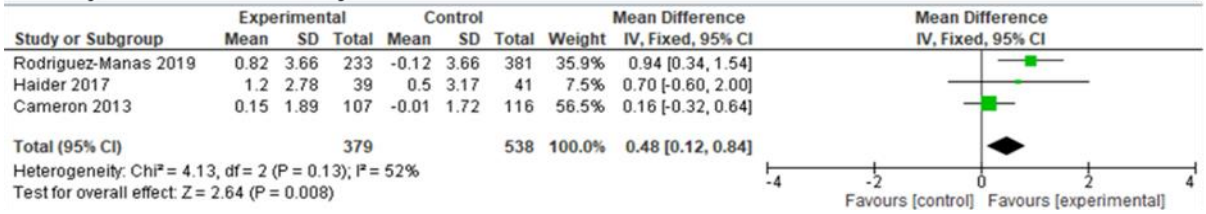
Effectiveness of combined exercise and nutrition interventions

The results from the meta-analyses (Figure 4) suggest that participants who received combined exercise and nutrition intervention had greater reduction in frailty scores (n=3, SMD 0.25; 95% CI 0.03-0.46; P=0.02) and improvement in short physical performance battery (SPPB) scores (n=3, MD 0.48; 95% CI 0.12-0.84; P=0.008) compared to standard care. Only chair-stand test (n=3) out of the three SPPB components was significantly improved (MD 0.26; 95% CI 0.09-0.43; P=0.003). Patients were more independent in activities of daily living in intervention groups, but high heterogeneity was observed (I2=96%, P<0.001). The pooled effect for grip (n=3) +/- knee extension muscle strength (n=4) was not statistically significant. Most studies assessed participants' nutritional status at baseline, while only one study[88] assessed it as an outcome. Luger et al reported a 1.54-point improvement in the Mini-Nutrition Assessment (MNA) long form tool, in participants who received combined exercise and nutrition intervention compared to those who received standard care (95% CI 0.51-2.56, P=0.004). Combined exercise and nutrition intervention did not affect cognitive status (mini-mental state examination (MMSE)) or mood (geriatric depression scale (GDS)).[100] Armamento-Villareal et al reported a significant decrease in total and free oestradiol in their frail obese older men (attributed to weight loss from lifestyle change rather than the intervention), without a clinically meaningful increase in total or free testosterone levels.[83] In one study that reported CRP levels, this inflammatory marker remained stable in the combined exercise and nutrition intervention group participants, compared to an increase in the social support control group at the end of 12 weeks (P=0.04).[103] Three studies[87, 92, 95] that evaluated QoL could not find statistically significant improvement in the intervention as compared to the control group. Fairhall et al[86] found that risk factors related to falls (physical tests as mentioned above) but not rate of falls were reduced while Kapan et al[91] found that a 10% reduction in fear of falling as ascertained by the falls efficacy scale.

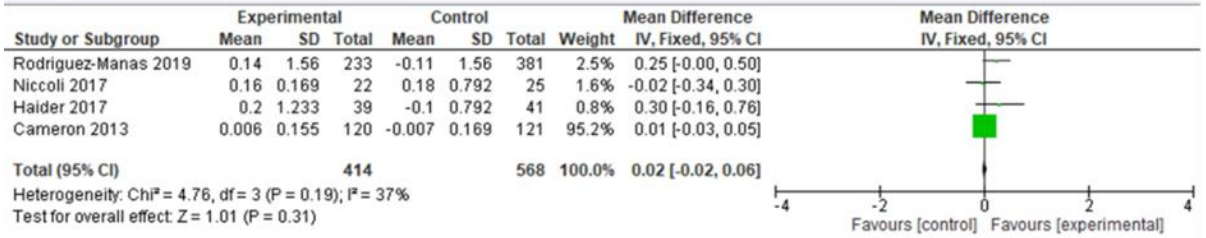
Frailty



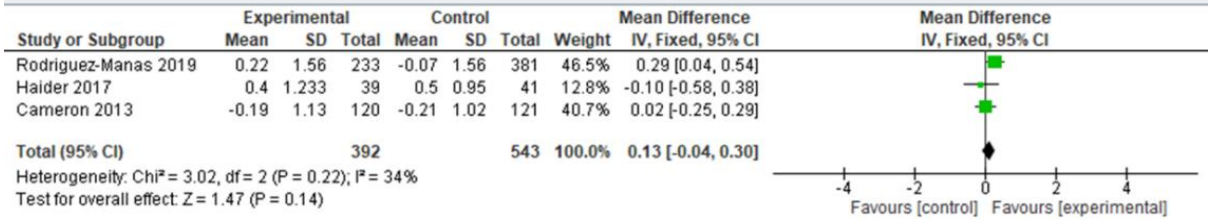
Short Physical Performance Battery



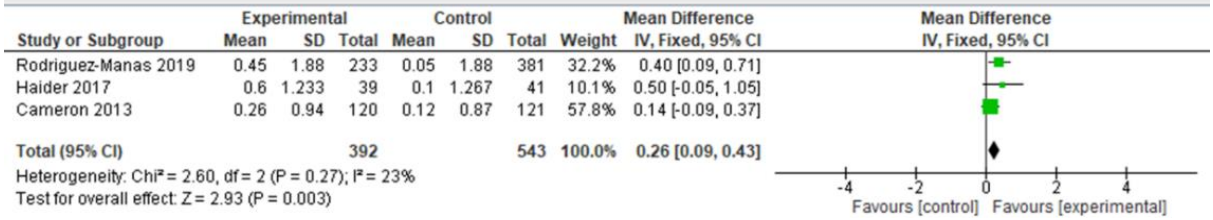
Gait speed



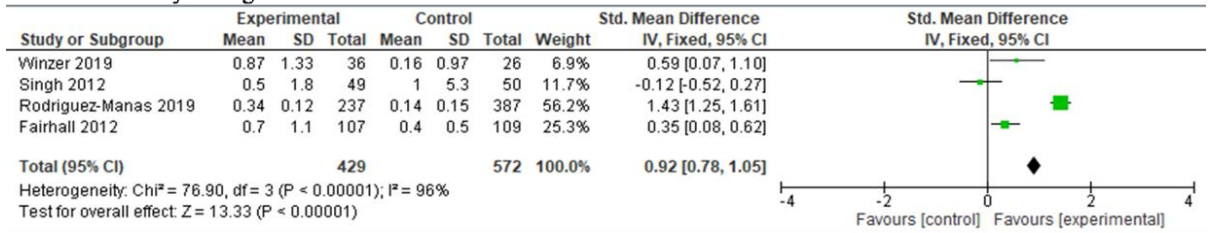
Balance test



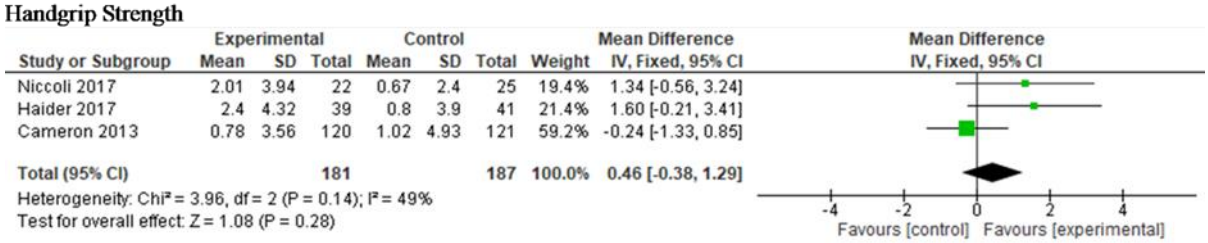
Chair stand test



Activities of Daily Living



Handgrip Strength



Abbreviations**:** CI, Confidence Interval; IV, Inverse Variance; SD, Standard deviation; Std, Standardised

Figure 4. Meta-analysis of reduction in pre-frailty and frailty and their related outcomes for combined exercise and nutrition intervention versus standard care

Economic analyses

Only two studies examined the cost-effectiveness of their combined exercise and nutrition interventions. Fairhall et a[87] reported no additional resource cost in terms of medical (P=0.87) or nursing and health professional appointments (P=0.32). Similarly, Milte et al[95] reported no cost differences between groups (P=0.868).

The INTERACTIVE study

From hand searching of the references of a study[95] identified in this review for publication of its clinical outcomes related to pre-frailty and frailty, the PhD candidate found its published protocol paper only.[104] As with its economic analysis article,[95] this study fits the criteria of the first systematic review and was a national study on older adults with hip fractures, that may also be pre-frail and frail – **I**ndividual **N**utrition **T**herapy and **E**xercise **R**egime: **A** **C**ontrolled **T**rial of **I**njured, **V**ulnerable **E**lderly (INTERACTIVE). The study evaluated a 6-month combined exercise and nutrition intervention, delivered within two weeks of surgical intervention in hospitalised older adults with hip fractures, that may also be pre-frail or frail. However, only economical outcomes were reported.[95] Thus, its outcomes related to pre-frailty and frailty could not be included in this section. The principal investigator for this study was contacted and the PhD candidate noted that results were not analysed due to limitation in resources then. As this was a one of the important studies in the early phases where pre-frailty and frailty were still poorly defined, the results would inform future design of such intervention in Australia.

1.6.3 Discussion

Main findings

Section 1.6 presents updated evidence that suggests combined exercise and nutrition intervention to be effective on pre-frailty and frailty, and their related physical outcomes in hospitalised older adult patients. When compared to standard care, combined exercise and nutrition interventions improved pre-frailty and frailty as determined by the Fried Frailty criteria[1] and the SHARE-FI.[101] They also improved physical function according to the SPPB and ADLs. Only one study measured and found significant improvement in nutritional status.[88] The two economic analyses included in the review of Section 1.6 suggested that combined exercise and nutrition interventions, though more effective, were not more costly than standard care.

Existing reviews of exercise and nutrition interventions have highlighted heterogeneity in study protocols (including intervention descriptions), which limit the potential for quantitative analysis. They have also focussed on community dwelling participants.[105] As discussed in the previous sections, there needs to be more research on the more vulnerable hospitalised populations.

From this review, the PhD candidate found that out of five studies in this review that used a validated pre-frailty and frailty assessment tool, only three had assessed pre-frailty and frailty at outcome, and available for quantitative analysis. This could be because the frailty phenotype was first described 2001, with a systematic evaluation of frailty tools a decade later.[1, 106] As previously discussed, the definition of pre-frailty and frailty, though better defined now than a decade ago, are still evolving. Nonetheless, the studies reviewed in this section additionally evaluated components such as physical function, nutrition, cognition and biomarkers as baseline and outcome measures that are related to pre-frailty and frailty. Although not specific to pre-frailty and frailty, these measures provide an insight to the effectiveness of combined exercise and nutrition interventions on improving various components of pre-frailty and frailty and may inform future studies.

Previous reviews have found mixed results[105] or have concluded that evidence for combined multi-domain interventions for pre-frailty and frailty is limited but increasing.[107] The results from this review concur with RCTs of combined exercise and nutrition interventions conducted in community dwelling pre-frail and frail older adults. Tarazona-santabalbina et al found significant improvement in SPPB in participants on a 24-weeks combined exercise and nutrition intervention as compared to controls in a community dwelling frail population – intervention group 9.5±1.8 versus control group 7.1±2.8, P=0.007.[108] Similarly, Kim et al reported a 12-weeks, community-based study of frail older adults that found SPPB to remain stable in the intervention group, while it decreased by 12.5% (1 point) in controls (P=0.039).[109] The meta-analysis of individual components of the SPPB in this review suggest that the significant improvements in functional muscle strength as represented by the chair stand component of the SPPB may be pivotal to the increase in overall SPPB post intervention and reflect the functional lower limb strength training focus of the exercise interventions. However, the meta-analysis of grip +/- quadriceps strength did not produce a similar trend. Diversity in outcome measures for pre-frailty and frailty, and their related domains like physical function can be a challenge for comparative analyses between studies. Future studies should carefully consider measure responsiveness when selecting outcome tools.

Nutrition is another important domain within pre-frailty and frailty. Yet the majority of studies included in this review only reported nutritional status at baseline, with only one study reporting follow-up nutrition assessment at the end of the intervention.[88] Luger et al described an improvement in nutritional status in a sample of at risk malnourished pre-frail and frail patients (thus likely to benefit most from nutrition therapy). As hospitalised patients have greater energy deficits due to catabolic stress of acute illness, they are a population that requires careful determination of energy/protein requirements and in whom additive effects of nutrition supplementation to exercise may have greatest impact on outcomes such as muscle strength.[108] As none of the studies in the present review reported on energy deficits, it is not known whether these patients received adequate replacement. Nutrition supplementation should also not be confused with nutrition or diet modifications. The provision of ONS alone is unlikely to

augment diet adequacy as completely as diet modification that involves a wider range of nutrients and non-nutrients[110] especially when led by dietitians.[111, 112]

For both exercise and nutrition based interventions, an understanding of patient participation dynamics and compliance is required because of how these factors can impact on effectiveness.[113] Only five studies in this review reported attendance to program/home visits or phone calls or adherence to prescribed exercise/diet or related advice at rates of 50-90% and 70-93% for nutrition and exercise interventions, respectively. Issues with participants resulting in poorer compliance were not reported in these articles, such that those authors recommend that future studies explore barriers and enablers to adherence in multimodal interventions.

Cognition is another important domain in the multi-dimensional nature of pre-frailty and frailty. Exercise[114] and nutrition interventions[115] may have a far reaching, positive effect on cognition in older adults. However, there was no evidence of an impact on cognition from the study[41] in this review. This is consistent with a network meta-analysis of 13 RCTs that examined combined exercise and nutrition interventions in frail older adults.[116] One suggested explanation is that different neuronal mechanisms could result in a misfit between combinatory approaches of nutrition and physical interventions[116] highlighting that more in-depth research is required.[117]

The economic delivery of new interventions and models of care is important to a range of stakeholders[118] but has been infrequently conducted in previous studies.[105] In this review contributing to the overall background of this thesis, only two out of 11 studies included an economic analysis, with the majority of costs coming from delivery of exercise and nutrition support. The types of consumables that were considered in analyses included nutrition supplements, ankle/wrist weights, mobility aids and medications. Elements of service provision that were considered included community, rehabilitation, residential and transition care service use, which were often reduced and contributed to the net result. The results of this review support previous findings of beneficial effects on pre-frailty and frailty-related outcomes, without increased costs.[105] However, results should be interpreted with caution as omission of other services (such as medication reviews) within a multimodal intervention can impact costing, and there are instances where interventions have not been found to be more cost-effective than usual care.[119] The approach of streamlining and reorganising existing services rather than creating entirely new systems may be preferred.

1.6.4 Summary of findings

Combined exercise and nutrition interventions that start while patients are admitted to hospital and continue in the community/post-hospital, or commence early post discharge, appear to be effective in reducing pre-frailty frailty and some of their related physical indicators. Though effective, the quality of the evidence in this review is low as most studies included had some concerns for risk of bias based

on the assessment of the RoB-2 tool. Given the paucity of high-quality studies on the effectiveness of combined exercise and nutrition interventions on hospitalised pre-frail and frail older adults, more robust research that pays attention to effect of assignment to intervention is needed to increase the confidence in results.

From this review, the PhD candidate identified some gaps in literature: (1) lack of understanding of involvement of dietitians in the nutrition interventions for pre-frailty and frailty (2) lack of understanding of interventions from an end-user point of view as none of the interventions were designed with inputs from end-users (3) lack of patient-centred approaches such as individualisation of combined exercise and nutrition interventions (4) lack of patient self-management components/models in combined exercise and nutrition interventions (5) lack of measurement of participation/compliance of exercise and nutrition interventions and factors affecting them.

1.7 Nutrition interventions and dietitian involvement in pre-frailty and frailty: a systematic review

In section 1.6, it was demonstrated that nutrition is an important domain within pre-frailty and frailty, but there was limited understanding in the nutrition interventions and a dietitian's involvement in them, for pre-frailty and frailty. Nutrition interventions were poorly reported compared to its exercise counterparts in multifaceted interventions involving exercise and nutrition.[120] The role of dietitians within nutrition interventions for pre-frailty and frailty are also unclear, as nutrition interventions may not necessarily be designed or delivered by dietitians in those studies reviewed in Section 1.6. Additionally, nutritional status was not always measured as an outcome. Only one of 11 studies included in the systematic review in Section 1.6 reported both nutritional status at baseline and follow-up.

In a systematic review summarising the effectiveness of interventions to prevent pre-frailty and frailty progression in older adults, Apostolo et al found mixed results.[105] Amongst those interventions, nutrition interventions were summarised as ONS, where evidence favouring ONS use was graded as low to moderate. In a later review, Cruz-Jentoft and Woo highlighted the importance of nutrition (sufficient energy and protein intake) in reversing frailty but this review did not discuss the type of nutrition interventions used and how they were delivered.[121]

Though these reviews proposed nutrition interventions to be beneficial in the treatment and prevention of pre-frailty and frailty, dietitians may not always be involved. Previous studies have demonstrated the potential of nutrition services by dietitians in improving nutritional status, readmission rates and reducing health care cost for older inpatients post discharge.[112, 122] The Academy of Nutrition and Dietetics has recently highlighted the increasing importance of dietitians, as part of a multi-domain approach to help prevent and treat frailty.[74] Furthermore, nutrition interventions that are delivered by dietitians can have different effects from those delivered by non-dietitians.[123] A study found that

including a dietitian in a geriatric discharge liaison-team reduced healthcare costs, compared to a team without dietitian.[122] In that study, older patients that received dietetics care reduced the length of inpatient stay and number of hospitalisations, compared to the control group without a dietitian.[122] The authors suggested that ONS use and the time spent with the dietitian as key factors towards effectiveness in improving nutritional status and thereby reducing hospitalisations.[122]

Dietetics is a profession that requires extensive training and sufficient clinical practice to gain proficiency. However, currently available reviews on nutrition interventions seldom take this important information into consideration. At present, there are no reviews that discussed the types of nutrition interventions and the role of dietitians in such interventions for pre-frailty and frailty. Using a systematic approach, the last section of the Chapter 1 in this thesis aimed to narratively summarise the types of nutrition interventions involving dietitians, and the role of dietitians in them, intended to improve pre-frailty and frailty in older adults, in hospital, community or nursing home settings

1.7.1 Methods

Protocol and registration

Using the Cochrane systematic review guidelines,[75] a protocol was completed and registered with the International Prospective Register on Systematic Reviews (PROSPERO), CRD42020166845. This section of the thesis is also reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[76]

Search methods

Electronic bibliographic databases (Medline, Emcare, CINAHL, Ageline, Scopus, Cochrane) were searched from inception until 10th February 2020. The searches were performed by the PhD candidate. An academic librarian reviewed the search strategies (see Appendix 2 for the search terms and strategies used). Furthermore, related citations to eligible items were identified using the suggested related citation function in Pubmed. Reference lists of eligible items were also screened.

Study selection and data extraction

Citations were uploaded into the Covidence web-based software[77] for systematic reviews for title and abstract, and full-text screening, in duplicate (the PhD candidate and another member of the research team). Any incongruity was resolved with discussion and consensus opinion with a third member of the research team. Using data extraction forms developed by the PhD candidate and the research team, the PhD candidate and a member of the research team performed data extraction independently, on relevant full-text articles. Information extracted included country; intervention arm description (duration, intensity of intervention and any accompanying interventions); control group description (standard,

minimal or no care); compliance to intervention; follow up period; participant characteristics (age, frail classification, and percentage; frailty diagnostic tool/criteria used; nutritional status

Quality of the studies

Similarly to the methods used in section 1.6, the risk of bias assessment, using the Cochrane Risk of Bias tool 2 (RoB-2), was performed independently by the PhD candidate and another member of the research team; discussions were held if there were any disagreements and consensus from a third member of the research team was requested when required.[78] Further details of the RoB-2 criteria was discussed in Section 1.6.1 previously.

1.7.2 Results

Study selection

Through the literature searches, 3476 articles were retrieved after removal of duplicates (Figure 5). Of these, 3334 articles were excluded after screening abstracts and a further 122 articles were excluded after full-text reading. A total of 20 articles describing 16 studies were included in qualitative synthesis. A total of three of 16 studies presented their results through separate publications. First, Luger et al reported results on frailty and nutritional status,[88] but physical function outcomes[89] through another publication. Second, Villareal et al reported their results on physical function outcomes[82] and cognition[124] through separate publications. Third, Rydwik et al reported their findings on physical function outcomes,[125] nutrition outcomes[126] and activities of daily living[127] results through separate publications.

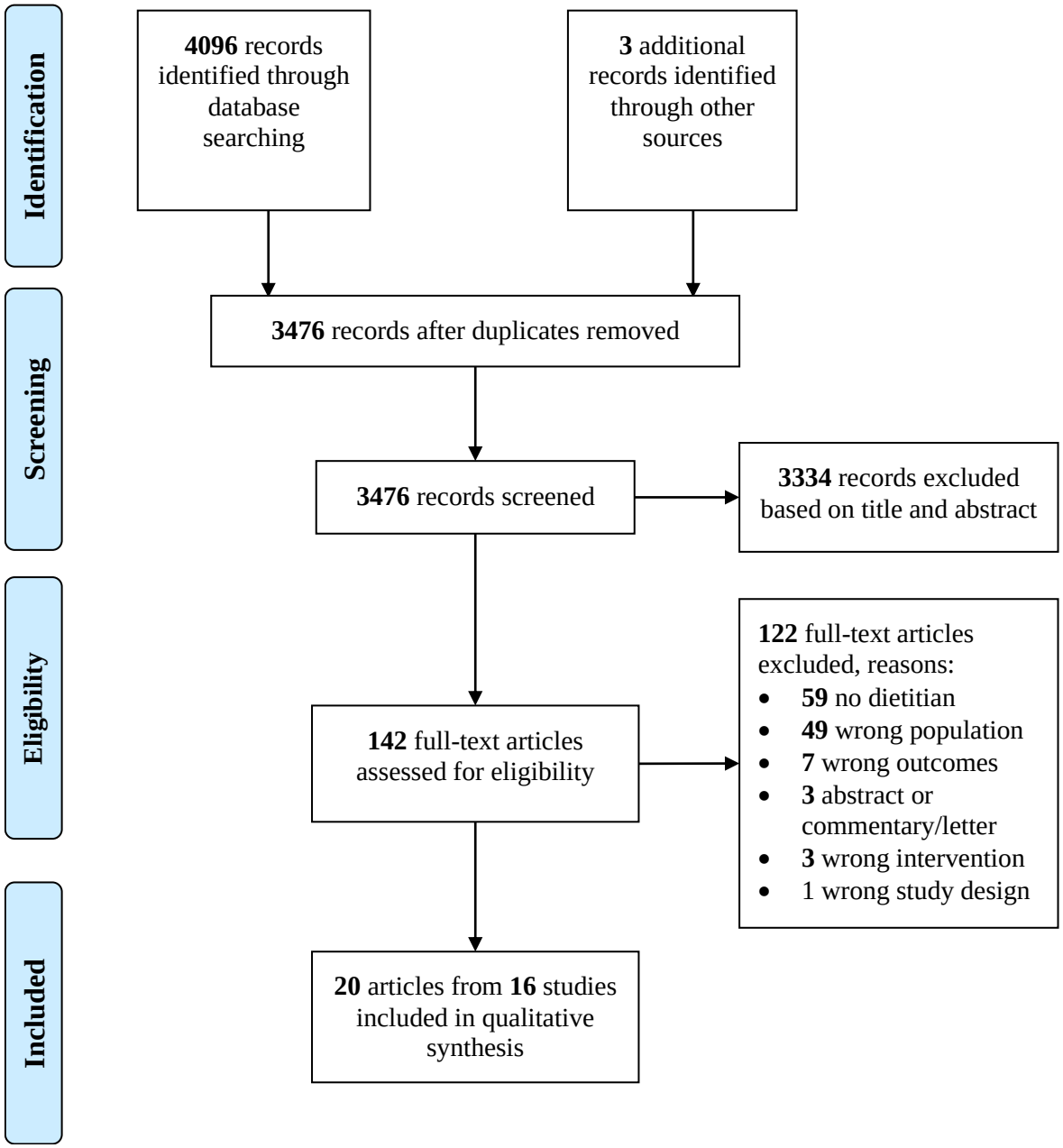


Figure 5. Flow diagram illustrating results of the search and study selection process as described in the PRISMA statement of second systematic review (Section 1.7)

Study and sample characteristics

The details of study characteristics in this review are reported in Table 7. Across all studies, a total of 2646 (range: 46-964) participants were investigated. Studies identified in this review were conducted in Europe (n=6),[88, 99, 125, 128-130] Asia (n=4),[68, 109, 131, 132] United States (n=3)[82, 100, 133] and Canada (n=3).[134-136] The mean age of participants across studies include in this review ranged from 69 to 88 years. Seven studies recruited participants from the community[109, 125, 128, 132, 133, 135, 136] while five studies recruited hospitalised patients[68, 129-131] only and four studies involved participants from both settings.[82, 88, 99, 100] The Fried frailty phenotype criteria was used most frequently to classify frailty (n=5),[68, 99, 109, 131, 132] where older adults were classified as either non-frail, pre-frail or frail if 0, 1-2, or 3-5 criteria were

present, respectively. Luger et al used the SHARE-FI which integrates components of exhaustion, appetite, handgrip strength, walking difficulties and physical activity.[88] A study from Netherlands used the Groningen Frailty Indicator (GFI), a 15-item questionnaire examining domains that include mobility, physical fitness, vision, hearing, nutrition, morbidity, cognition and psychosocial aspects of frailty.[128] One study used three criteria to identify frailty, namely, Functional Status Questionnaire, modified Physical Performance Test and, VO^2 max during incremental physical activity.[82] In other studies, frailty was identified by a chronic heart failure (CHF) coordinator,[100] who used either criteria of physical inactivity and weight loss,[125] or identified potential frail participants as those who needed daily help from the home care facilities or the community nurse.[130] Six studies did not report any assessment tools or pre-set criteria to define pre-frailty and frailty.[100, 129, 133-136]

Table 7. Demographic characteristics of included 16 randomised controlled trials examining nutrition intervention involving dietitians on pre-frail and frail older adults

Authors, y, reference, country	n	Mean age	Participants characteristics, BMI[a]	Recruitment site	Duration of nutrition intervention	Follow-up period	Frailty diagnostic tool/criteria used	Proportion of pre-frail, frail, non-frail (%)
Hsieh et al, 2019,[68] Taiwan	163	72.5 ±5.5, 70.4 ±5.3	Pre-frail and frail older men and women	Hospital (outpatient clinics)	3 mo	3, 6 mo	Fried frailty phenotype criteria	Pre-frail: 89.6% Frail: 10.4%
Rodriguez-Manas et al, 2019,[99]Spain	964	78.0 ±5.44	Pre-frail and frail older men and women with T2DM[f]	Hospital, Community	3.5-4 wk	1 y	Fried frailty phenotype criteria	Prefrail: 62.2% Frail:37.8%
Johnson et al, 2018,[136] Canada	61	79.7 ±9.4, 83.1 ±7.2	Frail older men and women	Community (rural)	6 mo	6 mo	Unreported tool/criteria	Frail: 100%
Terp et al, 2018,[129] Denmark	144	88.0 ±6, 87.0 ±6	Nutritional at risk frail, geriatric patients	Hospital	3 mo	3 mo	Unreported tool/criteria	NR
Van Lieshout et al, 2018,[128]Netherlands	281	73.3 ±6.7, 74.7 ±7.6	Pre-frail and frail older men and women	Community (semi-rural)	23 wk	6 mo, 1 y	Groningen Frailty Indicator	Pre-frail: 59.4% Frail: 40.6%
Wu et al, 2018,[131] Taiwan	36	75.9 ±1.7, 72.8 ±1.6	Pre-frail older men and women; BMI: 24.6 ±1.1, 28.4 ±1.2	Hospital	3 mo	1, 3 mo	Modified Fried phenotype criteria for Taiwan	Pre-frail: 90% Frail: 10%
Luger et al, 2016,[b,88] Austria	80	82.8 ±8.0	Pre-frail and frail older men and women;	Hospital, Community	3 mo	3 mo	SHARE-FI (female>0.315; male: >1.212 points)	Prefrail: 35% Frail: 64% Non-frail: 1%
Pedersen et al, 2016,[130] Denmark	208	86.3 ±6.2, 85.6 ±5.3, 86.4 ±5.5	Malnourished/at risk of malnutrition frail geriatric patients	Hospital	2 mo	Post-discharge, 2 mo post-discharge	Unreported tool; Patients who needed daily help from the home care facilities and help from the community nurse.	NR
Kwon et al, 2015,[132] Japan	53	76.9 ±3.9, 76.5 ±3.8	Pre-frail older men and women	Community	3 mo	3 mo, 1 y	Fried frailty phenotype criteria	Pre-frail: 100%

Starr et al, 2015,[133] United states	67	68.2 ±5.6	Frail, obese older hospitalised men and woman	Community	6 mo	3, 6 mo	Unreported tool/criteria	NR
Kim et al, 2013,[109] Korea	87	78.4 ±6.0, 78.9 ±5.5	Frail older men and women	Community	3 mo	3 mo	Fried frailty phenotype criteria	Frail: 100%
Villareal et al, 2011,[c,82] United States	107	69.3 ±4.1	Frail obese older men; BMI: 36.8 ± 4.6 kg/m^2	Hospital, community	1 y	6 mo, 1 y	≥2 criteria: Modified PPT score 18–32; VO^2 max of 11–18 ml ml/kg; difficulty in performing 2 IADL or 1 basic ADL	Mild-moderate frailty: 100%
Neelamat et al, 2011,[134]Canada	210	74.4 ±9.3, 74.6 ±9.7	Frail, malnourished older hospitalised men and woman	Hospital	During hospitalisation, 3 mo post-discharge	3 mo post-discharge	Unreported tool/criteria	NR
Azad et al, 2008,[100] United States	91	74.2, 75.8	Frail CHF older women	Hospital, community	6 wk	6 wk, 6 mo	Screened by a CHF coordinator, frailty assessment undefined	NR
Rydwik et al, 2008,[d,125]Sweden	46	82.4 ±3.9, 82.5 ±4.4	Frail older men and women	Community	3 mo	3, 9 mo	Combination of inactivity with weight loss	Frail: 100%
Gray-Donald et al, 1995,[135] Canada	48	79.0 ±8.0, 76.0 ±7.0	Frail older men and women	Community	3 mo	3 mo	Unreported tool/criteria	Frail: 100%

Abbreviations: BMI, Body Mass Index; w, Weeks; m, Months; y, Years; NR, not reported; SHARE-FI, Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; PPT, physical performance test; VO^2 max, maximal oxygen uptake; T2DM, Type 2 diabetes mellitus; IADL, Instrumental Activities of Daily Living; ADL, Activities of Daily Living; CHF, Chronic Heart Failure

[a]BMI, if reported in study; Multiple articles reported from same study, study chosen to represent other reports from the same study: [b]Luger et al, 2016[88] – Haider et al, 2017[89]; [c]Villareal et al, 2011[82] – Napoli et al, 2017[124]; [d]Rydwik et al 2009 – Rydwik et al 2010[127], Lammes et al 2012[126]

Characteristics of nutrition intervention components and (possible) roles of dietitians

Five characteristics of nutrition interventions involving dietitians were identified (Table 8).

1. Nutrition counselling (n=14)[68, 82, 88, 99, 100, 125, 128-135] – dietitians provided individualised therapy focusing on behaviour change either face-to-face in clinic or participants' home, or through telephone. These consultation and education sessions were also sometimes done in groups, some of which incorporated cooking.
2. Supplements (n=10)[68, 82, 109, 125, 129, 131, 133-136]
   i. *Commercial ONS* (n=8) – were used as a prescription to be taken daily or to make up for the deficits in the estimated energy/protein requirements. The ONS were typically 200-235ml per serve, providing approximately 200-300kcal energy, approximately 12g protein, and 140-400mg calcium. The frequency of administration ranged from one[136] to two[134, 135] servings per day. However, ONS prescription tailored according to individual participants' needs and requirements was not reported. Dietitian could be involved here to ensure that baseline requirements are met through diet and the optimal use of ONS.
   ii. *Micronutrient supplementation* (n=2) – calcium (400-1500mg/day) and vitamin D (400-1000IU/day). Dietitians could advise participants on its use in conjunction with diet.
   iii. *Food-based supplements* (n=4) – skim milk powder (25g/day); mixed nuts (10g/day);[68, 131] meal top-ups with cooked and chilled/frozen portions of lean beef;[133] between-meal workshop snack.[125] The dietitian could provide tailored instructions to ensure compliance and optimal use of food-based supplementation.
3. Customised dishware (n=2)[68, 131] – compartmentalised plates, bowls, mug, tablespoon; coloured meal pads. Dietitians educated participants implement the use of such tools to ensure its effectiveness.
4. Motivational cards (n=2)[68, 131] – dietitian penned inspirational cards to the intervention participants
5. Therapeutic meals (n=1)[134] – energy- and protein-enriched diet and assorted inpatient snacks in between meals, prescribed by attending dietitians in the hospitals.

Characteristics of accompanying components and compliance

Six studies had interventions other than nutrition interventions, delivered simultaneously to the participants.[88, 99, 100, 125, 128, 132] All six studies[88, 99, 100, 125, 128, 132] included an exercise component; two of which provided additional social support.[88, 128] The strength-based training exercises lasted 20 minutes to one hour per session, conducted once or twice a week individually or in groups, with overall 11 to 32 meetings throughout the intervention period, which ranged from three to six months. [88, 99, 100, 125, 128, 132] One study provided just one session of general physical training advice.[125] Social support provided was in the form of five empowerment workshops conducted by a nurse[128] and during home visits by trained lay volunteers.[88] Six studies did not report compliance. The reported compliance ranges for the intervention was 60-83 %, with only two have adherence rates to intervention >80%.

Table 8. Characteristics of nutrition intervention, other accompanying interventions, and controls of 16 randomised controlled trials examining nutrition intervention in pre-frail and frail older adults in second systematic review (Section 1.7)

Authors, y, reference	Nutrition intervention, and accompanying interventions if any	Control intervention	Compliance[a]
Hsieh et al, 2019[68]	**Nutrition counselling:** individualised nutrition therapy, with follow up telephone calls **Customised dishware:** a plate with four compartments for vegetables and protein foods, a bowl for rice and fruits, a mug for milk and juice, and a tablespoon. Colored meal pad to indicate the personalised food amount on the dishware. **Food Supplements:** 25g of skim milk powder and 10g of mixed nuts/d **Motivational cards**: received inspirational cards at the 1, 3 mo follow-ups, encouraging them to maintain their designated intervention schedules. **Accompanying intervention:** None	**Usual care:** usual medical check-ups, except telephone contacts (for greeting only) by case managers on the third day and at the end of the second mo	Compliance reported as increase in total energy intake and macronutrients, servings of food groups
Rodriguez-Manas et al, 2019[99]	**Nutrition counselling:** 7 educational sessions, each 45 min delivered by a trained researcher or nutritional therapist, twice a wk over 3.5-4 wk. Therapy focused on behavioural change, nutrition optimisation and diabetes. **Accompanying intervention:** 2 wk exercise pretraining phase followed by a 16 wk program consist of 2 d weekly; 20-30 min/session	**Usual care:** usual health care from local health system and/or general practitioner	>70% of the nutrition and exercise adherence to the intervention: defined as attending 5/7 nutrition intervention sessions
Johnson et al, 2018[136]	**ONS:** Instructions given by dietitian on the use of 235ml cans/d of a commercial ONS. ONS supplied weekly. **Accompanying intervention:** None	**Usual care:** no additional interventions other than patient's usual	Not reported
Terp et al, 2018[129]	**Nutrition counselling:** Individually tailored medical nutrition therapy inpatient by dietitian. Follow-ups conducted by nurse or healthcare assistant at 1, 4, 8 wk post-discharge. **ONS:** prescribed by dietitian **Accompanying intervention:** None	**Usual care:** standard inpatient nutrition care by dietitian but no planned follow ups	60% received three visits, 11% received two visits, 10% received one visit, 19% received no visits
Van Lieshout et al, 2018[128]	**Nutrition counselling:** 3 educational sessions, up to 2.5h each time, delivered by dietitian at a local community centre **Accompanying intervention:** 24 exercise sessions of 1h training (by physiotherapist) and 5 empowerment workshops (by nurse)	**Usual care:** wait-listed control used – invited to join intervention upon completion of control period	Not reported

Wu er al, 2018[131]	**Nutrition counselling:** individualised nutrition therapy, with follow up telephone calls **Customised dishware:** a plate with four compartments for vegetables and protein foods, a bowl for rice and fruits, a mug for milk and juice, and a tablespoon. Coloured meal pad to indicate the personalised food amount on the dishware. **Food Supplements:** 25g of skim milk powder and 10g of mixed nuts/d **Motivational cards**: received inspirational cards at the 1, 3 mo follow-ups, encouraging them to maintain their designated intervention schedules. **Accompanying intervention:** None	**Usual care:** usual medical check-ups, except telephone contacts (for greeting only) by case managers on the third day and at the end of the second mo	Not reported, compliance reported as increase in total energy intake and macronutrients, servings of food groups.
Luger et al, 2016[b,88]	**Nutrition counselling:** Trained lay volunteers, supervised by dietitian, visit twice/wk for dietary discussions aimed at achieving adequate energy, protein, and other nutrients. Educate on enriching food with protein; recipes, educational plate, food cards, play board. **Motivational interviewing**: Techniques utilised with nutrition goal setting and tools to reinforce self-efficacy. **Accompanying intervention:** Two sets of six strength exercises and social support from trained lay "buddies" and health-care professionals	**Attention control:** Trained lay "buddies" visit twice/wk but doing a portfolio of possible activities (go out, have a chat, and sharing interest), especially cognitive training	Retention rates 65.5% in nutrition group versus control group with 89.7% at 6 mo follow-up
Pedersen et al, 2016[130]	**Nutrition counselling:** Individually tailored nutritional counselling of the patient and the patient's daily home caregiver by a dietitian one, two, and four wk after discharge from hospital, either by (1) home visit or (2) telephone **Accompanying intervention:** None	**Usual care:** no follow-up after discharge	Not reported
Kwon et al, 2015[130]	**Nutrition counselling:** In the form of weekly cooking classes, lasting 2-3h **Accompanying intervention:** Weekly group-based exercise training sessions, 1h each	**Usual care:** Monthly general health education session	Not reported
Starr et al, 2015[133]	**Nutrition counselling:** Weight reduction diet by intervention dietitian, -500kcal energy deficit, protein 1.2g/kgBW/d, aimed at 0.6kg/wk weight loss. Weekly group classes from wk 3 onwards. Individualised support as per needed by participants. Counselling focused on protein quantity (30g per meal TDS[e]) and quality **Food Supplements:** meal top ups with cooked and chilled/frozen portions of lean beef. **Accompanying intervention:** None	**Nutrition consultation/education:** Weight reduction diet by dietitian, - 500kcal energy deficit, protein 0.8g/kgBW/d for 0.6kg/wk weight loss. Weekly group classes from 3 wk onwards. Individualised support PRN	Attendance at weekly group and weigh-in meetings (Control = 87 ±11%; Protein = 85 ±10%); Protein intake was 1.2 g/kg/d at both time points. In contrast, protein intake in the control group

			remained at 0.8 g/kg/d at 3, 6 mo.
Kim et al, 2013[109]	**ONS:** Instructions given by dietitian on the use of 200ml cans/d of a commercial ONS. **Accompanying intervention:** None	**Attention control:** monthly dietitian visits with small gift. Usual care suspended.	Supplement compliance among the intervention group was 79.4%.
Villareal et al, 2011[c,82]	**Nutrition counselling:** prescribed a balanced diet with energy deficit of 500-750 kcal/d from daily energy requirement, 1g of high-quality protein/kgBW/d. Weekly group consultation with dietitian for adjustments of their caloric intake, goals, and behavioural therapy. **ONS:** 1500mg of calcium/d and ~1000IU vitamin-D/d **Accompanying intervention:** None	**Usual care:** General healthy lifestyle advice **Supplements:** 1500mg of calcium/d and ~1000IU vitamin-D/d	Median attendance: 83% among participants in the diet group.
Neelamat et al, 2011[134]	**Nutrition counselling:** Six telephone counselling by a dietitian to give advice and to stimulate compliance to the proposed nutritional intake (every other wk post-discharge) **ONS:** Daily - two servings of ONS + 400IU vitamin-D3 and 500mg for 3 mo **Therapeutic meals:** inpatient energy and protein enriched diet during hospitalisation **Accompanying intervention:** None	**Usual care:** nutritional support given only on prescription by their treating physician	Adherence to ONS was 80%, complete follow-up on 71% of the patients
Azad et al, 2008[100]	**Nutrition counselling:** 3 sessions of individualised counselling about diet and nutrition in the management of CHF by dietitian **Accompanying intervention:** 11 exercise sessions + unspecified home exercises	**Usual care:** Optimal medical care	Not reported
Rydwik et al, 2008[d,125]	**Nutrition counselling:** Individual dietary counselling, lasting 1h, based on the baseline food record data focusing on food choices and meal patterns. Five group sessions for nutritional needs for elderly. **Food Supplements:** snack given by dietitian during session **Accompanying intervention:** 1 session of general physical training advice	**Usual care**: General advice regarding diet and physical training	Not reported
Gray-donald et al, 1995[135]	**Nutrition counselling:** Weekly home visits by dietitian **ONS:** two 235ml cans/d of a commercial ONS. **Accompanying intervention:** None	**Attention control:** subjects were visited each wk and given encouragement and suggestions to improve the quality of their diets.	68% of intervention were compliant. Average ONS intake: 9.8 cans/wk in experimental group

Abbreviations: ONS, oral nutrition supplements; BW, body weight; TDS, taken three times daily; PRN, Pro re nata; IU, International Units; CHF, Chronic Heart Failure; d, day; mo, month
[a]Compliance for nutrition intervention involving dietitians; Multiple articles reported from same study, study chosen to represent other reports from the same study: [b]Luger et al, 2016[88] – Haider et al, 2017[89]; [c]Villareal et al, 2011[82] – Napoli et al, 2017[124]; [d]Rydwik et al 2009 – Rydwik et al 2010[127], Lammes et al 2012[126]

Table 9. Assessment of methodology quality of included studies using Cochrane Risk of Rias 2.0 tool in first systematic review in second systematic review (Section 1.7)

Study, Year	Cochrane Risk of Bias 2.0 tool assessment domains					
	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of outcome	Selection of the reported result	Overall
Hsieh et al, 2019[68]	+[a]	+	+	+	?[b]	?
Rodriguez-Manas et al, 2019[99]	+	+	?	+	?	?
Johnson et al, 2018[136]	+	?	+	+	+	?
Terp et al, 2018[129]	+	?	—[c]	—	+	—
Van Lieshout et al, 2018[128]	+	?	+	+	+	?
Wu et al, 2018[131]	+	?	—	?	+	—
Luger et al, 2016[d],[88]	+	?	+	?	+	?
Pedersen et al, 2016[130]	+	?	+	+	+	?
Kwon et al, 2015[132]	+	+	+	+	+	+
Starr et al, 2015[133]	?	?	+	+	+	?
Kim et al, 2013[109]	+	+	+	+	+	+
Villareal et al, 2011[e],[82]	+	+	+	+	+	+
Neelamat et al, 2011[134]	+	?	+	?	+	?
Azad et al, 2008[100]	+	+	?	+	+	?
Rydwik et al, 2008[f],[125]	?	?	+	—	+	—
Gray-donald et al, 1995[135]	+	+	+	+	?	?

[a]+ =Low risk of bias; [b]? =Some concerns of risk of bias;[c]— =High risk of bias

Multiple articles reported from same study, study chosen to represent other reports from the same study: [b]Luger et al, 2016[88] – Haider et al, 2017[89]; [c]Villareal et al, 2011[82] – Napoli et al, 2017[124]; [d]Rydwik et al 2009 – Rydwik et al 2010[127], Lammes et al 2012[126]

R*isk of bias within individual studies*

The overall risk of bias of included studies ranged from low to high (Table 9). Twenty articles describing 16 studies were included and graded for risk of bias: low risk (n=3),[82, 109, 132] some concerns (n=10)[68, 88, 99, 100, 128, 130, 133-136] or high risk (n=3).[125, 129, 131] Of ten studies with some concerns, seven had concerns in only one out of five domains of the RoB-2 tool: deviations from intended interventions,[88, 128, 130, 136] missing outcome data,[100] measurement of outcome,[88] selection of reported result,[68] and all studies had a low risk for domain of randomisation. Some studies[88, 99, 100, 128, 132] that included exercise as part of combined intervention were graded as having some concerns for risk of bias. This was based on deviations from assignment to intervention due to the difficulty in blinding the participants, although attempts were made to reduce bias by use of attention controls (for example, a study had personnel assigned to control participants to talk about food and exercise during social visits[88]). The three remaining studies[99, 133, 134] with an overall risk of bias of some concerns, failed to clearly address two of five following domains: randomisation process,[133] deviations from intended interventions,[133, 134] missing outcome,[99] measurement of outcome,[134] or selection of reported result.[99, 135] Three studies were, classified as at high risk of bias by the RoB-2 tool, due to the fact that the assessors were not blinded to participant group allocation,[125, 129, 131] and/or due to the absence of intention-to-treat analysis.[125, 129, 131]

1.7.3 Discussion

This review summarised and described the components of nutrition interventions involving dietitians in a single or multicomponent pre-frailty and frailty intervention programs. The range of interventions summarised highlighted that nutrition interventions go beyond providing ONS. The effects were not extracted as the effects of combined exercise and nutrition interventions have already been summarised in Section 1.6, and effects of nutrition interventions were not the focus of this review.

In the previous review (Section 1.6), the PhD candidate identified that there is a lack of understanding of involvement of dietitians in the nutrition interventions for pre-frailty and frailty. This is echoed in the present review. One of the reasons could be that nutrition interventions often play a supplementary part in those multifaceted interventions involving exercise and nutrition. In this review, six of the 16 included studies in this review included other therapies such as exercise[99, 100, 125, 132] and social support[88, 128] delivered together with nutrition interventions. Furthermore, the types of nutrition counselling were not well-documented in the included studies. Therefore, it is likely that the term “nutrition counselling” used to describe the type of nutrition intervention in this review be an over-generalisation of different aspects of nutrition counselling.[138] In addition, compliance or adherence to nutrition interventions/therapies can be notoriously low, especially in the older adult populations.[139]

Similar to the previous review in Section 1.6, pre-frailty and frailty were not always formally assessed. Seven studies included in this review did not report the assessment tool used to define pre-frailty and frailty their study populations. This could be that the frailty phenotype was a relatively new concept, first described

in 2001,[1] and there could be limitations in identification and implementation of an appropriate assessment tool in earlier studies. Hence, there is a need for future studies to be more rigour in pre-frailty and frailty assessments (using validated multi-dimensional tools) and interventions, and measure adherence to multifaceted interventions involving exercise and nutrition.

1.7.4 Summary of findings

The current review using systematic methods provided a narrative summary of five nutrition interventions involving dietitians and their roles – nutrition counselling, supplements, customised dishware, motivational cards, therapeutic meals. The roles of the dietitians in nutrition interventions centred around individualisation and implementation of one or more strategies. However, as previously mentioned in Section 1.6, there was a lack of understanding towards patient self-management components and understanding of factors affecting adherence to interventions.

1.8 Summary of gaps in knowledge from literature reviews

Limited understanding of prevalence, associated factors and clinical outcomes with pre-frailty and frailty in hospitalised older adult patients – most studies in literature uses the physical frailty measures to report prevalence of pre-frailty and frailty. There are limited studies that reported prevalence of pre-frailty and frailty using multidimensional measures. There is a lack of observational studies conducted in hospital settings. Previous studies have also been focused on factors and clinical outcomes associated frailty, and pre-frailty was not always examined.

Limited tools to screen pre-frailty and frailty – there is no gold standard method to identify pre-frail and frail hospitalised older adults. Pre-frailty and frailty screening are also not mandated in hospitalised older adults due to the lack of evidence linking the practice to better clinical care or cost-effectiveness. There is a scarcity of validation studies on pre-existing tools commonly used in the hospital that can also detect pre-frailty and frailty.

Limited intervention studies using combined exercise and nutrition interventions to improve pre-frailty and frailty, and its related outcomes and inform future designs – in the review of multifaceted interventions combining exercise and nutrition for pre-frail and frail hospitalised older adults, the evidence found was weak due to the paucity of high-quality studies. The main outcome results (other than economical outcomes) from the multisite Australian study, INTERACTIVE, were not reported. There was also limited information on acceptability and adherence of these studies to inform future studies.

Limited understanding of perspectives of intervention services from end-users – existing reviews of exercise and nutrition interventions for pre-frail and frail older adults have highlighted heterogeneity in studies' intervention protocols. However, one commonality was the lack of understanding of interventions

from an end-user point of view as none of the interventions were designed with inputs from end-users.

Limited research on interventions targeted at pre-frailty and frailty that also promotes patient self-management – there is limited research that employs patient self-management models within their interventions combining exercise and nutrition e.g., chronic condition self-management, to determine delayed improvements and achieve long-lasting sustainability of interventions.

Patient participation and factors affecting them – for both exercise and nutrition based interventions, an understanding of patient participation dynamics and compliance is required because of how they can impact effectiveness.[113] Issues with participants resulting in poorer compliance are not always reported, such that the authors from this thesis review recommend that future studies explore barriers and enablers to adherence in multimodal interventions.

Overall aim of thesis

The overall aim of this thesis is to expand knowledge of pre-frailty and frailty in hospitalised older adults and improve their detection and treatment.

1.9 Research questions

1. What are the prevalence, associated factors and clinical outcomes of pre-frailty and frailty in a group of hospitalised older adults?
2. Can a commonly used malnutrition assessment tool that is not specifically used for pre-frailty or frailty also detect pre-frailty and frailty in hospitalised older adults?
3. What were the pre-frailty and frailty-related results of the INTERACTIVE study (identified from the first systematic review) and what can be learnt for pre-frail and frail hospitalised older adults?
4. What do pre-frail and frail hospitalised older adults want in self-managed, hospital-to-home, combined exercise and nutrition support programs?
5. Will a self-managed, hospital-to-home, combined exercise and nutrition support program, be acceptable and benefit pre-frail and frail hospitalised older adults when compared to usual care?
6. What are the barriers and enablers to a self-managed, hospital-to-home, combined exercise and nutrition support program for pre-frail and frail hospitalised older adults?

1.10 Research objectives

1. To investigate the prevalence, associated factors and clinical outcomes of pre-frailty and frailty in a group of hospitalised older adults.
2. To assess the validity (specificity and sensitivity) of the commonly used nutrition assessment tool, patient generated subjective global assessment (PG-SGA), to detect pre-frailty and frailty in hospitalised older adults.
3. To perform a secondary analysis of the INTERACTIVE study and learn the strengths and

limitations to develop an intervention program and pilot RCT for pre-frail and frail hospitalised older adults.

4. To further the understanding of what pre-frail and frail hospitalised older adults want in a self-managed, hospital-to-home, combined exercise and nutrition support program.
5. To develop and assess the benefits and acceptability of a self-managed, hospital-to-home, combined exercise and nutrition support program for pre-frail and frail hospitalised older adults, compared to usual care.
6. To explore the barriers and enablers to the self-managed, hospital-to-home, combined exercise and nutrition support program for pre-frail and frail hospitalised older adults.

1.11 Research Setting

Flinders Medical Centre (FMC) is a major public tertiary and teaching hospital with more than 590 beds. It is also the largest hospital providing medical care within the Southern Adelaide Local Health Network (SALHN), in Adelaide, South Australia. The FMC is co-located with Flinders University and supports leading clinicians and researchers to advance knowledge in healthcare, particularly in aged care and health services for older adults. All patients that are admitted to the hospital are either sent to the general long-stay inpatient wards or the acute medical unit (AMU), a 30-bed general medical unit that treats and discharge patients within 24-48 hours. The AMU may also review and transfer the patient to another unit/facility if longer care is required. The AMU also admits patients for the geriatric services of the hospital, including older patients who require input from the Older Persons Assessment Liaison team and nursing home patients who are seen by the Residential Care Outreach Service team. Flinders medical centre is supported by a range of allied health professionals e.g., physiotherapists, dietitian, occupational therapists, speech pathologists, pharmacists, social workers. Post-discharge care is not delivered by FMC staff but rather the Intermediate Care Services and Community Geriatric Services at SALHN. The primary studies within this thesis were conducted in the AMU.

1.12 Overview of methodology and structure

From February 2020 to January 2022, all research activities were carried out at AMU of FMC, with the exception of the final study (Chapters 6 and Chapter 7) that required home visits to participants. Both quantitative and qualitative methods was used. The detailed descriptions of its methods were outlined in respective chapters. All data/information were recorded on the pre-designed patient information sheets periodically from either patient interview, case notes or electronic medical records after written informed consent was provided (see Appendix 3 and Appendix 4). The main categories of data collected were demographic e.g., age, gender, income; biophysical e.g., pre-frailty and frailty, nutritional status; and psychosocial, e.g., cognition, mood, social support. Qualitative data were also coded from semi-structured interviews. Human ethics approval for all prospective studies required for this thesis were sought and obtained from Southern Adelaide Clinical Human Research Ethics Committee (HREC reference number: HREC/19/SAC/240) − within which the work was undertaken and conforms to the provisions of the

Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). Written informed consent was obtained from each participant by the PhD candidate who was not involved in the usual inpatient care of the patients. Figure 6 illustrates how each research question contribute to the aim of this thesis in expanding the knowledge in pre-frailty and frailty to better their detection and treatment in hospitalised older adults.

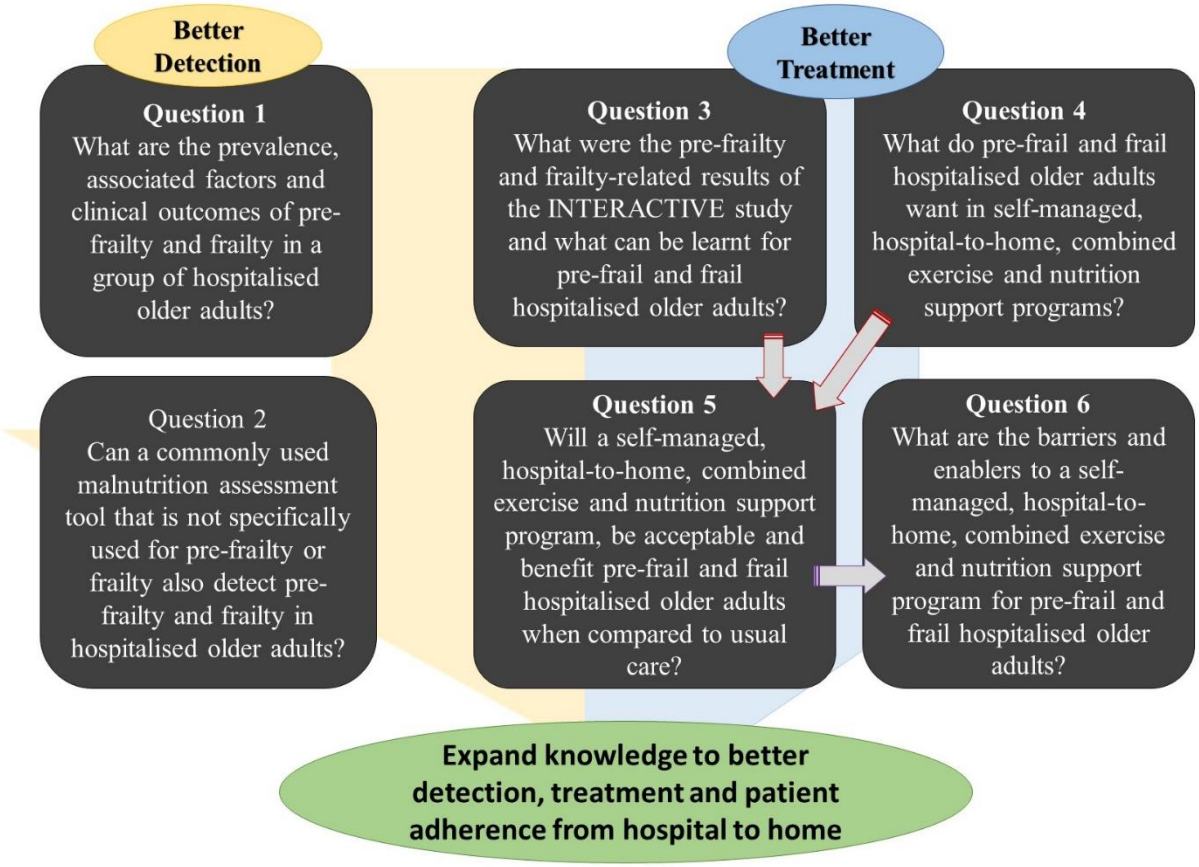


Figure 6. Conceptual framework encompassing research questions from thesis to expand knowledge in pre-frailty and frailty to better their detection and treatment in hospitalised older adults.

CHAPTER 2: PREVALENCE, FACTORS, AND CLINICAL OUTCOMES ASSOCIATED WITH PRE-FRAILTY AND FRAILTY IN HOSPITALISED OLDER ADULTS

2.1 Contribution to overall research objective

The overall objective of this thesis is to expand knowledge in pre-frailty and frailty to better their detection and treatment in hospitalised older adults. As discussed in Chapter 1, there are limited observational studies on pre-frailty and frailty in hospital settings, and the prevalence reported varied based on the type of assessment criteria used. These syndromes were also not often assessed with multidimensional tools to reflect their multidomain areas e.g., social, comorbidity. Prevalence, associated factors, and clinical outcomes associated with pre-frailty were also not as frequently reported as frailty. Therefore, an observational study design was undertaken to answer **Research Question 1 – What are the prevalence, associated factors and clinical outcomes of pre-frailty and frailty in a group of hospitalised older adults?**

2.2 Introduction

As discussed in Section 1.1, pre-frailty and frailty are concepts that are still evolving and described as an age-associated decline of physiological reserves and mechanisms.[140, 141] More recently, pre-frailty was agreed upon to be a multidimensional risk state, related to accumulation of physiological deficits and socioeconomic disadvantage that increases the risk of progression to frailty.[7] Although a systematic review recently investigated the prevalence of frailty, close to half (14/29) of the included studies did not categorise patients who were pre-frail.[142] Therefore, it would be useful to investigate the associations of both pre-frailty and frailty, and their associated factors and clinical outcomes in hospitalised older adults. The identification of factors which are associated with pre-frailty can be helpful in raising awareness of population at higher risk of progression to frailty. An observational study with hospitalised older adults can expand the limited knowledge of pre-frailty and frailty in the hospital setting.

2.3 Methods

All eligible patients ≥65 years, admitted between February to September 2020 to the AMU (Refer to Section 1.11) at FMC in Adelaide, Australia, were approached for participation in this study within 48 hours of their hospital admission. For this study, older patients who were under palliative care/severely or critically ill, unable to speak English, with cognitive impairment (standardised MMSE score ≤24) were excluded. The study was approved by the Southern Adelaide Clinical Human Research Ethics Committee (HREC reference number: HREC/19/SAC/240) − within which the work was undertaken and conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). A written informed consent was obtained from each participant. The recruitment of participants for this study was done by the PhD candidate not involved in their usual care.

Assessment of pre-frailty and frailty status

The Edmonton Frail Scale (EFS) was used to assess pre-frailty and frailty status.[57] As previously mentioned in details in Chapter 1, the EFS assesses nine domains contributing to frailty – cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance, and ranges from 0-17 points.[57] The points classifies the frailty categories of non-frail (0-5), pre-frail (6-7), and frail (≥8).

Factors and clinical outcomes

The age, sex, weight (kg), height (m), day of admission, and comorbidities, of all participants were recorded from the clinical case notes (see Appendix 4 – baseline data collection form part 1). The body mass index (BMI), kg/height (m^2), was calculated from weight and height. The standardised MMSE was used to ascertain cognition.[143] The following variables, which have previously been suggested as risk factors for frailty, were also collected at the time of hospital admission: number of medications, vitamin D supplementation, living status (living alone or with partner/friend), and education level. The Charlson Comorbidity Index (CCI) was used to assess the severity of comorbidities, as a continuous variable in this study.[144] Nutritional status was determined using the scored PG-SGA. The graded portions of the scored PG-SGA categorise a patient to either well-nourished, moderately/suspected of being malnourished, or severely malnourished, while the scored components comprise each of a score ranging from zero to four, based on the degree of impact of symptoms on nutritional status was totalled. Length of hospital stay (LOS), and inpatient mortality was also collected.

Statistical Analysis

All statistical analyses were performed with IBM SPSS Statistics version 27.0 (IBM Corp) and two-sided P-values <0.05 were considered as statistically significant. The sample size for this study was calculated using the sample size calculator accommodating "CI for one proportion" procedure based on previously reported prevalence of frailty (proportion of 0.7, alpha level of 0.05), deployed in the sample size calculator[145] from Australia Bureau of Statistics based on the population of older adults in South Australia in 2019 and the reported prevalence from two previous studies.[146, 147] The PhD candidate aimed to recruit a sample size of 329 participants for this study. One-way analysis of variance (ANOVA), t-test and Chi-square tests of independence using a range of demographic and clinical variables compared (1) non-frail, pre-frailty, and frailty, with post-hoc Bonferroni tests to determine specific differences between groups when necessary. Normality tests showed normal distribution for all measures except CCI. Additional Kruskal-Wallis H tests with Bonferroni correction were conducted for CCI. Next, the associations of factors and clinical outcomes with pre-frailty and frailty were examined by using the multinomial logistic regression models for pre-frailty and frailty, using non-frail as reference. The models were adjusted for variables which were found to be significant (P<0.05) after univariate analysis i.e., one-way ANOVA and Chi-square tests of independence. Additional VIF using linear regression was conducted to test for multicollinearity between CCI scores and number of medications between frailty statuses.

2.4 Results

Prevalence of pre-frailty and frailty

Figure 7. shows the flow of patient recruitment where 329 consecutive participants were included. The participants classified as non-frail, pre-frail, and frail, were 43%, 24% and 33%, respectively. The mean ±SD EFS was 6.2 ±2.9. The combined prevalence of pre-frailty and frailty in this cohort of hospitalised older adults was 57%.

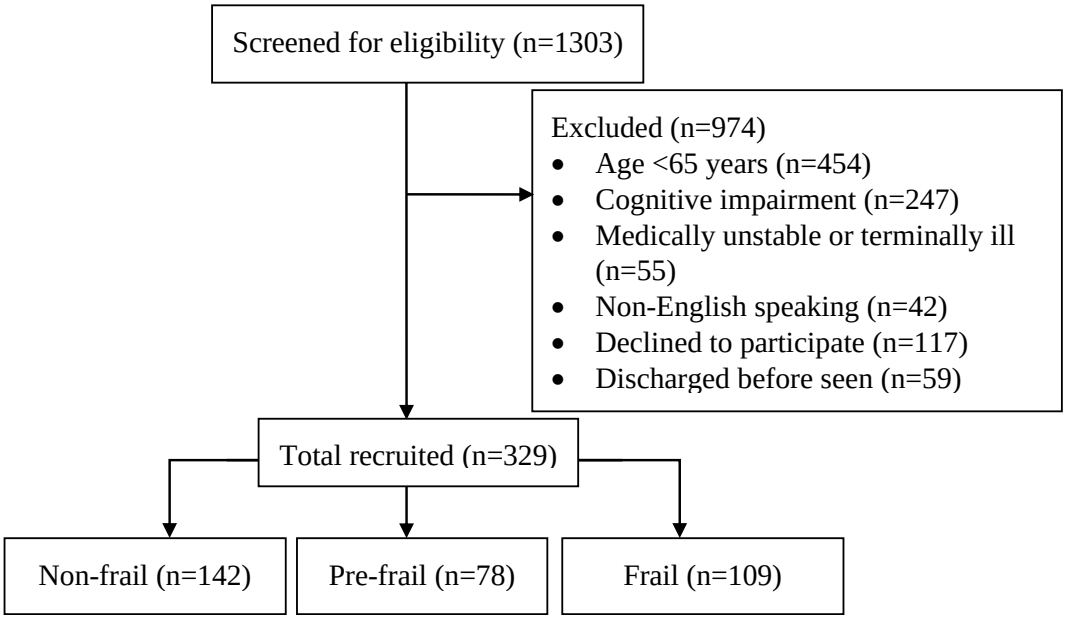


Figure 7. Study flow diagram of consecutive patient recruitment for observational study

Factors and clinical outcomes of cohort

Factors of participants (n=329), by non-frail, pre-frailty and frailty classifications are shown in Table 10. Overall, participants in this study were 79 ±8.2 years old, ranging 65-102. The age range for those non-frail, pre-frail and frail were 65-100 years, 66-93 years, and 65-102 years, respectively. Females made up 54% of the cohort. The mean ±SD score for cognition, as assessed by the MMSE, was 27.7 ±1.6 (range: 25-30). The mean BMI of the cohort is 27.0kg/m^2 and not significantly different between groups. Compared to non-frail participants, participants who were prefrail and frail were significantly older, with a higher comorbidity burden as reflected by the CCI, were more likely to be on polypharmacy and were less likely to have a tertiary-level education when compared to those who were non-frail ($P<0.05$ for all) (Table 10). Post hoc test revealed that CCI was not significantly different between pre-frailty and frailty in this cohort ($P=0.909$). The nutritional status of the participants, as reflected by the PG-SGA score, was significantly worse among those prefrail and frail, when compared to the non-frail group ($P<0.05$ for both). Other factors were not significantly different in the three frailty categories ($P>0.05$) (Table 10). Despite difference detected between all groups ($P=0.009$), LOS was significantly lower for non-frail participants compared to participants who were frail ($P=0.011$) but not different to participants who were pre-frail ($P=0.117$). Inpatient mortality was not compared as there was only one case found in the frail group within this cohort.

Table 10. Factors and length of hospital stay of cohort for each classification by pre-frailty and frailty statuses (n=329)

	Overall (n=329)	Non-frail (n=142)	Pre-frail (n=78)	Frail (n=109)	P-value[a]
Age (years)[b]	79.0 ± 8.2	77.2 ± 8.1	80.0 ± 7.4	80.7 ± 8.4	**0.002**
BMI[b]	27.0 ± 6.3	26.7 ± 6.3	27.2 ± 5.5	27.1 ± 6.7	0.762
Sex[c]					
Male	151 (46%)	69 (49%)	33 (42%)	49 (45%)	0.651
Female	178 (54%)	73 (51%)	45 (58%)	60 (55%)	
MMSE[b]	27.7 ± 1.6	28.2 ± 1.5	27.7 ± 1.7	27.2 ± 1.6	**<0.001**
CCI[b]	4.4 ± 1.5	4.0 ± 1.4	4.9 ± 1.6	4.6 ± 1.5	**<0.001**
No. of Medications[b]	6.3 ± 3.6	4.9 ± 3.5	7.0 ± 3.5	7.6 ± 3.3	**<0.001**
On vitamin D[c]					
Yes	109 (33%)	44 (31%)	27 (35%)	38 (35%)	0.771
No	220 (67%)	98 (69%)	51 (65%)	71 (65%)	
Living alone[c]					
Yes	141 (42%)	56 (40%)	32 (41%)	53 (49%)	0.322
No	188 (57%)	86 (60%)	46 (59%)	56 (51%)	
Education level[c]					
Up to secondary	184 (56%)	66 (47%)	53 (68%)	65 (60%)	**0.006**
Tertiary	145 (44%)	76 (54%)	25 (32%)	44 (44%)	
Income level[c]					
≤20k	141 (43%)	60 (42%)	31 (40%)	50 (46%)	0.693
>20k	188 (57%)	82 (58%)	47 (60%)	59 (54%)	
PG-SGA[c]					
Well-nourished	209 (64%)	120(85%)	47 (60%)	42 (39%)	**<0.001**
Malnourished	120 (36%)	22 (16%)	31 (40%)	67 (62%)	
Scored PG-SGA[b]	5.6 ± 4.5	3.4 ± 3.2	5.9 ± 4.2	8.2 ± 4.8	**<0.001**
Length of Hospital stay[b]	2 (2-5)	2 (1-4)	3 (2-6)	3 (2-6)	**0.009**

Abbreviations: BMI, Body Mass Index; CI, confidence interval; MMSE, Mini Mental State Examination; CCI, Charlson comorbidity index; PG-SGA, Patient Generated-Subjective Global Assessment; EFS, Edmonton Frail Scale [a]P-values obtained by One-way ANOVA tests for continuous variables and Chi-square tests for categorical variables; [b]Values reflect the mean (standard deviation) for continuous variables; [c]Values expressed as absolute numbers (percentage) for categorical variables; percentage may not add up due to rounding.

Factors associated with pre-frailty and frailty after adjusted analysis

Multinomial logistic regression model (Table 11) suggested differences in factors associated with pre-frailty and frailty. Pre-frailty was more likely to be associated with a higher comorbidity burden, polypharmacy, worse nutritional status and with a lower education level, when compared to non-frail participants. Frailty on the other hand, was more likely to be associated with increasing age, polypharmacy, and worse nutritional status. No multicollinearity was found between CCI scores or number of medications (VIF statistics range 1.1 for both).

Table 11. Multinomial adjusted associations of factors by pre-frailty and frailty classification.

	Pre-frail (n=78) OR (95% CI)	P-value	Frail (n=109) OR (95% CI)	P-value
Age	1.03 (0.98-1.07)	0.25	1.06 (1.02-1.10)	**0.008**
CCI	1.32 (1.03-1.70)	**0.028**	1.13 (0.88-1.46)	0.341
Number of medications	1.16 (1.05-1.27)	**0.003**	1.23 (1.12-1.36)	**<0.001**
PG-SGA grade				
Well-nourished	0.77 (0.24-2.54)	0.671	0.67 (0.21-2.09)	0.489
Malnourished	Ref		Ref	
Scored-PG-SGA	1.17 (1.01-1.36)	**0.033**	1.30 (1.13-1.49)	**<0.001**
Education level				
Up to secondary	2.40 (1.27-4.52)	**0.007**	1.67 (0.09-3.09)	0.112
Tertiary	Ref		Ref	

Abbreviations: OR, odds ratio; CI, confidence interval; CCI, Charlson comorbidity index; PG-SGA, Patient Generated-Subjective Global Assessment. Adjusted for all characteristics simultaneously, using participants who were non-frail (n=142) as reference.

2.5 Discussion

The findings of this study indicate an overall high prevalence of pre-frailty and frailty in hospitalised older adults from an AMU. Factors associated with pre-frailty and frailty were not entirely overlapping. When compared to participants who were non-frail, only pre-frailty was more likely to be associated with a higher CCI, and a lower education level. Although nutritional status and polypharmacy were relevant to both pre-frailty and frailty, age was associated with only frailty in this cohort. LOS was also observed to be significantly higher in frailty but not pre-frailty, compared to non-frail participants in this cohort, suggesting that pre-frailty may not be associated with LOS in this cohort of hospitalised older adults.

Prevalence of pre-frailty and frailty

The prevalence of pre-frailty and frailty in hospitalised older adults is high and the results of this study agree with those reported in a recent meta-analysis which included studies from 62 countries.[14] When comparing the participants included in this meta-analysis who were of the same age range (70-79 years) as this study (mean age of 79 years), participants in this study had a higher proportion who identified as frail (33% versus 20%), but a lower proportion of participants who were pre-frail (24% versus 49%). This discrepancy in the prevalence rates of pre-frailty and frailty between the present study in this thesis and the other,[14] may be because participants included here were likely to be acutely unwell, compared to those included in the meta-analysis that excluded participants from hospitals settings. It is well known that acute illness may lead to further worsening of the frailty status (due to factors such as deconditioning).[148] The nutritional status of the hospitalised acutely unwell patients may also decline due to factors such as poor appetite and polypharmacy.[149, 150] Thus, it may be useful to also report the types and frequency of the main diagnosis that led to hospitalisation in this cohort, in addition to reporting a summarised comorbidity score/burden.

Another reason could be that participants who may be pre-frail in the community may shift to a higher severity of frailty at the time of hospital admission and during the course of their hospital stay.[151] Contrary to the findings of this study, the pooled prevalence of pre-frailty and frailty in another meta-analysis of

older medical inpatients (a closer comparison) was higher (84% versus 57%).[142] In that study, the pooled prevalence of pre-frailty alone was also higher compared to this study (36% versus 24%). This could be due to the differences in the selection of participants.[142] Although the mean age in that pooled analysis[142] was not provided, the study reported a narrower mean age range of 73-85 years compared to 65-102 years in the present study. Old age is a risk factor for frailty reported in a review of previous studies.[14] The significant proportion of younger patients (approximately 40% between 65-75 years of age) in this study, could explain the differences in the prevalence rates. Furthermore, this study also excluded patients who were severely/critically ill, those who were palliated as well as those with cognitive impairment, all specific categories of patients who are at a high risk of frailty.[152] The primary role of any AMUs in the hospital is to provide a quick definitive assessment and treatment.[153] The study presented in this chapter provided a snapshot of a specific group of "short-stay" hospitalised older adults.

The other reason for the differences in the prevalence of pre-frailty and frailty could be related to the differences in the tools used for the assessment. The present study used the EFS which is a more holistic tool and assesses nine domains in relation to frailty, covering more breadth than depth of frailty, while the other meta-analysis, compiled studies with mostly physical frailty only.[14, 142]

Factors associated with pre-frailty and frailty

This study suggests that participants with pre-frailty were more likely to have a higher comorbidity burden and were more likely to have a lower education level than those who were non-frail. Although previous studies have determined the association between increasing comorbidity burden and frailty, its association with pre-frailty was only implied.[154, 155] As such, targeted interventions for pre-frail older adults should consider what may be helpful for those with lower education levels. The use of technology might be only suitable for those with higher levels of education. For example, an internet-based program for pre-frail older adults showed potential in improving QoL and health status but the cohort consist of majority (77%) with higher educational levels.[156] Interventions using face-to-face and telephone communications might be better suited for those that are pre-frail with lower education backgrounds. A qualitative study on perspectives of pre-frail older adults (83% pre-frail; 58% lower education levels) on being advised on exercise found that brochures with information, was preferred where advice/intervention was provided.[157] Hence, the mode of delivery (i.e., face-to-face/telephone) and provision of printed education materials may be equally important as the type of interventions in this population.

This study found a higher number of medications to be associated to both pre-frailty and frailty. However, a Spanish study which included 582 patients from primary health care centres, found that polypharmacy was a significant predictor for frailty but not pre-frailty.[158] The higher number of prescribed medications in this present cohort correspond to the fact that patients included in this study had a higher comorbidity burden (CCI 4.4 vs. 1.5) and were significantly older (age 79 vs. 73 years) when compared to the referenced study.[158] A recent systematic review of quantitative studies concluded that polypharmacy is a determinant

of frailty, and that reduction of medications could be a cautious strategy in its prevention and management.[159] This recommendation may be extended to pre-frailty. Pre-frailty and frailty represent a spectrum of the same condition, so the PhD candidate expected the comorbidity burden to be at least the same or much higher in frail patients. The overall CCI in this study was lower (4.4 versus 6.8) compared to a similar previous observational study.[160] This likely was because present cohort only included hospitalised older adults without cognitive impairment. Nonetheless, this study expanded knowledge in a gap identified in Chapter 1, where many studies on frailty did not consider pre-frailty.[160] Furthermore, a recent study also found an association only between increasing age and frailty (OR=1.03, 95% CI: 1.01-1.06), but not pre-frailty.[161] This indicates a need to screen for pre-frailty irrespective of age to optimise care for at risk groups e.g., individuals with multimorbidity.[162]

As mentioned in the earlier parts of this thesis, nutrition is a significant contributor to the spectrum of frailty and the results of this study concur with that i.e., a higher PG-SGA score increases the likelihood of being in the pre-frail (17% more) and frail (30% more) group, as compared to that non-frail. However, this was not seen in the PG-SGA grade. This disparity could be attributed to the responsiveness of the tool – the scored PG-SGA range from 1-20 in this cohort but could only be classified into three group using the grading system.

Strengths and limitations

In this study, pre-frailty and frailty were categorised with a validated multidimensional frailty tool. Factors and clinical outcome i.e., LOS associated with pre-frailty and frailty were also determined. The results of this study were not influenced by cognition as only participants with normal cognition were included. In the older adult population, it is already known that poor cognition has been associated with pre-frailty and frailty.[163, 164] Hence, the results of this study represents a cohort that are capable to self-manage these syndromes if given the chance and right education/training. As patient's height was collected from individual medical case notes, we were unable to determine if it was self-reported or measured during admission using a stadiometer. The sampling for this study was also limited to the AMU. As the participants included in this study were recruited from the AMU, the results cannot be generalised to other specific groups of hospitalised older adults.

2.5 Conclusions

In hospitalised older adults without cognitive impairment, pre-frailty is associated with a likelihood for higher CCI, a greater number of medications, higher PG-SGA score, and higher likelihood to have a lower education level, compared to non-frail participants; frailty is associated with higher age, a greater number of medications, and higher PG-SGA score. The associated factors and clinical outcome i.e., LOS presented in this study highlight that pre-frailty and frailty are different despite representing a spectrum of the same condition.

CHAPTER 3: VALIDITY OF THE PG-SGA TO DETECT PRE-FRAILTY AND FRAILTY IN GENERAL MEDICAL OLDER ADULT PATIENTS

The following section contains materials from a co-authored publication accepted in 2021. Please refer to Appendix 1 for the co-signed author statement and contribution.

Han CY, Sharma Y, Yaxley A, Baldwin C, Miller M. Use of the Patient-Generated Subjective Global Assessment to Identify Pre-Frailty and Frailty in Hospitalised Older Adults. The journal of nutrition, health & aging. 2021 Dec;25(10):1229-34.

3.1 Contribution to overall research objective

The use of a validated assessment tool to identify pre-frailty and frailty can be challenging for clinicians and nurses in the time-pressured hospital environment. As such, screening for pre-frailty and frailty may not be conducted. As discussed in Chapter 1 (Section 1.3.1), pre-frailty and frailty can and often overlap with malnutrition. The results from Chapter 2 also confirmed that malnutrition is associated with pre-frailty and frailty in a cohort of hospitalised older adults. This Chapter builds on Chapter 2 by using data from the same patient cohort to answer **Research Question 2 – can a commonly used malnutrition assessment tool that is not specifically used for pre-frailty or frailty also detect pre-frailty and frailty in the hospitalised older adults?**

3.2 Introduction

The comprehensive geriatric assessment (CGA) is a multidisciplinary endeavour and accepted as the gold standard to identify and care for frail hospitalised older adults.[165] However, CGA requires a team of doctors, nurses and physiotherapists in most cases. In the time-pressured acute care setting, pre-frailty and frailty are commonly assessed by clinical judgement or a range of frailty assessment tools[166] e.g., the EFS.[57] As discussed in Chapter 1, it is important to screen for pre-frailty and frailty in hospitalised older adults. However, due to the lack of evidence that screening translates to better clinical care or cost-effectiveness, it has not been mandated for pre-frailty and frailty. In the literature review in Chapter 1, a suggestion would be validating a pre-existing tool commonly used in the hospital that could also detect pre-frailty and frailty. That could potentially reduce the need of an additional screening process with a single-purpose screening tool. Due to the overlap of frailty and malnutrition,[32] researchers have previously suggested the use of a nutritional assessment tool to both assess nutritional status and also predict pre-frailty and frailty, suggesting benefits for time-pressured clinicians.[33, 167]

As discussed in Section 1.3.1, findings from the literature review suggest that many domains within pre-frailty and frailty overlap with that of malnutrition, especially in older adults. Malnutrition/undernutrition, characterised as a chronic state of nutrient inadequacy, is another common geriatric syndrome seen in the acute care setting.[28] Malnutrition in older adult patients is a significant predictor of negative outcomes such

as readmission or increased mortality.[168] Therefore, it is important to screen and assess hospitalised older adults for malnutrition, so timely interventions can be provided to reduce risk of complications. The PG-SGA is a nutrition assessment tool, commonly used in hospitals.[169] The PG-SGA provides a global rating of nutritional status and classifies a patient to one of three groups: well-nourished, moderately/suspected, or severely malnourished. The scored PG-SGA, is a continuous measure of impact of symptoms on nutritional status.[169] Under each component of the scored PG-SGA, a minimal of zero and maximum of four points are given dependent on the severity of the impact of the symptom on nutritional status. A higher score is indicative of greater risk for malnutrition. Based on the total score, nutritional triage recommendations differ. A score of 0-1 indicates no intervention required at the point of assessment, while score of nine or more implies a critical need for nutritional intervention. The scored PG-SGA consists of two sections: a patient-completed medical component and a clinician portion. The four medical components (weight loss, nutritional impact symptoms, oral intake, and functional capacity), presented in a check-box format, are completed by the patient. The remaining components (diagnosis, age, and metabolic stress), physical examinations, and performed the global assessment of nutritional status is completed by a clinician/nurse. For each component of the scored PG-SGA, points (0–4) are given based on the impact on nutritional status. A greater score suggesting a higher risk of malnutrition and scores ≥9 indicating a critical need for nutritional intervention.

If proven to be sufficiently sensitive and specific to detect pre-frailty and frailty in hospitalised older adults, the use of the scored PG-SGA, to both assess malnutrition and screen for pre-frailty and frailty may save clinicians and nurses much time in the hospital.

3.3 Methods

The present analysis uses the cohort recruited from Chapter 2. The details of methods for data collection have been fully described in Section 2.3. Only measures not discussed in detail in Chapter 2 and statistical analysis are presented.

Nutritional assessment

As mentioned in Chapter 2, the PG-SGA provides a global rating of nutritional status and can classify a person as either well-nourished or malnourished (which is further expanded into two categories: moderately or severely malnourished). The scored PG-SGA, is a continuous measure of impact of symptoms on nutritional status, and a higher score indicates a higher risk of malnutrition, with ≥9 indicating a critical need for nutritional intervention.[169] The scored PG-SGA was chosen as it showed a more accurate representation of malnutrition when compared to the International Statistical Classification of Diseases and Health Related Problems, 10th revision, Australian Modification, and showed strong concurrent validity (sensitivity and specificity) in the older adults, similar to the population of interest in this thesis.[170]

Pre-frailty and frailty assessment

As discussed in Chapter 2, pre-frailty and frailty were assessed using the EFS assessing nine domains – cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence and functional performance, to classify the participants as non-frail, pre-frail or frail[57]

Statistical Analysis

All analyses were performed using SPSS version 27.0 (SPSS Inc, Chicago, IL, USA). Two-sided p-values <0.05 were considered significant. Chi-square test or one-way ANOVA with post-hoc Tukey analysis or contrast test, was performed to compare characteristics between malnutrition status.[171] Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) were calculated to examine the ability of the scored PG-SGA to detect pre-frailty and frailty. The accuracy of scored PG-SGA in detecting pre-frailty and frailty, was assessed by the Receiver Operator Curve (ROC) and Area Under Curve (AUC) using sensitivity and specificity values for each scored PG-SGA cut-off point. To ascertain the most accurate scored PG-SGA cut-off score to reflect pre-frailty and frailty, the Youden Index (YI) (sensitivity + specificity -1) was calculated.[172] To obtain bootstrapped CIs for the YI, as well as for the cut-off score, the cutpt command available in STATA 16 was used.[173] This procedure also provided alternative Liu method for determining the value of the optimal cut point score.[174] Additional variance inflation factor using linear regression was conducted to test for multicollinearity between EFS, LOS and number of medications between nutrition statuses.

3.4 Results

Figure 8. shows the flow of patient recruitment where 329 consecutive patients were included, as presented in Chapter 2, with additional classification of nutritional status. In this cohort, 43%, 24% and 33% of the patients were classified as non-frail, pre-frail, and frail, respectively and the prevalence for combined pre-frailty and frailty in this sample was 57%. In addition, this analysis found 64% of the patients well-nourished and 36% malnourished (26% moderately malnourished, 10% severely malnourished).

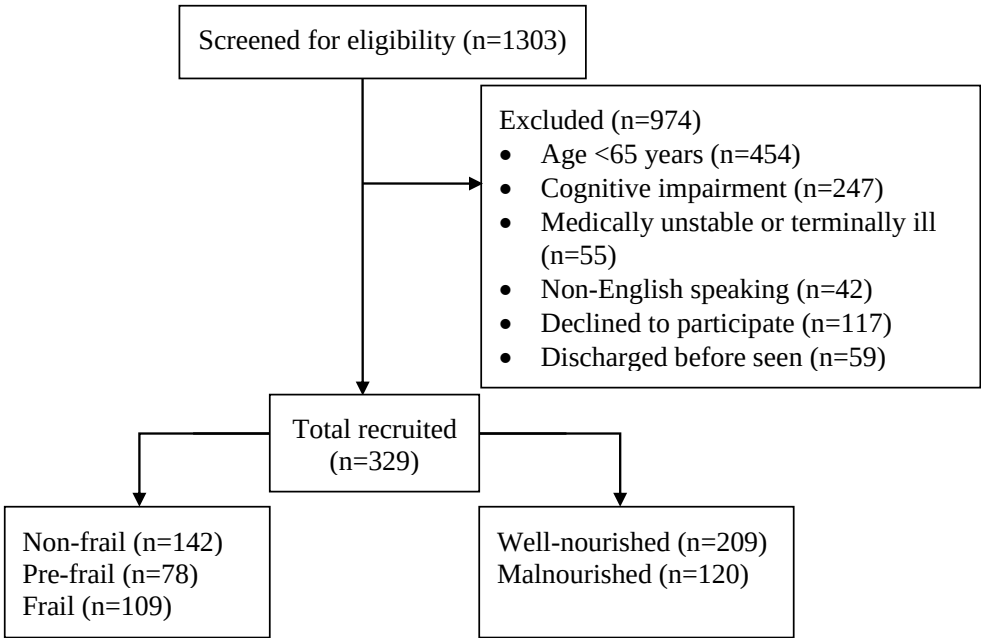


Figure 8. Flowchart of patient recruitment of validation study expanded from Chapter 2

The patient factors (n=329), by malnutrition classification are show in Table 12. LOS and EFS scores were significantly higher in those malnourished compared to well-nourished participants. There were no significant differences between other factors between malnourished and well-nourished participants. No multicollinearity was found between EFS, LOS or number of medications (VIF statistics range 1.0-1.3 for all).

Table 12. Factors and length of stay of cohort by malnutrition status

	Well-nourished (n=209)	Malnourished (n=120)	P-value[a]
Age (years)[b]	79.1 ± 8.3	78.9 ± 8.0	0.815
BMI[b]	27.5 ± 6.0	26.0 ± 6.6	0.043
Sex[c]			
Male	101 (49%)	50 (42%)	0.243
Female	108 (52%)	70 (58%)	
MMSE	27.8 ± 1.5	27.7 ± 1.7	0.545
CCI[b]	4.3 ± 1.4	4.5 ± 1.7	0.288
No. of Medications[b]	5.8 ± 3.6	7.0 ± 3.6	0.004
On vitamin D[c]			
Yes	145 (69%)	75 (63%)	0.202
No	64 (31%)	45 (38%)	
Living alone[c]			
Yes	118 (57%)	70 (58%)	0.741
No	91 (44%)	50 (42%)	
Education level[c]			
Up to secondary	116 (56%)	68 (57%)	0.84
Tertiary	93 (45%)	52 (43%)	
Income level[c]			
≤20k	89 (43%)	53 (43%)	0.90
>20k	120 (57%)	68 (57%)	
EFS[b]	5.3 ± 2.6	7.8 ± 2.7	**<0.001**
Length of hospital stay[b]	2 (1-4)	3 (2-6)	**0.006**

Abbreviations: BMI, Body Mass Index; CI, confidence interval; MMSE, Mini Mental State Examination; CCI, Charlson comorbidity index; EFS: Edmonton Frail Scale
[a]P-values obtained by One-way ANOVA or t-tests for continuous variables and Chi-square tests for categorical variables; [b]Values reflect the mean (standard deviation) for continuous variables, Length of hospital stay presented in median (interquartile range); [c]Values expressed as absolute numbers (percentage) for categorical variables; percentage may not add up due to rounding.

Overlap between pre-frailty and frailty, and malnutrition

The overlap between pre-frailty and frailty, and malnutrition is shown in the Venn diagram below (Figure 9). When examining those who were pre-frail and frail, and malnourished, the prevalence was 30%. This finding confirms the literature review finding in Chapter 1 that the co-occurrence of pre-frailty and frailty, and malnutrition in this cohort of hospitalised older adults admitted to the AMU.

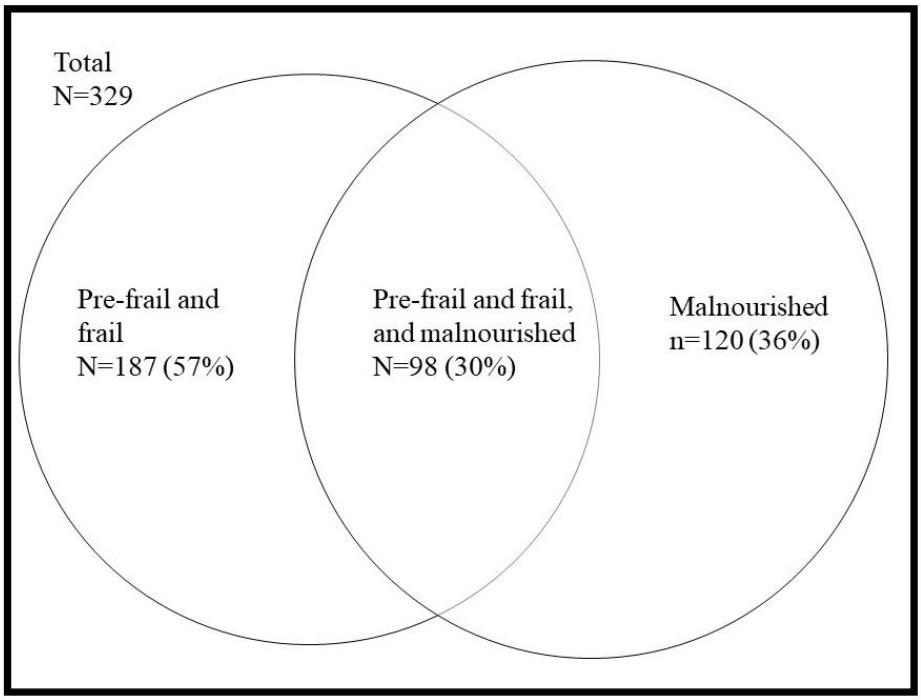


Figure 9. Venn diagram showing overlap of pre-frailty and frailty, and malnutrition in hospitalised older adults

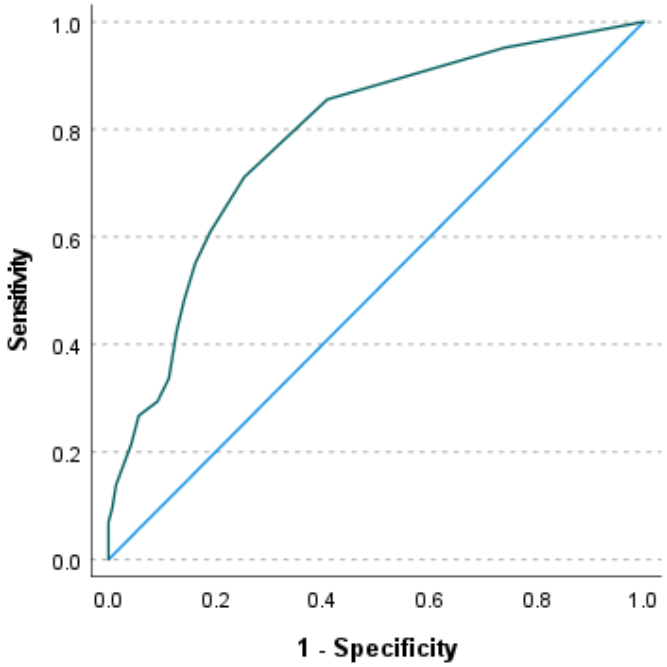
Table 13 shows the ability of the scored PG-SGA to detect pre-frailty and frailty at the selected cut-off points. The optimal scored PG-SGA cut-off score to predict pre-frailty and frailty, determined by the highest YI, was also >3, with a specificity and specificity of 0.711 and 0.746, respectively. Results from the STATA analysis showed optimal cut-off score to also be three (95% CI 1.8 to 4.2; YI 0.458; sensitivity 0.71, specificity 0.75; AUC 0.73). Results from the Liu index did not differ significantly from YI (cut-off score three; 95% CI 2.0 – 4.0; sensitivity 0.71; specificity 0.75; AUC 0.73). The cut-off to detect frailty without pre-frailty was the same (>3).

Table 13. Efficacy values of scored PG-SGA against pre-frailty and frailty classification by EFS

Scored PG-SGA cut-off scores for EFS above 5 (to pick up pre-frailty and frailty)									
	>1	>2	>3	>4	>5	>6	>7	>8	>9
Sensitivity	0.952	0.856	0.711	0.61	0.551	0.481	0.422	0.337	0.294
Specificity	0.261	0.592	0.746	0.81	0.838	0.859	0.873	0.887	0.908
PPV	0.629	0.734	0.786	0.809	0.817	0.818	0.814	0.797	0.808
NPV	0.805	0.758	0.663	0.612	0.587	0.557	0.535	0.504	0.495
Youden Index	0.213	0.448	0.457	0.42	0.389	0.34	0.295	0.224	0.202

PPV, positive predictive value (proportion of patients with positive test results that are correctly identified); NPV, negative predictive value (proportion of subjects with a negative test result that are correctly identified).

As shown in Figure 10, the total area under the ROC curve was 0.782 (95% CI 0.731 to 0.833) using scored PG-SGA for detection of pre-frailty and frailty.



AUC (95%CI): 0.782 (0.731-0.833)
Abbreviations: AUC, area under the receiver operator characteristics curve; CI, confidence interval

Figure 10. Receiver operator curves of Scored PG-SGA to detect pre-frailty and frailty

3.5 Discussion

In this study, an analysis was presented to support the use of the scored PG-SGA to detect both pre-frailty and frailty in older adults without cognitive impairments admitted to the AMU. The results of this study suggest that the scored PG-SGA is a suitable tool to identify hospitalised older adult patients at high risk of pre-frailty and frailty. In addition, the study confirms the co-occurrence of pre-frailty and frailty, and malnutrition in hospitalised older adults without cognitive impairments, admitted to the AMU.

The sensitivity, specificity, PPV, NPV, YI and AUC of the scored PG-SGA are all comparable to another tool, MNA, as evaluated previously.[33, 167] The sensitivity of the scored PG-SGA (at the optimal cut-off score) to detect pre-frailty and frailty is higher than the MNA, presented in a previous study (0.591[33]). A high sensitivity is important for any screening tool as there will be fewer false negatives. However, the specificity of the scored PG-SGA is lower than the MNA, when comparing across optimal cut-off scores of these two aforementioned studies (0.912[33] and 0.913[167]). The higher chance of false positive results could increase cost of additional assessments and patient burden. Nonetheless, leaving pre-frailty or frailty undetected and hence untreated, might incur worse implications and higher costs down the line.[46] Both pre-frailty and frailty increases risk of adverse health outcomes.[162, 175] Therefore, it is important that a screening tool used for these conditions to allow for early intervention.

There could be several reasons why the scored PG-SGA has good sensitivity and specificity in identifying pre-frail and frail hospitalised older adults. One of the shared common characteristics between pre-frail and frail older adults is that they are affected more by nutritional issues, as compared to their non-frail counterparts.[176] Nutritional issues resulting in deficits in energy intake that fail to compensate expenditures can result in weight loss, which can contribute to a higher risk of malnutrition, pre-frailty and frailty.[177] This overlapping symptom is reflected when contrasting the components within the scored PG-SGA and the EFS. Both tools assess and award points to patient with a significant degree of weight loss and loss of functional capacity. For example, one point is given if the patient experienced 2-5.9% weight loss in six months, in the scored PG-SGA. Similarly, one point is given to patients if they reported significant weight loss resulting in looser fitting garments, in the EFS. There are also components that overlap when assessing functional performance. While the scored PG-SGA assess muscle mass as a proxy to oral intake and function, the EFS assesses functional capacity directly with a time-up-and-go test.[178] As muscle mass is related to functional performance and capacity in older adults,[179] the scored PG-SGA indirectly evaluates another component of pre-frailty and frailty. However, there are several components within the EFS that are not assessed directly in the scored PG-SGA. For instance, cognition, social support, mood, and continence are not questioned in the scored PG-SGA. A total of four out of nine domains within the EFS were not assessed directly in the PG-SGA and thus its lack of sufficiency to assess all components of pre-frailty and frailty must be taken in consideration. Moreover, given the accuracy of scored PG-SGA to detect pre-frailty and frailty, nutritional status may have a far-reaching effect on other aspects of pre-frailty and frailty, than those discussed above.[180, 181]

According to the nutritional triage recommendations in the scored PG-SGA, nutritional intervention by a dietitian is required when a patient scores more than three.[169] Based on the results from this study, a scored PG-SGA of more than three indicates that patient is likely to be pre-frail or frail. Hence, the dietitian may likely be required to tackle nutritional issues related to pre-frailty and frailty concurrently, when treating malnutrition.[74] For example, through the use of early combined exercise and nutrition interventions for hospitalised older adults.[120]

As PG-SGA is originally designed to assess those with oncology and other chronic catabolic conditions, the appropriateness of this tool to screen for pre-frailty and frailty in specific settings i.e., AMU, can be further explored in an implementation study. Furthermore, there is an overlapping existence of frailty with chronic diseases including cancer. (Ethun et al 2017) The use of the PG-SGA to detect pre-frailty and frailty may be most useful in the context of geriatric oncology patients.

Strengths and limitations

As the first part of the scored PG-SGA requires patient to complete, the PhD candidate were unable to include those with cognitively impairment. Hence, further studies would be required to validate it for use in those with any cognitive impairments. Height was collected from patients' case notes, and it is unknown if height was self-reported or measured using a stadiometer. As the population was clinically unwell, this might have inflated the PPV. However, majority of the patients admitted to the AMU generally get

discharged within four days of admission, with only a fraction of patients requiring further medical attention and admitted into a general admissions ward. Cut-offs from the scored PG-SGA could not be differentiated to identify pre-frailty and frailty as separate conditions, as both cut-offs were the same. Given the dynamic nature of the two syndromes where patients can transit between pre-frail and frail status, detecting either syndrome would be sufficient to warrant further investigations in the clinical setting.[182] However, the PhD candidate acknowledge that it would be ideal that a tool is able to differentiate pre-frailty and frailty for research purposes, as the results from Chapter 2 suggest their associated factors and clinical outcomes differ.

As this was a pragmatic observational study, the PhD candidate was unable to accumulate sufficient patients to reflect the full range of scored PG-SGA. The highest scored PG-SGA in this population did not reach the maximum allowed. In terms of statistics, sufficient representation from each score within a scale would be ideal for such a validation study.[183] A different population group, with known higher prevalence of severe malnutrition issues e.g., oncology or intensive care unit patients, might be required. However, for clinical purposes, a score of more than four in the scored PG-SGA would already warrant nutritional intervention. Therefore, it might not have been clinically relevant to examine the beyond nine points of the scored PG-SGA, as it would not affect the triage recommendations.

3.6 Conclusion

The scored PG-SGA is useful to detect pre-frailty and frailty in hospitalised older adults. This provides a time-efficient alternative to screen hospitalised older adults for pre-frailty and frailty, simultaneously with nutritional assessment. The co-occurrence of pre-frailty and frailty, and malnutrition was also confirmed in this cohort of hospitalised older adults without cognitive impairments.

CHAPTER 4: EFFECTIVENESS OF EXERCISE AND NUTRITION ON HOSPITALISED OLDER ADULTS: THE INTERACTIVE RANDOMISED CONTROLLED TRIAL

The following section contains materials from a co-authored publication accepted in 2021. Please refer to Appendix 1 for the co-signed author statement and contribution.

Han CY, Crotty M, Thomas S, Cameron ID, Whitehead C, Kurrle S, Mackintosh S, Miller M. Effect of Individual Nutrition Therapy and Exercise Regime on Gait Speed, Physical Function, Strength and Balance, Body Composition, Energy and Protein, in Injured, Vulnerable Elderly: A Multisite Randomised Controlled Trial (INTERACTIVE). Nutrients. 2021 Sep;13(9):3182.

4.1 Contribution to overall research objective

The overall objective of this thesis is to expand knowledge in pre-frailty and frailty to better their detection and treatment in hospitalised older adults. The study in Chapters 2 and 3 expanded the knowledge to better the detection of pre-frailty and frailty in hospitalised older adults. The results from Chapter 2 revealed factors and clinical outcome associated with pre-frailty and frailty in a group of older adults admitted to an AMU. In Chapter 3, the scored PG-SGA was validated to detect pre-frailty and frailty in a group of hospitalised older adults without cognitive impairments.

The second part of the overall objective of this research program was to expand the knowledge to better the treatment of pre-frailty and frailty in hospitalised older adults. In Section 1.6, a systematic review of multifaceted interventions combining exercise and nutrition in pre-frail and frail hospitalised older adults, the PhD candidate found a very relevant study (INTERACTIVE) that had not published the main outcomes of their results nor shared about its acceptability of intervention; only the study protocol[104] and economic analysis[95] were available. The INTERACTIVE study was one of the first studies in Australia to investigate the effects of combined exercise and nutrition interventions on a group of hospitalised older surgical patients with hip fractures. In the economic analysis publication, the authors described the participants as frail though no formal assessments were conducted.[95] Notwithstanding that, it is still helpful to further expand on the results from the systematic review in Section 1.6 by examining the outcomes of the INTERACTIVE study and pooling it with those presented in section 1.6.2. As one of the pioneer studies in the area of combined exercise and nutrition interventions in hospitalised older adults, many lessons can be learnt to expand the knowledge in such multifaceted treatment.

The PhD candidate contacted one of the authors of the INTERACTIVE study, who then reached out to the Principal Investigator, and later was granted access to the blinded primary dataset. This secondary analysis of the pre-frailty- and frailty-related outcomes of the INTERACTIVE study can answer **Research Question 3 – what were the pre-frailty and frailty-related results of the INTERACTIVE study (identified from the first systematic review) and what can be learnt for pre-frail and frail hospitalised older adults?**

4.2 Introduction

Frailty is a common condition in older adults hospitalised for hip fractures, with studies reporting its rates as high as 51-53%.[184, 185] In frail older adults, hip fractures are strongly associated with poor QoL and mortality.[184, 186] More than 30% of these frail older adults die within the first year of hip fracture.[187, 188] This phenomenon suggests that hip fractures may be a symptom of frailty in this population, and the beginning of a downward spiral towards the end of life. Although surgery is a good option to fix hip fractures in older adults, it is imperative that such surgical treatments are followed up with rehabilitation using exercise and nutrition interventions to optimise recovery and enhance QoL.

In Chapter 1, it was shared that the ANZSSFR expert working group recommend multifaceted interventions combining exercise and nutrition as part of management strategies for pre-frail and frail hospitalised older adults.[72] This is similar to the guidelines to rehabilitation in hospitalised older adults with hip fracture who might be also prefrail and frail. The National Institute for Health and Clinical Excellence (NICE) guidelines recommends "*Early identification of individual goals for multidisciplinary rehabilitation to recover mobility and independence, and to facilitate the return of patients to their "pre-fracture" residence and to long term wellbeing*".[189(p.2)] Rehabilitation is usually made up of a multi-disciplinary healthcare team after hip fracture, and has been associated with better health outcomes e.g., better independence.[190, 191] This multi-disciplinary support usually involves medical, nursing and allied health professionals (e.g., physiotherapist, dietitians).[192] The concept and recommended use of combined exercise and nutrition interventions in rehabilitation is similar in pre-frail and frail hospitalised older adults.

The INTERACTIVE study was an RCT, investigating the effects of a 6-month, combined individualised exercise and nutrition program (involving physiotherapists and dietitians in its delivery), starting within two weeks of surgical intervention, in a cohort of older adults after hip fracture that might also be pre-frail and frail. Though not assessed formally for pre-frailty and frailty (concept and criteria were in the early phases of development in year 2008), it is presumable that the cohort consisted of a substantial proportion of hospitalised older adults that might also be pre-frail or frail. The data collection of the INTERACTIVE study has already been completed. The analysis of outcomes from the INTERACTIVE study can help build on the meta-analysis results from the systematic review presented in Section 1.6. In addition, many lessons can be learnt to expand the knowledge in such multifaceted intervention and translated to develop treatments for pre-frail and frail hospitalised older adults, towards the second objective of this thesis – expanding knowledge to better treatments of pre-frailty and frailty.

4.3 Methods

The study has been completed and the recruitment, intervention, and data collection described below were not performed by the PhD candidate. The research dietitian and physiotherapist referred to in this Chapter are also not members of the present research team described in this thesis. The PhD candidate performed all statistical analysis and interpretation of the results.

Study Design

This is a secondary analysis of the pre-frailty and frailty-related outcomes of the INTERACTIVE RCT conducted from June 2007 to September 2009. The INTERACTIVE trial was a multi-site RCT in Australia with blinded assessed outcomes, 12-month follow up of older adults hospitalised after proximal femoral fracture (PFF). The trial was registered at the Australian Clinical Trials Registry (ACTRNI2607000017426).

Participants and recruitment

Older adults aged over 70 years, with PFF confirmed by a radiology report, were recruited from four sites in Australia: Adelaide (Flinders Medical Centre, Flinders Private Hospital, Repatriation General Hospital) and Sydney (Hornsby Ku-ring-gai Hospital). The eligibility criteria for recruitment were ability to achieve a MMSE of ≥18/30, BMI between 18.5 and 35 kg/m^2 and resided in the community within existing local service boundaries. Exclusion criteria were: PFF was pathological or malignant, resided in residential care, unable to speak English, non-ambulatory pre-fracture, unable to tolerate any physical activity more than stand transfers post-operation, absence of a third party i.e., close relative or immediate caregiver to provide informed consent if participant not in full capacity to do so i.e., post-operative delirium or MMSE between 18 and 23 or not medically stable within 14 days post-operation as assessed by their respective primary care team.

Randomisation and blinding

The process of group allocation was managed externally by the Pharmacy Department, independent to the study, at one study site. Participants were randomly assigned to either the combined exercise and nutrition therapy group or the attention control group, after baseline measures were completed. The outcome assessors and PhD candidate were blinded to group allocation i.e., the data was sent to the PhD candidate after relabelling of the groupsIt was not feasible to blind therapists nor participants due to the nature of the intervention.

Intervention

The intervention provided was an individualised combined exercise and nutrition therapy that commenced during inpatient stay within two weeks post-surgery and continued for six months post-discharge to the community. The first part of the therapy involved a nutrition program delivered by a dietitian. Participants were measured with indirect calorimetry to best estimate caloric requirements to prevent clinically significant weight loss and to meet individual dietary requirements, especially energy and protein. Participants had fortnightly dietitian visits (alternate to physiotherapist), to monitor dietary fluctuations and optimise nutrition intake. Example of some strategies undertaken to optimise nutritional status included the introduction of small, frequent meals, food fortification, and use of ONS as appropriate. The second half of the therapy was a exercise component based on the Otago exercise program.[193] Exercises were supervised

until the participant was deemed safe to carry out this strength, balance, and walking program independently by the research physiotherapist. Participants were asked to perform the exercises three times a week and go for walks tri-weekly on their own. The research physiotherapist visited participants fortnightly to supervise and augment the program based on individual progress and needs.

Attention control

Participants in the attention control group received therapy as per standard care and respective hospital protocols i.e., continue therapy as prescribed during hospital admission (acute and rehabilitation). The participants also received visits by the study physiotherapist and dietitian, to match the length and frequency of social interactions received by the intervention participants. General nutrition, exercise, and information on falls prevention, which were provided to the intervention participants, were also discussed with participants in the attention control group. The same physiotherapist and dietitian who delivered the intervention also delivered the attention control – to ensure consistency and fidelity of intervention.

Primary and secondary outcome measures

The primary outcome was 3-metre gait speed, measured with a stopwatch.[194] The following methods were used to measure other physical functions, strength and balance, as secondary outcomes: Physical and instrumental activities of daily living (PADL/IADL) using the Older Americans Resources and Services Program (OARS) functional assessment questionnaire,[195] knee extensor strength using a Nicholas manual muscle tester (NMMT),[196] grip strength using a hand held dynamometer (TTM Advanced Hand Dynameter),[197] and functional balance using the modified Berg Balance scale (MoBERG).[198] The following methods were used as measures of the remaining secondary outcomes – body composition and nutrition outcomes. Percent weight changes were measured with calibrated weighing scales. Using the dual-energy x-ray absorptiometry (DEXA: Lunar Prodigy, GE Healthcare, UK), fat-free masses were measured. Dietary intakes were assessed with the 24-hour dietary recall method, using a standardised protocol used in the Australia National Nutrition Survey.[199] This method was adapted by the Australia Bureau of Statistics from the multiple-pass recall method from the United States Department of Agriculture, where three separate phrases were used in the 24-hour recall – completion of a quick list of food eaten or drunk during designated 24-hour period; collection of detailed information of each food and drink item listed in the quick list; a recall review which provided respondents with the opportunity to report any foods that may have been forgotten.[199]

QoL was measured with the Assessment of Quality of Life (AQoL) questionnaire.[200] Results for QoL together with a cost-effectiveness analysis of the intervention have been previously published, and reported in the literature review in Chapter 1.[95] Given the nature of the intervention which included individual goal setting with adaptations made in negotiation with the participant and informed by individual progress, the measurement of participant adherence to the intervention was unable to be determined using standard methodology.

Ethics approval and consent to participate

The study was approved by the Flinders Clinical Research Ethics Committee – 110/067 and the Hawkesbury Human Research Ethics Committee of the Northern Sydney Central Coast Health – 07/HAWKE/21. Written consent was obtained from all participants prior to baseline assessment and randomisation. A third-party consent from a close relative or immediate caregiver was sought additionally if a participant was deemed to not have the capacity to provide informed consent (i.e., post-operative delirium or MMSE between 18 and 23).

Sample size

Sample size was calculated based on the gait speed data derived from a smaller similar study (n=100) undertaken at one of the four RCT sites, prior to this study.[98] Using 80% power and alpha level of 0.05, it was calculated that a sample size of 176 participants in each group would be required to detect a 20% difference that would be clinically and statistically meaningful. Based on an assumed 30% drop out rate to account for deaths and withdrawals, the study aimed to recruit 460 participants (230 in each group).

Statistical analysis

Participants were assessed at baseline (before randomisation), 6-month and 12-month. Data were coded to allow for blinding to group allocation during statistical analysis. Normality tests (Kolmogorov–Smirnov and Shapiro–Wilk) showed normal distribution for all baseline characteristics and measures. Independent sample t-tests and Chi-square test of association were used, as appropriate, to compare groups at baseline. Primary and secondary outcomes were analysed with both per-protocol (PP) and intention-to-treat (ITT) analyses principles. Multiple imputation methods (Markov chain, Monte Carlo) including the entire dataset of measured outcomes, were used to derive any missing data points, with five imputations carried out for each missing value for the ITT analyses, as determined previously at conception.[201] To determine differences between the groups at 6-month and 12-month, linear regression models with follow-up changes from baseline as dependent variables, and baselines as covariates were used for continuous outcomes.[202] Statistical analysis was performed using SPSS version 27.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was set using a 2-sided Type 1 error rate of alpha level of 0.05 and differences between groups at 6-month and 12-month follow-up were described as mean and SD for continuous variables, as number (percent) for categorical variables, and differences between groups as mean difference with 95% CIs.

In addition, meta-analyses were performed for outcomes relevant to pre-frailty and frailty in Section 1.6.1, combining the previous studies reviewed with the results from the INTERACTIVE study i.e., ITT results of gait speed, grip strength and ADL at 12-month. Details of steps of the meta-analysis process have been described in Section 1.6.1.

4.4 Results

Recruitment

A total of the 1514 patients were screened consecutively at the four RCT sites over the recruitment period from June 2007 to April 2010. Due to unexpected slower recruitment rate and limited resources, the desired sample size calculated was not achieved. As per Figure 11, 175 out of the 319 patients who were eligible participated in the RCT. A total of 86 and 89 participants were randomised into intervention and attention control group, respectively. Follow-up data from 92% (79/86) of the intervention group and 87% (77/89) of the control group were available for analysis at 6-month (Figure 11). At 12-month, the availability of follow-up data was 79% (68/86) and 74% (66/89) of the intervention and control groups, respectively. The overall follow-up attrition rate was 23.4%, with 11 of the 41 losses due to death.

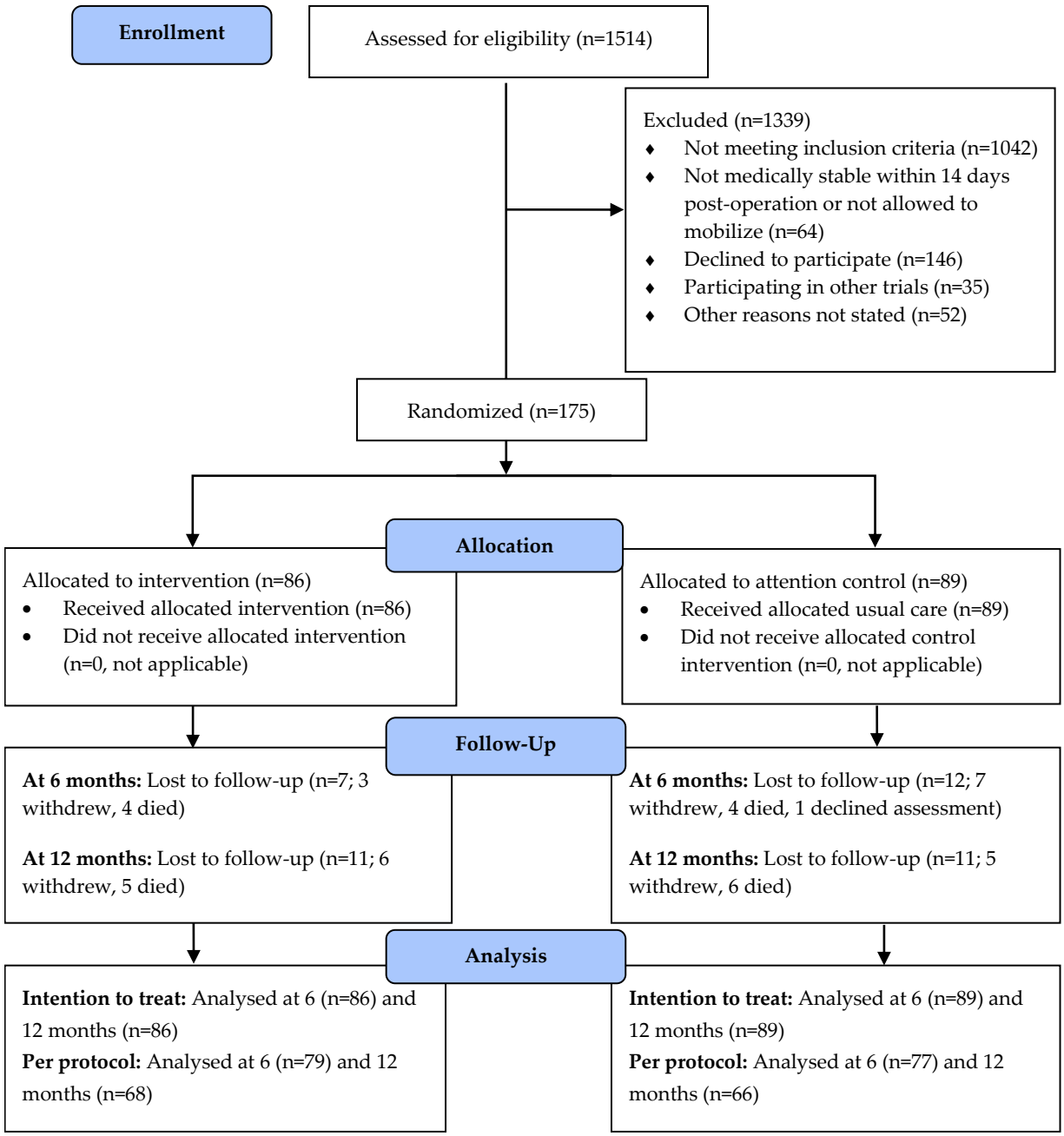


Figure 11. Flowchart of participants through the INTERACTIVE study

Characteristics of the study population

Participant characteristics are shown in Table 14. The mean age was 82.7 years and women made up of 77.1% of the participants. Baseline characteristics between groups were well matched with the exceptions of gender and grip strength. There were more females in the control group (P=0.002) and grip strength was significantly higher in the intervention group (P=0.011).

Table 14. Baseline characteristics of study population of the INTERACTIVE study

Characteristic	Intervention (n=86)	Control (n=89)	P-value[a]
Age, years, mean ±SD	86, 82.4 ±5.7	89, 83.0 ±6.2	0.51
Female, n (%)	86, 58 (67.4)	89, 77 (86.5)	0.002
BMI, kg/m^2, mean ±SD	86, 25.1 ±3.5	89, 24.8 ±4.2	0.67
MMSE score n, mean ±SD	59, 23.5 ±3.2	62, 23.9 ±3.4	0.53
Baseline resting energy expenditure (kJ/d) n, mean ±SD	36, 5583 ±1802	32, 5259 ±1847	0.47
Estimated energy requirement, (kJ/d) n, mean ±SD	86, 7254 ±1624	88, 6912 ±1381	0.14
Estimated protein requirement (g/d) n, mean ±SD	86, 78.2 ±16.9	88, 77.0 ±15.6	0.61
Physical function, strength and balance			
Gait speed (m/s) mean ± SD	86, 0.33 ±0.28	89, 0.28 ±0.28	0.25
Knee strength (injured) n, mean ±SD	74, 6.1 ±3.08	73, 5.2 ±3.08	0.06
Grip strength n, mean ±SD	85, 18.1 ±6.6	88, 15.7 ±5.9	0.01
MoBERG score n, mean ±SD	85, 16.3 ±7.8	87, 15.1 ±8.3	0.32
Physical Activities of Daily living mean ±SD	86, 9.63 ±1.72	89, 9.43 ±1.97	0.47
Instrumental Activities of Daily living mean ±SD	86, 12.0 ±2.0	89, 11.8 ±2.6	0.50
Body composition and nutrition measures			
Reported weight loss, n (%)	24 (13.7)	18 (10.3)	0.20
Reported amount of weight loss, n (%)			0.99
5 kg or less	9 (37.5)	7 (38.9)	
>5 kg	12 (50)	9 (50)	
unknown	3 (12.5)	2 (4.8)	
% Fat-free mass, DEXA n, mean ±SD	43, 67.4 ±9.4	36, 66.1 ±10.7	0.59
Estimated energy intake (kJ/d) n, mean ±SD	86, 4784 ±1766	88, 4706 ±1743	0.77
Estimated protein intake (g/d) n, mean ±SD	86, 49.5 ±19.0	88, 47.1 ±20.1	0.42

Abbreviations: BMI, Body Mass Index; MMSE, Mini mental state examinations; MoBERG, Modified Berg Balance Scale; DEXA, Dual-energy x-ray absorptiometry

[a]Chi-square, independent samples t-test as appropriate.

Primary outcome

Gait speed improved at 6-month and 12-month in both the ITT and PP analyses, irrespective of treatment group. However, there were no statistically significant differences in gait speed between the groups at 6-month and 12-month in either analysis (Table 15 and Table 16).

Table 15. Effects of intervention on primary and secondary outcomes, per protocol analyses of the INTERACTIVE study

	Intervention	Control	Coefficent[a]	P-value[b]
Primary outcome				
Gait speed				
6-month n, mean ±SD	77, 0.8 ±0.3	76, 0.83 ±0.3	-0.02 (-0.1 to 0.1)	0.64
12-month n, mean ±SD	65, 0.9 ±0.4	67, 0.84 ±0.3	0.08 (0 to 0.2)	0.19
Change from 0 to 6-month	77, 0.5 ±0.3	76, 0.5 ±0.3		
Change from 0 to 12-month	65, 0.6 ±0.5	67 0.6 ±0.4		
Secondary outcomes – Physical function, strength, and balance				
Knee strength (injured)				
6-month n, mean ±SD	74, 10.7 ±3.7	73, 10.7 ±4.7	-0.2 (-1.6 to 1.3)	0.84
12-month n, mean ±SD	63, 11.1 ±5.1	63, 11.1 ±5.1	0.1 (-2.0 to 1.8)	0.90
Change from 0 to 6-month	58, 4.8 ±3.9	65, 5.4 ±4.5		
Change from 0 to 12-month	52, 5.3 ±5.2	55, 5.8 ±5.2		
Grip strength				
6-month n, mean ±SD	79, 18.7 ±7.6	76, 17.7 ±6.4	-1.2 (-2.3 to -0.2)	0.02
12-month n, mean ±SD	64, 19.4 ±8.3	67, 17 ±5.7	2.4 (-0.2 to 4.9)	0.07
Change from 0 to 6-month	79, 0.6 ±3.6	76, 1.9 ±2.8		
Change from 0 to 12-month	64, 0.8 ±10.9	67, 0.7 ±8.1		
MoBERG score				
6-month n, mean ±SD	78, 38.2 ±11.9	74, 37.2 ±10.9	0.77 (-2.5 to 4.0)	0.64
12-month n, mean ±SD	63, 39.1 ±12.6	66, 36.5 ±11.8	3.04 (-1.3 to 7.4)	0.17
Change from 0 to 6-month	78, 22.1 ±10.9	73, 21.6 ±9.8		
Change from 0 to 12-month	62, 23.6 ±15.4	64, 21.8 ±14.6		
PADL score				
6-month n, mean ±SD	79, 12.6 ±1.5	78, 12.6 ±1.9	-0.1 (-0.5 to 0.4)	0.84
12-month n, mean ±SD	65, 11.0 ± 1.5	68, 10.9 ±1.2	0.1 (-0.3 to 0.6)	0.60
Change from 0 to 6-month	79, 3.1 ±1.9	78, 3.2 ±1.8		
Change from 0 to 12-month	65, 1.5 ±2.2	68, 1.51 ±2.3		
IADL score				
6-month n, mean ±SD	79, 10.9 ±2.8	78, 10.8 ±3.4	-0.1 (-0.8 to 0.7)	0.82
12-month n, mean ±SD	65, 11.4 ±2.9	68, 10.8 ±3.0	0.5 (-0.5 to 1.5)	0.33
Change from 0 to 6-month	79, -1.2 ±2.2	78, -1.1 ±2.5		
Change from 0 to 12-month	65, -0.9 ±3.6	68, -0.9 ±3.8		
Secondary outcomes – Body composition and nutrition measures				
Fat-free mass				
6-month n, mean ±SD	33, 69 ±9.7	36, 64 ±10.3	1.3 (-1.5 to 4.1)	0.37
12-month n, mean ±SD	41, 67.5 ±10.4	34, 65.7 ±10.6	-0.5 (-3.5 to 2.5)	0.72
Change from 0 to 6-month	29, 0.4 ±5.5	37, -1.0 ±6.0		
Change from 0 to 12-month	25, 0 ±5.9	30, 0.7 ±5.5		
Estimated energy intake				
6-month n, mean ±SD	79, 7117 ±1948	75, 6042 ±1858	984 (398 to 1570)	0.01
12-month n, mean ±SD	64, 6837 ±1825	67, 6779 ±2275	90 (-641 to 821)	0.81
Change from 0 to 6-month	76, 2357 ±2418	72, 1229 ±2129		
Change from 0 to 12-month	61, 2008 ±2496	64, 2105 ±2689		
Estimated protein Intake				
6-month n, mean ±SD	79, 67.4 ±25.8	75, 55.8 ±25.2	9.1 (1.5 to 16.8)	0.02
12-month n, mean ±SD	64, 65.1 ±23.6	67, 59.5 ±20.8	6.1 (-1.8 to 14.0)	0.13
Change from 0 to 6-month	76, 17.0 ±29.5	72, 7.9 ±26.9		
Change from 0 to 12-month	61, 14.8 ±30.3	64, 11.6 ±27.8		

Abbreviations: MoBERG, Modified Berg Balance Scale; PADL, Physical Activities of Daily Living using the Older Americans Resources and Services Program functional assessment questionnaire; IADL, Instrumental Activities of Daily Living using the

Older Americans Resources and Services Program functional assessment questionnaire; DEXA, Dual-energy x-ray absorptiometry.
Data presented as mean ±standard deviation. [a]Coefficient from a linear regression model with follow-up values as a dependent variable and baseline values as a covariate. [b]P-values, which were derived from linear regression models with baseline values as a covariate, are for the differences in mean between intervention and control group.

Table 16. Effects of intervention on primary and secondary outcomes, intention to treat analyses of the INTERACTIVE study

	Intervention (n=86)	Control (n=89)	Coefficent[a]	P-value[b]
Primary outcomes				
Gait speed				
6-month n, mean ±SD	0.8 ±0	0.8 ±0	0 (-0.1 to 0.1)	0.72
12-month n, mean ±SD	0.7 ±0	0.7 ±0	0.1 (-0.1 to 0.2)	0.36
Change from 0 to 6-month	0.5 ±0	0.5 ±0		
Change from 0 to 12-month	0.6 ±0.1	0.6 ±0.1		
Secondary outcomes – Physical function, strength, and balance				
Knee strength (injured)				
6-month, mean ±SD	10.4 ±0.5	10.3 ±0.5	-0.1 (-1.3 to 1.1)	0.85
12-month, mean ±SD	10.9 ±5.0	11.0 ±5.7	-0.3 (-2.0 to 1.3)	0.70
Change from 0 to 6-month	4.8 ±0.5	5.2 ±0.5		
Change from 0 to 12-month	4.9 ±0.8	5.7 ±0.7		
Grip strength				
6-month, mean ±SD	18.8 ±0.8	17.3 ±0.7	-0.9 (-1.9 to 0.1)	0.10
12-month, mean ±SD	18.8 ±1.0	17.3 ±0.8	0.2 (-0.7 to 3.9)	0.19
Change from 0 to 6-month	0.7 ±0.4	1.6 ±0.4		
Change from 0 to 12-month	0.7 ±1.2	1.7 ±1.0		
MoBERG score				
6-month, mean ±SD	38.0 ±1.3	36.8 ±1.3	0.4 (-2.8 to 3.6)	0.75
12-month, mean ±SD	39.3 ±1.8	37.2 ±1.5	2.2 (-1.6 to 6.0)	0.32
Change from 0 to 6-month	21.7 ±1.2	21.7 ±1.3		
Change from 0 to 12-month	23.0 ±2.0	22.11 ±1.8		
PADL score				
6-month, mean ±SD	12.6 ±0.2	12.6 ±0.2	-0.1 (-0.6 to 0.4)	0.72
12-month, mean ±SD	11.1 ±0.2	10.9 ±0.2	0.5 (-0.3 to 0.6)	0.49
Change from 0 to 6-month	3.0 ±0.2	3.2 ±0.2		
Change from 0 to 12-month	1.5 ±0.3	1.52 ±0.3		
IADL score				
6-month, mean ±SD	10.9 ±0.3	10.6 ±0.4	0.8 (-0.6 to 0.8)	0.76
12-month, mean ±SD	11.4 ±0.4	10.9 ±0.4	0.5 (-0.5 to 1.4)	0.38
Change from 0 to 6-month	-1.1 ±0.3	-1.2 ±0.3		
Change from 0 to 12-month	-0.6 ±0.5	-0.9 ±0.4		
Secondary outcomes – Body composition and nutrition measures				
Fat-free mass				
6-month, mean ±SD	68.1 ±2.4	67.1 ±2.1	1.07 (-1.71 to 3.86)	0.44
12-month, mean ±SD	67.9 ±3.7	68.7 ±3.7	-0.71 (0.47 to 0.96)	0.51
Change from 0 to 6-month	1.0 ±1.5	-0.1 ±1.1		
Change from 0 to 12-month	0.8 ±2.0	1.5 ±2.6		
Estimated energy intake				
6-month, mean ±SD	7065 ±1224	6024 ±243	1003 (421 to 1587)	0.01
12-month, mean ±SD	6926 ±264	6821 ±338	84 (-571 to 740)	0.68
Change from 0 to 6-month	2200 ±291	1340 ±279		
Change from 0 to 12-month	2061 ±344	2136 ±371		
Estimated protein intake				
6-month, mean ±SD	66.7 ±3.1	55.4 ±3.0	10.5 (2.7 to 18.4)	0.01
12-month, mean ±SD	64.1 ±3.4	59.9 ±2.9	4.1 (-3.0 to 11.2)	0.29
Change from 0 to 6-month	16.7 ±3.6	8.31 ±3.4		
Change from 0 to 12-month	14.1 ±4.1	12.8 ±3.4		

Abbreviations: MoBERG, Modified Berg Balance Scale; PADL, Physical Activities of Daily Living using the Older Americans Resources and Services Program functional assessment questionnaire; IADL, Instrumental Activities of Daily Living using the Older Americans Resources and Services Program functional assessment questionnaire; DEXA, Dual-energy x-ray absorptiometry.
Data presented as mean ±standard deviation. [a]Coefficient from a linear regression model with follow-up values as a dependent variable and baseline values as a covariate. [b]P-values, which were derived from linear regression models with baseline values as a covariate, are for the differences in mean between intervention and control group.

Secondary outcomes

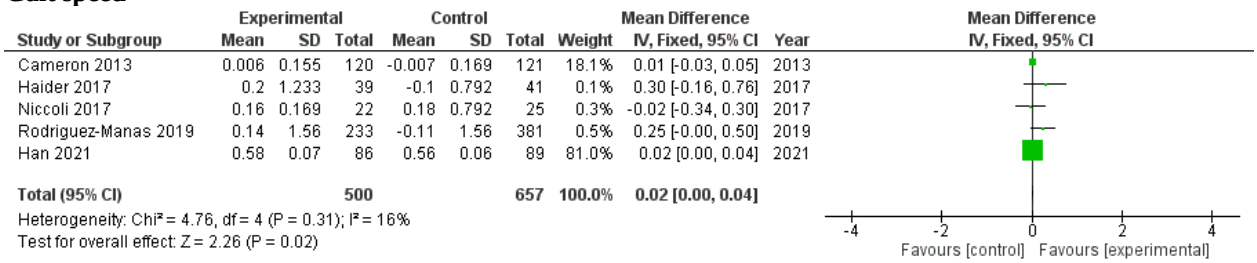
As shown in tables 15 and 16, there were no differences between groups with respect to the secondary outcomes of the trial, with exception of grip strength, estimated energy, and protein intake. Overall, there were improvements in knee strength, MoBERG, PADL, IADL scores in both groups at 6-month and 12-month. The intervention group had higher increase in fat-free mass compared to the control group though this difference was not statistically significant. In the PP analysis of grip strength, there was significantly better improvement in the control group as compared to the intervention group at 6-month. However, this improvement was not observed at 12-month follow-up and in the ITT analyses.

Participants in the intervention group had greater increment in energy intake compared to those in the control group at 6-month (between-group difference 984kJ; 95% CI, 398 to 1570; P=0.01). However, this increment was not significant at 12-month in both PP and ITT analyses. Participants in the intervention group had greater increment in protein intake compared to those in the control group at six months (between-group difference 9.1g; 95% CI, 1.5 to 16.8; P=0.02). Similar to energy intake, the increment in protein intake was not significant at 12-month in both PP and ITT analyses.

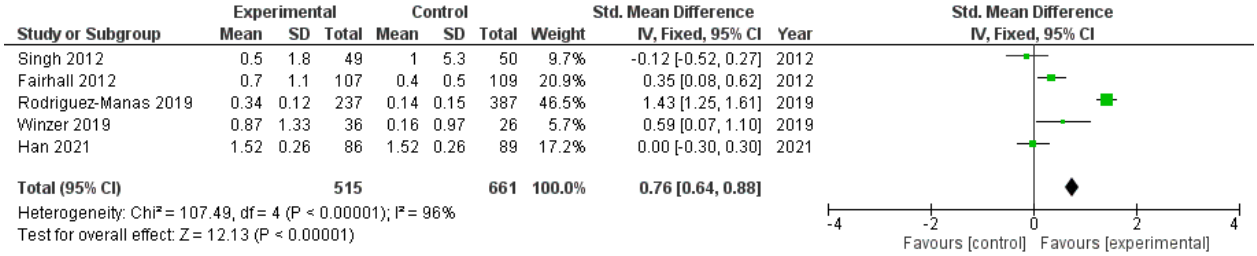
Pooled results from Section 1.6 – Gait speed, ADL, grip strength

Figure 12 presents the results from the meta-analysis from Section 1.6, with the incorporation of data from this Chapter. The addition of results of gait speed from the INTERACTIVE study added statistical power to the pooled analysis. The pooled analysis suggests that combined exercise and nutrition significantly improved gait speed in hospitalised older adults who may also be pre-frail and frail, compared to standard care. The addition of the results of ADL and grip strength from the INTERACTIVE study also did not make significant changes to the results presented in Section 1.6.2.

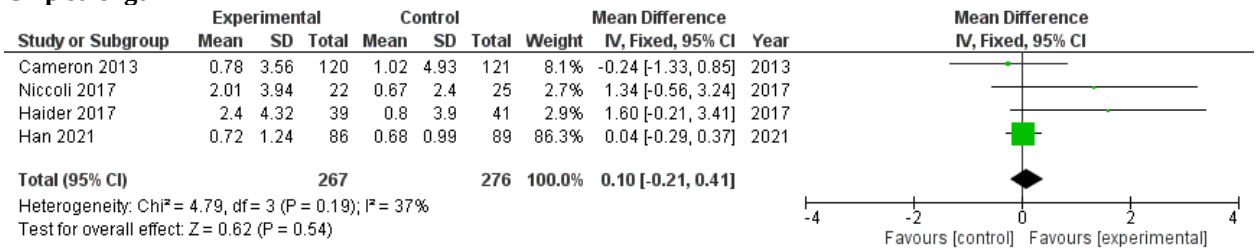
Gait speed



Activities of daily living



Grip strength



Abbreviations: AUC, area under the receiver operator characteristics curve; CI, confidence interval

Figure 12. Meta-analysis of reduction in pre-frailty and frailty-related outcomes for exercise and nutrition intervention versus standard care, adding results from the INTERACTIVE study to systematic review in Section 1.6

4.5 Discussion

The results from the present study showed positive trends of the intervention in improving grip strength (12-month), MoBERG, PADL, IADL, fat-free mass, and significant improvements in estimated energy and protein intake. There was no significant difference in the primary outcome (gait speed at 6-month) between groups, until results were pooled with other studies identified in Section 1.6. The lack of significant changes, with exception to energy and protein intake, may relate to a lack of statistical power. The benefits of the intervention may be more evident, if the desired sample size calculated was achieved. Nonetheless, pooling of the gait speed data in this Chapter with that in Section 1.6 improved statistical power to suggest a significant improvement through the use of combined exercise and nutrition interventions.

A recent similar trial (sufficiently powered) involving a multicomponent home-based physical therapy intervention in older adults with hip fracture reported a higher percentage of intervention compared to control participants with improved walking capabilities after 16 weeks, albeit the difference was also not statistically significantly different between groups.[203] Another trial using a 10-week home-based progressive resistance exercise program found significant improvement in gait speed but did not include a nutrition component.[204] There also could be other contributing factors that affected gait speed that were not measured in the present study. For example, impairments in lower body strength, perceived general health

and balance confidence were identified as predictors of gait speed in older adults after hip fractures.[205, 206] Potential confounders to gait speed, such as pain, was also not measured and accounted for.[207]

The better improvement in grip strength seen in the control group at 6-month, compared to the intervention group, could be contributed by the significant difference at baseline, though that has been considered during the statistical analysis by including the baseline as a covariate. The subsequent follow-up at 12-month later showed an observable trend that the intervention group had greater improvements in grip strength at 12-month, albeit not statistically significant.

The significantly better improvements in energy and protein intake in the intervention as compared to the control group were consistent with previous similar studies. Nutritional care significantly increased energy and protein intake in acute hip fracture patients.[208] Oral nutrition support provided by dietitians was previously reported to improve outcomes in older adult patients after surgical fixation of hip fractures.[209] The use of such individualised nutritional support is not novel, but still uncommon. Six out of seven RCTs from a systematic review on the effects of a geriatric team rehabilitation after hip fracture, provided no information on nutrition, with limited reports on multidisciplinary action on nutrition support.[210] In that review, only one RCT provided information that nutritional support was given in a form of a protein drink, with no individualised approach. The effect of **E**arly nutritional support on **F**railty, **F**unctional **O**utcomes and **R**ecovery of malnourished medical inpatients **T**rial (EFFORT) demonstrated that individualised nutrition support is associated with reduced adverse clinical outcomes, in medical inpatients at nutritional risk.[211] However, this effect was nullified when the same measurements were done at follow-up, suggesting the need for such individualised care to be extended beyond discharge, to the community, to sustain a "legacy effect", as observed in pharmacotherapies.[212, 213]

Furthermore, this study adds to previous research by demonstrating that it is possible to recruit older surgical patients that might be pre-frail and frail, in a RCT at an early stage during hospitalisation. It also showed that early combined exercise and nutrition intervention can improve energy and protein intake and suggest consequent improvements in body composition and functional outcomes.

Strengths and limitations

This RCT was completed with no deviations from the published protocol. The use of an attention control group that provided a sham/placebo intervention could be seen as one of the study's strengths. Although it was not possible to blind treating clinicians to the interventions, the outcome assessors were blinded. As all participants received equal number of home visits, treatment statuses were unlikely to be disclosed to the blinded assessors unless further probing was done (which was advised against during the outcome assessment). The primary outcome, gait speed, is a performance-based measure, that is less likely to be affected by observer bias. The remaining outcomes assessed were part self-reported and part performance based. The results presented in this study were supported with body composition analysis i.e., DEXA, which

corroborated with physical function outcomes. The use of DEXA scans in older adults for research is not common and provides for a more accurate measurement of fat-free mass than anthropometry which is the common substitute in research studies in this area.[214] A major limitation of the study is the lack of statistical power due to unexpected slower recruitment and limited resources. It was a challenge to complete data collection for many measurement outcomes due to logistical reasons i.e., immobile equipment used for body composition, resulting in missing data. There is a paucity of high-quality studies on combined exercise and nutrition interventions of the frail older adult populations.[120] A recent review of exercise and nutrition in managing hip fracture in older adults concluded that there are still few large, long term RCTs that involve multicomponent exercise and nutrition therapy interventions.[215]

4.6 Conclusion

Although the present study did not find significant effect of the intervention on functional outcomes and fat-free mass, it demonstrated that providing early, combined exercise and nutrition therapy may still be a practical therapeutic goal and can improve energy and protein intake for older adults with hip fractures that might also be pre-frail or frail. Analysis of the INTERACTIVE study added to the results from the review in Section 1.6 on combined exercise and nutrition interventions in hospitalised pre-frail and frail older adults. Future studies should also consider measuring and adjusting for known predictors to the outcomes of interest and track the type of usual care. Early and combined exercise and nutrition interventions can be feasible for older adults with hip fractures that might also be pre-frail and frail, but more research should be done to determine the optimal type, dose and combination of exercise and nutrition therapy that has the most benefit on functional outcomes.

4.7 Challenges and considerations for intervention study in pilot RCT (Chapter 6)

There were several lessons to be learnt for pre-frail and frail older adults from the analysis of this INTERACTIVE study. First, pre-frailty and frailty was not formally assessed in this study. This corroborates evidence presented from the review in Chapter 1 as formal assessment of pre-frailty and frailty was not a common practice in the past, due to a lack of consensus on their definitions then. In this study, there was no pre-frailty and frailty assessments at baseline or follow-ups, only surrogate measures of them e.g., gait speed were collected. Second, blinding treating clinicians or participants to the interventions group would not be possible due to the nature of the intervention, thus it would be essential, like in the INTERACTIVE study, to use a blinded outcome assessor to reduce bias. Third, the combined exercise and nutrition intervention described in the INTERACTIVE trial was delivered by allied health professionals and did not have a self-management component – a literature gap discussed when reviewing the literature in Chapter 1.

Fourth, there was a lack of a standardised method to measure adherence to therapy, given that it was individualised for each patient. Factors i.e., barriers and enablers, towards participation and adherence were not explored. As highlighted in Chapter 1, an understanding towards such factors is required to better

adherence as they can impact on effectiveness.[113] Fifth, the design of the INTERACTIVE intervention protocol was not informed directly by the end-user, thus future studies involving end-user input may improve acceptability. Existing reviews of exercise and nutrition interventions have highlighted heterogeneity in studies' intervention protocols. However, one commonality was the lack of understanding of interventions from an end-user point of view as none of the interventions were designed with inputs from end-users.

Lastly, there is limitation in the generalisability of results as the participants in the INTERACTIVE study was from a geriatric orthopaedic surgical population. The acceptability and benefits of a combined exercise and nutrition intervention in an acute generally medical population remains to be determined, especially where differences in standard care (with the involvement of allied health, in-hospital mobility, and nutrition care) tend to be less protocolised in the general medical population.

CHAPTER 5: PERCEPTIONS OF HOSPITALISED PRE-FRAIL AND FRAIL OLDER ADULTS ON PRE-FRAILTY AND FRAILTY AND EXERCISE AND NUTRITION PROGRAMS

5.1. Contribution to overall research objective

In Chapter 2 and Chapter 3, the PhD candidate identified factors associated with pre-frailty and frailty, and validated the scored PG-SGA as a screening tool to detect pre-frailty and frailty in hospitalised older adults. In Chapter 4, the PhD candidate retrieved data from the INTERACTIVE study, identified in the literature review (Section 1.6), examined its pre-frailty and frailty-related outcomes and pooled results relevant to those meta-analysed in section 1.6. In Chapter 4, lessons to be learnt about study design of combined exercise and nutrition interventions for pre-frail and frail hospitalised older adults were also discussed e.g., use of formal frailty assessment tools, need to explore factors adherence towards participation. While the intervention (and many other studies identified in this thesis's review) was designed by exercise and nutrition experts and with reference to guidelines, there was a lack of input from end-users.

In a meta-synthesis of qualitative evidence on stakeholders' views and experiences (including pre-frail and frail older adults) for interventions for pre-frailty and frailty, the view and experiences included (1) Capacity to care and person and family-centred service provision (2) Power and choice.[216] For capacity to care and person and family-centred service provision, a prominent theme highlighted was that stakeholders wanted to be included in decision-making.[216] One suggestion to improve patient-centred care was to incorporate home visits that could foster a "partnership" between the pre-frail and frail older adults and healthcare providers.[217, 218] In a way, the home visit provides an opportunity for pre-frail and frail older adults to discuss their needs to allow for autonomy, and requirements to implement the exercise and nutrition interventions prescribed.[217, 218] Under the theme of power and choice, many older adults reported challenges relating to the perception of a "diminished power" with health care services.[216] It was described that pre-frail and frail older adults had feelings of de-personalising and being perceived as incompetent.[216]

As discussed in Chapter 1 (Section 1.8) and highlighted above, interventions for pre-frailty and frailty should be patient-centred and allow for choice and power to be redirected to the patients themselves. Research using qualitative designs can benefit some research question such as those looking to provide unique perspectives and insights into a specific context, e.g., pre-frail and frail hospitalised older adults. Therefore, a qualitative descriptive design using principles from the grounded theory approach, was undertaken to answer **Research Question 4 – what do pre-frail and frail hospitalised older adults want in self-managed, hospital-to-home, combined exercise and nutrition support program?** This contributes to part of the thesis aim of improving treatment of pre-frailty and frailty by informing the development of a patient-centred, self-managed intervention program.

5.2. Introduction

In comparison to research studies focusing on treating pre-frailty and frailty, research to understand pre-frailty and frailty from the point of view of the end user (older adults) is scarce. In a local qualitative study of 39 South Australian older adults (ranged from non-frail to very frail), three representations of frailty were described.[219] First, participants described frailty as an inevitable domain of ageing with physical representations such as slow moving, skinny, and use of mobility aids. It was viewed as a "static state" nearing the end of life, and unlikely to be improved on. Second, through the lens of a disability model, participants viewed frailty as a condition that can happen regardless of age and related its onset to a life-threatening stressor event e.g., motor vehicle accident. In this schema unlike the first, frailty was viewed as a dynamic state that individuals can transit in and out of. Third, frailty was viewed in association with a loss of independence – an inability to control oneself and one's environment, with emphasis on whether a person can mobilise independently. In addition to the schemas, it was reported that there was a consensus about mental state/attitude in close relation to physical frailty. Overall, frailty was negatively viewed and a result of personal choice.[219] There is limited information on perspectives of pre-frailty.

To alleviate both pre-frailty and frailty and relevant health outcomes such as poor quality of life, interventions combining exercise and nutrition appear to have an overall benefit, as reported in Section 1.6.[105, 120] However, implementing and sustaining such intervention programs can be challenging, especially in older adults.[49] Poor adherence to exercise and nutrition interventions in older adults is a long-standing issue. A recent report has shown that adherence to exercise programs in older adults is poor and that this problem is multi-factorial with surrounding biopsychosocial influences.[139] Previous research on older adults has also reported poor uptake of dietetic referrals.[220] Amongst those referred, older adults can also be resistant to dietary interventions, for example, meal delivery.[221]

To increase the success rate of programs to treat pre-frailty and frailty, some studies have examined the perceptions of older adults towards possible treatments e.g., exercise. In a study by Broderick et al, exercise was viewed as a by-product of other purposeful activities such as manual work or social activities.[222] Frail older adults viewed exercise as accompanying more purposeful activities rather than on its own. Hence, to increase compliance to treatments, exercise programs focusing on functional outcomes may be more relevant from their point of view. Program may also employ strategies that involve the use of social support networks.[222] A review of reviews found some barriers towards strength and balance activities are not having enough time, perceived risk of heart attack/stroke/death, and surprisingly, fear of looking "too muscular".[223]

In the hospital setting, a study also found that mobilisation varied greatly between older adult inpatients; factors that affected walking were (1) connected devices or treatments that hindered walking (2) needing assistance and fear of falling.[224] Conversely, facilitators to strength and balance activities include improved ability to complete daily activities, preventing deterioration and disability, and decreasing the risk or fear of falling.[223] There was an overall positive attitude towards exercise, with a preference for advice given by

healthcare professional prior to performing physical activities.[157]

A recent guideline derived from the Frailty Management Optimisation through European Innovation Partnership on Active and Healthy Ageing Commitments and Utilisation of Stakeholder Input (FOCUS) project specifically recommended intervention programs with physical activity, nutrition or a combination of both, with an optional component of cognitive training, and those based on individualised care and/or geriatric evaluation or management.[225]

Regardless of intervention modality, it was agreed upon in a qualitative study by key stakeholders (older adults, carers, specialists and health care professionals), that services addressing pre-frailty and frailty should be individually tailored, address social networks and be delivered over a sustained period by non-specialist healthcare professionals/workers.[226] It was also reported that the service should aim to improve personal motivation with a focus on independence and behaviours that promote a sense of well-being.[226]

With the aforementioned indicators in mind, a research design that involves meaningful end-user engagement in designing/reshuffling of healthcare interventions seems to be that last stage to a successful intervention.[227] The involvement of end-user helps develop interventions that place the patient at the centre thus improving implementation and adherence.[228] An understanding of pre-frail and frail older adults' perspective of diet and exercise would be valuable in informing the design of such healthcare interventions targeted at them. However, there is limited information about the perspectives of pre-frail and frail older adults towards diet and exercise, particularly around participation in a transitional hospital-to-home program. Hence, this study aimed to gather qualitative data from the perspectives of hospitalised older adults on 1) pre-frailty and frailty, 2) diet and exercises changes through journey of home-hospital-home, 3) optimal diet and exercises practices and 4) a proposed self-managed hospital-to-home intervention protocol combining exercise and nutrition.

5.3. Methods

Using principles from the grounded theory

Grounded theory as first described by Glaser and Strauss, and explained for health researchers, was referenced for this study.[229] It is one of the canonical theories underpinning qualitative research methods to answer questions surrounding perspectives and experiences. As demonstrated in the previous chapters of this thesis, quantitative methods perform analysis only after all data has been collected. However, grounded theory has a process that is cyclical in nature that involves both data collection and analysis to be conducted concurrently.[229] The early analysis in this process, allow the researchers to solidify the developing theory through identifying directions and gaps.[229] Recruitment and interviews would continue until information redundancy was reached, where the interviewers reported to the researcher that the same comments are being heard repeatedly (data saturation).[229] Figure 13 showed a version of the research design framework adapted to the present study.[229]

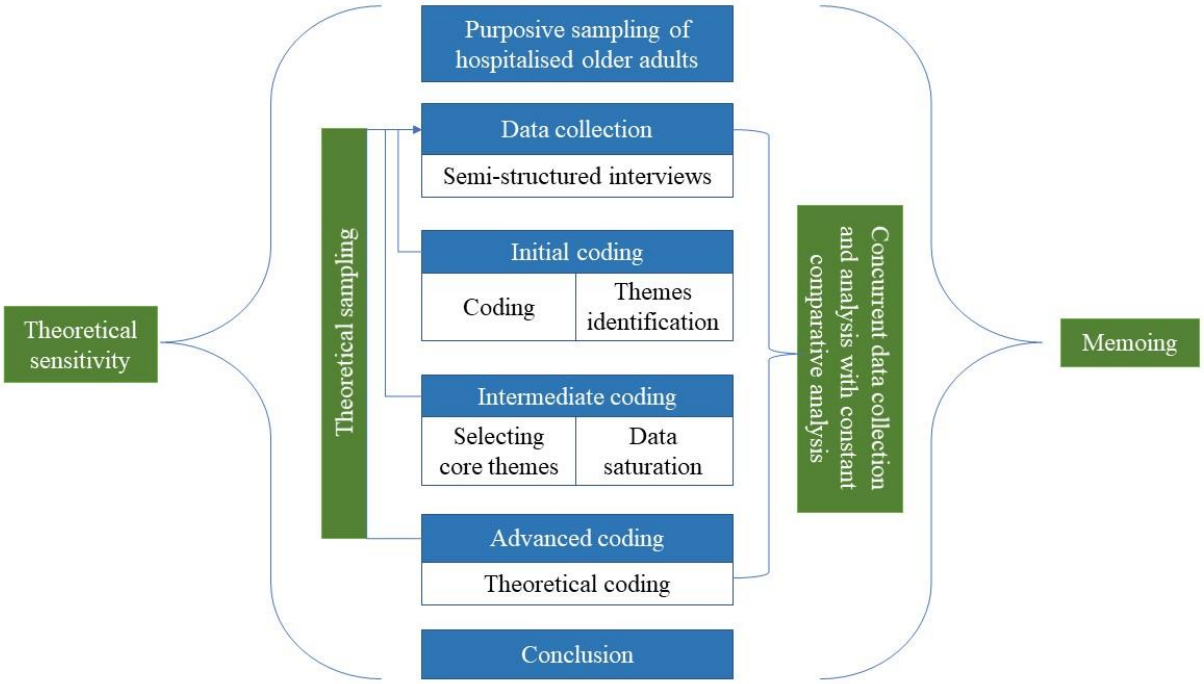


Figure 13. Framework of essential grounded theory methods applied on study processes of the first qualitative study (adapted from Tie, Birks and Francis 2019[229])

Demonstrating trustworthiness and rigour

The qualitative methods and findings in this study are reported in accordance with the COREQ (**CO**nsolidated criteria for **RE**porting **Q**ualitative research) statement/checklist.[230] Interview questions and prompts were developed with the guidance from the research team from multidisciplinary backgrounds – physiotherapy, dietetics, medicine, and with expertise in management of pre-frail and frail patients. For this study, an additional member of the research team included a final year undergraduate majoring in psychology and linguistics from an Australian University. The PhD candidate have had experience of delivering MNT to pre-frail and frail older adults, and prior experience in conducting semi-structured interviews for mixed methods research.[231] Additionally, the PhD candidate completed two certified course modules on qualitative research methods (conversational interviewing; analysing data) conducted online by Professor Susan Sibley from Massachusetts Institute of Technology.

Design of interview protocol

To explore the perspectives of pre-frail and frail hospitalised older adults on the aforementioned topics, an in-depth individual interviews protocol was designed to allow participants to freely express their personal views. The PhD candidate prepared the first draft of the interview questions. The research team provided critical revisions and approval to the final set of interview questions, to support participants to share in-depth thoughts and experiences. Interview questions addressed the following areas related to research questions of this chapter (see Appendix 5 for the full interview guide):

- Pre-frailty and frailty – what do the terms means to them
- Home diet and exercise habits – what was done and preferred prior to admission
- Diet and exercises when admitted to hospital – experience and perceived changes compared to home
- Diet and exercise post-discharge – anticipated changes to be made when home
- Optimal diet and exercise – what constitutes an optimal diet and exercise routine at home
- Perception of a proposed self-managed hospital-to-home intervention protocol combining exercise and nutrition – what they like and dislike, frequency and types of visits, any other components that should be added

During the interview, participants were asked to describe desired program features, and to comment on the proposed study intervention package (INDEPENDENCE). Feedback from the research team was incorporated before pilot testing. The interview questions were initially tested by the PhD candidate with a pre-frail and frail patient at Flinders Medical Centre prior to commencing formal data collection. No modifications were made after the initial testing.

Participants and baseline descriptive data

Purposive sampling was employed to recruit hospitalised older adult patients, that were pre-frail or frail, as determined by the EFS. These patients were admitted to the AMU at the FMC in Adelaide, Australia. Eligible patients were approached within 48 hours of admission, between February and August 2020, from the observational study described in Chapters 2 and Chapter 3,[232] if they were assessed to be pre-frail or frail as aforementioned. Participants, aged ≥65 years, who were able to converse in English were included. Those medically unstable or terminally ill patients were excluded from the study. Patients with cognitive impairment (Mini Mental State Examination (MMSE) of ≤24), were also excluded, as the interview was in-depth and required verbalisation of perceptions towards diet and exercise. Age, gender, education and living situations, frailty status (pre-frail, mild, moderate, severely as per the EFS) were collected as part to provide a description of the participant's sociodemographic information and pre-frailty and frailty statuses.

Interview process

The PhD candidate who was also the interviewer, has no prior casual or professional contact with any enrolled participants and was not involved with any inpatient care or MNT. The participants were briefed on the purpose of the study prior to informed consent and were informed about the role of the PhD candidate/interviewer as an independent researcher, not involved with inpatient care. The participant was also unaware that the PhD candidate was an Accredited Practising Dietitian. These measures aimed to reduce social desirability bias. In the event that participants were aware of the interviewer's background or thought that the interviewer was providing inpatient care, there is a potential for them to self-represent in a

certain manner. To ensure the privacy of participants, all interviews were conducted in individual patient rooms, or with curtains drawn if the room was shared by other non-participating patients. During the interview, pseudonyms i.e., Mary and John were used names accordingly to preserve anonymity. The interviews were audio recorded and transcribed verbatim. Recruitment and interviews continued until data saturation, as previously mentioned on the grounded theory approach.

Data analysis

The PhD candidate transcribed the recordings verbatim using a software program (Microsoft Word), before relistening to the recordings, to check and correct the transcriptions, and making notes on the interviews before coding transcriptions using the same software. The verification process to ensure transcription accuracy was also done by a member of the research team. Interview data were coded inductively by the PhD candidate throughout data collection. Additionally, all transcripts were then separately coded by another member of the research team when the data collection was completed to ensure rigour. Any coding discrepancies were resolved through a discussion with a third member of the research team until an agreement was reached. The interview data were initially sorted into four groups – (1) perceptions of pre-frailty and frailty (2) diet and exercises changes through journey of home-hospital-home (3) perception of optimal diet and exercise routine for pre-frailty and frailty, and (4) perceptions of a proposed self-managed hospital-to-home intervention protocol combining exercise and nutrition. Data were coded using a thematic analysis approach informed by Braun and Clarke.[233] A five-stage analytical method involving familiarising and identifying of key themes, creating a "thematic framework", coding, data sorting and summation/synthesis of data was referenced.[234, 235] Transcripts were repeatedly read to gain a sense of -generated codes initially while creating the thematic framework to help the researchers identify recurrent patterns. An initial conceptual model was generated by the PhD candidate after reading over the initial coding and organising data into major and minor themes. Meetings were taken with the PhD candidate and a member of the research team where revisions of themes were then undertaken, and the final conceptual models were produced. None of the themes were identified in advance. Rather, they were derived from the data solely. Feedback was also provided by two members of the research team – one dietitian, another physiotherapist by training. Number codes, age, gender, frailty status (pre-frail, mild, moderate, severely as per the EFS) of the participants were used, when describing their demographics in relation to the quotes.

Ethics

This study was approved by the Southern Adelaide Clinical Human Research Ethics Committee (HREC reference number: HREC/19/SAC/240) − within which the work was undertaken and conformed to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). All participants provided written informed consent; consent sought by the PhD candidate who was not involved in their usual inpatient care.

5.4. Results

A total of 22 pre-frail and frail older adults aged 67 – 90 years (mean age, 80.6 years; female 41%; living alone 41%) admitted to the AMU at the FMC, were interviewed (Table 17). The cohort was well represented in diversity of age, gender, living situation, and pre-frailty and frailty statuses. However, only one participant had received tertiary education at a university and thus the results presented could only be representative of older adults with lower levels of education. Sessions were audio-recorded, transcribed verbatim and analysed thematically, as described previously. The median (range) duration of the interviews was 16 (8-81) minutes, with one participant stopping the interview after completing one-third of the protocol questions due to flaring of acute symptoms.

Table 17. Demographic and health characteristics of study participants of the first qualitative study

Characteristics	Mean / n (%)
Mean age (range), years	80.6 (65-90)
60-69	3 (13.6)
70-79	3 (13.6)
80-89	15 (68.2)
≥90	1 (0.5)
Gender	
Female	13 (59)
Male	9 (40.9)
Education level	
Up to high school	13 (59)
Trade/Diploma	8 (36.4)
University and above	1 (0.5)
Living situation	
Living with someone	13 (59)
Living alone	9 (40.9)
Mean Edmonton Frail Scale score (range)	8.4 (6-12)
Vulnerable (pre-frail)	9 (40.9)
Mildly frail	6 (27.2)
Moderately frail	4 (18.2)
Severely frail	3 (13.6)

Perspectives of pre-frailty and frailty

Perspectives of pre-frailty and frailty from the point of view of hospitalised older adults are summarised and presented in Figure 12. Three themes overlapped between perspectives towards pre-frailty and frailty.

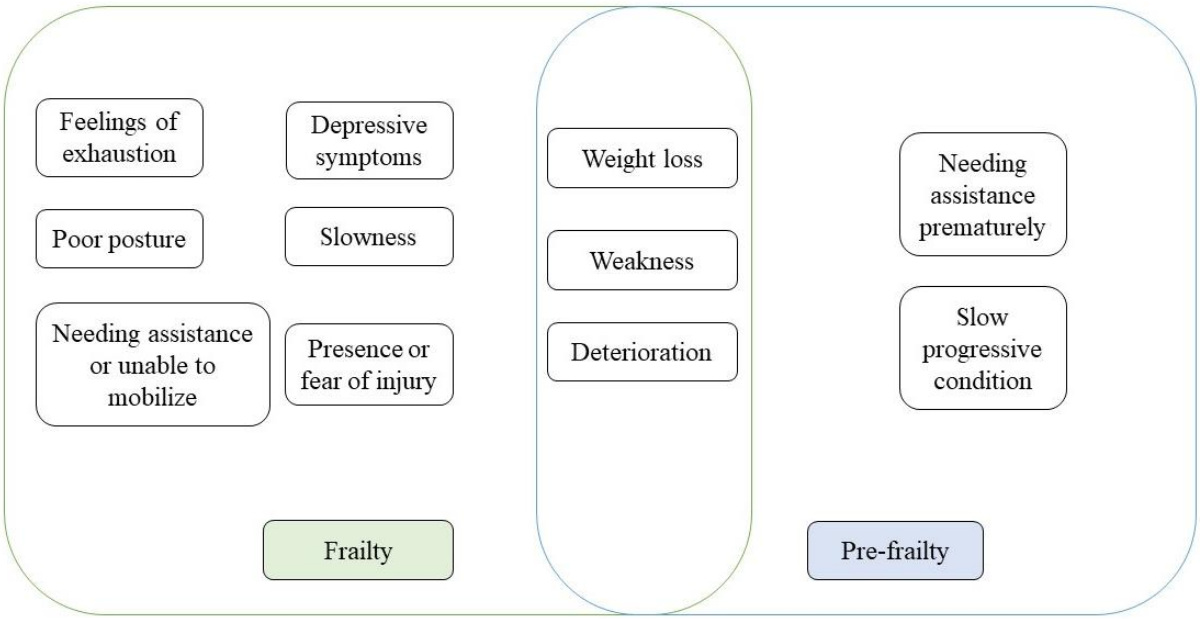


Figure 14. Perspectives of pre-frailty and frailty of hospitalised pre-frail and frail older adults in the first qualitative study

There was a general lack of awareness or misconception when it comes to pre-frailty in these study participants. Pre-frailty as the term suggest, is a condition that classifies one at a higher risk of progressing to frailty. However, this was not instinctive to all participants. Some participants depicted pre-frailty as a slow progressive condition that can sometime result in needing physical assistance prematurely.

"Pre-frail? Um…. Yes... it doesn't ring bells with me" **#1, 85 years, male, moderately frail**

"Needs help before they get old, the person is younger" **#14, 75 years, male, pre-frail**

"I think I've got that. It sort of comes on slowly…" **#11, 83 years, female, severely frail**

"they're prior to that, you know where it's sort of- you're not sort of, you know, most of them would walk with a walker…. Or something like that, a walking stick."
#7, 75 years, female, pre-frail

Frailty was viewed as largely under par physical form and function, with poor posture, slowness and needing assistance or seen as an inability to mobilise. Participants often drew links between frailty and injuries or a fear of injuries of the lower limbs, that could ultimately take away their capacity to mobilise. To several participants, frailty was described as a barrier to living the lives that they desire, often related to the physicality of tasks such as walking. Feelings of depression and mood swings were also viewed as components of frailty.

"It means that you're not able to do a lot of things, you don't have enough strength, and also the fact that your legs haven't got enough strength. You need help." **#4, 84 years, female, mildly frail**

"It's usually a person who's not quite able to do all the normal things that they want to do, and also... what they can do, is somewhat, you know, reduce fashion, or reduce manner. And sometimes people who are frail physically look, you know, like they're bent over or slow walking, like me and they often may use a support walking stick." **#5, 67 years, male, moderately frail**

"Being injured in some way" **#10, 65 years, male, severely frail**

"Feel low, ups and downs" **#6, 90 years, male, pre-frail**

Weight loss, weakness and deterioration were all viewed as components surrounding the concepts of both pre-frailty and frailty. Gradual weight loss over the years was often linked to physical weakness and the slow observable reduction in muscle mass. It was often expressed as a time where one starts to "*go downhill*". Deterioration was further described as either a reduced physical stability and capacity for day-to-day activities or a decline in cognition.

"Got no balance" "they got bad legs" **#15, 87 years, male, pre-frail**

"People are just sort of... getting old and a bit wobbly on their feet…" "they've lost weight over, you know the years, you know, you go from say, 80 to 60, they might have lost weight" **#7, 75 years, female, pre-frail**

"You start to go downhill, you just start to lose you- your strength your energy to do things and you just, you know, sit around and that's about it, you know" **#13, 82 years, male, pre-frail**

"Memory loss and that sort of thing." **#17, 80 years, female, mildly frail**

Diet and exercises changes through journey of home-hospital-home

The themes surrounding perspectives of own diet and exercise (and changes) through the journey of home-hospitalisation-home were summarised and illustrated in Figure 15.

Prior hospitalisation

The perspectives of the participants' own diet prior to hospitalisation were grouped into seven themes: preference for home-cooked food over store bought meals; three regular meals; unchanged since young/influenced by childhood; energy-balanced; variety; emphasis on particular food group(s); close watch on discretionary foods.

"I don't eat a lot of fast foods or anything of that nature. Between the wife and I we generally cook all our meals at home. It's a rarity for us to go out for a meal" **#1, 85 years, male, moderately frail**

"We don't drink alcohol nowadays and we don't smoke, neither of us. We don't- every now and again we might have a bit of a splurge on the- on the desserts or something like that, but generally try to keep it straight and narrow." **#13, 82 years, male, pre-frail**

"I'm doing my own cooking and, and all that sort of stuff, I do my own shopping." "Some sort of meat some sort of noodles some sort of chicken" "five or nearly five vegetables." **#15, 87 years, male, pre-frail**

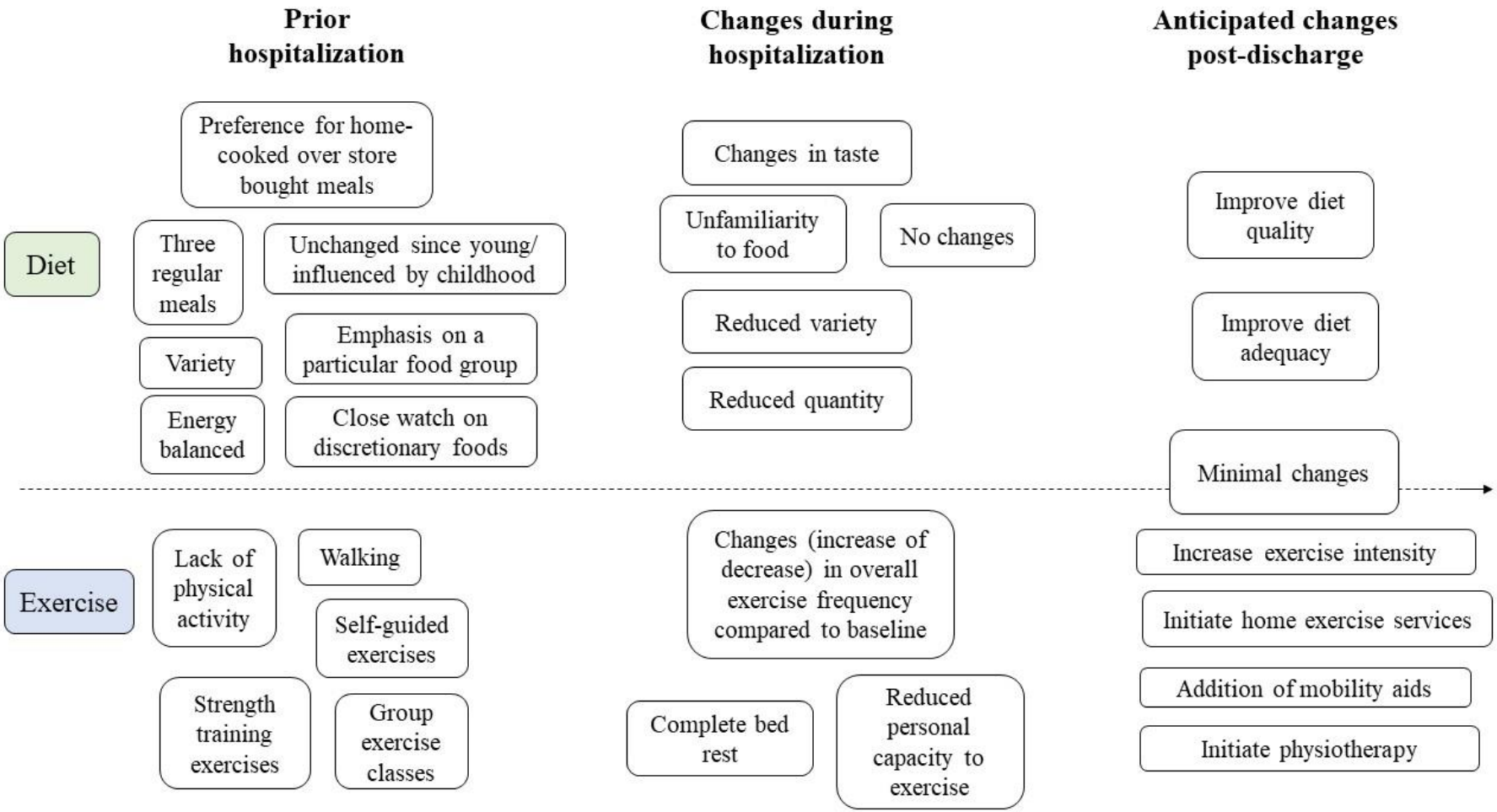


Figure 15. Themes summarising description of changes in diet and exercise through journey to home-hospital-home in the first qualitative study

Regarding exercise prior hospitalisation, participant responses typically fell into one of two opposing groups – (1) those that had a lack of exercises (who understood "enough exercise" be household chores and stretching) or (2) those who were self-reported active and involved in a range of exercises or types of physical activity prior to admission such as walking, strength-training, self-guided programs, and group exercise.

"Now as for the exercise, on a scale to 1 to 10 and one being 'you don't do any exercise at all', I would say probably 2 [laughing]. I don't like doing any exercise."
#5, 67 years, male, moderately frail

"We go a walk every- I take a walking frame, not one of them- one of the sit-on ones. And, uh, we go around for about 20 minutes. Sometimes twice a day, but mostly once a day."
#9, 89 years, male, pre-frail

During hospitalisation

During hospitalisation, participants noticed a difference in the taste of food served. There were also feelings of unfamiliarity in the type of food, and reduced variety and quantity compared to what is served at home. In this cohort of pre-frail and frail hospitalised older adults, the perceptions were more often negative than not.

"When in hospital, eating is as per the hospitals menus and it always feels a little undersized in my opinion, cause I'm a big guy." **#5, 67 years, male, moderately frail**

"Well, you got to get used to the hospital food. Is not the same as our own, and uh, feel a bit tired."
#18, 68 years, male, pre-frail

Participants also described a wide range of changes in exercise during hospitalisation, from complete bed rest to increased exercise from baseline. This was relative to their baseline physical activity at home. Those that were more sedentary and asked to mobilise by hospital staff perceived that they were exercising more while those that were active prior hospitalisation felt the opposite. The acute medical conditions that led to orders, for example, bed rest, was another reason for the change.

"Well I suppose it's important when you're in hospital since I've been unable to walk as much, I've gradually gone downhill." **#4, 84 years, female, mildly frail**

"You can't do much exercise in here." **#13, 82 years, male, pre-frail**

"if they said to me "you have to get up and walk". Well, I've done that in the past, when I've been in hospital. I've sort of, once I sort of feel, you know, I'll walk round the bay and come back, you know, sort of do that, so you know, just to sort of keep- keep the bones moving"
#7, 75 years, female, pre-frail

Post-hospitalisation

Post-hospitalisation, some participants felt that they did not need to change any parts of their diets and would return to what their previous eating patterns were like. Others looked forward to an improvement in

diet adequacy and quality. The general consensus towards exercise post-hospitalisation was the initiation of home exercise services or physiotherapy, increasing exercise intensity, and exercising with mobility aids if necessary. Some participants that felt that there would be minimal changes to either their exercise routines or diets.

"Yes! Eating well! Always getting it down. And I think I'm going to get back to that.", "I'm going to get back to that, I'm going to get back to that when I get home."
#21, 84 years, female, moderately frail

"I probably will go back to some of the things I've got at home there. I always like to have fruit; I might have vegetables too" **#4, 84 years, female, mildly frail**

"I'll try and go back to my normal exercises of walking half an hour day.", "I'll try if I get stronger to add." **#18, 68 years, male, pre-frail**

"No" "you get set in your ways." **#16, 85 years, male, pre-frail**

Perception of optimal diet and exercise routine for pre-frailty and frailty

Participants provided a rich description of their desires for components of an optimal diet and exercise routine from their point of view, and further details were presented in Table 18. The following main themes were all identified as components of an ideal diet for older adults: variety, sufficient in food groups, sufficient in hydration, moderation of some food groups, nutritionally balanced meals; self-made meals, professionally planned and delivered meals, and three-regular meals. Participants generally perceive that any exercise prescription should be age appropriate and promote the maintenance of their body weight. Regular walking and golfing were also described as examples of ideal types of exercises.

Table 18. Sample quotes on perception of components of an optimal diet and exercise routine for pre-frailty and frailty by themes in the first qualitative study

Main theme Sub-theme	*Participant's quote example*, **participant demographic**
Components of an optimal diet routine for pre-frailty and frailty	
Variety	
Contains variety of food groups	*"Yeah, I've got to eat the right things and I know- that's why I have a bit of everything"* **#4, 84 years, female, mildly frail** *"Well, you should eat- some… bit of fruit, a bit of meat, get your protein and… your fruit, you get your vitamin C, tomatoes and vits and that"* **#13, 82 years, male, pre-frail**
Contains different courses in a meal	*"The time I've got to the last fork full, our meal was cold. That was all right. As long as I've got it down and um, dessert always came with it And I would say must have the dessert and soup can have for the evening meal"* **#20, 80 years, male, mildly frail**
Sufficient in food groups	
Fruits and vegetables	*"Well, I mean you should eat veggies. You should eat fruit"* **#8, 85 years, male, mildly frail** *"With uh, with… with five or nearly five vegetables."* **#15, 87 years, male, pre-frail** *"Plenty of fruits and vegetables"* **#17, 80, female, mildly frail**
Grains and wholegrains	*"Wholemeal bread"* **#21, 84 years, female, moderately frail** *"I suppose Weetbix"* **#4, 84 years, female, mild frail**
Fish	*"Fish, two or three times a week"* **#17, 80, female, mildly frail**
Meat	*"Oh, pork yeah, something like that every day, every day and one probably. Leg of lamb or something"* **#9, 89 years, male, pre-frail** *"Oh, nutritious is a nice piece of steak."* **#14, 75 years, female, pre-frail**
Sufficient hydration	*"And some fluid. I know I've got to drink"* **#4, 84 years, female, mild frail**
Moderation of some food groups	
Red and processed meats	*"… can't eat a lot of red meat…. and things like sausages is too high in cholesterol."* **#5, 67 years, male, moderate frail** *"In my opinion, um, red meat small amounts"* **#17, 80, female, mildly frail**
Discretionary foods	*"they're my treats if I have treats, you know, there's sort of snacks in between. But don't have many. I mean.... sweet things but um, don't have a lot of cakes and things like that."* **#7, 75 years, female, pre-frail**
Alcohol	*"I mean, like some people, they get caught up where they, smoke and some people, they drink (alcohol) too excess"* **#8, 85 years, male, mildly frail**
Nutritionally balanced	
Energy-balanced	*"I don't think I should start eating more until I- I'm doing more, you know, working, doing my own jobs."* **#17, 80, female, mildly frail**

	Sufficient protein	*"Well, you should eat some…, a bit of meat, get your protein and…"* **#13, 82 years, male, pre-frail**
	Use of oral vitamin, mineral supplements	*"Um… magnesium from the Chemist and Vitamin B12."* **#11, 83 years, male, moderately frail**
Self-made meals		
	Meals are prepared at home by self or family	*"I'd rather prepare my own stuff. Uh, Yeah, I think home cooking and my daughter comes home and cooks for me sometimes."* **#21, 84 years, female, moderately frail**
Professionally planned and delivered meals		
	Meals are prepared and delivered	*"I have Meals on Wheels and I'll get their pre ordered meals. They're quite healthy."* **#10, 65 years, male, severely frail**
	Meals are prepared with input by dietitian	*"I think my diet is reasonably good because my diet that I have now is actually done by a dietitian."* **#16, 85 years, male, pre-frail**
Three regular meals a day		*"…three meals a day."* **#18, 68 years, male, pre-frail** *"I'm eating well I have my breakfast, morning. I have my lunch at lunchtime and that's a big lunch because our main meal is lunch time and, in the evening, something like that."* **#14, 75 years, female, pre-frail**
Components of an optimal exercise routine for pre-frailty and frailty		
Exercises that are low intensity		
	Walking	*"Should walk a mile or something every day"* **#13, 82 years, male, pre-frail** *"Walking in the garden"* **#21, 84 years, female, moderately frail**
	Golf	*"Good exercises when I was a bit younger, and I played golf"* **#22, 88 years, male, severely frail**
Exercises that support maintenance of healthy body weight		*"You know, and they put weight on a little bit easy, but in most cases I think it's because they don't exercise"* **#8, 85 years, male, mildly frail**
Exercises adapted for older age		*"You know when you're young, you have a different exercise than when you grow older, and on and on"* **#12, 83 years, male, moderately frail**

Perception of a proposed self-managed hospital-to-home intervention protocol combining exercise and nutrition

Participants perception of the contents of a proposed self-managed hospital-to-home intervention program was that it had to accommodate to current schedules, live-in partners, and the patients' changing physical capabilities.

"*As long as you sort of, I mean, if you let them know that you're likely to ring on a Tuesday at 11 o'clock or something."* **#7, 75 years, female, pre-frail**

While there was a general unanimity that the proposed program had a sense of familiarity and would benefit pre-frail and frail older adults, there were varying viewpoints on the amount of effort required as some

anticipated they would find it manageable while others thought it to be overly demanding and drawn out.

"They probably will- they would benefit yes" **#9, 89 years, male, pre-frail**

Concerns was raised by one participant about the timeliness of the intervention as some older adults might be too far into the condition and unable to participate to reap its benefits.

"I'm 89 and… I don't know. I don't think so. I think it's a bit too much" **#9, 89 years, male, pre-frail**

The program was also seen as one that required the participant's own motivation. There was feedback on the draft education resource booklet that it might be edits on the design to appear less condescending and the content to be more informative. For example, one participant thought the photos depicting the exercises were too elementary. The education material also was thought to need more references to an older person's current conditions i.e., cancer, other chronic diseases, not just pre-frailty and frailty. The proposed intervention period was also viewed as acceptable and not too lengthy. Participants verbalised that intervention touchpoints should be weekly, conducted in the later part of the day and general agreement that three months should suffice for interaction and support within the program. With regard to the mode of follow-ups post-discharge, there was agreement amongst participants against video conference calls. Generally, most participants were receptive to telephone calls, as long as they were planned in advance and "not too lengthy".

"I'm just wondering whether they are… telephone calls .. We use… WhatsApp", "Uh… video conference calls… I know they're around but I don't think I'll bother with them at the moment." **#9, 89 years, male, pre-frail**

There were some reservations towards home visits, but most were receptive, and more so, if the visiting health provider was previously acquainted. The gender of the visiting health provider was also a concern for female participants, unless previously acquainted. Table 19 presents more details on sample quotes on perception of a proposed self-managed hospital-to-home intervention protocol involving combined exercise and nutrition by themes.

Table 19. Samples quotes on perception of a proposed self-managed hospital-to-home intervention protocol involving combined exercise and nutrition by themes in the first qualitative study

Main theme Sub-theme	*Participant's quote example*, **participant demographic**
Combined exercise and nutrition program contents	
Accommodating to current conditions	
Must blend with existing schedules	"depends whether the four visits at home will coincide with whatever we're doing on that given day. That's the only disadvantage there **#1, 85 years, male, moderately frail**
Patient-partner lifestyle	"I don't think so because when my wife is so independent about cooking…*"* **#9, 89 years, male, pre-frail**
Patient's changing physical capabilities	*"I mean it it keeping it small in light because. A lot of these older people. Yeah, they can't really pick up more than 5 kilos"* **#8, 85 years, male, mildly frail**
Emphasis on patient-led approach	*"I don't like to be pigeonholed.", "I don't like being told what to do"* **#15, 87 years, male, pre-frail**
Beneficial	*"I'm optimistic about that exercising (program)."* **#11, 83 years, female, severely frail** *"Helpful"* **#6, 90 years, male, pre-frail**
Sense of familiarity	*"I've done all of these… this sort of thing I've done, yeah, they sort of, explain fairly well."* **#7, 75 years, female, pre-frail**
Different viewpoints on effort	
Manageable	*"I think I might be able to manage it, yeah."* **#4, 84, female, mildly frail**
Drawn-out	*"Wishy Washy", "It's pretty drawn out.", "A lot of effort."* **#10, 65 years, male, severely frail**
Timely	*"I have passed that time.", "Home visit is a good idea if it's early enough, even telephone calls are hard on me."* **#12, 83 years, male, moderately frail**
Requires patient motivation	*"so at the moment I had, I've really had no- I've not been very inspired to do anything, you know. But I think it's a good idea, but I've still got to get my head around a lot of things at the- you know that- but I think I mean, I think it is a good idea. But whether the oldies would be keen to do it, I don't know. It will follow it through. It's more the follow through that's sort of, you know… you don't want to be under any pressure."* **#7, 75 years, female, pre-frail**
Program accompanied by educational resources	
Education booklet must be informative	*"Maybe some good reading material.", "Yeah, relevant to, you know, cancer or whatever the person has."* **#20, 80 years, male, mildly frail**
Booklet appears condescending	*"The illustration that shows the person doing something. Makes it almost feel like you're training a child", "that looks a little demeaning to me"* **#5, 67 years, male, moderately frail**
Frequency and time of intervention	

	Total intervention	*"Yeah, I think three months is a reasonable approach to it, yeah."* **#1, 85 years, male, moderately frail**
	Weekly or fortnightly	*"Once a week is better.", "if every fortnight, then by the fortnight, you forget what you have done, and your muscles forget what you have done"* **#2, 84 years, female, mildly frail** *"Probably fortnightly I would think. So, there's only four over the three-month period is there?"* **#1, 85 years, male, moderately frail**
	Later in the day	*"Quite often older people don't get out of bed until later in the day.", "would be better between 10:00 and 12:00 or something."* **#13, 82 years, male, pre-frail**
Delivery method i.e., home visits and telehealth		
Reservation towards technology		
	Video conferencing	*'I- I mean a video call still one on one but it's not the same."* **#16, 85 years, male, pre-frail**
	Phone calls	*"Um, I'm not very keen on telephone calls."* **#14, 75 years, female, pre-frail**
Receptive to telehealth		*"Oh, I don't mind people calling on me! And in fact, I'm happy to even come to the medical centre and involve myself with questionnaires and things."* **#5, 67 years, male, moderate frail** *"As long as you sort of, I mean, if you let them know that you're likely to ring on a Tuesday at 11 o'clock or something"* **#7, 75 years, female, pre-frail**
Social aspect of home visits		*"I've got somebody next to me (home visits)."* **#18, 68 years, male, pre-frail**
Opposite viewpoints on home visits		
	Agree to home visits	*"Yeah, the home visits… they might be a great idea"* **#9, 89 years, male, pre-frail**
	Reservations towards home visits	*"I'm not one for home visits anyway"* **#5, 67 years, male, moderately frail** *"Invade your privacy."* **#16, 85 years, male, pre-frail**
	Must be delivered by acquainted health provider	*"They would be a little bit wary of having a young lad come into their house. I'm talking about a woman on her own.", "ladies might be inclined to sort of have a, uh, a lass come in.", "Well, they've got to know you"* **#7, 75 years, female, pre-frail**

5.5. Discussion

The findings of this study provide insights into the perceptions of pre-frailty and frailty, diet, and exercise from the point of view of a cohort of hospitalised pre-frail and frail older adults. There is a shared narrative among participants in this study, that pre-frailty and frailty are vulnerable age-related processes contributed by biopsychosocial factors. A range of diet and exercise habits were reported prior to hospitalisation; older adults tended to follow dietary practices from their younger years and walked as a common form of exercise. Hospitalisation was unanimously viewed as an event that drastically changed their diet and exercise routines, regardless of pre-hospitalisation practices. A majority in this cohort was positively affected by

hospitalisation, in that they expressed the desire to augment diet quality and improve exercise practices post-hospitalisation. However, not all components of an optimal diet and exercise regime that participants perceived and described, had elements aligned to the recommended national dietary and physical activity guidelines for community dwelling older adults. For example, for both aerobic activity as well as resistance training, some thought they were doing enough (e.g., exercise as a by-product of household chores), which suggested a mismatch between what participants think was enough activity compared to what actually is (moderate-greater intensity multicomponent physical activity ≥3 days a week to enhance functional capacity and prevent falls).[236] A rich dataset about perceptions towards a self-managed hospital-to-home intervention protocol as obtained in this study, will also serve as a guide for healthcare providers/researchers in codesigning programs that match end-users' needs with service provided.

Perceptions towards pre-frailty and frailty

The narrative among hospitalised pre-frail and frail older adults in this study (that pre-frailty and frailty are vulnerable age-related processes contributed to by biopsychosocial factors) is consistent with previous qualitative studies on frailty in healthcare providers and policy makers.[216, 237, 238] However, environmental, and economic factors were not identified in this cohort. Environmental factors may be related to infrastructure/living environment (e.g., housing, falling hazards while economic factors have been defined as costs (e.g., living expenses, access to services).[237] Data from this study highlight that pre-frail and frail older adults may tend to attribute their condition to intrinsic personal factors such as ageing, and fail to acknowledge the contribution of environmental and economic factors to the condition; particularly a lack of recognition of the external constraints of the hospital environment on their current capacity to be active.[239] This may in part be due to the fact that research exploring factors related to the physical environment and economic factors is lacking, especially during acute hospitalisation. The influence of these two aforementioned factors have been documented in a handful of studies albeit less recognised.[240, 241] Also, public education on pre-frailty and frailty may need to be prioritised before intervening.

Data from this study suggest that pre-frailty was not automatically thought of as a phase prior to frailty. In the literature review (Chapter 1), it was discussed that an International Delphi consensus suggested that pre-frailty is a multidimensional risk states related to physiological and socioeconomical disadvantages, that increases the risk of developing frailty.[8] However, that is from the point of view of "experts". This study expands the definition of pre-frailty defined by experts, by evaluating pre-frail and frail older adults' perceptions on pre-frailty. The themes identified and its descriptions could help researchers better understanding pre-frailty as a concept encompassing all dimensions including that of clinical and anthropological.[7]

Perception of diet and exercise

To the knowledge of the PhD candidate, this is the only study that presented described components of diet and exercise in pre-frail and frail older adults as a continuum from at home to when in hospitalisation and anticipated changes when home. It is also one of the first studies that explored what they perceive as

components of an optimal diet and exercise regime for pre-frail and frail older adults. A meta-synthesis of qualitative evidence on stakeholders' views and experience of interventions addressing pre-frailty and frailty suggest that it is a necessity to use a bottom-up approach to match the values, goals, priorities of pre-frail and frail older adults to the services offered in order to optimise the effectiveness of any care rendered.[216] The themes identified in this study and its descriptions could help researchers understand how pre-frail and frail older adults perceive diet and exercise. The deeper understanding can help healthcare providers/policy makers design interventions that are both supported by the scientific community and acceptable by its end-user. For example, having three regular meals was described as a diet habit practiced at home, and also perceived as part of an optimal diet for pre-frail and frail older adults. A study examining use of snacks in older adults to improve nutrient intake, found perceived lack of need for additional food and perceived adequate health status from the participant to be barriers towards the program.[221] This suggest that for between-meal snacks to be implemented as a strategy, prior education to the end-users may be needed. The present study also found a similar theme to another qualitative study of older New Zealanders perspective of food intake; "*we prefer foods we grew up with and we trust*" [242]. The participants of Pacific Islanders background had strong preferences for cultural foods grown in Samoa and Tonga.[242] In a qualitative study of influences on diet quality in older adults from the United Kingdom, Bloom et al also reported their perception of a "proper meal" consisted of traditional, familiar foods.[243]Therefore, nutrition interventions designed for older adults should consider also factors relating to cultural backgrounds and traditions.

Regardless of baseline physical activity levels, participants agree that exercises that if of a lower intensity (i.e., walking), adapted for old age and support weight maintenance, could benefit pre-frailty and frailty. This concurs with a previous study of institutionalised older adults that identified walking as part of any optimal exercise interventions.[244] The study further described that exercise programs often failed to meet participant's expectation of individualisation towards difficulty level of the recommended exercise (i.e., either too easy or overly difficult). Hence, it is crucial that exercise interventions provided must be adaptable to different needs. On that same note, walking was often seen as part of optimal exercise for the fact that a majority of older adults can do, albeit some with mobility aids, but intensity controlled by its participant (pace versus capacity).

In a qualitative study Gwyther et al reported a consensus from with healthcare policymakers, "*potential for frailty to be managed in a more integrated and person-centred manner, overcoming the challenges associated with niche ownership within the healthcare system*."[238(p.1)] Pre-frail and frail older adults should be more involved in management of this condition. Further details of implications for design of intervention protocol in pilot RCT in Chapter 6, would be discussed in Section 5.7.

Strength and limitations

This study captured a wide range of views of participants from a range of age, gender, living situation, nutritional status, and degrees of frailty, including pre-frailty. However, the PhD candidate only managed to recruit one participant with university level of education and the findings could only represent older

adults with lower levels of education. Nonetheless, the perception of pre-frailty and frailty in older adults (not specifically pre-frail and frail) has been most commonly explored in community settings. It is unsurprising that it would be hard to conduct interviews in a hospital setting, particularly when the patient is acutely unwell. One of the strengths of this study was that it presents data from specifically the hospitalised, pre-frail and frail population. The interview guide protocol was developed with reference to literature of combined exercise and nutrition interventions and a range of clinical expertise of the investigators representing different fields within pre-frailty and frailty care, with open-ended questions and prompts to elicit unleaded responses. The purposive sampling method allowed the PhD candidate and research team to recruit from their population of interest, gaining new insights to the issue surrounding a common group of hospitalised older adults. The use of principles from grounded theory ensured that data saturation was attained. The risk for social desirability bias was minimal in this study, as measures had been put in place, mentioned in the methods section. None of the participants knew that the PhD candidate/interviewer was a dietitian, and it was stressed that he was an independent researcher, without any influence over any aspect within the inpatient care.

As the interview was conducted within 48 hours of admission, the risk of recall bias related to home might be low in this cohort. Regardless, this potential for recall bias was acknowledged during data collection and analysis, and the PhD candidate/interviewer was careful to delineate views between hospital and home components. The PhD candidate also asked specific questions about the experiences across settings (i.e., hospital, home).

Some of the interviews were as short as eight minutes. While this may limit data, the difficulty of conducting interviews during admission must be acknowledged as many of the participants were admitted very recently with acute medical conditions. As majority of participants were not clear as to what pre-frailty constitute, their perceptions could represent more of frailty.

The applicability of the results from this study is limited to pre-frail and frail older adults without cognitive impairment as only those MMSE 25 and above were recruited. The results could only represent Caucasian older Australians, as none of the participants were from ethnically diverse and multicultural backgrounds.

5.6. Conclusion

This study has provided insights into the perception of pre-frailty and frailty and the role and acceptability of combined exercise and nutrition support programs in the context of health services spanning hospital-to-homes.

5.7 Implications for design of intervention program protocol in pilot RCT (Chapter 6)

Pre-frailty and frailty

The data on the perception of pre-frailty and frailty highlighted the importance of education as part of an intervention program to improve knowledge of these syndromes to facilitate behavioral change. The PhD

candidate further considered the perceptions of components of an optimal diet and exercise routine and perceptions of when improving the intervention program protocol for the pilot RCT in Chapter 8.

Nutrition

Prior to this qualitative study, the prototype resource booklet only focused on energy and protein. This focus on nutritional support was largely due to the anticipation that a high proportion of pre-frail and frail participants might also be malnourished. As such, there were only protein-rich food and calorie dense snacks suggestions within the education resource booklet. In response to the perception of having variety, sufficient and moderation in food groups as components of an optimal diet for pre-frailty and frailty, the Australian Guide to Healthy Eating was included as part of nutrition component of the program.

This finding concurs with another study that found that optimal diet was described by older adults to comprise of "*adequate eating and avoidance from under or over nutrition, having a balanced diet according to the age and consumption of recommended daily allowance of fruits and vegetables*".[245(p.291)]

The theme "sufficient hydration" viewed by pre-frail and frail older adults as part of an optimal diet also prompted the PhD candidate and study investigators to include a topic on fluids within the educational aspect of the program. Fluid restrictions might also be in place for some participants i.e., those with heart conditions, and adding it to the program would not only ensure sufficient hydration but also help monitor participants and prevent risks of overload. Both the healthy eating and hydration components were reflected in the nutritional component of the education resource booklet (see pages 31 and 32 within Appendix 6).

Exercise

Initially, only strength-based exercises were included in the program, as one of the goals of the program was to improve physical domains within frailty. Following this qualitative study, the component of daily walking was considered before inclusion to the exercise component of the program. The PhD candidate discussed with the research team and decided that it would help provide variety, especially in the hospital component of the program, where bedside exercises can be as restrictive as they are safe. The only concern was that the participant may not participate in the strength-based exercises once walking was completed. Therefore, the PhD candidate and the team decided to include walking three times a week as an additional recommendation, while still prioritising strength-based exercise components. One of the sub-themes of perceived optimal exercise, golf, was not an option due to resources, as it would be impossible to facilitate based on the resources allocated for the pilot RCT. In response to the perception that exercises had to support weight, it was highlighted in education that the exercises recommended helped to build/maintain lean body mass. In response to the perception that the exercises are adapted for old age, the PhD candidate and the study investigators retained the pictorial instructions (using photographs of actual older adults) within the exercise domain of the education resource booklet to demonstrate its age-appropriateness (see pages 9 to 18 within Appendix 6). As only one participant found the pictorials within the exercise to be demeaning, the PhD candidate sought to add relevant images featuring real older adults, to balance the

infographic/cartoons used throughout the education resource booklet (see pages 6, 22, 49 within Appendix 6).

Others

Remaining aspects of the programs were retained as they were deemed already reflective of what the interview data suggested. For example, participants wanted an "emphasis on patient-led approach", covered by the Flinders Chronic Condition Model (covered more in detail in Chapter 6). This one-on-one patient-provider model enables participants to act as their own principal source of care daily, with healthcare provider only facilitating that care as consultants. This was in accordance with a meta-synthesis of qualitative evidence on stakeholders view of pre-frailty and frailty interventions that suggested greater use of psychological skills, improve communication.[216] As the proposed program did not include video conference as a mode of intervention delivery, there wasn't a need for any changes on that aspect. However, some aspects of the perception of the program could not be addressed. For example, a minority of two participants mentioned that the program required much effort. On balance with other participant responses, and as the components of the programs were carefully picked for specific purposes, it was decided that none would be taken out for the next stage of pilot testing. The idea of home visit was also not always well-received. Therefore, the proposed program would appeal to pre-frail and frail older adults that are motivated to self-manage. In the pilot trial of the intervention (Chapter 7), there would be opportunity to measure real-world (rather than hypothetical/perceived) adherence to the updated and actual program.

CHAPTER 6: EFFECTS OF INDIVIDUALISED THERAPY FOR ELDERLY PATIENTS USING EXERCISE AND NUTRITION TO REDUCE DEPENDENCE POST DISCHARGE (INDEPENDENCE): A PILOT RANDOMISED CONTROLLED TRIAL

6.1 Contribution to overall research objective

The study in this chapter contributes to the overall aim of this thesis to expand knowledge in pre-frailty and frailty to better treatment in hospitalised older adults. The literature review in Chapter 1 and results from Chapter 4 highlighted that exercise and nutrition interventions for hospitalised pre-frail and frail older adults were not designed with input from its end-users. In this Chapter, the study incorporates lessons learnt from Chapter 4 e.g., need for formal assessment of pre-frailty and frailty, and inputs from the qualitative data from Chapter 5 (details in Section 5.7) to develop a self-managed combined exercise and nutrition intervention program. Thus, the protocol in this study has been heavily influenced by the cumulative findings of results from Chapter 4 and Chapter 5. A pilot RCT was undertaken to answer **Research Question 6 – will a self-managed, hospital-to-home, combined exercise and nutrition support program, be acceptable and benefit pre-frail and frail hospitalised older adults, when compared to usual care?** In this study, acceptability refers to drop-out rates and adherence to program, while benefits refer to improvement in pre-frailty and frailty measured by EFS and pre-frailty and frailty-related outcomes e.g., SPPB, grip strength.

6.2 Introduction

Given the significant impact that pre-frailty and frailty can have on public health systems, research on interventions to treat and prevent them is on the rise.[71] In Chapter 1 (Section 1.6), the systematic review of combined exercise and nutrition intervention for pre-frailty and frailty in hospitalised older adults has suggested promising results on pre-frailty and frailty and their related health indicators.[120] Exercise, and in particular strength training, can improve muscle strength and frailty.[246] Physical training within such interventions also benefits physical status outcomes,[84] and may be effectively delivered by physiotherapists, or in some trials other health professionals such as nurses[247] or trained lay individuals.[88] At the same time, individualised MNT and counselling conducted by a dietitian can improve nutritional status in three months.[112] As highlighted in Chapter 1, many RCTs supporting the effectiveness of combined exercise and nutrition interventions to reverse frailty are limited to community dwelling pre-frail and frail older adults.[67, 68] As the studies were conducted in community dwelling older adults, the applicability of the results to hospitalised older adults is limited. As mentioned in Section 1.4, hospitalisation is a vulnerable period for older adults, especially if they are pre-frail and frail, because acute catabolic stress and physical deconditioning due to immobility can further aggravate these syndromes.[248, 249] Overall, there is a paucity of high-quality studies on the effectiveness of combined exercise and nutrition interventions for pre-frail and frail hospitalised older adults, and even fewer that examine them using a patient self-managed model.[120]

The present **IND**ividualised therapy for **E**lderly **P**atients using **E**xercise and **N**utrition to reduce depen**DENCE** post discharge (INDEPENDENCE) pilot RCT aimed to investigate the benefits and acceptability of an individualised community-extended, combined exercise and nutrition intervention on pre-frailty and frailty. The exercise and nutrition components of this intervention were designed to be minimally supervised and delivered by a team of allied health professionals (dietitians, physiotherapists) and trained allied health assistants. However, the unique parts of the program is that it was informed by end-users as discussed in Chapter 5 and the inclusion of a patient self-management model[250] designed for chronic conditions. This would allow participants to take the lead in reversing pre-frailty and frailty through independent exercises and nutritional self-care.

The intervention was described with reference to the Template for Intervention Description and Replication (TIDieR) checklist.[251] The description of the INDEPENDENCE study protocol version 1.0 is reported in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist, a list of the recommended items to be included when reporting clinical trial protocols.[252] In conjunction with the SPIRIT checklist, the intervention is also described with reference to the TIDieR checklist.[251]

6.3 Methods

Study Design

This study (INDEPENDENCE) was a pilot RCT conducted among older adults who were pre-frail or frail and hospitalised for an acute medical illness. The study is reported with the Consolidated Standards of Reporting Trials (CONSORT) statement – randomised pilot and feasibility trials,[253] This study was prospectively registered with the Australia New Zealand Clinical trials Register ACTRN12619001367134.

Participant recruitment

Potential pre-frail and frail older adult participants, aged ≥65 years, were approached within 48 hours of admission and recruited from a single acute care site – patients admitted through the AMU at the FMC. A minute-long recruitment video was produced by the PhD Candidate using licensed stock videoclips and software, VideoPad video editor, version 8.63 (see Appendix 6 for screenshot and link to example).

Inclusion and exclusion criteria

Participants who met the following criteria were invited to participate – older adults aged ≥65 years, residing within Southern Adelaide Local Health Network (SALHN), an EFS score of ≥6 (the higher the score, the more severe the frailty), able to understand English instructions and without cognitive impairment (standardised MMSE) ≥25),[254] with access to a mobile or home phone. Those receiving palliative care, on home oxygen or assessed by the treating physician as unsafe to participate were not eligible.

Sample size calculation

During the conception of this study, there was no RCT that had investigated the effect of a self-managed combined exercise and nutrition intervention in pre-frail and frail hospitalised older adults. Hence, the study aimed to recruit 16 participants in each study arm, considering a minimal of 12 per group,[255] and accounting for a 25% attrition rate.[256] The proposed sample size also falls within the range reported in an audit of pilot trials.[257] Moreover, to determine the statistical power of this study, post-hoc power estimates were calculated for the mean and SD EFS scores at 3- and 6-months, alpha level of 0.05.

Randomisation and blinding

After screening, consent, enrolment and baseline assessments, the PhD candidate sent an identification number to a member of the research team not involved in the operations of this study, at which time the participant was randomised into either the intervention or control group. The randomisation schedule was created by an external research officer (not part of the research team) through computerised randomisation using randomly permuted blocks of size eight. Treatment codes were concealed in numbered opaque envelopes and opened by a research staff member not involved with participants directly, at the time of randomisation. Therapists and participants were aware of the allocated group, as it was not possible to blind the participants or research staff administering the intervention due to the nature of the intervention. However, another external research officer (not the PhD candidate nor other members of the research team for this thesis) performing outcome assessments and data analyses were blinded to group allocation.

Control

Participants in the control group received usual care available to older adults within SALHN, from their acute hospitalisation to post-discharge community care, and from health professionals across the spectrum of attending medical consultants, general practitioners, allied health, and nursing. The usual standard of care involved referral to a dietitian, physiotherapist and or other allied health care personnel such as allied health attendants, occupational therapist, speech pathologist, but only if requested by participants' treating medical team, with no dedicated outpatient follow up plan.

Intervention

Participants assigned to the intervention group received an individualised exercise and nutrition care plan while acutely admitted and that continued for three months post discharge, through an ambulatory service in the form of four home visits and four telephone calls (Figure 16).

Activities	Hospital stay	After Discharge (Week)											
		1	2	3	4	5	6	7	8	9	10	11	12
Nutrition therapy	×	×	×	×	×	×	×	×	×	×	×	×	×
Exercise therapy	×	×	×	×	×	×	×	×	×	×	×	×	×
Home visits		×	×		×				×				
Telephone calls				×			×				×		×

Figure 16. Outline of participant activities (intervention group) of the INDEPENDENCE pilot RCT

In addition to any usual physiotherapy care, inpatient participants in the intervention group were offered a daily (weekdays) supervised physical activity program of up to 30 minutes duration, that was individualised to their physical capabilities. Participants who were able to safely walk either independently or with minimal assistance (may have included a gait aid) were firstly offered the opportunity to walk for as long as they could. Then with any remaining session time, they completed exercises adapted from the STAND-Cph trial.[258] For the STAND-Cph component, following a range of motion 'warmup', participants completed chair stand and heel raise exercises at their maximum tolerated intensity, with options for progression and regression as per the STAND-Cph program. Participants who were physically dependent or unable to move away from the bedside due to requiring more than the available 1x assist, completed the STAND-Cph program only. All participants were encouraged to work at their highest level of function for as long as they could. Each session was supervised by the PhD candidate who had also been specially trained to the level of an allied health assistant to deliver this exercise program. Program oversight was provided by each participant's treating physiotherapist during the inpatient phase, and participants were assisted to self-regulate their effort by monitoring perceived exertion, ensuring safe program delivery.

For all participants, including those identified as malnourished, as ascertained by the PG-SGA, the research dietitian formulated an individualised nutrition care plan to maintain/improve diet quality with a focus on (1) ensuring 100 per cent of their energy requirements to achieve ideal body weight, estimated from the Harris Benedict equation[259] and (2) meeting the recommended protein intake (1-1.2g/kg body weight/d) to maintain and regain lean body mass.[260] The Australian Guide to Healthy Eating was also referred to when optimising diet quality and ensuring sufficient hydration.[261] For some participants, the medical nutrition therapy provided included the use of ONS, mid-meal snacks (limited to hospital's food service menu) and food fortification strategies, catered to the individual participant's preferences and tolerance. Optimal care in terms of frequency of reviews and input was left to the discretion of the dietitian as individualised therapy will vary between participants. Nutrition counselling delivered by the PhD candidate in the capacity of a dietitian, with a focus to augment energy and protein intake, was provided to participants prior to discharge to ensure continuity of the nutritional care plan at home. For participants who were well-nourished as per the PG-SGA, nutrition counselling prior discharge was focused on optimisation of diet quality, protein, and hydration.

Post-discharge, participants were provided with an ambulatory combined exercise and nutrition service to encourage patient-management of both exercise and nutrition therapies, and to troubleshoot related issues. For the post-discharge follow ups, participants were guided by the PhD candidate working both in scope as a dietitian and as a trained allied health assistant following training in the Flinders chronic condition self-management program, and training from the physiotherapist to facilitate the home exercise program. Ideally, an additional member of the research team would function as the allied heath assistant to facilitate the program. However, due to lack of resources, the PhD candidate had to take both roles. The aim of the intervention was to ensure continuity of care from hospital-to-home and to build participants confidence for self-management through empowering the participants with knowledge about exercise and nutrition specific to their needs. This may improve the adherence to this self-managed program as the "onus of care" is placed upon the participant. For the home based exercise program, the focus was resistance training for completion three days a week, with strength exercises from the Otago community exercise program.[262] The Otago exercise program consist of 17 strength (e.g., knee extensor, hip adductor) and balance (e.g., heel walking, one leg stand) exercises and a walking routine, performed three times per week. Balance exercises were not included as the home exercises were almost always unsupervised in this self-managed program. Consistent with the Otago program, participants were also provided with advice about walking three times a week, in between strength training exercises. To embed self-management in the intervention design, both exercise and nutrition care was supported by the Flinders chronic condition management model – a one-on-one patient-health provider approach with motivational interviewing.[250] As the information and instructions were rather extensive, each intervention participant was provided with a printed program guidebook (Table 20), with all the above-mentioned information, full details available in Appendix 6.

Table 20. Content of program resource booklet for intervention participants of the INDEPENDENCE pilot RCT

Section	Content
Introduction	
- About the program	Information about the program, the team working on this research and contact details of the liaison officer. Information about the structure of intervention program i.e., dedicated space to record scheduled visits.
- What is frailty	Information about pre-frailty and frailty; compiled by the research physician
Exercise	Written information and diagrams about exercise and its relation to frailty/pre-frailty. Also contain guided activities with pictorials i.e. warm up, exercise from the STAND-Cph trial,[258] Otago program;[247] compiled by research physiotherapist.
Nutrition	Information on nutrition and its role in frailty/pre-frailty. Information explaining the importance of sufficient energy and protein, maintaining hydration and the Australia guide to healthy eating; compiled by the research dietitian.

Self-management	Guided activities to help participants to think about and understand their concerns surrounding frailty/pre-frailty. Activities include understanding their strengths, needs and worries, what they see as their main worry, and a section on goal setting, using the Flinders chronic condition management model. Contains exercise and diet monitoring diaries where participants can self-monitor actual physical activities done and diet records.

To maintain a participatory/co-design approach while designing the protocol,[263] the PhD candidate took into consideration the results of the qualitative study conducted in Chapter 5. There was a general consensus that the type of intervention proposed for delivery was familiar and anticipated to be manageable and to reasonably be capable of obtaining the desired benefits. The intervention period was also viewed as acceptable and not too lengthy. There was acceptance towards the intervention for (1) its emphasis on a patient-led self-managed approach that would be able to accommodate participants' current situation (existing schedules and lifestyle; changing physical capabilities that requires adaptive interventions), (2) its delivery by a trusted health provider whom participants would get acquainted with from the daily inpatient therapy and (3) its timeliness to attempt to treat the problem early. However, there appeared to be a unanimous agreement that the program would likely only appear to older adults with particular motivations and who were receptive to the idea of home visits. In addition, the use of an educational resource such as a printed booklet was also suggested to accompany the intervention.

Outcome measures

The following outcomes were used to assess the benefits of the INDEPENDENCE program in pre-frail and frail hospitalised older adults improved the following outcomes at 3- and 6-months, compared to baseline (see Appendix 4 part 1 and part 2):

1. Pre-frailty and frailty scores as determined by EFS[57]
    - Assesses nine domains – cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance, score ranges from 0-17 points with higher scores indicative of a greater severity of frailty.
2. Lower extremity physical function as assessed by SPPB[264]
    - Consist of three components: ability to stand with feet together side by side, semi-tandem, and tandem, timed trials of 4-meter walk, and sit-to-stand test. Score range from 0-12 points with higher scores indicating better function and 10 or more indicates robustness.
3. Grip strength as measured with a hand held dynamometer[197]
    - Average of three attempts with dominant hand using the TTM Advanced Hand Dynamometer, measured in kilograms.
4. Nutritional status as measured with the PG-SGA and Scored PG-SGA[265]
    - Consist of a grade and score component. The grade component consists of five categories – weight, nutritional intake, nutrition impact symptoms (NIS), functioning, physical exam. An overall grade of A, B or C indicates well-nourished, moderate/suspected malnutrition or severely malnourished, respectively. The score components consist of seven categories

– weight, food intake, NIS, activities and function, disease and relation to nutrition requirements, metabolic demand, physical examination, with a global assessment of nutritional status. A higher score would suggest a greater degree of malnutrition.

5. Cognition as assessed with the mini-mental state examinations (MMSE)[143]
    - Consist of tests of orientation, attention, memory, language, and visual-spatial skills, ranging 0-30, with 25-30 indicating normal cognition, 24 and below suggesting mild to severe cognitive impairment as scores get lower.
6. Mood as assessed using the 15-item geriatric depression scale, validated for older adults in hospital setting.[266]
    - A set of 15 questions describing the respondent's feeling over the past week. Score ranging from 0-15. A score of 0-5 is normal while a score greater than five suggests depression.
7. Health-related QoL as assessed with the EuroQol-5-Dimension-5-Level (EQ-5D-5L)[267]
    - The EQ-5D-5L consists of five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems that is combined into a 5-digit number that describes the patient's health state. The EQ-5D Visual Analog Scale (VAS) quantifies the participant's self-rated health on a vertical visual analogue scale from 0-100, with zero being the worst and 100 being the best health imagined.
8. Risk of functional decline as assessed with the Hospital Admission Risk Profile (HARP) tool[268]
    - Calculated with age, cognitive status, and self-reported Instrumental Activities of Daily Living (IADL) upon admission, ranging from 0-5, with higher scores indicative of higher risk of functional decline.
9. The inpatient length of stay (LOS), total visits to the emergency department within 180-days post-discharge, total number of reported unplanned readmissions (defined as a hospital admission resulting in an overnight stay) and total hospital LOS within 180-dayspost discharge, was also recorded at three and six months.

Program adherence

The degree of adherence to the intervention was recorded for completed intervention participants (n=12) as (1) attendance to the inpatient and home visits, (2) adherence as a reasonable attempt at each 3x/week strength focussed training and walking session from the exercise monitoring diaries in the education booklet and (3) percentage of energy and protein intake over estimated requirements as per suggested by dietitian, from the diet monitoring diaries in the education booklet. The other participants (n=4) were not recorded as one died during inpatient stay, one died before start of community visits, one died before completion of community visits, and one withdrew from the program prior to start of community visits.

Statistical Analysis

Participants data were assessed at baseline (before randomisation), 3-month and 6-month. Treatment groups

were coded to blind the PhD candidate prior statistical tests. Normality tests (Kolmogorov–Smirnov and Shapiro–Wilk) showed normal distribution for all baseline measures, except PG-SGA and scored PG-SGA. Baseline data were described and compared with the use of independent sample t-tests or Mann-Whitney U test for continuous data and chi square or Fisher's exact test, for categorical data. The primary analyses were conducted with PP and also ITT principles with all participants randomised included in the analysis and assigned to the group they were randomised to regardless of their received treatment.[269] Multiple imputation method (Markov chain, Monte Carlo) including the entire dataset of measured outcomes, was used to derive any missing data points, with 20 imputations carried out for each missing value for the ITT analyses.[201] This was conducted on the recommendation of a biostatistician to improve the reliability of the results compared to the RCT described in Chapter 4, which used five imputations. To determine differences between the groups at three and six months, linear regression models with follow-up changes from baseline as dependent variables, and baselines as covariates were used for continuous outcomes.[202] Statistical analysis was performed using SPSS version 28.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was set using a 2-sided Type 1 error rate of alpha level of 0.05 and differences between groups at 3-month and 6-month follow-up were described as mean and SD for continuous variables, as number (percent) for categorical variables, and differences between groups as mean difference with 95% CI.

6.4 Results

Recruitment

A total of 1371 participants were screened consecutively at the AMU at FMC from September 2020 – June 2021. A total of 723 (54%) of patients screened were not eligible due to age <65 years. As per the CONSORT flow diagram in Figure 17, 32 participants were randomised into intervention and control groups each.[270] Follow-up data from 75% (12/16) of the intervention and 100% (16/16) of the control group were available for analysis at 3-month. At 6-month, the availability of follow-up data was 69% (11/16) and 94% (15/16) of the intervention and control group, respectively. The follow-up attrition rate at 6-month was 16%, with 4/5 losses due to death.

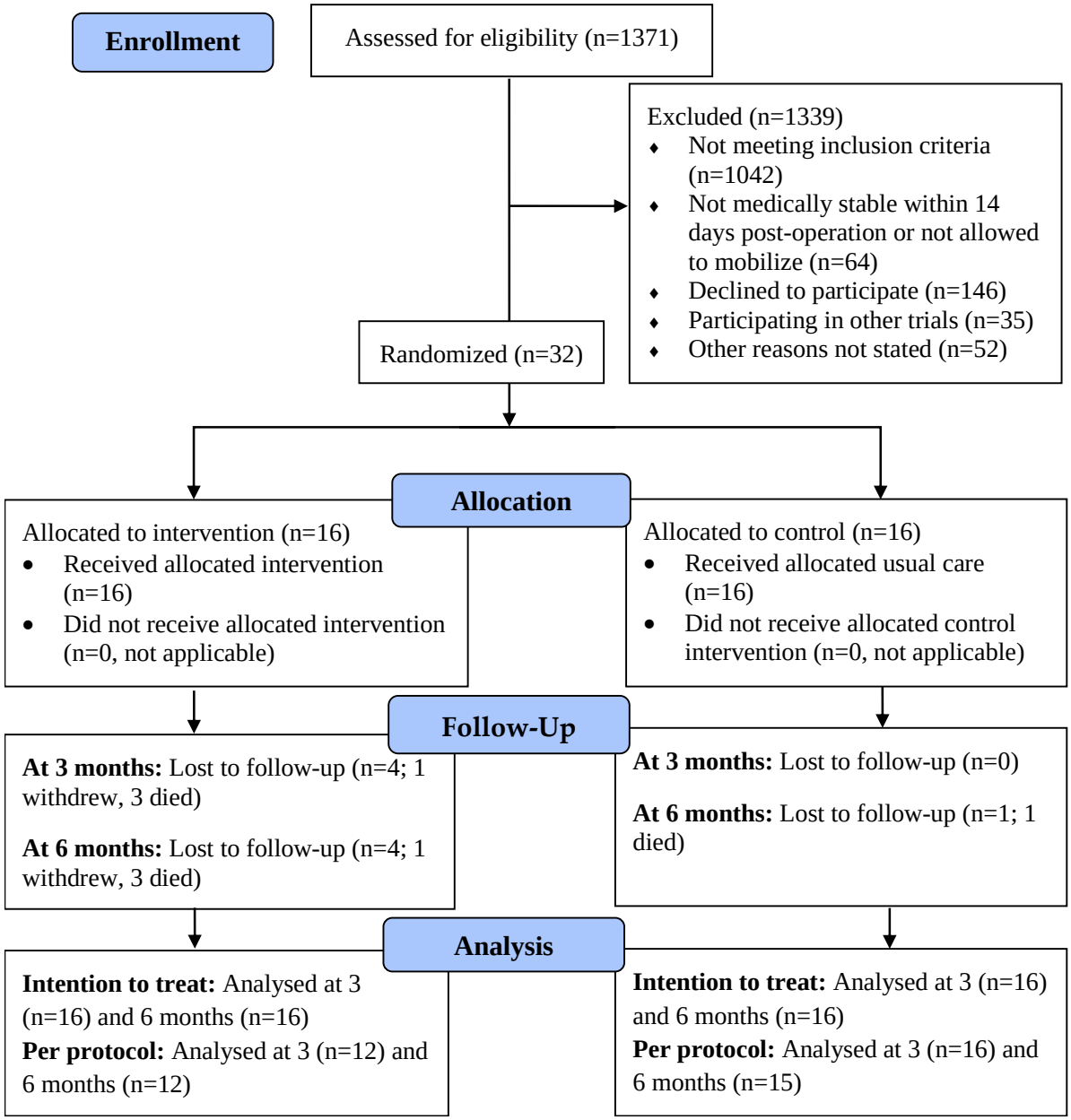


Figure 17. Overview of the INDEPENDENCE RCT with CONSORT Flow Diagram

Characteristics of the study population

Participant characteristics are shown in Table 21. Baseline characteristics between groups were well matched with the exceptions of overall SPPB, specifically the balance component.

Table 21. Baseline characteristics of study participants in the INDEPENDENCE pilot RCT

Characteristic	Intervention (n=16)	Control (n=16)	*P*-value[a]
Age, years, mean ±SD	80.0 ±7.6	78.3 ±5.8	0.484
Female, n (%)	11 (69)	9 (56)	0.264
Weight, kg, mean ±SD	72.5 ±18.5	86.8 ±29.2	0.110
Height, cm, mean ±SD	166.6 ±8.6	168.0 ±10.8	0.694
BMI[b], kg/m^2, mean ±SD	26.1 ±6.2	30.5 ± 8.1	0.095
MMSE[c] score, mean ±SD	28 ±2.0	28 ±2.0	1.0
Charleson Comorbidity Index, mean ±SD	4.4 ±1.6	4.4 ±1.4	1.0
Number of medications, mean ±SD	7.5 ±3.7	8.9 ±4.7	0.345
On vitamin D supplements, n (%)	8 (50)	6 (43)	0.476
Education level tertiary and above, n (%)	4 (25)	5 (31)	0.723
Very low income, n (%)	4 (25)	4 (25)	1.0
Living status alone, n (%)	8 (50)	6 (43)	0.476
Alcohol (>2 standard drinks a day), n (%)	0 (0)	1 (6)	0.310
Smokers (former and current), n (%)	6 (38)	4 (25)	0.446
Pre-frailty and Frailty			
Edmonton Frail Scale, mean ±SD	9.1 ±1.8	8.0 ±2.0	0.107
Frail participants, n (%)			
Pre-frail	3 (19)	9 (56)	0.172
Mild frail	6 (38)	3 (19)	
Moderately frail	6 (38)	3 (19)	
Severely frail	1 (6)	1 (6)	
Physical function, strength, and balance			
Short Physical Performance Battery, mean ±SD	2.1 ±1.9	3.9 ±2.5	0.02
Gait speed score, mean ±SD	1.0 ±1.0	1.6 ± 1.2	0.13
Chair stand test score, mean ±SD	0.06 ±0.25	0.38 ± 0.72	0.11
Balance test score, mean ±SD	1.0 ±1.1	1.94 ± 1.12	0.02
Grip strength, kg, mean ±SD	16.8 ±6.8	22.6 ± 10.1	0.07
Nutrition, mental, quality of life and readmission risk			
Scored PG-SGA[d], mean ±SD	8.8 ±5.0	6.2 ±5.5	0.061
PG-SGA[d] grade, n (%)			0.076
Well-nourished	5 (31)	11 (69)	
Malnourished	11 (69)	5 (31)	
Geriatric Depression Scale, mean ±SD	5.6 ±3.6	4.3 ±2.6	0.246
EQ-5D-5L UI[e], mean ± SD	0.55 ±0.35	0.38 ±0.35	0.158
EQ-5D VAS[f], mean ± SD	57.7 ±23.0	54.9 ±19.9	0.721
HARP[g], mean ± SD	2.2 ±1.3	1.8 ±1.3	0.422

Data expressed as mean ± SD for continuous variables; absolute numbers (percentage) for categorical variables. [a]t-tests, Mann Whitey U, Chi-square or Fisher's exact test, as appropriate. [b]Body Mass Index. [c]Mini Mental State Examinations. [d]Patient-generated subjective global assessment: has scores between 0 and 35 with higher scores indicating worse nutritional status. [e]Geriatric Depression Scale has scores has scores between 0 and 15 with a higher score indicating more depressive symptoms. [f]Quality of life measured with the EQ-5D-5L utility index: has scores between 0 and 1 with higher scores indicating better health-related quality of life. [g]EQ-5D visual analogue scale: has scores between 0 and 100 with higher scores indicating better health-related quality of life. [h]Hospital Admission Risk Profile: has scores between 0 and 5 with higher scores indicating higher readmission risk.

Adherence to program

The mean ±SD attendance (completion) of the inpatient and home visits/telehealth follow-ups were 91% ±13% and 92% ±21%, of sessions attended respectively. For the home-based component, the mean adherence to the exercise program was 66% ±33%. At home, the percentages of energy and protein being met were 89% ±17% and 82% ±20%, respectively. The daily mean ±SD energy and protein intake were

1604 ±471kcal and 71.1 ±24.0g, respectively.

Responsiveness of assessment tools (EFS, GDS, MMSE)

The effect sizes as measured by Cohen's D for responsiveness of tools were calculated for EFS, GDS and MMSE. The effect sizes using PP analyses at 3- and 6-months were >1.0 and 0.83 for EFS; 0.70 and 0.56 for GDS, and 0.89 and 0.37 for MMSE, respectively. The effect sizes using ITT analyses at 3- and 6-months were 0.91 and 0.71 for EFS; 0.35 and 0.50 for GDS, and 0.81 and 0.31 for MMSE, respectively.

Pre-frailty and frailty

As shown in Table 22 and Table 23, participants in the intervention group had a significantly greater reduction in EFS score, as compared to those in the control group at three and six months ($P<0.001$ for both time points) in both PP and ITT analyses. Based on the results of ITT analyses, the prevalence of pre-frailty and frailty at 3-month was 46% more for control than intervention (14 out of 16, 88% versus 5 out of 12, 42%, $P=0.028$. However, that was not significant at 6-month, albeit there was a trend that the prevalence of pre-frailty and frailty at 6-month was 40% more for control than intervention (11 out of 15 (73%) versus 4 out of 12 (33%), $P=0.051$). PP analyses showed significance for both 3-month and 6-month ($P<0.05$). Post-hoc power estimates were 72.6% and 62.6% at 3- and 6-months, respectively.

Table 22. Effects of intervention on primary and secondary outcomes, per protocol analyses in the INDEPENDENCE pilot RCT

	Intervention	Control	*Coefficent*[a]	*P*-value[b]
Primary outcomes				
Edmonton Frail scale				
3-month, n, mean ±SD	12, 5.3 ±3.3	16, 8.2 ±2.5	-3.5 (-5.4 to -1.6)	<0.001
6-month, n, mean ±SD	12, 4.6 ±3.3	15, 6.8 ±2.0	-2.8 (-4.3 to -1.3)	<0.001
Change from 0 to 3-month	12, -3.4 ±2.3	16, 0.2 ±2.3		
Change from 0 to 6-month	12, -4.2 ±2.6	15, -1.3 ±1.0		
Secondary outcomes – Physical function, strength, and balance				
Short Physical Performance Battery – Overall				
3-month, n, mean ±SD	12, 7.5 ±4.1	15, 3.8 ±3.1	4.7 (1.8 to 7.6)	0.003
6-month, n, mean ±SD	12, 7.3 ±4.1	15, 3.6 ±4.1	4.8 (1.3 to 8.3)	0.009
Change from 0 to 3-month	12, 5.1 ±4.4	15, -0.3 ±2.5		
Change from 0 to 6-month	12, 4.9 ±4.1	15, -0.6 ±3.7		
Short Physical Performance Battery – Gait speed				
3-month, n, mean ±SD	12, 3.0 ±1.5	15, 1.3 ±1.3	1.9 (0.7 to 3.0)	0.003
6-month, n, mean ±SD	12, 2.9 ±1.3	15, 1.4 ±1.6	1.7 (0.4 to 2.9)	0.011
Change from 0 to 3-month	12, 1.8 ±2.0	15, -0.5 ±1.2		
Change from 0 to 6-month	12, 1.8 ±1.9	15, -0.3 ±1.6		
Short Physical Performance Battery – Chair stand				
3-month, n, mean ± SD	12, 1.8 ±1.3	15, 0.4 ±0.6	1.7 (1.0 to 2.4)	<0.001
6-month, n, mean ± SD	12, 2.0 ±1.5	15, 0.7 ±1.3	1.5 (0.3 to 2.7)	0.013
Change from 0 to 3-month	12, 1.8 ±1.1	15, 0 ±0.4		
Change from 0 to 6-month	12, 1.9 ±1.4	15, 0.3 ±1.3		
Short Physical Performance Battery – Balance				
3-month, n, mean ± SD	12, 2.7 ±1.8	15, 2.1 ±1.7	0.9 (-0.6 to2.4)	0.201
6-month, n, mean ± SD	12, 2.4 ±1.7	15, 1.5 ±1.7	1.6 (0.3 to 3.0)	0.017
Change from 0 to 3-month	12, 1.5 ±2.0	15, 0.1 ±1.6		
Change from 0 to 6-month	12, 1.2 ±1.5	15, -0.6 ±1.5		
Grip Strength				
3-month, n, mean ± SD	12, 19.4 ±7.6	13, 20.9 ±13.6	4.0 (-1.5 to 9.6)	0.147
6-month, n, mean ± SD	11, 19.2 ±8.7	14, 21.2 ±12.0	4.8 (0.3 to 9.2)	0.037
Change from 0 to 3-month	12, 2.0 ±3.9	13, -2.0 ±7.8		
Change from 0 to 6-month	11, 3.0 ±5.2	14, -1.3 ±4.7		
Secondary outcomes – Nutrition, mental, quality of life and readmission risk				
Scored Patient Generated-Subjective Global Assessment[c]				
3-month, n, mean ± SD	12, 3.7 ±2.8	16, 6.3 ±3.8	-2.9 (-5.5 to -0.2)	0.036
6-month, n, mean ± SD	12, 3.7 ±3.6	15, 4.7 ±4.3	-1.4 (-4.5 to 1.6)	0.341
Change from 0 to 3-month	12, -3.9 ±4.3	16, 0.1 ±5.6		
Change from 0 to 6-month	12, -3.9 ±4.8	15, -1.7 ±5.2		
Geriatric Depression Scale[d]				

3-month, n, mean ± SD	12, 2.8 ±2.9	13, 3.9 ±3.4	-1.6 (-3.8 to 0.6)	0.137
6-month, n, mean ± SD	12, 2.5 ±3.3	15, 4.4 ±3.5	-2.7 (-4.9 to -0.5)	0.018
Change from 0 to 3-month	12, -2.4 ±3.5	13, -0.4 ±2.3		
Change from 0 to 6-month	12, -2.8 ±3.4	15, 0.3 ±2.3		
EQ-5D-5L Utility Index[e]				
3-month, n, mean ± SD	12, 0.8 ±0.3	16, 0.6 ±0.4	0.2 (-0.1 to 0.5)	0.16
6-month, n, mean ± SD	12, 0.7 ±0.4	15, 0.7 ±0.2	0.1 (-0.2 to 0.4)	0.57
Change from 0 to 3-month	12, 0.3 ±0.4	16, 0.1 ±0.3		
Change from 0 to 6-month	12, 0.3 ±0.4	15, 0.1 ±0.1		
EQ-5D Visual analogue scale [f]				
3-month, n, mean ± SD	12, 62.3 ±30.5	16, 58.6 ±23.5	2.4 (-18.6 to 23.3)	0.819
6-month, n, mean ± SD	12, 68.7 ±24.4	15, 65.5 ±15.6	1.5 (-11.2 to 14.1)	0.815
Change from 0 to 3-month	12, 2.4 ±35.4	16, 3.6 ±26.5		
Change from 0 to 6-month	12, 8.8 ±22.6	15, 8.6 ±13.3		
Hospital Admission Risk Profile[g]				
3-month, n, mean ± SD	12, 1.7 ±1.2	15, 1.9 ±1.5	-0.5 (-1.5 to 0.5)	0.343
6-month, n, mean ± SD	12, 1.5 ±1.2	15, 2.0 ±1.2	-0.6 (-1.4 to 0.2)	0.356
Change from 0 to 3-month	12, -0.7 ±1.2	15, 0.1 ±1.4		
Change from 0 to 6-month	12, -0.7 ±1.0	15, 0.1 ±1.2		
Mini Mental State Examination[h]				
3-month, n, mean ± SD	12, 28.7 ±1.2	15, 25.6 ±4.0	2.6 (0.3 to 4.8)	0.025
6-month, n, mean ± SD	12, 28.8 ±1.0	15, 28.3 ±1.5	0.4 (-0.6 to 1.4)	0.422
Change from 0 to 3-month	12, 0.6 ±2.2	15, -1.8 ±3.0		
Change from 0 to 6-month	12, 0.8 ±1.9	15, 0.6 ±1.6		

Data presented as mean ±standard deviation. [a] Coefficient from a linear regression model with follow-up values as a dependent variable and baseline values as a covariate. [b]P-values, which were derived from linear regression models with baseline values as a covariate, are for the differences in mean between intervention and control group. [c]Patient-generated subjective global assessment: has scores between 0 and 35 with higher scores indicating worse nutritional status. [d]Geriatric Depression Scale has scores has scores between 0 and 15 with a higher score indicating more depressive symptoms. [e]Quality of life measured with the EQ-5D-5L utility index: has scores between 0 and 1 with higher scores indicating better health-related quality of life. [f]EQ-5D visual analogue scale: has scores between 0 and 100 with higher scores indicating better health-related quality of life. [g]Hospital Admission Risk Profile: has scores between 0 and 5 with higher scores indicating higher readmission risk. [h]Mini Mental State Examinations: has scores between 0 and 30 with higher scores indicating better cognition.

Table 23. Effects of intervention on primary and secondary outcomes, intention-to-treat analyses in the INDEPENDENCE pilot RCT

	Intervention	Control	*Coefficent*[a]	*P*-value[b]
Primary outcomes				
Edmonton Frail scale				
3-month, mean ± SD	5.7 ±3.0	8.2 ±2.5	-3.0 (-4.8 to -3.0)	<0.001
6-month, mean ± SD	4.9 ±3.0	6.7 ±2.0	-2.5 (-3.8 to -1.0)	<0.001
Change from 0 to 3-month	-2.8 ±2.4	0.2 ±2.3		
Change from 0 to 6-month	-3.8 ±2.5	-1.4 ±1.0		
Secondary outcomes – Physical function, strength, and balance				
Short Physical Performance Battery – Overall				
3-month, mean ± SD	7.1 ±3.7	3.9 ±3.1	4.0 (1.3 to 6.6)	0.003
6-month, mean ± SD	6.9 ±3.7	3.7 ±4.0	3.9 (1.0 to 6.9)	0.009
Change from 0 to 3-month	4.4 ±4.1	-0.2 ±2.5		
Change from 0 to 6-month	4.1 ±43.9	-0.4 ±3.7		
Short Physical Performance Battery – Gait speed				
3-month, mean ± SD	2.7 ±1.5	1.3 ±1.3	1.5 (0.3 to 2.7)	0.015
6-month, mean ± SD	2.7 ±1.3	1.4 ±1.6	1.4 (0.2 to 2.6)	0.022
Change from 0 to 3-month	1.5 ±2.0	-0.4 ±1.3		
Change from 0 to 6-month	1.5 ±1.8	0.3 ±1.6		
Short Physical Performance Battery – Chair stand				
3-month, mean ± SD	1.6 ±1.2	0.5 ±0.7	1.4 (0.6 to 2.2)	<0.001
6-month, mean ± SD	1.9 ±1.4	0.8 ±1.3	1.2 (0.2-2.2)	0.022
Change from 0 to 3-month	1.5 ±1.2	0.1 ±0.5		
Change from 0 to 6-month	1.7 ±1.4	0.4 ±1.3		
Short Physical Performance Battery – Balance				
3-month, mean ± SD	2.6 ±1.7	2.2 ±1.7	0.8 (-0.6 to 2.1)	0.261
6-month, mean ± SD	2.3 ±1.6	1.5 ±1.7	1.4 (0.2 to 2.6)	0.022
Change from 0 to 3-month	1.3 ±1.9	0.1 ±1.6		
Change from 0 to 6-month	1.0 ±1.5	-0.5 ±1.5		
Grip Strength				
3-month, mean ± SD	19.7 ±6.8	20.9 ±12.3	3.3 (-1.1 to 7.6)	0.140
6-month, mean ± SD	19.6 ±7.5	21.1 ±11.2	3.7 (0.2 to 7.1)	0.039
Change from 0 to 3-month	1.5 ±3.7	-1.7 ±7.1		
Change from 0 to 6-month	2.4 ±4.6	-1.0 ±4.5		
Secondary outcomes – Nutrition, mental, quality of life and readmission risk				
Scored Patient Generated-Subjective Global Assessment[c]				
3-month, mean ± SD	4.1 ±2.7	6.3 ±3.8	-1.9 (-4.7 to 0.9)	0.176
6-month, mean ± SD	3.8 ±3.3	4.7 ±4.1	-0.7 (-3.6 to 2.2)	0.649
Change from 0 to 3-month	-3.4 ±4.0	0.1 ±5.6		
Change from 0 to 6-month	-3.7 ±4.3	-1.7 ±5.1		
Geriatric Depression Scale[d]				

3-month, mean ± SD	2.9 ±2.6	3.9 ±3.1	-1.2 (-3.0 to 0.7)	0.211
6-month, mean ± SD	2.8 ±3.0	4.4 ±3.4	-2.2 (-4.1 to -0.3)	0.026
Change from 0 to 3-month	-2.2 ±3.1	-0.6 ±2.2		
Change from 0 to 6-month	-2.3 ±3.2	0.2 ±2.3		
EQ-5D-5L Utility Index[e]				
3-month, mean ± SD	0.7 ±0.3	0.6 ±0.4	0.2 (-0.1 to 0.5)	0.274
6-month, mean ± SD	0.7 ±0.4	0.7 ±0.2	0.1 (-0.2 to 0.3)	0.674
Change 0 to 3-month	0.3 ±0.5	0.1 ±0.3		
Change 0 to 6-month	0.3 ±0.5	0.1 ±0.4		
EQ-5D Visual analogue scale [f]				
3-month, mean ± SD	61.8 ±26.4	58.6 ±23.5	0.9 (-16.7 to 18.4)	0.924
6-month, mean ± SD	68.3 ±21.2	65.7 ±15.1	1.2 (-9.2 to 11.7)	0.819
Change from 0 to 3-month	8.8 ±30.7	8.5 ±26.5		
Change from 0 to 6-month	8.8 ±19.6	8.6 ±13.0		
Hospital Admission Risk Profile[g]				
3-month, mean ± SD	1.8 ±1.2	1.9 ±1.5	-0.4 (-1.3 to 0.5)	0.419
6-month, mean ± SD	1.5 ±1.1	2.0 ±1.2	-0.5 (-1.3 to 0.2)	0.180
Change from 0 to 3-month	-0.4 ±1.2	0.1 ±1.4		
Change from 0 to 6-month	-0.6 ±1.0	0.1 ±1.2		
Mini Mental State Examination[h]				
3-month, mean ± SD	28.1 ±1.6	25.7 ±3.9	2.1 (0.2 to 3.9)	0.029
6-month, mean ± Sd	28.8 ±1.0	28.4 ±1.5	0.2 (-0.8 to 1.2)	0.702
Change from 0 to 3-month	0.3 ±2.1	-1.8 ±3.0		
Change from 0 to 6-month	0.8 ±1.8	0.6 ±1.6		

Data presented as mean ±standard deviation. [a] Coefficient from a linear regression model with follow-up values as a dependent variable and baseline values as a covariate. [b]P-values, which were derived from linear regression models with baseline values as a covariate, are for the differences in mean between intervention and control group. [c]Patient-generated subjective global assessment: has scores between 0 and 35 with higher scores indicating worse nutritional status. [d]Geriatric Depression Scale has scores has scores between 0 and 15 with a higher score indicating more depressive symptoms. [e]Quality of life measured with the EQ-5D-5L utility index: has scores between 0 and 1 with higher scores indicating better health-related quality of life. [f]EQ-5D-5L visual analogue scale: has scores between 0 and 100 with higher scores indicating better health-related quality of life. [g]Hospital Admission Risk Profile: has scores between 0 and 5 with higher scores indicating higher readmission risk. [h]Mini Mental State Examinations: has scores between 0 and 30 with higher scores indicating better cognition.

Other outcomes

In both PP and ITT analyses, there were significantly greater improvements in total SPPB score in intervention than control, specifically in its gait speed and chair-stand components, at 3-month and 6-month. The significant difference in mean change from baseline between groups in SPPB-balance can be observed during 6-month follow up but not immediately after the intervention. In both PP and ITT analyses, participants in the intervention group also had significantly greater improvement in cognition (2.6; 95% 0.3-4.8, P=0.029) at 3-month, and grip strength (3.7; 95% CI: 0.2-7.1, P=0.039) and mood at 6-month (-2.2; 95% CI: -4.1 to -0.30, P=0.026). A trend for greater improvements in nutritional status was observed at 3-month as the effect could not be seen with ITT analyses. Moreover, there was a trend that the proportion of well-nourished participants was higher for intervention than control at 3-month (75% versus 56%), and 6-month (83% versus 67%).

There were no significant differences between groups with respect to EQ-5D-5L UI and VAS, and HARP at 3-month or 6-month in both PP and ITT analyses. It is noteworthy to mention that the proportion of well-nourished participants trended to be higher for intervention than control at 3-month (75% versus 56%), and 6-month (83% versus 67%). The total incidence of hospital readmissions, defined as at least one hospital admission resulting in an overnight stay, also trended lower for intervention compared to control at 3-month (33% versus 63%), and 6-month (25% versus 53%).

Length of hospital stay, readmissions, and visits to emergency department

There were no significant differences in inpatient LOS and total LOS in unplanned readmission within 180-days post-discharge between groups (Table 24). Although the total number of readmissions within 180 days post discharge was not significantly different between groups (Table 24), there was a trend towards reduced hospital readmission rate in the intervention group when compared to the control group at both 3-month (33% versus 63%, P=0.132) and 6-month (25% versus 53%, P=0.431). Participants in the intervention group had significantly lesser visits to the emergency department compared to those in the control group (Table 24).

Table 24. Effects of intervention on clinical outcomes, intention-to-treat analyses

	Intervention	Control	P-value[a]
Inpatient length of stay	8.5 (3-18)	5.5 (3-7.8)	0.402
Total length of stay in unplanned readmission within 180 days post discharge	0 (0-5.5)	1 (1-16.8)	0.160
Number of visits to emergency department within 180 days post discharge	0 (0-1)	1 (1-1.8)	0.039
Number of unplanned readmissions within 180 days post-discharge	0 (0-1)	1 (0-1.8)	0.128

Data presented in median (interquartile range). [a]P-values, derived from Mann-Whitney U test.

Adverse events

No adverse events or deaths due to the intervention, as defined as injuries or medical events due to the trial that result in medical attention or restriction of daily living activities for more than two days, were documented or reported to ethics.

6.5 Discussion

This study suggests preliminary evidence on benefits and acceptability of a new approach in pre-frailty and frailty care in hospitalised older adults. This intervention re-directed autonomy of care back to patients, with a self-managed, exercise-nutrition intervention and mixed modes (telehealth/in-person care) facilitated by an allied health assistant with support from a team of physiotherapist and dietitian. To the best of the PhD candidate's knowledge, this study is one of the first pilot RCT to evaluate the effects of such an intervention compared to usual care, to alleviate pre-frailty and frailty, as determined by the EFS scores in hospitalised older adults. The findings suggest that such a program can improve pre-frailty and frailty status,

physical strength and possibly have far reaching effects on cognition and mood in hospitalised older adults. This study demonstrated that the INDEPENDENCE intervention, compared to usual care, may produce approximately a 3-point difference in EFS, and greater chance at reversal of pre-frailty and frailty. Delivered during early detection of pre-frailty and frailty in the acute setting, such self-managed, exercise-nutrition model of intervention seems practicable in older adults. The results also suggested that effects were durable as there were good retention of positive effects on pre-frailty and frailty at 6-month. It is also noteworthy to mention that the intervention appeared to be well accepted, as reflected by good patient adherence to both supervised and non-supervised components in hospital and at home, and a low voluntary drop-out rate. However, the ability to draw any firm conclusions from the results is limited as this was a pilot study and the post-hoc power estimates of EFS scores were <0.8 at both 3- and 6-months.

This study contributes new knowledge to self-managed programs for pre-frailty and frailty in hospitalised older adults. This area is understudied, and more information is needed to be able to improve such services. Previous studies have demonstrated the effectiveness of combined exercise and nutrition programs managed by healthcare professionals to tackle pre-frailty and frailty starting predominantly in the community setting.[105] Nevertheless, intervention studies to ameliorate pre-frailty and frailty in hospitalised older adults remain limited.[120] To allow for better community reach, Luger et al have shown the use of trained non-professional volunteers to deliver a home-based physical training and nutritional intervention, to halt/slow down the progression of pre-frailty and frailty.[88] In that study, there was a also significant improvement in frailty in the intervention group compared to the control group after 12 weeks, as measured with the SHARE-FI (-0.71 discrete factor score values, 95% CI -1.07 to -0.35; P<0.001). The present study provides preliminary evidence to such a program but using a patient self-managed model, to help hospitalised older adults who are pre-frail and frail take a more active role in its management. This study also recruited solely hospitalised pre-frail and frail older adults based on a validated frailty assessment tool, making up for the lack of data from this population.

The improvement in SPPB may be explained by the high adherence to both supervised and unsupervised exercise components of the program in this study. Cameron et al demonstrated that higher levels of adherence to intervention produced a greater effect on physical performance in the previous Frailty Intervention Trial (FIT).[84] The greater improvement in SPPB was likely contributed significantly by better gait-speed and chair stand scores at 3-month. Similarly, Haider et al found an increased in SPPB score but not in the SPPB-balance component at the end of intervention.[89] One explanation may be that the exercises in the referenced study and within the INDEPENDENCE program were focused on strength training, and in particular functional sit-to-stand. However, at 6-month, there was a significant difference between was observed for total and individual SPPB scores, including balance. This could reflect different patient trajectories based on acquired ADL impairment as a result of hospitalisation.[271] The improved balance at 6-months could be part of a general recovery trajectory post hospitalisation, the pathway to which was smoothed by INDEPENDENCE participation, even though the exercises did not target balance specifically.

Conversely the control group did not have such a trajectory and either plateaued (health took a hit) or continued to decline post hospitalisation. Future studies could also measure community participation or other changes in lifestyle/activity post-hospitalisation to elucidate this.

Another possibility could be a far-reaching effect of the strength training exercises on balance and stability. Balance training have been shown to improve only the performance of trained tasks.[272] However, strength training exercises can benefit both strength and balance (by proxy), as balance is dependent on lower limb muscle strength.[273] This suggest that strength training exercises might be prioritised when time for physical activities are limited in pre-frail and frail older adults.

In the intervention group, grip strength increased by 3.3kg and 3.7kg at 3-month and 6-month, respectively, though statistical significance was only observed at 6-month. This finding is comparable to a similar study by Haider et al, that found combined physical activity and nutritional intervention delivered by trained non-professionals for older adults with pre-frailty and frailty, to improve grip strength by 2.4kg but no difference when compared to their attention-controlled group.[89] It was also reported that participants who were frail were 2.8 times (95% CI: 1.0 to 7.7) more likely to benefit from the intervention than those assessed to be pre-frail.[89] The proportion of participants who were pre-frail in both the referenced and present study were similar (34% versus 33%). Also, the INDEPENDENCE program did not include any upper limb or upper body specific training, so with a program lacking that specificity, grip strength may not be expected to change.

Nutritional status trended to improve more in intervention group. In particular, the significant improvement in the "activities and function" section concur with the findings from our physical function tests, while the improving trend in "weight loss" section suggest trends that weight loss was alleviated in intervention compared to control. This observation supports the involvement of dietitians in providing MNT to alleviate malnutrition in pre-frail and frail hospitalised older adults.[112] However, the effect was not large enough to detect a difference with the more rigorous ITT analyses. A possible explanation of this could be that participants in the usual care group might have received nutritional therapy, improving their nutritional status, albeit slower than those in the intervention group. A recent qualitative study on older patient's perception of nutritional care in the transition between hospital and home care highlighted the need for a comprehensive and individualised approach.[274] The present study is amongst the first to demonstrate that a combined exercise and nutrition intervention can improve malnutrition in hospitalised older adults who were also pre-frail and frail.

Cognitive status as determined by the MMSE scores was significantly better in the intervention group when compared to the control group at 3-month, however, this improvement in cognition was not sustained at 6-month. These results concur with a trial examining physiotherapist-delivered exercise intervention with protein supplementation on frail older adults in the community (EFS >8; MMSE >24), where MMSE was

improved in intervention but declined in control group (28.9 ±3.9 versus 25.9 ±7.3) post intervention.[108] However, there was no follow-up data in that study. The short-term beneficial effects of intervention on cognition with later weaning of effect is unexplained but it is possible that some control patients also received nutritional and physiotherapy intervention post discharge, which led to dilution of the beneficial effects of intervention.

The present study observed a trend of improvement in GDS in the intervention group at 3-month, and a significant difference between groups at 6-month. Exercise can improve mood in older adults, especially in those suffering from depression.[275] Hence, the improvement in GDS could be attributed to good adherence to the exercise components of the INDEPENDENCE program. Furthermore, the nutrition intervention within the INDEPENDENCE program focusses on sufficient protein and encourages intake of foods such as olive oil, fish, fruits, vegetables, legumes, poultry, dairy, and meat (unprocessed). This could have contributed to the improvement in GDS as a dietary pattern high in consumption of these aforementioned foods have been associated with depression risk and suggested to improve depressive symptoms.[276]

The intervention had no remarkable effects on the QoL as assessed by the EuroQoL questionnaire and on the risk of predicting functional decline as assessed by HARP tool. The evidence for exercise or multi-modal interventions including exercise and nutrition for these two measurements are inconsistent and largely dependent on the assessment tool used.[277] Previous studies have reported differing results depending upon the assessment tools used with one study which used the 36-item short form survey (SF-36) questionnaire reporting significant differences while another which used the EQ5D reporting non-significant results on the quality of life in this population.[277] Like grip strength, the effects of interventions on quality of life may also require a longer period to show effect.[278] Therefore, additional studies should explore the effects of self-managed combined exercise and nutrition interventions on QoL using multiple or an assessment tool that is sensitive enough to measure as an older adult transit through different settings and have a longer follow-up period.

The HARP tool assesses risk of hospital admission by age, an abbreviated MMSE and reported IADL, which are all factors related to hospital admissions. The lack of significance found between groups could be to the following three reasons. First, age was a non-modifiable risk factor, and no interventions will be able to reverse that. Second, the abbreviated MMSE might have a greater differentiating power if participants were recruited regardless of cognitive functions; only those with MMSE ≥25 were included. Considering that both factors were less likely to be impacted by intervention, the HARP tool probably only measured one risk factor for hospital admission, which was independent of IADL in this study.

Nevertheless, the trend for incidences of unplanned hospital readmissions within 180-days post-discharge was double for participants in control when compared to intervention in this study. A large-scale study of over a million hospitalised frail older adults 65 years and above, admitted with coronary heart diseases,

reported ascending trends of readmission rates as frailty risk increased.[279] Hence, the INDEPENDENCE intervention should be further studied to assess its impact on clinical outcomes i.e., hospital readmission, LOS post-discharge.

Strengths and limitations

The INDEPENDENCE trial is one of the first studies to investigate the feasibility of a patient self-management model, multimodal cross-continuum therapy to treat pre-frailty and frailty in hospitalised older adults. The novelty of this intervention lies in the application of a chronic disease care model to an otherwise established method (combined exercise and nutrition), to attempt to alleviate pre-frailty and frailty with a legacy effect. This study offers new perspectives and expands the knowledge to better and sustainable clinical pathways to overcome such geriatric syndromes. This proof of concept of a patient self-managed system could be referenced in the design and exploration of future public health services, to help reduce the burden of health professionals and overall health care system.

The study is not without limitation. First, although it meets the sampling standards for a pilot study, it is not powered sufficiently and should only be used as a proof of concept. The results cannot be extrapolated to assume an improvement on hospital and economical outcomes at this stage. Hence, a larger, statistically powered clinical trial would be needed to confirm the evidence presented here and to further examine its impact on mortality rates, length of stay, readmission rates. The inclusion of a cost-effectiveness analysis could further support its implementation and uptake by existing geriatric clinical services, if also found to be effective.

Second, participants cannot be blinded to group allocation as modifications made to usual care for the sole purpose of research would not be justified for ethical reasons. The lack of frequency matched social visits within the control group also meant that the impact of the social aspect of the intervention cannot be excluded. Thus, there would be a potential source of bias in self-reported measures i.e., exhaustion, mood within the EFS. However, all outcomes were conducted by a blinded assessor. Most components within the EFS and many other outcomes i.e., grip strength, SPPB, were objective performance-based assessments and that should significantly reduce such bias.

Third, the program was built around a self-management model and might not be as useful for older adults with cognitive deficits affecting functional independence. While the present study recognises Rockwood's frailty model and the importance for poor cognition to be included as one of the possible deficits, the study recruited only participants without any cognitive impairment, due to the design of the intervention relying heavily on patient self-management. Nonetheless, this program may still be a viable option to self-motivated pre-frail and frail older adults that are markedly deconditioned by episodes of hospitalisation.

Lastly, the combined exercise and nutrition intervention also made it difficult to narrow down to particular

components that contributed most to its effectiveness. However, it might not be necessary to differentiate between them because combined interventions have been suggested to tackle pre-frailty and frailty.

Challenges and considerations for implementation

Recruitment and retention of pre-frail and frail participants was a challenge identified by a previous study.[280] The low recruitment rate (10% amongst those meeting the inclusion criteria) in the present study was likely due to the recruitment site being an AMU and majority of potential participants screened were <65 years old (54%). Offering the program to a more targeted population might improve recruitment rates. The good retention rates in this study could be attributed to its daily brief visits by PhD candidate in the capacity of an allied health assistant during inpatient stay so that rapport and relationship could be established. This partnership was then continued to be built on through home visits and telehealth follow-ups, when the participant was discharged to the community. This healthcare provider-patient partnership likely led to mutual collaboration and reduced nonadherence amongst participants.[281] Due to the lack of resources, the PhD candidate also took on the role of the dietitian and allied health assistant. Considerations about training and the skill set of personnel should be considered and planned for in future iterations and testing of the intervention program.

6.6 Conclusion

In conclusion, this study provided preliminary evidence on the acceptability and benefits of a patient self-managed combined exercise and nutrition program to reverse or slow down the progression of pre-frailty and frailty in hospitalised older adults. Older adults who are motivated, can take a more proactive role in management of pre-frailty/frailty. The result of this study provides preliminary evidence to support further studies on the benefits of such self-managed, nutritional/exercise intervention on these two conditions in hospitalised older patients.

CHAPTER 7: BARRIERS AND ENABLERS TO A HOSPITAL-TO-HOME, COMBINED EXERCISE AND NUTRITION SELF-MANAGED PROGRAM FOR PRE-FRAIL AND FRAIL HOSPITALISED OLDER ADULTS?

7.1 Contribution to overall research objective

The intervention presented in Chapter 6 was designed with both inputs from a previous similar RCT (Chapter 4) and influenced by the data from Chapter 5. However, actual participant experience of the intervention and factors affecting participants' adherence remains to be understood. As mentioned in Chapter 5, qualitative method study designs can benefit certain types of research questions such as those looking to provide unique insights to a specific experience, in this case, a self-managed hospital-to-home support program. Therefore, a qualitative design was again used but this time analysed with the Theoretical Domains Framework (TDF) as the topic of interest (barriers and enablers) are of behavioural nature.[282] This Chapter presents the results of an embedded qualitative study to the pilot RCT of Chapter 6, to answer **Research Question 6 – what are the barriers and enablers to the self-managed, hospital-to-home, combined exercise and nutrition support program for pre-frail and frail hospitalised older adults?**

7.2 Introduction

A range of interventions involving exercise and nutrition have been developed to improve pre-frailty and frailty and its related health aspects, and support community-dwelling older adults to preserve their autonomy in life at home.[283] It was demonstrated in the pilot RCT in Chapter 6, that such interventions can bring about significant improvements in pre-frailty and frailty and frailty-related health outcomes. However, these positive changes were observed in a selected group of older adults with high adherence to the said combined exercise and nutrition program. Lower adherence to a similar combined exercise and nutrition program delivered by physiotherapists and dietitians, was previously reported to have corresponded to potentially smaller magnitude, towards alleviating frailty.[84] Adherence to treatment is a key factor to the success of such programs.

According to the World Health Organisation (WHO), treatment adherence is defined by the extent of a person's behaviour i.e., taking medications, following exercise and diet changes, that is consistent with what was agreed and recommended by the healthcare provider.[284] The WHO highlighted the seriousness of poor adherence to treatment of chronic diseases. They also further stated that the health system, socio-economic and patient-related factors all affect adherence simultaneously. So, it is pivotal that healthcare providers not only assess adherence but also investigate factors that influence it. Adherence to prescribed diet and exercise advice can be notoriously low, especially older adult populations.[139] Treatment adherence is multifaceted, often with causes that can be linked to environment, resources, and social influences; none of which are mutually exclusive. Therefore, it is essential to describe barriers and enablers to adherence to diet and exercise recommendations since they are not always described in interventional studies.

In brief, barriers are factors that prevent the adoption of said behavioural changes, whereas enablers facilitate them. Connecting barriers and enablers to intervention strategies can help in their implementation and that can be done by the application of a relevant theoretical framework. Moreover, a theoretical framework to identify barriers and enablers affecting health behaviours might be more successful at changing them, when compared to a non-theory driven one.[285] One of the most commonly used frameworks is the TDF.[282] The TDF comprises 14 domains from numerous unique theoretical constructs, anchored by theories of behaviours and its changes. These domains can be applied to barriers or enablers of health behaviours, and they include (1) Knowledge (2) Skills (3) Social/Professional role and identity (4) Beliefs About capabilities (5) Optimism, (6) Beliefs about consequences (7) Reinforcement (8) Intentions (9) Goals (10) Memory, attention, and decision processes (11) Environmental context and resources (12) Social influences (13) Emotion and (14) Behavioural regulation. The TDF has also been used in the context of frailty.[286]

Identifying barriers and enablers to treatment adherence can ensure that the design of future interventions could be as effective as they are efficacious, by reducing the lack of effect caused by poor adherence. Understanding themes of barriers and enablers can serve as a valuable guide for the development of health services, particularly those of transitional care nature, from hospital-to-home. The objective of this study was to address the above mentioned, by exploring the experience, and barriers and enablers to a self-managed combined exercise and nutrition program from the point of view of hospitalised older adults living with pre-frailty and frailty.

7.3 Methods

Theoretical Framework

Components of grounded theory were referenced in this study, in the aspect that there were simultaneous data collection and analyses was carried out.[229] This allowed the PhD candidate to solidify the developing theory through identifying directions and gaps. However, due to the limitations in sample of this pilot study, data collection could not be determined by data saturation. This is because interviews were carried out for all intervention participants as explained during recruitment, unless the participant chose not to partake. Therefore, data collection could not be stopped even if similar comments were being heard repeatedly and saturation was attained. Similarly, in the event that information redundancy was not attained, there were no additional sources of data available to tap into. To better guide the identification of barriers and enablers, the TDF (Figure 18) was also drawn on to distinguish behavioural elements associated with barriers/enablers influencing adherence to the nutrition and exercise components of the program.

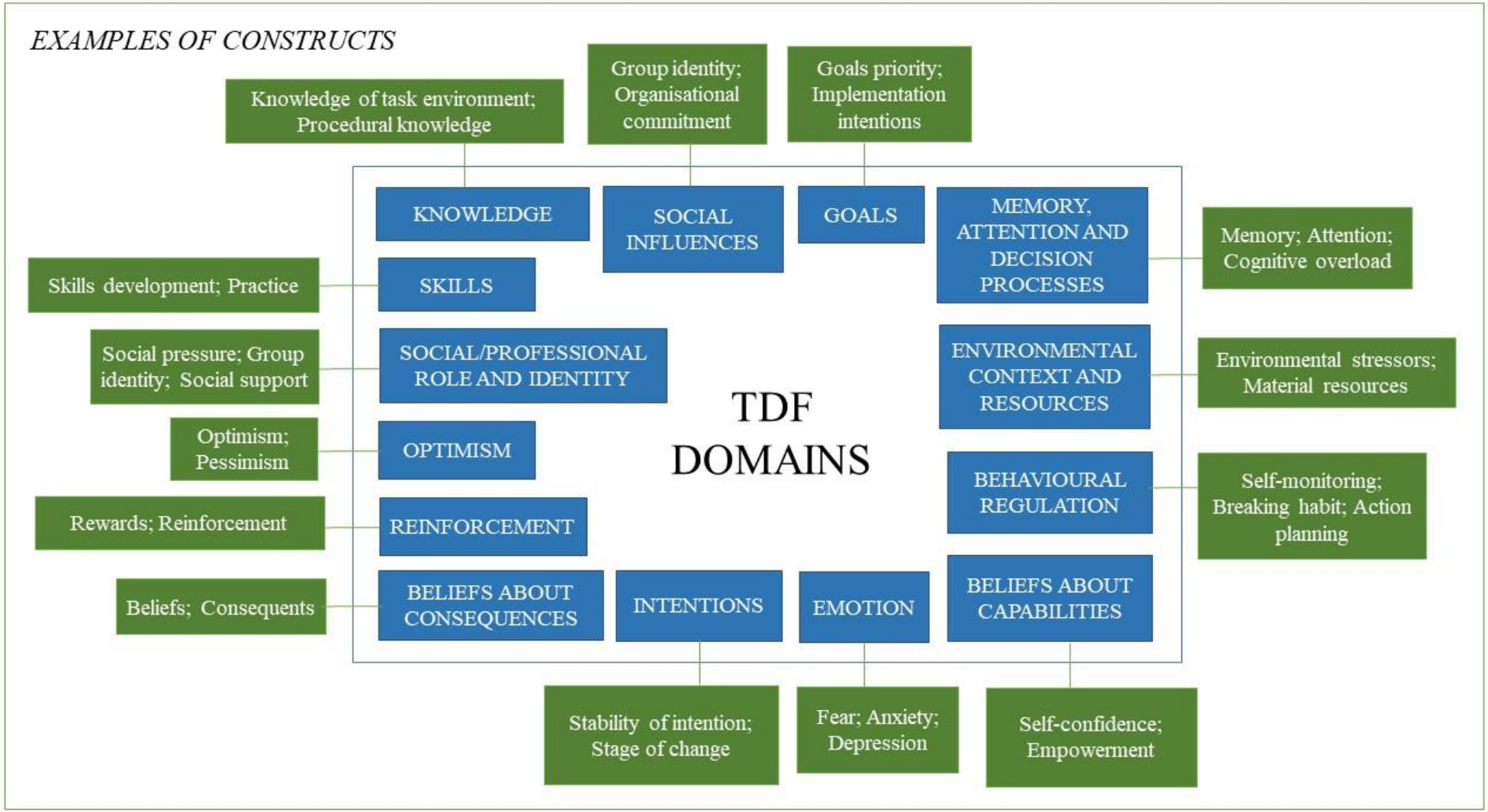


Figure 18. Theoretical Domains Framework (constructed with information from Cane, Connor and Michie 2012)[287]

Demonstrating trustworthiness and rigour

As per Chapter 5, the present qualitative study was conducted using semi-structured interviews, and was reported in accordance to the COREQ research statement.[230] The research team and reflexivity i.e., personal characteristics and relationship with participants, are important aspects to in demonstrating trustworthiness and rigour of a qualitative study.[230] For example, the credentials and occupation of the members in the research team should be clarified, providing the readers with information to assess how that might have influenced the researcher's interpretation, in turn improving the trustworthiness of findings.[230] Further details demonstrating trustworthiness and rigour have been previously described in Chapter 5.

Design of interview protocol

To explore the experience of the program, and barriers and enablers to its diet and exercise components, the interview guide was designed with the aim to allow participants to freely express their personal views, i.e., with open-ended questions, ques, and prompts. The PhD candidate planned the first draft of the interview guide. The member of the research team then provided essential revisions to support participants to share in-depth thoughts and experiences, to ensure the richness of the data (see Appendix 7 for the full interview guide).

- Experience of program – what were their overall feelings and opinions towards the program
- Barriers and enablers to diet – what helped or deterred them from adhering to the diet recommendations/changes
- Barriers and enablers to exercise – what helped or deterred them from adhering to the exercises prescribed

Feedback from members of the research team were incorporated before commencing formal data collection. All members of the research team approved the final set of interview questions prior to commencement of data collection.

Participants

Purposive sampling was employed to recruit hospitalised older adults, that were pre-frail or frail, as determined by the EFS, and that took part in a hospital-to-home, self-managed combined exercise and nutrition intervention program (i.e., only those allocated to the intervention group) in Chapter 6. As part of the recruitment for the pilot RCT in Chapter 6, eligible patients were approached within 48 hours of admission, between September 2020 to June 2021, if they were assessed to be pre-frail or frail as aforementioned.[232] The inclusion and exclusion criteria have been previously mentioned in Chapter 6.

Interview process

For this study, the PhD candidate was also the interviewer. This is due to a lack of resources and a suitable research assistant trained in qualitative interviews could not be engaged. It is acknowledged that this increased the risk of social desirability bias, especially since the interviewer was also the person who

delivered the intervention. Nonetheless, measures were put in place to counter that. First, the participants were briefed on the purpose of the study prior to informed consent and were informed about the role of the interviewer, as an independent researcher, prior to enrolment. Second, it was emphasised to the participant that the PhD candidate/interviewer was not involved with any other parts of the participants standard (non-project related) care and would not have influence over any health care practices delivered by their local health network. Lastly, like in the first qualitative study described in Chapter 5, pseudonyms i.e., Mary and John were used as names accordingly during interviews to preserve anonymity during the interview processes. All interviews were conducted in homes of the participant to ensure their privacy, and to allow them to freely express their personal views. Participants were also interviewed privately, in the absence of other family members. The interviews were audio recorded and transcribed verbatim, using a software program (Microsoft word), before relistening to the recordings, to examine the transcriptions, and note down on the interviews before coding transcriptions, similar to the study in Chapter 5. Recruitment and interviews were conducted for all participants regardless of program completion or degree of adherence to ensure accurate representation of data.

Data analysis

The PhD candidate transcribed the interviews, and the blinded transcripts were verified by a member of the research team. The coded transcripts were rechecked by two other members of the research team. A thematic framework of coding, data sorting and summation/synthesis of data was referenced to assess the content of all interviews.[234, 235] The transcripts were repeatedly read to gain a sense of generated codes initially while creating the thematic framework to help the researchers identify recurrent patterns. The PhD candidate coded, described, and recorded key and recurring ideas in the transcripts. This was followed by a further deductive approach, using the TDF, to identify influences on self-managed exercise and nutrition behaviours.[282] This is so ensure that context and details from an inductive approach was not lost from the restriction of the analysis to the TDF domains.[288] Discussions with the research team were carried out until an agreement was reached for any coding discrepancies. Statistical analysis (t-test and chi-square test) were carried out between the interviewed participants (n=11) and the entire intervention cohort (n=16) to determine if the interviewed cohort was not significantly different from the intervention cohort. All statistical analyses were performed with IBM SPSS Statistics version 28.0 (IBM Corp) and two-sided P-values <0.05 were considered as statistically significant.

Ethics

This study was approved by the Southern Adelaide Clinical Human Research Ethics Committee (HREC reference number: HREC/19/SAC/240) − within which the work was undertaken and conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). All participants provided written informed by a research staff not involved in the usual care of the patients, prior to the start of the study.

7.4 Results

A total of 11 pre-frail and frail older adults aged 68–93 years (mean age, 80.4 years); female 64%; living alone 55% that participated in a self-managed, combined exercise and nutrition, hospital-to-home support program (i.e., the intervention group), were interviewed (Table 25). A range of degrees of frailty were represented in the interview cohort – 2/11 pre-frail; 6/11 mildly frail; 2/11 moderately frail; 1/11 severely frail. The median (range) duration of the interviews was 25 (15-60) minutes. Out of the 16 participants in the intervention group, 11 were interviewed as three died, one withdrew, one declined to be interviewed. Further insights to the characteristics and demographic information of those not interviewed were presented in Table 25. Themes identified inductively could fit within domains of the TDF and no additional unique domains were identified.

Table 25. Demographic and health characteristics of study participants prior to program in the second qualitative study

Characteristics	Interview cohort (n=11)	Cohort not interviewed (n=5)	Entire intervention cohort (n=16)
Age, years, mean ±SD	80.4 ±6.3	78.8 ±6.9	80.0 ±6.6
Female, n (%)	7 (64%)	4 (90%)	11 (69%)
Body Mass Index, kg/m^2, mean ±SD	26.1 ±6.2	27.4 ±6.3	26.1 ±6.2
Mini Mental State Examination score, mean ±SD	28.3 ±1.4	26.6 ±1.8	28.0 ±2.0
Charlson Comorbidity Index, mean ±SD	4.6 ±1.7	4.4 ±1.3	4.4 ±1.6
Tertiary education level	3 (27%)	2 (40%)	4 (25%)
Living alone	6 (55%)	2 (40%)	8 (50%)
Mean Edmonton Frail Scale	8.9 ±1.9	9.3 ±2.1	9.1 ±1.8
Pre-frail	2 (18%)	1 (10%)	3 (19%)
Frail	9 (82%)	4 (90%)	13 (81%)
PG-SGA grade – Malnourished, n (%)	6 (55%)	5 (100%)	11 (69%)
Scored PG-SGA, mean ±SD	7.9 ±3.8	10.2 ±6.6	8.8 ±5.0
Short Physical Performance Battery, mean ±SD	2.6 ±1.8	3.6 ±3.3	2.1 ±1.9
Geriatric Depression Scale, mean ±SD	5.6 ±3.6	5.7 ±2.9	5.6 ±3.6
EQ-5D-5L Utility Index, mean ±SD	0.37 ±0.37	0.47 ±0.28	0.55 ±0.35
EQ-5D VAS, mean ±SD	61.6 ±23.9	46.4 ±17.6	57.7 ±20.9

Data expressed as mean ± SD for continuous variables; absolute numbers (percentage) for categorical variables. [a]Body Mass Index. [b]Mini Mental State Examinations. [c]Quality of life measured with the EQ-5D-5L utility index: has scores between 0 and 1 with higher scores indicating better health-related quality of life. [d]Quality of life measured with the EQ-5D visual analogue: has scores between 0 and 100 with higher scores indicating better health-related quality of life.

Experience of the self-managed hospital-to-home program

There were both positive and negative experiences of the program. Sample quotes of the experience of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes are presented in Table 26 below.

Table 26. Sample quotes of experience of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes in the second qualitative study

Experience		
TDF Domain	**Themes**	*Participant's quote example*, **Participant demographic**
Knowledge	**Increased awareness about lifestyle behaviours**	*"I've not thought so much about diet, so it made me think about diet a little bit more on what I was eating in in terms of exercise, because I was fairly active before the exercise component"* **#02, 77 years, male, pre-frail**
		"I think the benefit the benefit is mainly being that I become more diet conscious." **#10, 85 years, female, mildly frail**
Social identity	**Participant of a program**	*"I just think it was really helpful that I that [name of therapist] invited me to connect into this program, it's been really helpful.* **#06, 76 years, female, mildly frail**
Beliefs about capabilities	**Perceived lack of ability to participate**	*"Well, all my life I was born with a muscle weakness yes. And all my life was a struggle"* **#03, 77 years, male, mildly frail**
		"I'm so sorry to say and I just can't do it because I enjoy his visits and his advice, but I can't do it." **#05, 79 years, female, severely frail**
Optimism	**Optimism about effects of program**	*"Getting used to eating and have regular meals. That was the most important thing for me and be able to walk again and to move again"* **#05, 79 years, female, severely frail**
Reinforcement	**Reward of getting back to pre-hospitalised activities**	*"I did get back to you know, sorting out some stamps and picked up my ukulele and trying to get back in things"* **#02, 77 years, male, pre-frail**
Environmental context/resource	**Disruptions to program by readmissions**	*"Yeah, yeah, in admissions into hospital 'cause I injured my leg then I've had that funny thing that grew on the top of my foot and so it interrupted it all. It wasn't a continuous flow"* **#01, 77 years, female, mildly frail**
	Lack of time for program	*"I didn't expect that when I came out of hospital, I thought I was going to have time"* **#02, 77 years, male, pre-frail**
	Positive affect for home visits	*"I think the home visits have been very helpful"* **#03, 77 years, male, mildly frail**
	Flexibility of program	*"Yeah, I like that arrangement. I looked in my on the weekend. I looked in my diary for today and I thought, oh yes, three o'clock OK, I just like that planning ahead thing that."* **#06, 76 years, female, mildly frail**

Social influence	**Individualised support**	*"This was more personal. You know the help that you I get at each time that [name of home therapist] came out. And then I am improved as I went on"* **#04, 93 years, female, moderately frail** *"But [name of therapist] is beautiful, I love to participate in the program. He is a beautiful person, and he brings it in. Acceptable they and I have really appreciated him"* **#05, 79 years, female, severely frail**
Behavioural regulation	**Habit forming**	*"I'm quite happy to do them. And try to do them at least before 2 meals."* **#04, 93 years, female, moderately frail**

Study participants felt that knowledge was improved as they felt an increased awareness towards exercise and diet in general. While some concerns were raised regarding their perceived lack of ability to participate even if they desired to (due to doubts in their own capabilities), others felt optimistic about the program, citing that they looked forward to benefitting and returning to their baseline diet patterns and physical activity levels. There was a sense of group identity as participants felt like part of a program. Some participants also felt that they were rewarded, when they were able to return to some pre-hospitalisation activities, such as playing a musical instrument. Participants also overestimated the time available at home to participate in the program, citing follow-up medical appointments as one of the reasons for a lack of time. However, they appreciated the flexibility of the program that helped fit its components into their schedule. Participants reported positive affects for the home visits, and appreciated them, citing them to be helpful. The social influence brought upon by the individualised support also made the experience personal. With regard to the behavioural regulation, participants stated that habits were formed as they reported to have integrated components of the program into their daily routine.

Barriers and enablers to the nutrition component of the self-managed hospital-to-home program

Sample quotes of the barriers and enablers to the nutrition component of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes are presented in Table 27 below.

Table 27. Sample quotes of barriers and enablers to the nutrition component of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes in the second qualitative study

TDF Domain	**Themes**	*Participant's quote example*, **Participant demographic**
		Barriers
Intentions	**Lack of motivation to cook**	*"Only laziness"* ***#06, 76 years, female, mildly frail*** *"Or I don't feel like cooking"* **#08, 68 years, female, mildly frail**
Environmental context/resource	**Dietary restrictions from multimorbidity**	*"I've got to stick virtually the three different diets don't I low sodium gout diet and potassium diet, don't I, you know?"* **#01, 77 years, female, mildly frail**
	Side effect from medications/ treatments	*"When they give me the first injection, I was sick in the stomach. I couldn't eat. I had to force myself to eat"* **#04, 93 years, female, moderately frail**
	Limited transport	*"If I forget something or if I feel like something I can't get it because there's no way really. Well, there's no transport around here"* **#09, 81 years, female, moderately frail**
	Physical limitation to prepare food	*"Yeah, the rheumatoid yeah. I'm only you know if I go to lift the pan or a sauce pan up, I find it very hard."* **#07, 86 years, female, mildly frail**
Social influence	**Loneliness**	*"Eating alone, I think I've told you haven't heard that. My husband had restaurants and yes, and I'm, you know, always get stuff cooked for me and then you know I go into the restaurant and if he's got people that are coming in, I sit down and eat with them. And yeah, yeah so"* **#09, 81 years, female, moderately frail**
	Peer pressure	*"The only thing that interferes with me doing it is it I go out and put people like people asking me out. And give me a meal I feel obliged to eat what they put in front of me"* **#10, 85 years, male, mildly frail**
Emotion	**Lack of enjoyment**	*"I put pressure on myself to eat something and I used to be a good eater. Uh, food used to be celebration for me and now food is a punishment"* **#05, 79 years, female, severely frail** *'I still have trouble tasting. I don't get the nice time able to drink tea now."* **#08, 68 years, female, mildly frail**
	Fear of insufficient funds	*"I was afraid that my money wouldn't go as far as I needed it to go, but it was just unreasonable fear."* **#06, 76 years, female, mildly frail**
	Lack of appetite	*"Oh, especially now sometimes I just don't feel hungry at all. But I'm forcing myself to eat."* **#08, 68 years, female, mildly frail**
	Depressive mood	*"Now I hate getting out. I just like staying in my bed. I think the earlier I get up, the longer the day is."* **#09, 81 years, female, moderately frail**
		Enablers

Knowledge	**Improved awareness and knowledge of food on health**	*"what the program did was made me look at what we were preparing or what was on the plate. And making sure that we had a good balance of food but with a bias towards the proteins."* **#02, 77 years, male, pre-frail**
	Increased importance of protein	*"Yeah, I'll make sure I put some protein in it"* **#08, 68 years, female, mildly frail**
Skills	**Consistent dietary advice from healthcare staff across services**	*"I think it was seamless from the hospital and you and my GP. And before I think I was using water. So, to put the sustagen, mix it with water."* **#03, 77 years, male, mildly frail**
	Portioning of food	*"Right, yeah, well understand about the portions bit better from (home visit therapist)."* **#10, 85 years, male, mildly frail**
Social identity	**Caregiver to others**	*"Yeah, it's. She has dementia. So, it's where she needs me badly"* **#03, 77 years, male, mildly frail**
Optimism	**Trust and confidence in healthcare provider**	*"Yeah, and I respected the fact, I suppose that [therapist] done that. [therapist] have done the hard yards and got qualification in it"* **#10, 85 years, male, mildly frail**
Beliefs about consequences	**Perception that nutrition will improve weight/strength**	*"Realising that I had to work on the dietary program, but I did find having lost 12 kilos in weight between going to hospital and coming out the [hospital]."* **#02, 77 years, male, pre-frail**
	Perception that nutrition can improve blood glucose	*"That's an obvious improvement. Which is helping with the BGL, because that's coming down."* **#10, 85 years, male, mildly frail**
Reinforcement	**Exercise-induced appetite**	*"I felt with the exercise it did give me a little more appetite than I had before"* **#02, 77 years, male, pre-frail**
	Mental benefits	*"Because I'm I feel better."* **#06, 76 years, female, mildly frail**
Goals	**Weight gain**	*"I've got the scales in the bathroom. I weigh myself every morning when I get out of the chair and I'm just hoping to see that. It's really not. Yeah. Get up a little bit more than it has"* **#03, 77 years, male, mildly frail**
Environmental context/resource	**Government funding**	*"No, it [government funding support] helps me because something go out shopping, buy anything I want, you know"* **#01, 77 years, female, mildly frail**
	Meal delivery service	*"Well, you know I was on light and easy (pre-prepared meal program)"* **#01, 77 years, female, mildly frail**
	Education resource booklet	*"Yeah, like it's you know I try to refer to this book"* **#01, 77 years, female, mildly frail**
Social influences	**Support from family**	*"[Daughter] suggested that she get high protein milk for the coffee because she said that'll take care of two proteins straight away. So, then I only had to worry about 5."* **#01, 77 years, female, mildly frail**
	Company of a spouse	*"I'm very lucky to still have my partner so someone I can talk to and eat with and prepare food with is very beneficial"* **#02, 77 years, male, pre-frail**

	Support from peers	*"Oh, people encouraging me and saying gosh, you're looking good"* **#06, 76 years, female, mildly frail**
Emotions	**Increased enjoyment in food/supplements**	*"Well, it's it seems to be taste here. It tastes smoother, Yes, yeah I do. I do like the protein drinks I really do like them"* **#09, 81 years, female, moderately frail**

The barriers reported were from four domains – Intentions; Environmental context/resource; Social influence; Emotion. A total of 11 themes were identified as barriers to the nutrition component of the program. A majority of themes were related to environmental context/resource and emotion. Three of four themes within the environmental context/resource stemmed from past/present illnesses. It was reported that there were pre-existing conditions that restricted some participants diets e.g., potassium restriction, and conditions that were debilitating and limited the ability to prepare food. The side effects from medications prescribed for those conditions affected dietary intake or adherence. The fourth theme was that the lack of transport to get groceries limited the types of food, as there was no chance to get additional food/ingredients if they forgot to pick it up in the planned shopping trip. A lack of enjoyment of food and appetite was reported as a barrier towards dietary adherence. Participants felt that there was reduced feelings of hunger and the pleasure of eating/drinking had made it hard to keeping to what was recommended in the program. There was also a lack of motivation to cook. Two themes from the social influence domains were also identified. While the lack of social support and company (loneliness/eating alone) was a barrier to adhering to diet, pressure from peers was also raised as an issue as participants felt that they were obliged to what they were asked to eat when dining in social settings.

Eighteen themes from 10 domains of the TDF (Knowledge, Skills, Social identity, Optimism, Beliefs about consequences, Reinforcement, Goals, Environmental context/resource; Social influences; Emotion) were identified as enablers of the nutrition component of the program. There was a general consensus on the improvement of knowledge and skills. Participants reported improved awareness and knowledge of food and protein on health and felt better equipped in terms of skills needed to adhere to the diet recommendations i.e., portioning of food. There were themes surrounding the social identity and influences that encouraged dietary adherence. Participants who were caregivers to others felt a responsibility to eat better. Company of a spouse during mealtimes and social support from family members and friends were also cited as positive influences towards keeping to what was recommended in terms of diet. Participants reported to have trust and confidences in the healthcare provider (home visit therapist) and perceive nutrition to be something that can improve their weight/strength/blood glucose. The perceived menta and physiological benefit were also raised as enablers to diet adherence. For example, an increased appetite from adhering to the exercise component of the program. The attainment of a goal i.e., weight gain also facilitated better dietary adherence. In some participants, emotions played a part as they experienced increased enjoyment in food/supplements recommended. There was a general agreement by more than half of the participants on the usefulness of the education resource booklet as a reference guide. Other resources that facilitated dietary adherence were financial support from government and meal delivery services.

Barriers and enablers to the exercise component of the self-managed hospital-to-home program

Sample quotes of the barriers and enablers to the nutrition component of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes are presented in Table 28 below.

Table 28. Sample quotes of barriers and enablers to the exercise component of the self-managed, combined exercise and nutrition, hospital-to-home support program by themes in the second qualitative study

TDF Domain	**Themes**	*Participant's quote example*, **Participant demographic**
	Barriers	
Beliefs about capabilities	**Lack of coordination and balance**	*"I can't stand on my feet very well"* **#01, 77 years, female, mildly frail**
	Lack of self-efficacy	*"Yeah, but now I realise that some people in their 80s they're a lot better than what I am."* **#09, 81 years, female, moderately frail**
Intentions	**Lack of internal motivation**	*"I didn't have the motivation to do it"* **#01, 77 years, female, mildly frail** *"I don't think I have much motivation"* **#08, 68 years, female, mildly frail**
Memory, attention, decision processes	**Forgetfulness**	*"It just doesn't come up. I don't think about it. A lot of the times that I should be doing it."* **#03, 77 years, male, mildly frail**
Environmental context/resource	**Cold/wet weather**	*"Too cold and wet….and when it's wet, I don't go out for a sweat"* **#06, 76 years, female, mildly frail** *"Right now, cold weather"* **#11, 85 years, male, pre-frail**
	Comorbidities and injuries	*"Itch… it's constant. I didn't get any sleep. So, you know it was very hard you see. It consumed my life."* **#01, 77 years, female, mildly frail**
	Lack of sleep	*"You know and lack of sleep."* **#01, 77 years, female, mildly frail**
	Lack of energy	*"No, yeah, well I was tired. So tired."* **#01, 77 years, female, mildly frail**
	Lack of time	*"The simple answer is time… you know, routines even within the house. And the day just never seems long enough"* **#02, 77 years, male, pre-frail**
Social influences	**Prioritising social activities over exercise**	*"If I get an invitation to go out somewhere with somebody, I'll drop the exercise and go out."* **#06, 76 years, female, mildly frail**
Emotion	**Stress from dealing with physical ailments**	"*Pain, yeah. Just the pain that it caused me and then. I have to do it in the kitchen because I can hold on to the bench and then I can't get back, but there's only so much pain here*" **#05, 79 years, female, severely frail**
	Depression and anxiety	"*All depression and anxiety*" **#09, 81 years, female, moderately frail**

	Fear from pending diagnosis	"*I was waiting to get the results. From this these tests. No, no waiting for them to give me the green light so that I didn't overdo it*" **#10, 85 years, male, mildly frail**
Behavioural regulation	**Not part of daily routine**	"*Yeah, I just never thought of it. Perhaps that day*." **#03, 77 years, male, mildly frail**
	Enablers	
Knowledge	**Increased awareness of importance to not stay sedentary**	"*I'm more aware that I'm sitting. I need to move. Yeah, yeah. So I am more aware of that, yes*?" **#08, 68 years, female, mildly frail**
Skills	**Less reliant on gait aids**	"*at times I don't even use the Walker or, you know I can open if I've got something to grab on that I can. Do that*" **#04, 93 years, female, moderately frail**
	Level of difficulty of home exercises were manageable	"*I don't find it difficult at all*." **#07, 86 years, female, mildly frail**
	Learnt skill from health care provider	"*You've explained yourself so well, and I haven't felt. The need to call you*" **#06, 76 years, female, mildly frail**
Social identity	**Participant of a program**	*"I thought, you know, I've started it. I've got to finish it."* **#01, 77 years, female, mildly frail**
	Independent person/parent	*"As I say. Some people expect their child to be there every five minutes, and that's just not the way that we are... I just think sometimes that some parents think expect too much of their children because they've got their own lives. They've got their own family to look after. So there. You really should. Be stronger and more independent."* **#07, 86 years, female, mildly frail**
	Worthy patient	*"They said that they see me see me as his old. He is a patient worth working on. Otherwise, once you get over 80, they're not interested"* **#10, 85 years, male, mildly frail**
Beliefs about capabilities	**Perceived competence from previous program**	*"I mean just doing them more often and you know I've always done a lot of walking anyway. You know but haven't necessarily done all the other things."* **#07, 86 years, female, mildly frail**
Optimism	**Confidence in prescribed exercises**	*"I think the answer is the exercises when they're given by an external organisation rather than me just thinking them up myself. You know, they have been developed for a reason."* **#02, 77 years, male, pre-frail**
	Optimism of increasing physical capabilities	*"This though, because I think I might get better"* **#05, 79 years, female, severely frail** *"I've liked doing the exercise to getting out and seeing what I can do."* **#06, 76 years, female, mildly frail**

Beliefs about consequences	**Perception that exercise will maintain or improve strength/health**	*"I know if I don't keep the exercise up that my strengths not going to come back, you know. So, I've tried to do them when I can, yeah"* **#01, 77 years, female, mildly frail** *"And I knew it was going to build up stamina and give me strength again. So there was a big incentive"* **#02, 77 years, male, pre-frail**
	Perception that exercise helped maintain independence	*"Well, I like to keep fit to a certain extent. I'm on my own so I have to do things for myself. Yes, that's how I try to keep fit to enable me to do them"* **#07, 86 years, female, mildly frail**
	Perception that exercise will improve appetite	*"I'm underweight and I feel that it may improve my appetite with the exercises"* **#03, 77 years, male, mildly frail**
	Accountability to health support workers	*"I think when you realise that you have some supervision, you have some external help. These sorts of things are motivators as well that you know you are wanting to do it for yourself, but you're wanting to do it for the tutor so that they can see the benefit of their work and their recommendations"* **#02, 77 years, male, pre-frail**
	Fall prevention	*"Actually, we're keeping the lower body very strong, which enables us not to fall over, which is the whole idea."* **#07, 86 years, female, mildly frail**
Reinforcement	**Physical/health benefits**	*"Yeah and getting up out of the chair. A great deal"* **#04, 93 years, female, moderately frail** *"These simple exercises done around the chair and their added weight in nature. Uhm, they have more effect on the weight control and the sugar control than what the other exercises I do."* **#10, 85 years, male, mildly frail**
Intentions	**Intrinsic motivation**	*"I say to myself, I've got to do them, and I do them."* **#07, 86 years, female, mildly frail** *"my own will power"* **#10, 85 years, male, mildly frail**
	Constant decision to stay active	*"Sometimes if I'm busy or going to be busy. I'll just go along a walk up on the block that went along halls. You know?"* **#04, 93 years, female, moderately frail**
Goals	**To reclaim life prior hospitalisation**	*"You, well, you know I wanted to, you know, resume my life and start instead of watching the church service on the tablet that I could go back to church as well, you know"* **#01, 77 years, female, mildly frail**
Memory, attention, and decision processes	**No reliance on memory for exercises**	*"The fact that all the exercises are illustrated so that you can't make a mistake because you can see it."* **#06, 76 years, female, mildly frail**

Environmental context/resource	**Education resource booklet**	*"Well, I do the exercises in the book, but perhaps without I wouldn't have done them so often"* **#10, 85 years, male, mildly frail**
	Presence of outdoor facility	*"There's an open-air gym down the road. There we go down there"* **#06, 76 years, female, mildly frail**
Social influence	**Support from family/partner**	*"Must my wife and myself. And she was an in great Encourager all the time but she never really interfered with me"* **#02, 77 years, male, pre-frail**
	Support from health care providers	*"The very fact that [therapist] come here and we do what we do and then [therapist] ring up and we talk about what we talk about. It's just that continual connection, yeah?."* **#06, 76 years, female, mildly frail**
Behavioural regulation	**Fitting exercises into daily routine**	*"Trying to get the exercises in, especially when I get about to go out"* **#01, 77 years, female, mildly frail**
		"Yeah, I should get up in the morning after breakfast. Do my exercise, then get on with the rest of the day." **#03, 77 years, male, mildly frail**

The barriers reported were from seven domains – Beliefs about capabilities, Intentions, Memory attention and decision processes, Environmental context/resource; Social influences; Emotion, and Behavioural regulation. A total of 14 themes were identified as barriers to the exercise component of the program. A majority of the themes rose from the domain, Environmental context/resource. Participants described that a lack of sleep, energy and time all contributed to poor adherence to the prescribed exercises. Participants also stated pre-existing illnesses and injuries as another barrier. Despite the prescribed exercises being indoors, participants quote cold/wet weather as something that will deter them from exercising that day. Linked to the lack of time (*the day just never seems long enough, #02, 77 years, male, pre-frail*) as above mentioned, participants could prioritise social activities over adhering to the exercises if they happened to coincide. For some, the exercises were also hard to adhere to, if they were not integrated as part of the participants' daily routine. In addition, participants reported memory to be an issue, that there could be a lack of cues and they simply "forgot" about exercising. The participants' perceived lack of physical capabilities (such as coordination and balance) and low self-efficacy (individual's belief in their own capacity to achieve said goal) discouraged them from performing some or at times all exercises. Intrinsically, for some participants they conveyed both explicitly and through implication that a lack of motivation (individual desire to achieve goal) was a barrier to exercise. One of the emotions that dissuaded participants from exercise was mental stress from dealing with pre-existing illnesses. For example, the stress of having to deal with persistent pain from a physical ailment. From one participant, their report of fear from a pending diagnosis discouraged them from exercising to the prescribed level. Lastly, depression and anxiety were verbalised as factors that prevented adherence to exercises within the program.

Twenty-four themes from 13 domains of the TDF (Knowledge, Skills, Social identity, Beliefs about capabilities, Optimism, Beliefs about consequences, Reinforcement, Intentions, Goals, Memory attention and decision processes, Environmental context/resource; Social influences; Behavioural regulation) identified as enablers to the nutrition component of the program. A majority of themes were identified from the domain, Beliefs about consequences. Participants described their perception around positive effects of exercise to maintain or improve strength/health/independence, and that it could also improve their appetite, and help prevent falls. They also felt accountable to the healthcare provider supporting them. Similar to enablers to the nutrition component of the program, there was a general consensus that the improvement of knowledge and skills was a enabler to exercise adherence. Participants reported improved awareness of the importance to not be sedentary. They described that the reduced reliance on gait aids, a perception that the level of difficulty of the home exercises were manageable and learnt skills from their home visit therapist all helped facilitate adherence. As the exercises were not unfamiliar, participants perceived that they were competent based on previous experience with similar programs. They were also optimistic about the prescribed exercises and that adhering to them would increase their physical capability. This adherence was further encouraged as many expressed that they experienced meaningful physical and health benefits as they progressed through the program. For example, one participant reflected that they could now get up out of her chair and another felt that it benefitted his blood sugar control. Participants who integrated the exercise regime as part of their daily routine found that it helped them adhere to the exercise component of the program. While some participants stated poor memory as a barrier, others reported that memory was not required as they did not feel like they needed to remember them due to the education resource booklet. The education resource booklet was also described as a cue to exercise. An enabler related to environment was a participant who enjoyed options to exercise in an outdoor facility despite the fact that home exercises could be done indoors. There were themes surrounding the social identity that encouraged adherence to the exercises. Participants felt the responsibility as a part of the program, contributing individually to a collective group. Two themes from social identity were identified – responsible parents (perceived to be those that took care of their own health and not having to rely on their children) and a worthy patient (perceived that healthcare providers will take individuals who made efforts toward exercising more seriously). Like with the nutrition component, social support from family/partner and healthcare providers facilitated better adherence to exercises within the program. Furthermore, participants described having both intentions and a goal to "reclaim" their life prior hospitalisation as an enabler towards exercise adherence. A constant decision to stay active and presence of intrinsic motivation were identified under the domain, Intentions.

7.5 Discussion

The findings of this study provided insights to the perceptions and lived experiences of pre-frail and frail older adults after a self-managed hospital-to-home support program. Positive experiences were around those of improved knowledge, skills, formed habits and the program's social elements. There was a sense of reward when improvement could be felt in participants' day-to-day activities as the program progressed. Negative experiences were related to a mismatch in expectations versus reality, particularly around personal

capabilities, time, and salient events during participation. Many barriers to adherence identified were modifiable by the individualised support aspect of the program. On the same note, what were perceived as enablers can be brought upon or reinforced by personalising care. The data suggested that treatment adherence can be heavily influenced by tailoring the combined exercise and nutrition interventions to individual participants.

Knowledge and skills

Education and improving knowledge are essential as part of delivering nutrition interventions, as a lack of knowledge/skills were reported as barriers towards participation and behavioural change.[289, 290] This also applied to exercise. The provision of a customisable educational resource booklet, such as the one used in the programs, (i.e., with personalised recommended serving sizes for protein, exercise pictorial instructions, food/exercise diary) complement the knowledge and skills taught during intervention. Participants also valued the expertise of the healthcare provider. The trust and confidence towards the healthcare provider brought about optimism of effect of the nutrition recommendations. Many participants described receiving advice that was consistent to the program, (i.e., their general practitioner (GP) also encouraged them to engage in behaviours around nutrition and exercise). This has been previously reported where regular contact with GP was highlighted as a facilitator towards exercise and protein-rich foods.[291, 292] The present study therefore emphasised the importance of consistent advice between healthcare providers across health systems.

Social/Professional role and identity

There were a handful of participants that felt responsibility towards the program, their social role as a parent/caregiver, and as an older patient, to adhere to the recommended diet and exercise. Being a caregiver to others has previously been cited as barrier towards exercise.[293] However, in this study, and at the individual level, this was not the experience of one participant who adhered to supplements recommended as he felt a responsibility to take care of himself so he could care for his wife with dementia. Consistent with some of the participant views in the present study, Hardy and Grogan found feelings of superiority to younger generation an enabler to exercise in older adults,[294] where exercise may be viewed as a form of "token" to remain relevant in their social networks.

Beliefs about capabilities and Optimism

Some participants had past experiences of exercise programs which gave them a perceived competence towards the present exercises recommended in the present program. Positive past experiences with physical activity and exercise has been previously reported as a motivator towards exercise adherence in older adults.[295] Perceived symptoms from health-related problems such as impaired balance and fear of falling were expressed as barriers to physical activity and exercise. However, familiarity with exercise tasks have been reported to improve motivation that help retain older adults in exercise programs.[289] Adapting exercises gradually in daily life was expressed as an important factor influencing adherence.[296]

For this program, participants were encouraged to maintain the exercises prescribed as the regime was individualised and constantly adapted to their changing capabilities, with support from the healthcare professional.[297] This could reduce the reliance of having the exercise session delivered by an exercise professional over time, as co-monitoring was deemed sufficient.[292] In fact, a formal regime of scheduled exercises was quoted as a barrier towards exercise.[298]

The program participants who were in a uniquely vulnerable time of recent discharge from hospital (and where there is comparatively less research evidence on diet-exercise interventions in this period compared to stable community dwelling older adults), it appears that there is a balance to be had, between program structure/schedule and personalisation with flexibility. This appears important to meet both the individual motivators and values/preferences, but also the environmental and health factors such as concurrent medical conditions and constraints on time with ADLs taking longer or other appointment e.g., a re-calibration of self.

Beliefs about consequences

Overall, the perceived benefits of nutrition and exercise facilitated program adherence. Participants described beliefs that nutrition and exercise would help improve their strength, blood glucose (nutrition), appetite (exercise) and prevent falls (exercise). This perceived increased chance of success to prevent falls was also previously reported in another qualitative study on a group of Scandinavian older adults.[299]

Reinforcement

A handful of participants have reported that they perceived that exercise brought upon better appetite. This was described in a recent systematic review and meta-analysis of exercise on older adults, that exercise to significantly reduce leptin (a hunger inhibiting hormone), concurring with the perception of exercise-induced appetite.[300]

Intentions and Goals

Motivation appears to operate on a continuum in that its presence or lack can respectively either enable or deter older adults from exercising.[301, 302] Having goals facilitated better adherence to the present program; consistent with previous research where having a weight goal has helped adherence to supplements recommended while returning to leisure activity enabled exercise.[303] Moving forward, setting goals appears to be a vital component of self-managed intervention programs to sustain habits formed.[304]

Memory, attention, and decision processes

For participants that were still working towards making the exercise components habitual, forgetfulness was described as a barrier. However, another participant found that there wasn't a need to rely on one's memory as the presence of instructional exercise pictorials within the educational resource booklet

facilitated her exercises. Combined exercise and nutrition program for pre-frail and frail older adults may need to consider the use of cues, such as reminder alarms, to prompt participants. Moreover, participants in the program were relatively cognitively good, based on the eligibility and MMSE scores, meaning there would likely be considerations in the design of future programs if being adapted for delivery to a more cognitively diverse population.

Environmental context and resources

When delivering the nutritional components of pre-frailty and frailty intervention programs for older adults, the data suggest that it is essential to consider the participant's existing health conditions that may limit the extent of adherence. For nutrition support to be effective, nutrition-related goals ideally need to be individualised by a trained dietitian e.g., protein set higher to adjust for increased breakdown during acute disease and lower targets in those with renal issues.[211] Each unique medical condition may have a different set of nutritional issues. A combination of dietary issues and restrictions from multiple concurrent conditions present challenges towards nutritional adequacy. The data suggested that when prescribing diet recommendations and ONS, physical limitations of the pre-frail and frail older adult should also be considered. Pre-frail and frail older adults may have disabilities limiting their mobility, and thus ability to prepare food. Conditions such as arthritis can affect grip and food preparation.[305] For example, there could be difficulties in performing basic kitchen related tasks such as opening a cap.[306] A previous study also reported that frailty was described to be a physical limitation to prepare food; a lack of strength to cook.[307] Limited transport has also been cited previously as barrier towards healthy eating and disease self-management among older adults.[308] Future programs may need to consider logistics of purchasing food, while trying to prioritise nutrition content. For example, for interventions using food-based dietary modifications, milk powder may be a better option as opposed to fresh milk, if participant only goes grocery shopping once every fortnight. Meal delivery services could also be explored as a component of nutrition intervention for frailty, to reach the neediest individuals, and government could work with and fund such services, if economic benefits could also be demonstrated.[309]

The perceived barrier of lack of energy and time when it comes to exercise have both been reported many times in previous literature.[310, 311] This would suggest that healthcare providers need to address these issues by tailoring prescribed exercises, keeping in mind the length of session, time set for set-up and transportation. For example, centre-based exercises would require much more time traveling, compared to home-based ones. Although the exercise recommended were indoors, one participant chose to do it at an outdoor gym. A review suggested that enjoyment of physical activity relies on individual preferences for location (indoors or outdoors).[312] While home exercises are "weatherproof", future interventions may consider including an option for outdoor exercises, or at least ensuring that participants are more clearly made aware of safe and suitable alternatives, if preferred. Participants in this cohort were asked to walk three times a week in the program they participated in. On the same note, wet/cold weather was cited as a barrier to exercise in this study and could have impacted adherence to the walking component in particular.

Chan and Ryan found a negative correlation between rainfall and physical activity.[313] Considering that fact that the exercises (other than walking) recommended were indoors, the effects of wet weather on exercise may be affected more by factors other than logistical reasons. Interventions may need to consider change of season/temperature on the type of exercises recommended.

Social influences

Loneliness impacts dietary adherence and choice greatly. The perceived lack of social support or social opposition have been reported across other populations as well.[314] Older adults with partners/family members described social support as a significant enabler to dietary adherence to the program. It has been previously reported that older adults living with their partners tended to have more variety and larger meal size.[315] Studies have also shown shared meals to be effective in improving energy intake, albeit demonstrated in institutionalised older adults.[316] Social support is a frailty domain and assessed within the EFS. The finding of loneliness and peer pressure correspond to another study citing the lack of social support and social opposition to be barriers towards dietary and exercise adherence.[317] Social frailty has recently garnered increasing interest, with some studies defining it as insufficient or no participation in social networks with a perception of absence of contacts/supports.[318] It would be helpful for future RCTs to also compare social frailty at baseline.

Emotion

A range of emotions (fear, lack of enjoyment and appetite, depressive mood) that negatively impact on dietary adherence were described in this study. The lack of appetite and enjoyment could be linked to changes across physiological systems. Reduced hunger and early satiety are common issues raised by older adults; ageing is related to many physiological changes that favour reduced intake.[319] There are ways to respond to that barrier using a patient-centred approach.[320] Pre-prepared meals in the forms of ready-to-eat chilled or frozen meals can, keep nutritional intake adequate when there is a lack motivation to cook. The lack of enjoyment presents opportunities for healthcare providers to get creative. Again, individualised support, as opposed to prescribing more ONS, would help the participant navigate around this issue (i.e., improving the flavours of food with stronger herbs and spices). The simple process of matching food/supplements prescriptions with preferences is often overlooked. Emotions identified as barriers to exercises were stress from dealing with pain, depression and anxiety, fear of pending medical diagnosis. Depressive symptoms and perceived poor health were described as a barrier to physical activity and exercise.[296] [321] The range of emotional factors affecting adherence could be alleviated by inclusion of psychological interventions. Future programs can consider including components of psychological interventions as needed.[107] The program in the present study was underpinned by the Flinders Chronic Condition Model, based on Cognitive Behavioural Therapy. Social support was also reported to be negatively associated with depressive mood,[322] highlighting the importance of social aspect of any pre-frailty and frailty when it comes to overcoming barriers to program adherence.

Behavioural regulation

The self-management component of the program provided opportunities for self-monitoring and action planning. The food diary allowed participants to record, reflect and discuss with the home visit therapist on changes needed to break or form habits that bring them closer to their goals from the participation in the program. Interventions applying theoretical behavioural change models, for example motivational interviewing and transtheoretical model of behaviour change have been successful at establishing physical activity habits.[323] [324] Hence, future interventions involving exercise and nutrition should be designed with elements of any behavioural change models.

Demographic and health characteristics of study population on themes

A total of 11 pre-frail and frail older adults aged 68–93 years (mean age, 80.4 years); female 64%; living alone 55% that participated in a self-managed, combined exercise and nutrition, hospital-to-home support program (i.e., the intervention group), were interviewed (Table 25). A range of degrees of frailty were represented in the interview cohort – 2/11 pre-frail; 6/11 mildly frail; 2/11 moderately frail; 1/11 severely frail. The intervention cohort was well represented by the cohort presented in this study, as there were no significant differences ($P>0.05$ for all) between any of the baseline characteristics between groups. The median (range) duration of the interviews was 25 (15-60) minutes. Out of the 16 participants in the intervention group, 11 were interviewed as three died, one withdrew, one declined to be interviewed. Further insights to the characteristics and demographic information of those not interviewed were presented in Table 25. Themes identified inductively could fit within domains of the TDF and no additional unique domains were identified.

Strength and limitations

The cohort interviewed was representative of all participants who were assigned intervention at baseline. The study captured a wide range of views of participants from a range of age, nutritional status, and degrees of frailty, including pre-frailty. The interview guide protocol was developed with reference to literature of combined exercise and nutrition interventions and a range of clinical expertise of the investigators representing different fields within pre-frailty and frailty care, and not based on the TDF. Using this method, the questions and responses were direct and thus more focused to the program, rather than restricted to questions specific to each of the 14 theoretical domains. Notwithstanding that, all coded themes in this study could be matched to a domain within the TDF, further highlighting the framework's comprehensiveness.

A major limitation in this study was that the same person that delivered the intervention conducted the interviews. Social desirability bias may have occurred where participants exaggerated positive aspects of the program or could not report all personal barriers. More enablers than barriers were reported by participants for both nutrition and exercise components. Measures put in place such as briefing the participant about the role of the interviewer as a researcher, anonymity using pseudonyms, and non-

involvement of formal care within the Local Health Network might have lessened said bias. A possible benefit of conducting the interview using the PhD candidate who also delivered the intervention might be his status as an "insider" and perceived as an "advocate" for the participant. This may allow for more thorough engagement in issues, encourage disclosure, elicit a more "private" account and richer data.[325, 326] It may also be possible that participants would be more inclined to share more sensitive issues or unpopular opinions. A study suggested that shared knowledge and interest between the interviewer and participants may boost the interviewer's credibility.[327] While the use of an independent person unrelated to the program can reduce bias, their status as an "outsider" may also elicit reticence. There were also no additional checks for accuracy between the transcription and recording by another member of the research team. As discussed in methods of this Chapter, data saturation could not be determined, and the results presented in this thesis may only provide all barriers and enablers to the adherence to said program.

Another potential issue was that the participants were interviewed about their experiences of the program as a whole (including those of hospital), while at home. Most parts of the program were carried out at home post discharge, and that could have contributed to a potential for recall bias toward home as opposed to hospital care. This potential for recall bias was acknowledged during data collection and analysis, and the PhD candidate was careful to delineate views between hospital and home components. However, the authors could have asked specific questions about the experiences during the hospital component of the program in addition, or to conduct a separate interview right after discharge, prior to starting the home component. Fortunately, a recent review had already been conducted exploring barriers and enablers to physical activity during hospital stay.[328]

As the data analysis was conducted by the interviewer (PhD candidate), he would have held personal views about the participants' experiences with the interventions during their role delivering the intervention, and from the literature. Hence, it is not possible to completely bracket or dismiss these views and eliminate their impact on the data analysis process. However, this limitation was considered in the data analysis. Two members of the research team not involved in delivery of intervention nor data collection, also examined the analysed data with the TDF domains/constructs. Moreover, the findings should be interpreted in light of these limitations mentioned.

7.6 Conclusion

Healthcare providers and policy makers planning interventions to alleviate pre-frailty and frailty should be aware of the multitude of factors affecting the adherence to a self-managed combined exercise and nutrition program in this population. The present study described lessons and provided insights into the factors to adherence of such self-managed programs in pre-frail and frail older adults. While exercise and nutrition interventions can be straightforward, implementation is often tangled. Potential self-managed programs targeting pre-frail and frail older adults would require taking a multifaceted approach. Programs that emphasis patient-centredness may be more relevant for this population. The complexity of delivering

multiple components within a program could also be solved by using a single healthcare personnel to bridge healthcare providers and consumers. A single healthcare personnel can tailor the components of a structured program, to suit the different and changing needs of individual participants. A befriending element could be considered to foster social network, especially for those without support from spouse, family, or friends.

CHAPTER 8: DISCUSSION OF OVERALL FINDINGS AND CONCLUSION

8.1 Summary of findings and original contribution to knowledge

Pre-frailty and frailty syndromes are growing public health concerns.[46] In the literature review (Chapter 1), it was identified that their prevalence varied when measured with different tools[14] and are higher in hospital settings.[16] Due to the lack resources and evidence linking the practice to improve care or cost in the time-pressured hospital setting, pre-frailty and frailty screening are yet mandated in older adults.[49] The systematic review and meta-analysis (Section 1.6) of existing literature on combined exercise and nutrition interventions for pre-frailty and frailty in hospitalised older adults is the first original contribution of knowledge from this thesis, as it demonstrated there are a limited number of RCTs in hospitals[329] and evidence on combined exercise and nutrition interventions for pre-frailty and frailty in hospitalised older adults that are self-managed.[120]

The first part of the research presented in this thesis expanded knowledge on identification of pre-frailty and frailty in hospitalised older adults. The second part of the research presented in this thesis augmented knowledge on self-managed combined exercise and nutrition interventions for pre-frail and frail hospitalised older adults to warrant more research in this area.

A high prevalence of pre-frailty (24%) and frailty (33%) was observed during the assessment of these geriatric syndromes using the EFS in the observational study of this thesis. This result concurs with current prevalence reports.[14, 16] As compared to non-frail participants, the nutritional status of the pre-frail and frail participants, according to the PG-SGA score, was also significantly worse. The co-occurrence of pre-frailty and frailty, and malnutrition was confirmed in this cohort of hospitalised older adults without cognitive impairments. From the observational study in this thesis, the presence of frailty was significantly associated with a longer hospital LOS compared to older adults in a non-frail state. This echo results from meta-analysis of six cohorts – frail hospitalised older adults had statistically higher LOS compared with their non-frail counterparts (13.5 days; 95% CI: 11.51 to 15.63 versus 8.3 days; 95% CI: 6.40 to 10.38, P=0.001).[38] There was also no significant difference in LOS between pre-frail and non-frail participants.[38] The factors associated with pre-frailty and frailty were also not entirely overlapping in this thesis (Chapter 2). For instance, older age was associated with higher likelihood for frailty but not pre-frailty. There were also more factors associated with pre-frailty than frailty. While the associated factors are different, it is not so much about differentiating pre-frailty from frailty but highlighting that pre-frailty is as important as frailty in hospitalised older adults.

As a original contribution to knowledge, research conducted as part of this thesis was the first to evaluate the scored PG-SGA to also detect pre-frailty and frailty in cognitively well, hospitalised older adults admitted to the AMU.[232] The results of this study provided an alternative to screening for pre-frailty and

frailty using a specific pre-frailty and frailty screening tool. However, the scored PG-SGA is unable to differentiate pre-frailty and frailty as the cut-offs for both syndromes were the same for the hospitalised older adults in the AMU studied. Moreover, it is not so much about differentiating these two syndromes but including pre-frailty as part of frailty screening and interventions. The simultaneous detection of these three overlapping syndromes can be a time-efficient way to screen while more evidence is developed to provide a basis to mandate routine pre-frailty and frailty screening of older adults in hospitals. This thesis supports the use of a tool nonspecific to pre-frailty and frailty to serve a secondary function of detecting pre-frailty and frailty in the hospital, and adds to a previous study using the MNA to identify frailty.[33]

A cost-benefit analysis has not been conducted as part of this thesis as this involves implementation of the pre-frailty and frailty screening process, using the scored PG-SGA, which is beyond the scope of this thesis. As mentioned in Section 1.4, the clinical management of hospitalised frail older adults adds an estimate of AUD$2400/frail patient per year on health expenditures. Hence, future implementation studies of the scored PG-SGA as a screening tool for pre-frailty and frailty can consider including economic analysis to investigate if it can result in cost-savings in the care of pre-frailty and frailty in hospitalised older adults.

The analysis of the INTERACTIVE study added to the findings of the systematic review (Section 1.6) of combined exercise and nutrition interventions for pre-frail and frail hospitalised older adults in this thesis. The significant finding of improvement in gait speed was only seen with the combined statistical strength adding data from the INTERACTIVE study to the meta-analysis in the review. Many areas of the study design and intervention were also studied to inform future research. The evaluation of the INTERACTIVE study highlighted the importance of assessments of pre-frailty and frailty with validated tools e.g., EFS, instead of surrogate measures such as gait speed. As an original contribution to knowledge, the qualitative analysis of perceptions from pre-frail and frail hospitalised older adults provided valuable insights to understanding this vulnerable population from their perspectives. It is interesting to know that while the perception of frailty was largely aligned with definitions provided by experts, pre-frailty was not automatically understood as a stage prior to frailty. The evidence from this thesis also highlights that they can have different associations to factors and clinical outcomes e.g., LOS. The range of home diet and exercise practices of pre-frail and frail older adults described in this thesis highlights that exercise and nutrition interventions should not be “one-size fits all”. Hospitalisation was also viewed almost unanimously as an event that drastically changed home practices. The information collected serves as a voice from the service end-users and can be a guide to pre-frailty and frailty researchers when designing interventions involving exercise and nutrition.

The research presented in this thesis is one of the first to develop a self-managed combined exercise and nutrition intervention (INDEPENDENCE) for pre-frail and frail hospitalised older adults, as an original contribution to knowledge. The INDEPENDENCE program appears to benefit pre-frailty and frailty by reducing EFS scores, and improving other domains within pre-frailty and frailty, such as mood, cognition,

grip strength, and physical performance. The INDEPENDENCE program also appeared to have a positive impact on reduction in number of visits to the emergency department within 6-month/180-days post discharge, when compared to usual care, though it was uncertain if the observed benefits were an independent or spurious relationship confounded by other unknown factors not accounted for in this study. The high adherence to the inpatient and home visits, and exercise and nutrition components of the program might be a result of the fact that it was designed with the inputs of the end-users. However, a cost-effective analysis has not been conducted for the INDEPENDENCE program as the aims of this thesis was only to develop the program and assess the acceptability and benefits. At this stage, the PhD candidate can only provide a proof of concept, and an economic analysis should be conducted to investigate this in a statistically powered effectiveness RCT. Nonetheless, this thesis provides preliminary evidence of the benefits and acceptability of such a self-managed exercise and nutrition intervention.

The barriers and enablers identified from the final study is an original contribution to knowledge as they provided insights into the factors impacting adherence of such novel self-managed programs in pre-frail and frail older adults. While domains identified as barriers towards the program were largely environmental, many of which could be attenuated with empowerment of knowledge, skills, social influences, and beliefs about capabilities, all found within the INDEPENDENCE program.

In the climate of resource constraints, this thesis expanded knowledge in pre-frailty and frailty care in hospitalised older adults – prevalence, validation of a non-specific screening tool, and a self-managed intervention program. These findings warrant further creative exploration of re-purposing existing hospital tools and developing new/modifying current programs to re-direct autonomy back to pre-frail and frail older adults. Table 29 summarises the key original contributions of knowledge discussed throughout this thesis.

Table 29: Key original contributions to knowledge from thesis

Chapter	Contribution
1	There is weak evidence showing that combined exercise and nutrition interventions are effective to improve pre-frailty and frailty and their related indicators in hospitalised older adults.[120]
2	The prevalence of pre-frailty and frailty is high amongst hospitalised older adults in the AMU, and the factors associated with pre-frailty and frailty are not identical.
3	The Scored PG-SGA can identify pre-frailty, frailty, and malnutrition in older hospitalised adults concurrently in hospitalised older adults in the AMU[330]
4	An early, combined exercise and nutrition therapy can improve dietary energy and protein intake in older adults with hip fractures that might also be pre-frail or frail.[331]
5	There are unique perspectives of pre-frailty and frailty (e.g., pre-frailty is not automatically perceived as a syndrome before frailty) and the role and acceptability of a self-managed combined exercise and nutrition support program from the point of view of pre-frail and frail hospitalised older adults.
6	There is preliminary evidence that a patient self-managed combined exercise and nutrition program developed for pre-frail and frail hospitalised older adults is acceptable, and may benefit pre-frailty and frailty, and their related indicators.
7	There are important factors, as categorised by the TDF domains, that affect the adherence to exercise and nutrition in pre-frail and frail older adults that should be considered when designing future self-managed intervention programs for pre-frail and frail hospitalised older adults.

8.2 Overall strengths of thesis

There are several strengths in this PhD thesis. The overall objective of this PhD thesis was to improve care through early identification and intervention of pre-frailty and frailty in hospitalised older adults. A particular strength was that all the methods used were robust and adhered to respective reporting guidelines based on their study designs, e.g., CONSORT for RCTs and COREQ checklist for qualitative studies. For parts of the literature review in Chapter 1, the methods used were systematic (Section 1.6 and Section 1.7) and the search strategies were verified by an academic librarian.

The observational study within this thesis (Chapter 4 and Chapter 5) classified pre-frailty with a validated multidimensional frailty tool and attempted to address the lack of inclusion of pre-frailty in frailty research. The use of validated assessment tools throughout the studies within this thesis was also a strength. This thesis consists of studies designed by a multidisciplinary team from medicine, physiotherapy, and dietetics, and gave assurance that the assessment tools selected were optimal and content validated. This is important because pre-frailty and frailty should be assessed with a validated assessment tool to ensure accurate classification of the research participants. Furthermore, as only participants without cognitive impairments were included, the results in this thesis represent a cohort of pre-frail and frail hospitalised older adults could potentially play a more active role in patientcare, i.e., self-care.

The rich qualitative data within this thesis captured a wide range of views of pre-frail and frail participants, specifically in the hospital setting, expanded existing knowledge which largely had been built around data from older adults not specifically pre-frail and frail in community settings.

The strength of the pilot RCT examining the INDEPENDENCE program is that it is one of the first studies to pilot test a multifaceted intervention involving a patient self-management model to treat pre-frailty and frailty in hospitalised older adults. Whilst unable to provide evidence on effectiveness to alleviate pre-frailty and frailty, the creative application of an existing chronic disease care model to an otherwise recommended method i.e., Flinders Chronic Condition Model to the combined exercise and nutrition intervention in this thesis provides a new perspective and encourages repurposing existing models of care for new problems.

8.3 Overall limitations of thesis

While there were several strengths to this PhD thesis, its limitations must be acknowledged. The original studies within this PhD thesis were conducted in a single AMU within a public health institution. Therefore, the results cannot be generalised to other specific groups of hospitalised older adults (i.e., oncology, surgical), until further research has been conducted. In addition, the applicability of the results from this thesis could be limited to pre-frail and frail Caucasian older adults without cognitive impairment as none of the participants were from ethnically diverse and multicultural backgrounds, nor had any cognitive deficits.

The second qualitative study within the PhD thesis should also be interpreted with caution. While the first qualitative study (Chapter 5) used principles from the grounded theory approach, with measures taken to ensure rigor/trustworthiness and minimise bias e.g., social desirability bias, the interviews in the second study (Chapter 7) were conducted by the PhD candidate who also delivered the interventions due to limitations of resources. The thesis also contained results from analyses of a RCT that was conducted a decade ago, on a specific group of hospitalised older adults that belonged to the surgical specialty, different from the new participants recruited for the purpose of this thesis. While the secondary analysis of this study (Chapter 4) was useful to inform current interventions and had valuable objective measure such as DEXA body composition analysis, the outcomes could only provide preliminary data, and direct future research to the present cohort.

The intervention designed in Chapter 6 was also meant to be facilitated by a trained allied health assistant, supervised by a physiotherapist and dietitian. However, due to the lack of resources, the PhD candidate functioned as the trained allied health assistant, as well as in his capacity as an APD.

Finally, the intervention studies (Chapter 4 and Chapter 6) described within this thesis were not statistically powered. Therefore, the results presented can only provide a justification for further investigations but not evidence to direct changes to clinical practice.

8.4 Future studies

This research has contributed to the development of expert recommendations (multifaceted interventions combining exercise and nutrition) for pre-frail and frail hospitalised older adults in Australia and New Zealand,[72] expanded the knowledge of pre-frailty in the AMU, validated the scored PG-SGA to detect pre-frail and frail older adults in the AMU, and developed a self-managed intervention with preliminary evidence showing benefits and acceptability in a group of hospitalised older adults without cognitive impairments. With much groundwork laid, it is important to consider future directions regarding potential changes to relevant health services and research, to grow this body of work.

While the EFS is a multi-dimensional tool validated for use even by non-geriatric trained staff in hospitalised older adults, it still requires manpower to perform the assessment. It would be very costly to perform pre-frailty and frailty assessment on all hospitalised older adults, and screening is essential to first identify those at-risk to reduce unnecessary assessments. Some organisations have a system-based screening approach using electronic health records, e.g., Electronic Frailty Index and Hospital Frailty Risk Score, to automate a frailty risk score for older adults upon admission.[332, 333] However, not all acute care settings have access to that, and it also requires reconfigurations to existing electronic health records system. Moreover, such systems have yet to be extended to identification of pre-frailty. As the results of this PhD suggest, equal attention should be given to pre-frailty. Instead of using a single-purpose pre-frailty and

frailty screening tool, another way would be validating commonly used geriatric assessment tools, relevant to pre-frailty and frailty, that are already part of the hospital system's protocols. Other pre-existing tools e.g., MMSE, de Morton Mobility Index (DEMMI),[334] could be validated and/or modified to serve a dual function – assessment of its primary purpose e.g., cognition, physical performance, and also pre-frailty and frailty screening. For example, the scored PG-SGA was able to assess malnutrition and detect pre-frailty and frailty in this thesis.

While the scored PG-SGA was shown in this PhD to be valid to identify both pre-frailty and frailty in older medical inpatients, the feasibility and practicality for use in other settings is yet to be determined. Hence, the immediate next step would be to explore ways to implement the use of scored PG-SGA by healthcare professionals such as dietitians, to improve identification of pre-frailty and frailty in hospitalised older adults. This can be done using a translational research framework that is established in Australia, to determine if the assessment tool would also work in other populations. An example of such framework would be the seven steps developed by the SAX institute – idea generation, feasibility, efficacy, replicability and adaptability, effectiveness, scalability, monitoring.[335] Further research including a nation-wide survey could be conducted to assess the feasibility and acceptability of dietitians in acute care settings in the use of scored PG-SGA to also identify pre-frail and frail older patients, on top of its primary function as a malnutrition assessment tool.[335]

After examining its feasibility and acceptability, the next step would be to explore its efficacy and if implementation of the score PG-SGA to identify older patients at-risk of pre-frailty and frailty would have a positive impact on patient outcomes.[335] The implication of cost and resources to facilitate that should also be included in this step. As discussed in Chapter 3, dietitians were not always involved in multifaceted interventions involving nutritional care. Thus, it could explore whether this screening process can raise awareness of pre-frailty and frailty in hospitalised older adults and improve collaboration between dietetics and different disciplines within the healthcare system such as acute care medicine/geriatrics, physiotherapy, exercise physiology. If results from the previous step deemed this screening process to be efficacious, the replicability and adaptability of the screening process using the scored PG-SGA should be examined further to determine whether it ultimately improve patient outcomes, e.g., if more patients received treatment from the screening and as a result reduced complications, LOS. This could be done with a RCT comparing the outcomes of older patients screened using the scored PG-SGA and managed thereafter to those who receive usual care i.e., standard pre-frailty and frailty screening and management pathway. The above steps described could also be adapted to other pre-existing tools in acute care settings, relevant to pre-frailty and frailty, such as the DEMMI.[334]

Results from the pilot RCT in this thesis prompt further research into efficacy, replicability and adaptability, effectiveness, scalability, and monitoring of the INDEPENDENCE program.[335] As the INDEPENDENCE program was designed with input from its end-users, further qualitative study might be optional unless

adapted for a different population e.g., cultural diverse group. Further research could be conducted to focus on assessing the efficacy and replicability of the INDEPENDENCE program through conducting a statistically powered single centre RCT, in various departments e.g., AMU general surgical unit, geriatric unit.[335]

The pilot RCT in this thesis (Chapter 8) had the PhD candidate deliver the program in the capacity of the dietitian and, in an inter-disciplinary capacity to facilitate the home exercise program (to the level of a trained allied health assistant following training and with access to distance supervision by a physiotherapist). With more resources, future studies could have trained allied health assistants to facilitate the exercise and nutrition components under the supervision of physiotherapists and dietitians; that would better represent the INDEPENDENCE program, which designed to be facilitated by allied health assistants. The implication of cost and resources to facilitate the INDEPENDENCE program that should also be included in this step, i.e., perform an economic analysis embedded in the RCT. Considering that frailty has an estimated increment of AUD$2400 per patient on health expenditures annually (pre-frailty a similar trajectory)[44] and with increasing with total number of frailty symptoms,[45] evaluating cost-effectiveness of pre-frailty and frailty interventions would be useful to estimate costs and outcomes associated with them.[336]

If deemed to have good efficacy and replicability, the next step would be to explore its effectiveness with a multi-centred RCT.[335] If results from the previous step deemed the INDEPENDENCE program to be effective, the implementation process involving scalability and monitoring would then be examined to determine whether the program could be sustained in the health system, using principles of implementation science to promote uptake in clinical, organisational or policy context.[337]

8.5 Conclusion

This thesis brought attention to pre-frailty by demonstrating its importance while being different to frailty. To make progress towards a complete system of care for frailty from detection to intervention, pre-frailty must be considered and included. While there are many pre-frailty and frailty screening tools in the hospital, implementation would pose new challenges. To overcome such challenges, the traditional model of screening for any conditions, including pre-frailty and frailty, using a specific screening tool must be reimagined. Existing assessment tools already implemented by doctors, nurses, and allied health professionals in the hospital systems for older adults might have the potential to serve a secondary function, and that should be explored.

Multifaceted interventions combining exercise and nutrition are also recommended for hospitalised pre-frail and frail older adults in Australia. While the optimal types of exercise and nutrition components for pre-frail and frail hospitalised older adults remain to be confirmed, individualisation appears to be one of the keys to adherence. A major part of this thesis (Chapter 4-7) aimed to develop an evidenced-based, self-managed intervention to improve pre-frailty and frailty in hospitalised older adults. The rich evidence

generated on target users' desires, capitalising on a well-tested patient self-management model i.e., Flinders Chronic Condition Model, could contribute to the development of other such self-management programs to alleviate pre-frailty and frailty. A self-managed intervention program was demonstrated in this PhD to be a feasible solution to pre-frailty and frailty intervention services, that could offer hospitalised older adults more autonomy. In other words, a "patient-active" self-management model, with reduced inputs from healthcare providers (i.e., facilitation by trained allied health assistant with supervision from physiotherapists and dietitians), might challenge a "patient-passive" system that relies on healthcare system for the delivery of all education/intervention, in terms of sustainability of impacts. The roles of trained allied health assistants in facilitating such self-managed combined exercise and nutrition interventions under the supervision of physiotherapists and dietitians remain to be explored and developed.

In consideration of that, this work has identified new options for such a "patient-active" model to be integrated into pre-frailty and frailty management, at least for hospitalised older adults initially. Such a "patient-active" model may provide a sustainable solution to allow for more autonomous care in pre-frailty and frailty, thus posing a viable alternative to healthcare-personnel dependent strategies.

APPENDIX 1: AUTHORSHIP CO-SIGNING AND DETAILS ON CONTRIBUTIONS

A. STUDENT'S DETAILS (to be completed by the Student)

Name: Chad Yixian Han Student ID: 2078159

Degree: Doctor of Philosophy College: Nursing and Health Sciences

Title of Thesis: Pre-frailty and frailty in hospitalised older adults: Prevalence, identification, and development of a self-managed exercise and nutrition program

B. CO-AUTHORSHIP APPROVALS (To be completed by the student and co-authors)

If there are more than four co-authors (student plus 3 others), only the three co-authors with the most significant contributions are required to sign below.

Please note: A copy of this page will be provided to the Examiners.

1. Full publication Details Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a systematic review and meta-analysis. BMJ open. 2020 Dec 1;10(12):e040146.

Section of the thesis where the publication is referred to Chapter 1

Student's Contribution to the publication:

Research Design 80 %

Data Collection and analysis 75 %

Writing and editing 80 %

Outline your (the student's) contribution to the publication:

The PhD Candidate made major contributions to the conception and design of the review. He read and screened titles and abstracts of potentially relevant studies before evaluating the selected ones and performed data extraction. He also reviewed the collated evidence and conducted meta-analyses. The PhD candidate also drafted and led the manuscript, including rebuttals and edits during review process.

☑ I confirm that the details above are an accurate record of the student's contribution to the work.

Name of Co-Author 1: Michelle Miller Signed: Michelle Miller Digitally signed by Michelle Miller Date: 2022.06.10 11:01:11 +09'30' Date: 10/06/2022

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 2: Alison Yaxley Signed: Alison Yaxley Digitally signed by Alison Yaxley Date: 2022.06.07 13:56:39 +09'30' Date: 07/06/2022

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 3: Claire Baldwin Signed: Claire Baldwin Digitally signed by Claire Baldwin Date: 2022.06.21 13:52:19 +09'30' Date: 21/06/2022

2. Full publication Details Use of the Patient-Generated Subjective Global Assessment to Identify Pre-Frailty and Frailty in Hospitalized Older Adults. The journal of nutrition, health & aging. 2021 Dec;25(12):1229-34.

Section of the thesis where the publication is referred to Chapter 3

Student's Contribution to the publication:

Research Design 80 %

Data Collection and analysis 75 %

Writing and editing 85 %

Outline your (the student's) contribution to the publication:

The PhD Candidate made major contributions to the conception and design of the study, including ethics application.

He collected the data and performed the analyses under the guidance of statistician and the supervisory team.

He also drafted the manuscript and amended any necessary edits. There were no rebuttals during the review process.

☑ I confirm that the details above are an accurate record of the student's contribution to the work.

Name of Co-Author 1: Michelle Miller Signed: Michelle Miller Digitally signed by Michelle Miller Date: 2022.06.10 11:02:26 +09'30' Date: 10/06/2022

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 2: Alison Yaxley Signed: Alison Yaxley Digitally signed by Alison Yaxley Date: 2022.06.07 13:30:31 +09'30' Date: 07/06/2022

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 3: Claire Baldwin Signed: Claire Baldwin Digitally signed by Claire Baldwin Date: 2022.06.21 13:32:39 +09'30' Date: 21/06/2022

3. Full publication Details Han CY, Crotty M, Thomas S, Cameron ID, Whitehead C, Kurrle S, Macdonald S, Miller M. Effect of individual nutrition Therapy and Exercise Regime on Gait Speed, Physical Function, Strength and

Section of the thesis where the publication is referred to Chapter 4

Student's Contribution to the publication:

Research Design	50 %
Data Collection and analysis	50 %
Writing and editing	85 %

Outline your (the student's) contribution to the publication:

The PhD candidate performed the all of the formal analyses and visual presentation of the results. He interpreted the results and drafted the manuscript and edited with inputs from all other authors, that included reviewers rebuttals and edits during review process.

☐ I confirm that the details above are an accurate record of the student's contribution to the work.

Name of Co-Author 1: Michelle Miller Signed: Michelle Miller Digitally signed by Michelle Miller Date: 2022.06.10 11:02:48 +09'30' Date: 10/06/202

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 2: Maria Crotty Signed: Maria Crotty (RGH) Digitally signed by Maria Crotty (RGH) Date: 2022.06.21 11:11:57 +09'30' Date: 21/6/22

☐ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 3: Ian Cameron Signed: Ian Cameron Digitally signed by Ian Cameron Date: 2022.06.10 15:17:29 +10'00' Date: 10/06/202

4. Full publication Details Ho CY, Blanche Y, Yaxley A, Baldwin C, Miller M. Prevalence, factors and clinical outcomes associated with nutritional status and frailty in hospitalised older adult patients: a cross sectional observati

Section of the thesis where the publication is referred to Chapter 2

Student's Contribution to the publication:

Research Design 75 %

Data Collection and analysis 85 %

Writing and editing 85 %

Outline your (the student's) contribution to the publication:

The PhD Candidate made major contributions to the conception and design of the study, including ethics application.

He collected the data and performed the analyses under the guidance of statistician and the supervisory team.

He also drafted the manuscript and amended any necessary edits. There were no rebuttals during the review process.

☑ I confirm that the details above are an accurate record of the student's contribution to the work.

Name of Co-Author 1: Michelle Miller Signed: Michelle Miller Digitally signed by Michelle Miller Date: 2022.06.10 11:03:04 +09'30' Date: 10/06/20

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 2: Alison Yaxley Signed: Alison Yaxley Digitally signed by Alison Yaxley Date: 2022.06.07 13:40:13 +09'30' Date: 07/06/20

☑ I confirm that the details above are an accurate record of the student's contribution to the work

Name of Co-Author 3: Claire Baldwin Signed: Claire Baldwin Digitally signed by Claire Baldwin Date: 2022.06.21 13:33:05 +09'30' Date: 21/06/2022

APPENDIX 2: SEARCH STRATEGIES FOR CHAPTER 1

Systematic Review for section 1.6

Search Strategy – Medline

#	Searches
1	"diet, food, AND nutrition"/ or food/ or diet/
2	dietary proteins/ or dietary supplements/
3	Nutritional Status/ or Feeding Behavior/
4	Dietitian/
5	Nutrition Assessment/ or Nutrition Therapy/
6	((diet* or nutrition* or food*) adj5 (intervention or program or supplement or educat* or assess* or advic* or counsel* or treat*)).tw,kf.
7	or/1-6
8	motor activity/ or exercise/ or muscle strength/ or physical endurance/ or physical fitness.mp.
9	Exercise/ or resistance training/
10	(exercis* or "resistance training" or "exercis* therapy" or "muscle stretching exercis*" or "physical exercis*" or "strength train*" or "aerobic exercis*" or hydrotherapy or rehabilitat* or walk* or cycl* or conditioning* or "leg press" or flexib*).mp.
11	Physiotherapy/
12	((exercise* or resistan* or strength) adj5 (intervention or program or educat* or advice* or treat* or train* or rehabilit*)).tw,kf.
13	or/8-12
14	frail elderly/ or pre-frail elderly/
15	frail*.mp.
16	(functional* adj2 (declin* or impair*) adj3 (aged or aging or elderly or elder* or old* or senior*)).mp.
17	(frail* and (geriatric* or gerontolog* or (vulnerable and older))).mp.
18	(frail* and (aged or aging or elderly or elder* or older or senior*)).mp.
19	(frail* and (geriatric* or gerontolog* or aging)).mp.
20	("geriatric assess*" or "functionally-impaired elder*").mp.
21	14 or 15 or 16 or 17 or 18 or 19 or 20
22	7 and 13 and 21

Translated above strategy for other databases: **CINAHL, Emcare, Scopus, Cochrane, Ageline and PEDro**

Systematic Review for section 1.7

Search Strategy 1 - Medline

#	Searches
1	"diet, food, AND nutrition"/ or food/ or diet/
2	dietary proteins/ or dietary supplements/
3	Nutritional Status/ or Feeding Behavior/
4	Nutrition Assessment/ or Nutrition Therapy/
5	((diet* or nutrition* or food*) adj5 (intervention or program or supplement or educat* or assess* or advic* or counsel* or treat*)).tw.kf
6	Dietitian/ or Nutritionist/
7	or/1-6
8	frail elderly/ or pre-frail elderly/
9	frail*
10	(functional* adj2 (declin* or impair*) adj3 (aged or aging or elderly or elder* or old* or senior*))
11	(frail* and (geriatric* or gerontolog* or (vulnerable and older)))
12	(frail* and (aged or aging or elderly or elder* or older or senior*))
13	(frail* and (geriatric* or gerontolog* or aging))
14	("geriatric assess*" or "functionally-impaired elder*")
15	or/8-14
16	7 and 15

Translated above strategy for other databases: **CINAHL, Emcare, Scopus, Cochrane, Ageline**

APPENDIX 3: PARTICIPANTS INFORMATION SHEET FOR CHAPTERS 2-3, 5-7

Flinders University of South Australia

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Flinders Medical Centre

Title	Individualised therapy for elderly patients using exercise and nutrition to reduce dependence post discharge (the INDEPENDENCE trial)
Short Title	Extended nutritional and exercise therapy in elderly patients.
Protocol Number	U1111-1237-1587
Project Sponsor	N.A.
Coordinating Principal Investigator/ Principal Investigator	Prof. Michelle Miller Dr. Yogesh Sharma
Associate Investigator(s)	Dr. Alison Yaxley Mr. Chad Han Yixian Dr. Claire Baldwin
Location	Flinders Medical Centre

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have been admitted to the General Medicine Unit at Flinders Medical Centre and have been identified for frailty assessment by your attending physician.

There are 2 parts to this project:

- Part 1: The research project attempts to validate a nutrition assessment tool against a frailty assessment tool and may involve an anonymous, audio-recorded interview on your opinions on frailty and related services.
- Part 2: The research project is also testing a new management procedure for frailty in the older adults who are admitted to the General Medicine Unit at Flinders Medical Centre. The new procedure is called community extended nutrition-exercise therapy in the older adults.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether you want to take part in this research, you might want to talk about it with a relative, friend or your local doctor.

Your participation is voluntary – Your participation in this study is completely voluntary and there will be no cost to you. If you do not want to take part in this study, you do not have to. You

should feel under no obligation to participate in this study. Choosing not to take part in this study will not affect your current and future medical care in any way.

Your withdrawal from the study – You are under no obligation to continue with the research study. You may change your mind at any time about participating in the research. People withdraw from studies for various reasons and you do not need to provide a reason. You can withdraw from the study at any time by completing and signing the 'Participant Withdrawal of Consent Form'. This form is provided at the end of this document and is to be completed by you and supplied to the research team if you choose to withdraw later. If you withdraw from the study, you will be able to choose whether the study will destroy or retain the information it has collected about you. You should only choose one of these options. Where both boxes are ticked in error or neither box is ticked, the study will destroy all information it has collected about you. You may choose to withdraw from the whole study or just parts relating to your Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) information in the withdrawal of consent form should you choose to do it.

If you decide to take part in the research project, you will be asked to sign the consent section. By signing it, you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the assessments and treatments that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

Part 1: Determine whether a single tool can be used to determine both frailty and nutritional status. Nutritional status is an integral component of frailty assessment. We hope to verify whether a single tool can be used to assess both nutrition and frailty status. This may reduce the burden of multiple tools used by professionals in busy health care settings. It may also help in improving the nutrition/frailty assessment rates of hospitalised patients. Sharing your opinions on frailty and related services will help inform future health programs.

Part 2: Determine whether an extended nutrition and exercise therapy can improve pre-frail and frailty status in the older adults, results in beneficial effects on the health of the patients and if it is cost effective. The beneficial effects of an extended nutrition/exercise therapy on health outcomes in frail older hospitalised patients are unclear. This is because only limited number of studies have been performed in hospitalised patients and even fewer studies have extended the intervention into the community following hospital discharge.

This study intends to shed further light on the outcomes of prolonged nutrition and exercise therapy in the older adults which may help to amend the guidelines for management of frail patients in the hospital.

The results of this research will be used by the study dietitian Mr Chad Han to obtain a PhD degree. This research has been initiated by the study doctors and allied health professionals, Dr. Yogesh Sharma, Prof. Michelle Miller, Dr Alison Yaxley and Dr Claire Baldwin.

This research is not funded by any grant at this stage. There is also no commercial sponsor for this study.

3 What does participation in this research involve?

If you are willing to take part in this study, you will first be required to sign a consent form. Then, the following will entail,

Part 1: There will be a comprehensive nutrition and frailty assessment by a research dietitian, which will inform us about your nutrition and frailty status. These assessments will take approximately ~1 hour. You can also choose to participate in an optional interview, length and what to share or answer, is entirely decided by you. You can choose to proceed to part 2 of this study if you are found to be either pre-frail or frail and if you meet certain eligibility criteria.

Part 2: There will be further assessments such as measurement of height and weight, and non-invasive tests of muscle strength of the hand (hand-grip strength measurement) with the help of instruments which will not cause any pain. In addition, we will assist you to fill up questionnaires to assess quality of life, mood. We will also assess your physical function level with a chair-stand and walking/balance tests within the ward premises. The assessments will not take more than an hour and you will be approached by the researchers during the hospital stay and thereafter.

There will **no** additional blood test in any part of the study for the purpose of this study.
You will be randomly allocated to intervention or control group by opening an opaque envelope. There will be 50% chance that the participant will come in the intervention arm of this study.

If you are involved with part 2 of the study, you will be participating in a randomised controlled research project. Sometimes, we do not know which treatment is best for treating a condition. To find out we need to compare different treatments by putting people into groups and giving each group a different treatment. The results are then compared to see if one is better. To try to ensure that the groups are the same, each participant is put into a group by chance (random). There will be two groups in this study - a control group and an interventional group. Although both groups will undergo assessments and fill questionnaires, only the interventional group will receive a nutrition-exercise therapy plan and will be required to follow the plan. The participant has one in two chances of being put in the interventional group. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way, avoiding study doctors or participants jumping to conclusions.

Intervention group
If you are allocated to the intervention group, you will receive a nutrition and exercise plan provided by allied health professionals, which includes a dietitian and a physiotherapist. The intervention will be individualised according to your energy needs and capacity to exercise and will include optimisation of your diet (including oral nutrition supplements) and additional exercise therapy.

Follow-up
Once you are discharged from the hospital, you will be required to continue the nutrition and exercise plan under the supervision of an allied health personnel. This will include home visits at week 1, 2, 4 and 8, with telephone calls at weeks 3, 6, 10, 12 post discharge.

Control group
If you are allocated to control group, then you will receive usual care provided routinely at Flinders Medical Centre. This may include referral to the dietitian/physiotherapist on advice by their treating clinicians.

Regardless of the groups allocated, you will be assessed by researchers at your residential address at the end of 3 and 6 months, to see if there has been any difference in your frailty and health status. The assessments will include questionnaires and physical function tests that you have completed at the start of the study. These assessments will take approximately 2 hours. If you had received intervention, then you may be asked to do an interview to share your experience at the end of 3 months.

This study requires your commitment for time and compliance with the nutrition and exercise advice from your assigned allied health professional, if you are randomised to the intervention group. Table 1. shows the outline of your activities in the research project.

Table 1: Outline of participant activities in the research project part 2 *(for the intervention group)*

Activities	Hospital stay	After Discharge (Week)											
		1	2	3	4	5	6	7	8	9	10	11	12
Nutritional assessment	✓	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	✓
Physical function assessments	✓	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	✓
Nutrition therapy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Exercise therapy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Filling questionnaires	✓	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	✓
Home visits	Nil	✓	✓		✓				✓				
Telephone calls	Nil			✓			✓				✓		✓

The data collected from these assessments will be stored in a password protected computer file within a locked office at Department of Nutrition and Dietetics, Flinders University. Participation in this study is voluntary and you can withdraw from the study at any time.

There are no additional costs associated with participating in either parts of the research project, nor will you be paid. If randomised to the intervention group, the nutrition and exercise consultation and medical care required as part of the research project in part 2 will be provided to you, free of charge.

It is desirable that your local doctor be advised of your decision to participate in part 2 of this research project. If you have a local doctor, we strongly recommend that you inform them of the participant's participation in this research project.

4 What do I have to do?

There is no restriction on your standard of care in both parts of the projects. You can participate in all activities as advised by your treating doctor.

Part 1 of the project requires only simple assessments that last no more than an hour; the interview is optional, and should you decide to do it, the length is entirely up to you. After that, if you do not wish to partake in part 2 of the project, there will be no further commitments.

If you are eligible and willing to participate in part 2 of the project, you will undergo further assessments that is anticipated to be no more than an hour. You will also have to follow the dietary advice of the dietitian of this project and will receive additional exercise therapy. You should continue taking your regular medication as advised by your treating doctor. There is no restriction on taking any medication. However, you are advised to inform the researcher of any new medication started. You can donate blood as done previously. This study may require your time and commitment to comply with the nutrition and exercise advice which may include the extended support services provided (i.e. home visits and telephone calls) depending on the group you are randomised to.

5 Other relevant information about the research project

The project is being conducted at Flinders Medical Centre only and does not include any other hospitals. Part 1 of the study is cross-sectional and only require your participation for not more

than an hour; and the time taken for the optional interview is up to you. For part 2 of the study, you will be followed for 6 months. Both parts of the project involve academics from the Nutrition and Dietetics Department of Flinders University and clinicians from Flinders Medical Centre and University of Adelaide.

6 Do I have to take part in this research project?

Participation in any parts of this research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. You **do not** have to take part in this research project to receive treatment at this hospital.

If you do decide that you can take part, you will be asked to sign this Participant Information and Consent Form and you will be given a copy to keep. Your decision to participate or not to, or if you decide to withdraw from this study at a later stage, **will not** affect your routine treatment, or your relationship with the treating medical team, or your relationship with Flinders Medical Centre.

7 What are the alternatives to participation?

You do not have to take part in any parts of this research project to receive treatment at this hospital. Other options are available; these include standard treatment which is the treatment given by your attending medical team and other allied health care providers as advised by your attending medical team. One of the members of the research team will discuss these options with you before you decide whether you can take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits of part 1 of the study include increased awareness of personal frailty and nutritional status. Possible benefits of part 2 may include improvement in your health and quality of life, decrease in number of visits to the hospital and reduction in the length of the participant's stay in the hospital. This may reduce your dependence on acute health services and thus reduce health care costs. There may be potential amendments in the guidelines for management of older frail hospitalised patients thus benefitting community.

9 What are the possible risks and disadvantages of taking part?

This study will verify assessment tool and study the long-term benefits of nutrition and exercise therapy. The chance of any risks or discomfort is negligible. You will be involved in assessments (physical examination, filling up of questionnaires, walking) conducted in your ward. If you take part in the interview, you have the chance to provide opinions that may inform future health programs. Pseudonyms will be given during the audio-recorded interviews, to protect your privacy and ensure confidentiality is respected. In part 2 of the project, you may be involved in a nutrition-exercise based intervention. Although we anticipate minimal risks/discomfort, you may raise any concerns regarding anticipated or actual risks or discomfort at any time with the investigator.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

10 What will happen to my test samples?

No additional blood samples will be required for this study.

11 What if new information arises during this research project?

Sometimes during a research project, new information becomes available about the treatment that is being studied. If this happens, then your study doctor will inform you about this new information and discuss with you whether you want to continue in the research project. If you decide to withdraw from this study, your study doctor will arrange for your regular health care to continue. If you decide to continue in the research project, you will be asked to sign an updated consent form.

Also, on receiving any new information, your study doctor might consider in your best interests to be withdrawn from the research project. If this happens, the doctor will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Although you can have all other treatments as advised by your treating doctor, it is advised that you tell the study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you, which treatments or medications need to be stopped for the time you are involved in the research project.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow the research supervisor to discuss any health risks linked to withdrawing i.e., you will not be receiving further therapies related to the intervention and may not benefit further from the exercise and nutrition intervention provided. **You will not be questioned should you choose to withdraw from the study.** If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly. You should be aware that data collected by the investigator (through a qualified assessor that is unaware of your group allocation) up to the time you withdraw will form part of the research project results If you do not want them to do this, you must tell them before you join the research project. Once the data has been deidentified/analysed, it cannot be destroyed.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• The assessment tool or procedure being shown not to be effective
• The assessment tool or procedure being shown to work and not need further testing

15 What happens when the research project ends?

The assessment in part 1 is free and you will not be charged any fees. The nutrition-exercise therapy program is available through this project for three months and you will not be charged any fees. To access the services of an allied health professional after that, you will have to follow the usual method of approaching one through your local doctor and may have to pay for their services. Outcomes from the project will be summarised and will be provided to the participant on request. The summary of this research will be available at the SALHN website after approximately 12 months from the start of the project.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form, you consent to the study doctor and relevant research staff collecting and using your personal information for this and future research projects, subject to approval from the relevant Human Research Ethics Committee (HREC). Any information obtained in connection with the data collection of this research project that can identify your participation will remain confidential. MBS/PBS data will be stored on servers, or hosted through cloud computing providers, physically located within Australian borders. All the information collected will be stored on password protected computers within locked offices of the Department of Nutrition and Dietetics of Flinders University, with passwords only known to primary investigators. The data will be stored for 15 years and will be appropriately deleted from the computers. Your information will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form, you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subjected to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities, Flinders Medical Centre or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Your name and identification number will not be used, and you will be de-identified and anonymous within this study. Your name and identification numbers will be converted into code numbers. The code numbers will be stored in password protected computers. MBS/PBS data will not be used in any future or unspecified research outside of the approved study.

Information about your participation in this research project will be recorded in your health records. In accordance with relevant Australian and South Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information. Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. In case of an unexpected adverse effect, compensation may be paid automatically but you may have to commence legal proceedings to determine if you should be compensated. Since this is a nutrition-exercise therapy-based study and no pharmacological drug is being tested in this research project, there are negligible chances of any adverse effects. In case of an unexpected adverse effect, compensation will be provided in accordance with the law.

18 Who is organising and funding the research?

This research project is conducted by Prof. Michelle Miller and Dr. Yogesh Sharma. No additional funding is required for this research project. The research is being supported in-kind by the Departments of General Medicine, Nutrition and Dietetics and Physiotherapy.

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Southern Adelaide Clinical HREC of Flinders University. This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on +61 8 82046694 or any of the following people.

Clinical contact person

Name	Yogesh Sharma
Position	Senior Consultant, Department of Medicine
Telephone	+61 8 82046694
Email	yogesh.sharma@sa.gov.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Michelle Miller
Position	Dean (People and resources), College of Nursing and Health sciences, Flinders University
Telephone	+61 8 82045328
Email	michelle.miller@flinders.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Southern Adelaide Clinical Human Research Ethics Committee
HREC Executive Officer	Paula Davies
Telephone	+61 8 8204 6453
Email	health.SALHNOfficeforResearch@sa.gov.au

Local HREC Office contact (Single Site - Research Governance Officer)

Name	Danielle Eley
Position	Administration Officer
Telephone	+61 8 8204 6453
Email	health.SALHNOfficeforResearch@sa.gov.au; danielle.eley@sa.gov.au

Consent Form - *Adult providing own consent*

Title	Individualised therapy for elderly patients using exercise and nutrition to reduce dependence post discharge (the INDEPENDENCE trial)	
Short Title	Extended nutritional and exercise therapy in elderly patients.	
Protocol Number	ACTRN12614000833662	
Project Sponsor	N.A.	
Coordinating Principal Investigator/ Principal Investigator	Prof. Michelle Miller Dr. Yogesh Sharma	
Associate Investigator(s)	Dr. Alison Yaxley Dr. Claire Baldwin	Mr. Chad Han Yixian
Location	Flinders Medical Centre	

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Flinders University concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project; its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.
Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

Title	Individualised therapy for elderly patients using exercise and nutrition to reduce dependence post discharge (the INDEPENDENCE trial)	
Short Title	Extended nutritional and exercise therapy in elderly patients.	
Protocol Number	ACTRN12614000833662	
Project Sponsor	N.A.	
Coordinating Principal Investigator/ Principal Investigator	Prof. Michelle Miller Dr. Yogesh Sharma	
Associate Investigator(s)	Dr. Alison Yaxley Dr. Claire Baldwin	Mr. Chad Han Yixian
Location	Flinders Medical Centre	

Declaration by Participant

I wish to WITHDRAW my participation in the study effective from the date below. I request that the study handles the information they have collected about me in the following way (choose one option):

Type of participation to be withdrawn: ☐ WHOLE study

☐ DESTROY all information collected about me so it can no longer be used for research
☐ RETAIN all information collected about me so it can continue to be used for research

I understand that (1) no further information about me will be collected for the study from the withdrawal date; (2)information about me that has already been analysed and/or included in a publication by the study, may not be able to be destroyed; and (3) choosing to withdraw from the study will not affect my access to Health Services or Government benefits.

Name of Participant (please print) _____

Signature _____ Date _____

Description of circumstances for withdrawal of study

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.
Note: All parties signing the consent section must date their own signature.

BASELINE DATA ASSESSMENT

(White PACK)

Part 1: • Baseline data collection form • Edmonton Frail Scale (EFS) • Patient-generated Subjective Global Assessment (PG-SGA) • Mini mental state examination (MMSE)
Part 2: • EQ-5D-5L • Hospital Admission Risk Profile (HARP) • Geriatric depression scale (GDS) • Handgrip strength • Short Physical Performance Battery (SPPB)

Baseline data Collection Form

Participant Code:

ANTHROPOMETRIC DATA Today's Date: _____ /_____ /_____

Height: _____(m) Weight___ (kg) BMI: _____(kg/m^2)

CLINICAL DATA

Primary diagnosis:

_____

_____

Comorbidities (tick and circle):

☐ Myocardial Infarction	☐ Congestive Heart Failure	☐ Peripheral Vascular Disease	☐ Cerebrovascular Disease
☐ Dementia	☐ COPD	☐ Connective Tissue Disease	☐ Peptic Ulcer Disease
☐ Liver Disease (Mild/ Moderate/ Severe)		☐ Diabetes Mellitus (Uncomplicated / End-organ damage)	
☐ Hemiplegia	☐ Moderate to Severe CKD	☐ Solid tumour (Metastasis / No metastasis)	☐ Leukemia
☐ AIDS		☐ Malignant Lymphoma	
☐ Arthritis	☐ Osteoporosis	☐ Asthma	☐ ARDS/emphysema
☐ Angina	☐ neurological disease	☐ stroke/ TIA	☐ Upper GI disease (hermia/reflux)
☐ Depression	☐ Anxiety/panic disorders	☐ Visual impairment (cataracts, glaucoma. MD)	☐ Hearing impairment (very hard of hearing even with hearing aid)
☐ Degenerative disc disease (back disease, spinal stenosis or severe chronic back pain			

Others (please specify):_____

SOCIAL AND LIFESTYLE DATA

☐ Home alone ☐ Home with _____

☐ Residential Aged Care Facility/ Nursing Home: High level care OR Low level care (please circle)

☐ Other: _____

_____

Highest Education level:
☐ Up to secondary ☐ Trade/certificate/diploma ☐ Bachelor degree and above

Income group:
☐ up to $20K ☐ more than $20 – less than 40K ☐ $40 – less than 60K ☐ More than $60K

Marital status:
☐ Married/De facto ☐ Separated/Divorced ☐ Widowed ☐ Never married

Smoking status:
☐ Never smoked ☐ Former smoker ☐ Current smoker: _____ sticks/day

Alcohol consumption: _____ standard drinks/week

MEDICATIONS/SUPPLEMENTS CONSUMPTION

Number of medications used prior admission: _____Vitamin D/Calcium: ☐ Yes ☐ No
Others (specify): _____

EFS **if already done, note final score from participant's case notes*

Frailty domain	Item	0 point	1 point	2 points
Cognition	Please imagine that this pre-drawn circle is a clock. I would like you to place the numbers in the correct positions then place the hands to indicate a time of 'ten after eleven'	No errors	Minor spacing errors	Other errors
General health status	In the past year, how many times have you been admitted to a hospital?	0	1–2	≥2
	In general, how would you describe your health?	'Excellent', 'Very good', 'Good'	'Fair'	'Poor'
Functional independence	With how many of the following activities do you require help? (meal preparation, shopping, transportation, telephone, housekeeping, laundry, managing money, taking medications)	0–1	2–4	5–8
Social support	When you need help, can you count on someone who is willing and able to meet your needs?	Always	Sometimes	Never
Medication use	Do you use five or more different prescription medications on a regular basis?	No	Yes	
	At times, do you forget to take your prescription medications?	No	Yes	
Nutrition	Have you recently lost weight such that your clothing has become looser?	No	Yes	
Mood	Do you often feel sad or depressed?	No	Yes	
Continence	Do you have a problem with losing control of urine when you don't want to?	No	Yes	
Functional performance	I would like you to sit in this chair with your back and arms resting. Then, when I say 'GO', please stand up and walk at a safe and comfortable pace to the mark on the floor (approximately 3 m away), return to the chair and sit	0–10 s	11–20 s	One of: >20s, or patient unwilling, or requires assistance

	down’			
Totals	Final score is the sum of column totals			
Scoring: 0 - 5 = Not Frail 6 - 7 = Vulnerable 8 - 9 = Mild Frailty 10-11 = Moderate Frailty 12-17 = Severe Frailty Functional performance ❑ Walking aid use: _____(type)				Total: /17

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

Patient Identification Information

History: Boxes 1 - 4 are designed to be completed by the patient.
[Boxes 1-4 are referred to as the PG-SGA Short Form (SF)]

1. Weight *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____kg
I am about _____ cm tall

One month ago I weighed about _____ kg
Six months ago I weighed about _____ kg

During the past two weeks my weight has:

☐ decreased (1) ☐ not changed (0) ☐ increased (0)

Box 1 ☐

☐ unchanged (0)
☐ more than usual (0)
☐ less than usual (1)

I am now taking

☐ *normal food* but less than normal amount (1)
☐ little solid food (2)
☐ only liquids (3)
☐ only nutritional supplements (3)
☐ very little of anything (4)
☐ only tube feedings or only nutrition by vein (0) **Box 2** ☐

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)

☐ no problems eating (0)
☐ no appetite, just did not feel like eating (3)
☐ nausea (1)
☐ constipation (1)
☐ mouth sores (2)
☐ things taste funny or have no taste (1)
☐ problems swallowing (2)
☐ pain; where? (3) _____
☐ other (1)** _____
**Examples: depression, money, or dental problems

☐ vomiting (3)
☐ diarrhea (3)
☐ dry mouth (1)
☐ smells bother me (1)
☐ feel full quickly (1)
☐ fatigue (1)

Box 3 ☐

4. Activities and Function:
Over the past month, I would generally rate my activity as:

☐ normal with no limitations (0)
☐ not my normal self, but able to be up and about with fairly normal activities (1)
☐ not feeling up to most things, but in bed or chair less than half the day (2)
☐ able to do little activity and spend most of the day in bed or chair (3)
☐ pretty much bed ridden, rarely out of bed (3)

Box 4 ☐

The remainder of this form is to be completed by your doctor, nurse, dietitian, or therapist. Thank you.

Additive Score of Boxes 1-4 ☐ **A**

email: faithotterymdphd@aol.com or info@pt-global.org

Worksheet 1 – Scoring Weight Loss

To determine score, use 1-month weight data if available. Use 6-month data only if there is no 1-month weight data. Use points below to score weight change and add one extra point if patient has lost weight during the past 2 weeks. Enter total point score in Box 1 of PG-SGA.

Weight loss in 1 month	Points	Weight loss in 6 months
10% or greater	4	20% or greater
5-9.9%	3	10- 19.9%
3-4.9%	2	6- 9.9%
2-2.9%	1	2- 5.9%
0-1.9%	0	0- 1.9%

Numerical score from Worksheet 1 ☐

Additive Score of Boxes 1-4 (See Side 1) ☐ **A**

5. Worksheet 2 – Disease and its relation to nutritional requirements:

Score is derived by adding 1 point for each of the following conditions:

- ☐ Cancer
- ☐ AIDS
- ☐ Pulmonary or cardiac cachexia
- ☐ Chronic renal insufficiency
- ☐ Presence of decubitus, open wound or fistula
- ☐ Presence of trauma
- ☐ Age greater than 65

Other relevant diagnoses (specify) _____

Primary disease staging (circle if known or appropriate) I II III IV Other ____

Numerical score from Worksheet 2 ☐ **B**

6. Worksheet 3 – Metabolic Demand

Score for metabolic stress is determined by a number of variables known to increase protein & caloric needs. **Note:** Score fever intensity or duration, whichever is greater. The score is additive so that a patient who has a fever of 38.8 °C (3 points) for < 72 hrs (1 point) and who is on 10 mg of prednisone chronically (2 points) would have an additive score for this section of 5 points.

Stress	none (0)	low (1)	moderate (2)	high (3)
Fever	no fever	> 37.2 and < 38.3	≥ 38.3 and < 38.8	≥ 38.8 °C
Fever duration	no fever	< 72 hours	72 hours	> 72 hours
Corticosteroids	no corticosteroids	low dose (< 10 mg prednisone equivalents/day)	moderate dose (≥ 10 and < 30 mg prednisone equivalents/day)	high dose (≥ 30 mg prednisone equivalents/day)

Numerical score from Worksheet 3 ☐ **C**

7. Worksheet 4 – Physical Exam

Exam includes a subjective evaluation of 3 aspects of body composition: fat, muscle, & fluid. Since this is subjective, each aspect of the exam is rated for degree. Muscle deficit/loss impacts point score more than fat deficit/loss. Definition of categories: 0 = no abnormality, 1+ = mild, 2+ = moderate, 3+ = severe. Rating in these categories is *not* additive but are used to clinically assess the degree of deficit (or presence of excess fluid).

Muscle Status		Fat Stores	
temples (temporalis muscle)	0 1+ 2+ 3+	orbital fat pads	0 1+ 2+ 3+
clavicles (pectoralis & deltoids)	0 1+ 2+ 3+	triceps skin fold	0 1+ 2+ 3+
shoulders (deltoids)	0 1+ 2+ 3+	fat overlying lower ribs	0 1+ 2+ 3+
interosseous muscles	0 1+ 2+ 3+	**Global fat deficit rating**	**0 1+ 2+ 3+**
scapula (latissimus dorsi, trapezius, deltoids)	0 1+ 2+ 3+	**Fluid status**	
thigh (quadriceps)	0 1+ 2+ 3+	ankle edema	0 1+ 2+ 3+
calf (gastrocnemius)	0 1+ 2+ 3+	sacral edema	0 1+ 2+ 3+
Global muscle status rating	**0 1+ 2+ 3+**	ascites	0 1+ 2+ 3+
		Global fluid status rating	**0 1+ 2+ 3+**

Point score for the physical exam is determined by the overall subjective rating of the total body deficit.

No deficit	score = 0 points
Mild deficit	score = 1 point
Moderate deficit	score = 2 points
Severe deficit	score = 3 points

Again, muscle deficit/loss takes precedence over fat loss or fluid excess.

Numerical Score for Worksheet 4 ☐ **D**

Total PG-SGA Score (Total numerical score of A+B+C+D) ☐

Clinician Signature _____ RD RN PA MD DO Other _____ Date _____

Global PG-SGA Category Rating (Stage A, Stage B or Stage C) ☐

Worksheet 5 – PG-SGA Global Assessment Categories

	Stage A	Stage B	Stage C
Category	**Well-nourished**	**Moderate/suspected malnutrition**	**Severely malnourished**
Weight	No weight loss **OR** recent non-fluid wt gain	≤ 5% loss in 1 month (≤10% in 6 months) **OR** Progressive weight loss	> 5% loss in 1 month (>10% in 6 months) **OR** Progressive weight loss
Nutrient intake	No deficit **OR** Significant recent improvement	Definite decrease in intake	Severe deficit in intake
Nutrition Impact Symptoms (NIS)	None **OR** significant recent improvement allowing adequate intake	Presence of NIS (Box 3 of PG-SGA)	Presence of NIS (Box 3 of PG-SGA)
Functioning	No deficit **OR** Significant recent improvement	Moderate functional deficit **OR** Recent deterioration	Severe functional deficit **OR** Recent significant deterioration
Physical Exam	No deficit **OR** chronic deficit but with recent clinical improvement	Evidence of mild to moderate loss of muscle mass &/or muscle tone on palpation &/or loss of SQ fat	Obvious signs of malnutrition (e.g., severe loss muscle, fat, possible edema)

Nutritional Triage Recommendations: Additive score is used to define specific nutritional interventions including patient & family education, symptom management including pharmacologic intervention, and appropriate nutrient intervention (food, nutritional supplements, enteral, or parenteral triage).

First line nutrition intervention includes optimal symptom management.

Triage based on PG-SGA point score

0-1	No intervention required at this time. Re-assessment on routine and regular basis during treatment.
2-3	Patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey (Box 3) and lab values as appropriate.
4-8	Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms (Box 3).
≥ 9	Indicates a critical need for improved symptom management and/or nutrient intervention options.

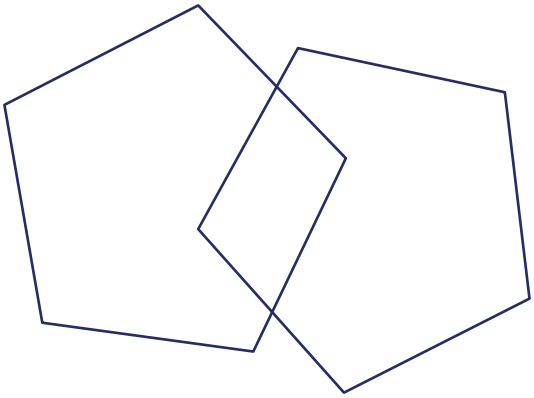
email: faithottervmdphd@aol.com or info@pt-global.org

MMSE **record individual sections and final score from participant's case notes*

Say: *I am going to ask you some questions and give you some problems to solve. Please try to answer as best you can*

1. Allow ten seconds for each reply. **Say:** *a) What year is this?* (accept exact answer only) *b) What season is this?* (during the last week of the old season or first week of a new season, accept either) *c) What month is this?* (on the first day of a new month or the last day of the previous month, accept either) *d) What is today's date?* (accept previous or next date) *e) What day of the week is this?* (accept exact answer only)	/1 /1 /1 /1 /1
2. Allow ten seconds for each reply. **Say:** a) *What country are we in?* (accept exact answer only) b) *What state are we in?* (accept exact answer only) c) *What city/town are we in?* (accept exact answer only) d) <At home> *What is the street address of this house?* (accept street name and house number or equivalent in rural areas) **OR**<In facility> *What is the name of this building?* (accept exact name of institution only) e) <At home> *What room are we in?* (accept exact answer only) **OR** <In facility> *What floor of the building are we on?* (accept exact answer only)	/1 /1 /1 /1 /1
3. **Say:** *I am going to name three objects. When I am finished, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes* (say slowly at approximately one-second intervals). **Ball Car Man** For repeated use: Bell, jar, fan; bill, tar, can; bull, bar, pan **Say:** *Please repeat the three items for me* (score one point for each correct reply on the first attempt) Allow 20 seconds for reply; if the person did not repeat all three, repeat until they are learned or up to a maximum of five times (but only score first attempt)	/3
4. **Say:** Spell the word WORLD (you may help the person to spell the word correctly). **Say:** Now spell it backwards please (allow 30 seconds; if the person cannot spell world even with assistance, score zero). Refer to accompanying guide for scoring instructions (score on reverse of this sheet)	/5
5. **Say:** *Now what were the three objects I asked you to remember?* (score one point for each correct answer regardless of order; allow ten seconds)	/3
6. Show wristwatch. **Ask:** *What is this called?* (score one point for correct response; accept 'wristwatch' or 'watch'; do not accept 'clock' or 'time', etc.; allow ten seconds)	/1

7. **Show pencil. Ask:** *What is this called?* (score one point for correct response; accept 'pencil' only; score zero for pen; allow ten seconds for reply)	/1
8. **Say:** *I would like you to repeat a phrase after me: No ifs, ands, or buts*	/1
9. **Say:** *Read the words on this page and then do what it says* Then, **hand** the person the sheet with CLOSE YOUR EYES (score on reverse of this sheet) on it. If the subject just reads and does not close eyes, you may repeat: *Read the words on this page and then do what it says*, a maximum of three times. See point number three in Directions for Administration section of accompanying guidelines. Allow ten seconds; score one point only if the person closes their eyes. The person does not have to read aloud.	/1
10. **Hand** the person a pencil and paper. **Say:** *Write any complete sentence on that piece of paper (*allow 30 seconds. Score one point. The sentence must make sense. Ignore spelling errors).	/1
11. **Place** design (see page 3), pencil, eraser and paper in front of the person. **Say:** *Copy this design please.* Allow multiple tries	/1
12. **Ask** the person if he is right or left handed. **Take** a piece of paper, hold it up in front of the person and **say** the following: *Take this paper in your right/left hand* (whichever is non-dominant), *fold the paper in half once with both hands and put the paper down on the floor*. Takes paper in correct hand____ Folds it in half_____ Puts it on the floor_____	/1 /1 /1 /1
Total Test score	/30



Time:

D	L	R	O	W

=

CLOSE YOUR EYES

EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems with walking around ❑
I have slight problems with walking around ❑
I have moderate problems with walking around ❑
I have severe problems with walking around ❑
I am unable to walk around ❑

PERSONAL CARE

I have no problems with washing or dressing myself ❑
I have slight problems with washing or dressing myself ❑
I have moderate problems with washing or dressing myself ❑
I have severe problems with washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

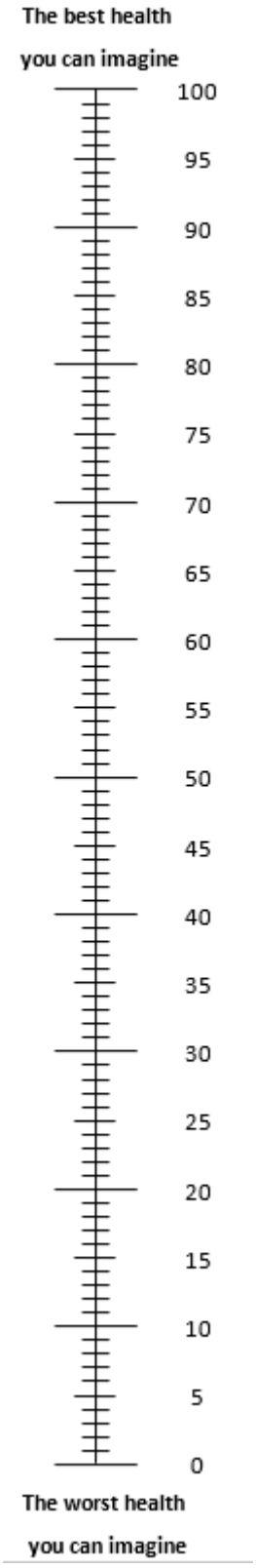
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



HARP

1. Scoring range 0-5

A. Age

AGE CATEGORY	RISK SCORE	
<75	0	
75-84	1	**SCORE =**
≥85	2	

B. Cognitive function (abbreviated 21 components MMSE- to **retrieve from above MMSE**)*

MMSE SCORE	RISK SCORE	
15-21	0	
0-14	1	**SCORE =**

C. IADL function prior to admission**

INDEPENDENT IADL's	RISK SCORE	
6-7	0	
0-5	2	**SCORE =**

*Abbreviated MMSE includes only the following 21 components of the original 30 item test: orientation (10 items: year, season, month, date, day, city, county, state, hospital, floor); registration (3 unrelated items, such as hat, ball, tree); attention (5 items, such as spelling WORLD backwards); and recall (same 3 items as in registration). Each correct answer is scored one point.

** IADL activities include telephoning, shopping, cooking, doing housework, taking medications, using transportation and managing finances.

Ability to Use Telephone 1. Operates telephone on own initiative; looks up and dials numbers.....1 2. Dials a few well-known numbers .....1 3. Answers telephone, but does not dial.....1 4. Does not use telephone at all…….0	**Laundry** 1. Does personal laundry completely……1 2. Launders small items, rinses socks, stockings, etc…..1 3. All laundry must be done by others…….0
Shopping 1. Takes care of all shopping needs independently ...1 2. Shops independently for small purchases.....0 3. Needs to be accompanied on any shopping trip ....0 4. Completely unable to shop.....0	**Mode of Transportation** 1. Travels independently on public transportation or drives own car.....1 2. Arranges own travel via taxi, but does not otherwise use public transportation .....1 3. Travels on public transportation when assisted or accompanied by another.....1 4. Travel limited to taxi or automobile with assistance of another .....0 5. Does not travel at all 0

Food Preparation 1.Plans, prepares, and serves adequate meals independently..... 1 2. Prepares adequate meals if supplied with ingredients……0 3. Heats and serves prepared meals or prepares meals but does not maintain adequate diet……...1 4. Needs to have meals prepared and served..... 0	**Responsibility for Own Medications** 1. Is responsible for taking medication in correct dosages at correct time…….1 2. Takes responsibility if medication is prepared in advance in separate dosage……..0 3. Is not capable of dispensing own medication…..0
Housekeeping 1.Maintains house alone with occasion assistance (heavy work)……1 2. Performs light daily tasks such as dishwashing, bed making…….1 3. Performs light daily tasks, but cannot maintain acceptable level of cleanliness……1 4. Needs help with all home maintenance tasks….1 5. Does not participate in any housekeeping tasks…0	**Ability to Handle Finances** 1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income…….1 2. Manages day-to-day purchases, but needs help with banking, major purchases, etc……1 3. Incapable of handling money……..0

2. Risk categories TOTAL = _____

TOTAL SCORE	RISK OF DECLINE IN ADL FUNCTION
4 or 5	High risk
2 or 3	Intermediate risk
0 or 1	Low risk

GDS

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life?	YES / **NO**
2. Have you dropped many of your activities and interests?	**YES** / NO
3. Do you feel that your life is empty?	**YES** / NO
4. Do you often get bored?	**YES** / NO
5. Are you in good spirits most of the time?	YES / **NO**
6. Are you afraid that something bad is going to happen to you?	**YES** / NO
7. Do you feel happy most of the time?	YES / **NO**
8. Do you often feel helpless?	**YES** / NO
9. Do you prefer to stay at home, rather than going out and doing new things?	**YES** / NO
10. Do you feel you have more problems with memory than most?	**YES** / NO
11. Do you think it is wonderful to be alive now?	YES / **NO**
12. Do you feel pretty worthless the way you are now?	**YES** / NO
13. Do you feel full of energy?	YES / **NO**
14. Do you feel that your situation is hopeless?	**YES** / NO
15. Do you think that most people are better off than you are?	**YES** / NO
Answers in **bold** indicate 1 point Scoring: 0 - 4 = No depression 5 - 8 = mild 9 - 11 = moderate 10-15 = severe	Total: /15

PHYSICAL TESTS ***Please refer to attached protocol prior to conducting measurements***

Handgrip Strength

Attempt	1	2	3	Average
Kilograms				

Dominant Hand ☐ Left ☐ Right

SPPB – Balance test

❑ Walking aid: _____

A. Side-by-Side stand

Held for 10 sec ❒1 point
Not held for 10 sec ❒0 points
Not attempted ❒0 points
If 0 points, end Balance Tests

Number of seconds held if less than 10 sec:
____.___ Sec

If participant did not attempt test or failed, circle why:
Tried but unable 1
Participant could not hold position unassisted 2
Not attempted, you felt unsafe 3
Not attempted, participant felt unsafe 4
Participant unable to understand instructions 5
Other (specify) 6
Participant refused 7

B. Semi-Tandem Stand

Held for 10 sec ❒1 point
Not held for 10 sec ❒0 points
Not attempted ❒0 points
(circle reason to the right)
If 0 points, end Balance Tests

Number of seconds held if less than 10 sec:
____.___ Sec

If participant did not attempt test or failed, circle why:
Tried but unable 1
Participant could not hold position unassisted 2
Not attempted, you felt unsafe 3
Not attempted, participant felt unsafe 4
Participant unable to understand instructions 5
Other (specify) 6
Participant refused 7

C. Tandem Stand

Held for 10 sec ❒2 point
Held for 3 to 9.99 sec ❒1 points
Held for < than 3 sec ❒0 points
Not attempted ❒0 points
(circle reason above)

Number of seconds held if less than 10 sec:
____.___Sec

If participant did not attempt test or failed, circle why:
Tried but unable 1
Participant could not hold position unassisted 2
Not attempted, you felt unsafe 3
Not attempted, participant felt unsafe 4
Participant unable to understand instructions 5
Other (specify) 6
Participant refused 7

Total balance test score:_____ (sum points)

SPPB – 4-metre Gait Speed

❑ Walking aid: _____

A. Time for First Gait Speed Test (sec)

1. Time for 3 or 4 meters _____.___ sec
2. If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not walk unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (Specify) _____	6
Participant refused	7

Complete score sheet and go to chair stand test

3. Aids for first walk..... None ❒ Cane ❒ Other ❒

B. Time for Second Gait Speed Test (sec)

1. Time for 3 or 4 meters _____.___ sec
2. If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not walk unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (Specify)	6
Participant refused	7

3. Aids for second walk..... None ❒ Cane ❒ Other ❒

What is the time for the faster of the two walks?

Record the shorter of the two times _____.___ sec

[If only 1 walk done, record that time] _____.___ sec

If the participant was unable to do the walk: ❒ 0 points

If time is more than 8.70 sec:	❒ 1 point
If time is 6.21 to 8.70 sec:	❒ 2 points
If time is 4.82 to 6.20 sec:	❒ 3 points
If time is less than 4.82 sec:	❒ 4 points

SPPB – Chair stand test

❑ Walking aid: _____

Single Chair Stand Test

	Yes	No	
A. Safe to stand without help	❒	❒	
B. Results:			
Participant stood without using arms	❒		→ Go to Repeated Chair Stand Test
Participant used arms to stand	❒		→ End test; score as 0 points
Test not completed	❒		→ End test; score as 0 points
C. If participant did not attempt test or failed, circle why:			
Tried but unable	1		
Participant could not stand unassisted	2		
Not attempted, you felt unsafe	3		
Not attempted, participant felt unsafe	4		
Participant unable to understand instructions	5		
Other (Specify)	6		
Participant refused	7		

Repeated Chair Stand Test

	Yes	No
A. Safe to stand five times	❒	❒
B. If five stands done successfully, record time in seconds. Time to complete five stands ____.___ sec		
C. If participant did not attempt test or failed, circle why:		
Tried but unable	1	
Participant could not stand unassisted	2	
Not attempted, you felt unsafe	3	
Not attempted, participant felt unsafe	4	
Participant unable to understand instructions	5	
Other (Specify)	6	
Participant refused	7	

Scoring the Repeated Chair Test

Participant unable to complete 5 chair stands or completes stands in >60 sec:	❒0 points
If chair stand time is 16.70 sec or more:	❒1 points
If chair stand time is 13.70 to 16.69 sec or more:	❒2 points
If chair stand time is 11.20 to 13.69 sec:	❒3 points
If chair stand time is 11.19 sec or less:	❒4 points

Total Score: /12 points (sum of points above)

Assessor's Initials and Signature: _____

Hand Grip Strength Protocol:

1) Grip strength will be measured using a **hand-held dynamometer** located from the studies allocated set of equipment
2) Participants will be instructed to stand with **legs straight** and **feet approximately 15cm apart**, and to hold the dynamometer in their dominant hand, so that it **does not touch the hand or clothes**.
3) They will then be instructed to squeeze the dynamometer with their dominant hand with **maximum force**, **without swinging the arm, for three seconds. This test will be repeated within 15 seconds.**
4) This will be performed **three times** and the **mean of three measures** used in calculations.

Short Physical Performance Battery (SPPB) Protocol: *Introduction, Balance*

You may help the participant to get up. The participant can use a cane or walker in this adapted SPPB, please record if the participant uses a walking aid and type. Instructions to the participants are shown ***in bold italic*** and should be given exactly as they are written in this script.

Now let's begin the evaluation. I would now like you to try to move your body in different movements. I will first describe and show each movement to you. Then I'd like you to try to do it. If you do it, tell me and we'll move on to the next one. Let me emphasise that I do not want you to try to do any exercise that you feel might be unsafe.

Do you have any questions before we begin?

A. Side-by-Side Stand

1. ***Now I will show you the first movement***.

2. (Demonstrate) ***I want you to try to stand with your feet together, side-by-side, for about 10 seconds.***

3. ***You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.***

4. Stand next to the participant to help him/her into the side-by-side position.

5. Supply just enough support to the participant's arm to prevent loss of balance.

6. When the participant has his/her feet together, ask ***"Are you ready?"***

7. Then let go and begin timing as you say, ***"Ready, begin."***

8. Stop the stopwatch and say **"*Stop*"** after 10 seconds or when the participant steps out of position or grabs your arm.

9. If participant is unable to hold the position for 10 seconds, record result and go to the gait speed test

B. Semi-Tandem Stand

1. ***Now I will show you the second movement***.

2. (Demonstrate) ***Now I want you to try to stand with the side of the heel of one foot touching the big toe of the other foot for about 10 seconds. You may put either foot in front, whichever is more comfortable for you.***

3. ***You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.***

4. Stand next to the participant to help him/her into the semi-tandem position

5. Supply just enough support to the participant's arm to prevent loss of balance.

6. When the participant has his/her feet together, ask ***"Are you ready?"***

7. Then let go and begin timing as you say ***"Ready, begin."***

8. Stop the stopwatch and say ***"Stop"*** after 10 seconds or when the participant steps out of position or grabs your arm.

9. If participant is unable to hold the position for 10 seconds, record result and go to the gait speed test.

C. Tandem Stand

1. ***Now I will show you the third movement.***

2. (Demonstrate) ***Now I want you to try to stand with the heel of one foot in front of and touching the toes of the other foot for about 10 seconds. You may put either foot in front, whichever is more comfortable for you.***

3. ***You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.***

4. Stand next to the participant to help him/her into the tandem position.

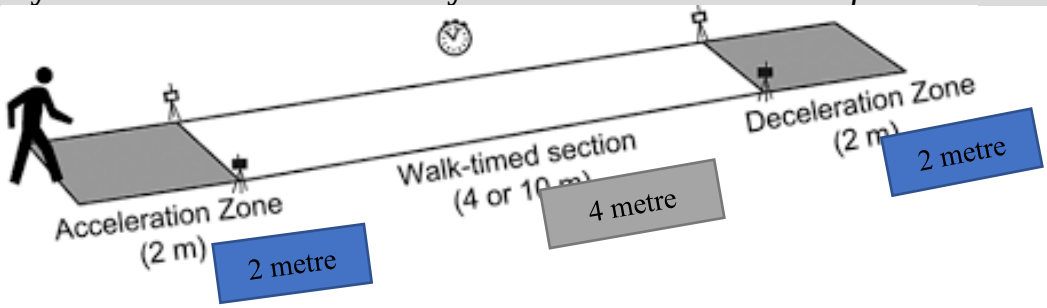
5. Supply just enough support to the participant's arm to prevent loss of balance.

6. When the participant has his/her feet together, ask ***"Are you ready?"***

7. Then let go and begin timing as you say, ***"Ready, begin."***

8. Stop the stopwatch and say ***"Stop"*** after 10 seconds or when the participant steps out of position or grabs your arm.

Short Physical Performance Battery Protocol: *4-metre Gait Speed*



Now I am going to observe how you normally walk. If you use a cane or other walking aid and you feel you need it to walk a short distance, then you may use it.

A. First Gait Speed Test

1. ***This is our walking course. I want you to walk to the other end of the course at your usual speed, just as if you were walking down the street to go to the store.***

2. Demonstrate the walk for the participant.

3. ***Walk all the way past the other end of the tape before you stop. I will walk with you. Do you feel*** this would be safe?

4. Have the participant stand with both feet touching the starting line.

5. ***When I want you to start, I will say: "Ready, begin."*** When the participant acknowledges this instruction say: "***Ready, begin."***

6. Press the start/stop button to start the stopwatch as the participant begins walking.

7. Walk behind and to the side of the participant.

8. Stop timing when one of the participant's feet is completely across the end line.

B. Second Gait Speed Test

1. ***Now I want you to repeat the walk. Remember to walk at your usual pace and go all the way past the other end of the course.***

2. Have the participant stand with both feet touching the starting line.

3. ***When I want you to start, I will say: "Ready, begin."*** When the participant acknowledges this instruction say: "Ready, begin."

4. Press the start/stop button to start the stopwatch as the participant begins walking.

5. Walk behind and to the side of the participant.

6. Stop timing when one of the participant's feet is completely across the end line.

Short Physical Performance Battery Protocol: *Sit-to-Stand 5* (*stand next to patient for safety)**:**

A. Single Chair Stand

1) ***Let's do the last movement test. Do you think it would be safe for you to try to stand up from a*** chair without using your arms?
2) ***The next test measures the strength in your legs.***
3) (Demonstrate and explain the procedure.) ***First, fold your arms across your chest and sit so that your feet are on the floor; then stand up keeping your arms folded across your chest.***
4) Please stand up keeping your arms folded across your chest. (Record result).
5) If participant cannot rise without using arms, say "Okay, try to stand up using your arms." This is the end of their test. Record result and go to the scoring page.

B. Repeated Chair Stands

1) ***Do you think it would be safe for you to try to stand up from a chair five times without using your arms?***
2) (Demonstrate and explain the procedure): ***Please stand up straight as QUICKLY as you can five times, without stopping in between. After standing up each time, sit down and then stand up again. Keep your arms folded across your chest. I'll be timing you with a stopwatch.***
3) When the participant is properly seated, say: ***"Ready? Stand"*** and begin timing.
4) Count out loud as the participant arises each time, up to five times.
5) Stop if participant becomes tired or short of breath during repeated chair stands.

6) Stop the stopwatch when he/she has straightened up completely for the fifth time.

Also stop:

- If participant uses his/her arms
- After 1 minute, if participant has not completed rises
- At your discretion, if concerned for participant's safety

If the participant stops and appears to be fatigued before completing the five stands, confirm this by asking ***"Can you continue?"***

If participant says "Yes," continue timing. If participant says "No," stop and reset the stopwatch

3-month follow up data collection form

ANTHROPOMETRIC DATA Today's Date: _____ /_____ /_____

Height: _____(m) Weight_____ (kg) BMI: _____(kg/m^2)

CLINICAL DATA

Any new diagnosis since discharged:

_____

Comorbidities (tick and circle):

☐ Myocardial Infarction	☐ Congestive Heart Failure	☐ Peripheral Vascular Disease	☐ Cerebrovascular Disease
☐ Dementia	☐ COPD	☐ Connective Tissue Disease	☐ Peptic Ulcer Disease
☐ Liver Disease (Mild/ Moderate/ Severe)		☐ Diabetes Mellitus (Uncomplicated / End-organ damage)	
☐ Hemiplegia	☐ Moderate to Severe CKD	☐ Solid tumour (Metastasis / No metastasis)	☐ Leukemia
☐ AIDS		☐ Malignant Lymphoma	
☐ Arthritis	☐ Osteoporosis	☐ Asthma	☐ ARDS/emphysema
☐ Angina	☐ neurological disease	☐ stroke/ TIA	☐ Upper GI disease (hermia/reflux)
☐ Depression	☐ Anxiety/panic disorders	☐ Visual impairment (cataracts, glaucoma. MD)	☐ Hearing impairment (very hard of hearing even with hearing aid)
☐ Degenerative disc disease (back disease, spinal stenosis or severe chronic back pain			

Others (please specify):_____

Total number of reported readmissions:_____

SOCIAL DATA

Any changes to living situations:

☐ Home alone ☐ Home with _____

☐ Residential Aged Care Facility/ Nursing Home: High level care **OR** Low level care *(please circle)*

☐ Other:

_____

NEW MEDICATIONS/SUPPLEMENTS BEING USED

Vitamin D/Calcium ☐ Yes ☐ No

Others (specify):_____

REMAINING DATA COLLECTION FORM EXACTLY THE SAME AS BASELINE

6-month follow up data collection form

ANTHROPOMETRIC DATA Today's Date: _____ /_____ /_____

Height: _____(m) Weight_____ (kg) BMI: _____(kg/m^2)

CLINICAL DATA

Any new diagnosis since discharged:

_____

Comorbidities (tick and circle):

☐ Myocardial Infarction	☐ Congestive Heart Failure	☐ Peripheral Vascular Disease	☐ Cerebrovascular Disease
☐ Dementia	☐ COPD	☐ Connective Tissue Disease	☐ Peptic Ulcer Disease
☐ Liver Disease (Mild/ Moderate/ Severe)		☐ Diabetes Mellitus (Uncomplicated / End-organ damage)	
☐ Hemiplegia	☐ Moderate to Severe CKD	☐ Solid tumour (Metastasis / No metastasis)	☐ Leukemia
☐ AIDS		☐ Malignant Lymphoma	
☐ Arthritis	☐ Osteoporosis	☐ Asthma	☐ ARDS/emphysema
☐ Angina	☐ neurological disease	☐ stroke/ TIA	☐ Upper GI disease (hermia/reflux)
☐ Depression	☐ Anxiety/panic disorders	☐ Visual impairment (cataracts, glaucoma. MD)	☐ Hearing impairment (very hard of hearing even with hearing aid)
☐ Degenerative disc disease (back disease, spinal stenosis or severe chronic back pain			

Others (please specify):_____

Total number of reported readmissions:_____

SOCIAL DATA

Any changes to living situations:

☐ Home alone ☐ Home with _____

☐ Residential Aged Care Facility/ Nursing Home: High level care **OR** Low level care *(please circle)*

☐ Other:

_____

NEW MEDICATIONS/SUPPLEMENTS BEING USED

Vitamin D/Calcium ☐ Yes ☐ No

Others (specify):_____

REMAINING DATA COLLECTION FORM EXACTLY THE SAME AS BASELINE, 3-MONTH DATA COLLECTION FORMS

APPENDIX 5: CHAPTER 5 INTERVIEW PROTOCOL

INDEPENDENCE STUDY
PRE-INTERVENTION INTERVIEW PROTOCOL

Instructions

Good morning (afternoon). My name is _____. Thank you for participating in our research. The purpose of this interview is to get your help on the design of a health program involving exercise and nutrition to restore health for older adults, starting in hospitals and followed up when they get home. You may refer to past experiences of such programs, if any. I must highlight that there are no right or wrong, desirable, or undesirable answers. I would like you to feel comfortable with saying what you really think and how you really feel. Please feel free to stop at any point during the interview for any reason(s) should you not wish to continue.

Audio recorder instructions

If it is okay with you, I will be recording our conversation. This is to get all the details but at the same time be able to carry on an attentive conversation with you. I assure you that your confidentiality is respected. I will be compiling a report which will contain all participants' comments without any reference to individuals.

Part 1. Introduction – Getting both parties comfortable with the conversation and brief information of what is frailty *(keep to 5-10 minutes)*

- Have you heard of the word frail or frailty? If yes, describe how you understand by being frail i.e., what does that mean to you and what comes to your mind?
- How about pre-frailty? Have you heard about it before? If yes, describe how you understand by being pre-frail i.e., what does that mean to you and what comes to your mind?

Interviewer can provide information if participant is not familiar with the term frailty: *Frailty is more common as people get older, but it is not something that all older adults get. Some common signs are weight loss, walking slower, weaker strength, more feelings of exhaustion, less physical activities. For example, Mr. Jackson has all 5 of the symptoms and is frail, his wife always feels exhausted, used to be 60kg but now 55kg and is pre-frail.*

Part 2. Open conversation – Seeking stories that provide general information about their attitudes about diet and exercise before and after hospital admission, how they think it will change when they return home.

- How is your diet and exercise before this trip to the hospital? Can you share with me your views on eating well and exercising?
- How do you think that changes when you are in the hospital?
- How important do you think nutrition and exercise when we are admitted in the hospital? And why?
- How do you feel about going home? Do you think it will change any of your diet and exercise practices?

- Have you come across any interventions or therapies that in your opinion will be beneficial to restore your strength back to re-admission?
- Have you had any experiences taking part in such exercise or nutrition support programs in the past? (*prompts: what did you like or dislike about it?)*
- What are some of the factors that make you want OR not want, to join such a health program? i.e. draw factors or barriers

Part 3. Clean up – Ask specific questions on the INDEPENDENCE protocol, feasibility
We have designed this program to help patients such as yourself make a better recovery to where you used to be before this admission, and we would like opinion on it. *Interviewer explains the components of the INDEPENDENCE intervention.*

- What do you think about the program?
- Are there things that you like about it? And why?
- Are there things you dislike? And why?
- What is your opinion on the frequency and length of the intervention? Why?
- What do you think about home visits? And how frequently might these home visits be conducted *i.e. weekly, fortnightly, monthly*?

When we are in the hospital, healthcare workers like the doctors and nurses can come by daily but this is not possible when the patient is home.

- What do you think about using telephone calls to check on the participants in the program? to ensure that people are eating well and getting along with the exercises to keep them fit, when they are home?
- Any other ideas that you might have that is not in the program and you would like to see?

Part 4. Wrap up – Ask if there is anything the respondent would like to add, anything they want you to know
We have come to the end of our questions. I would like to reassure you that all your responses are kept strictly confidential.

Now that you know what the interview was about, and you know what we've been talking about, is there anything else that we should have talked about but didn't?

Thank you for your time!

Prompts and probes

- *Can you explain the situation? What occurred?*
- *How did you respond to that?*
- *What did you do next?*
- *Who was involved?*
- *Was there anything else that you could have done?*
- *How often did it happen?*
- *How was it resolved?*
- *How would you have liked events to have worked?*
- *What do you mean by _____? Can you help me to understand this _____?*

APPENDIX 6: INDEPENDENCE PROGRAM RECRUITMENT VIDEO AND INTERVENTION GROUP RESOURCE BOOKLET

RECRUITMENT VIDEO

Screenshot; Link: https://www.youtube.com/watch?v=MxjwxaFF0xw

PROGRAM RESOURCE BOOKLET

INDEPENDENCE

an early and extended restorative program for adults above 65

Flinders UNIVERSITY

1

About INDEPENDENCE

We welcome you to the **INDEPENDENCE** program, aimed at helping you restore nutrition and strength.

This ***hospital to home program*** starts during admission at Flinders Medical Centre and continues 3 months after discharge, at your home. The continuity of care ensures that we are with you every step of the way through your journey of restoration.

We will work together to help you make positive changes to your life but you have the choice as to how far to take the programme. There will be ups and downs over the next few months. So, we should expect that, and together, will work through any difficulties that crop up.

After the ***4 home visits*** and ***4 telephone sessions***, we hope you will have the skills and the confidence to maintain the positive changes you choose to make.

We look forward to working with you over the next few months.

MAIN TEAM MEMBERS

Professor Michelle Miller
Principal Investigator, Flinders University
Adv. Accredited Practising Dietitian

Dr Yogesh Sharma
Principal Investigator, Flinders University
Senior Medical Consultant

Dr Alison Yaxley
Co-Investigator, Flinders University
Accredited Practising Dietitian

Dr Claire Baldwin
Co-investigator, Flinders University
Registered Physiotherapist

Mr Chad Han
PhD Candidate, Flinders University
Accredited Practising Dietitian
Mobile: 0452091109

MY SHARED SUPPORT PLAN

My ward visits

Name:.....
Start Date: ...../...../.....
D.O.B:...../...../.....

My planned visits for the next 3 months after I get home

HOME VISITS	1st visit	2nd visit	3rd visit	4th visit
Scheduled date/time				
Actual visit				

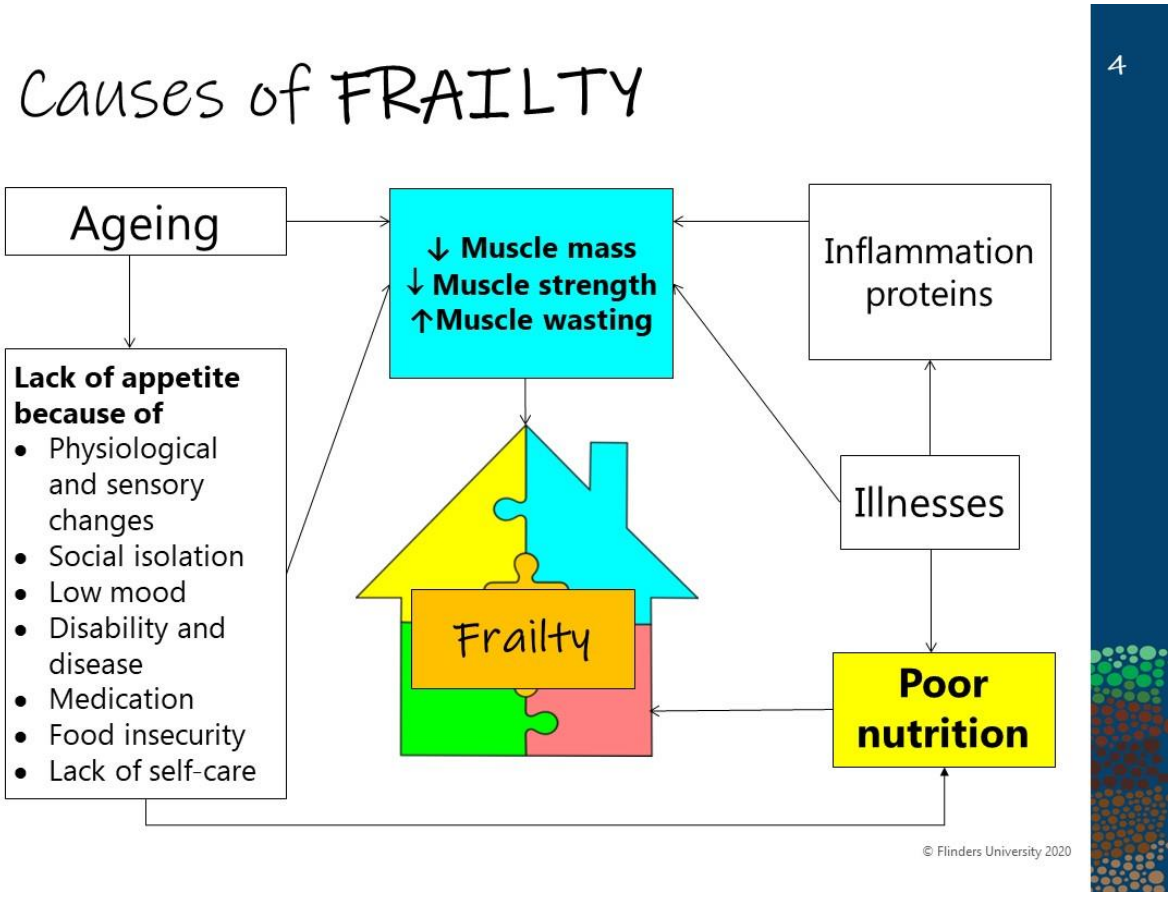
TELEPHONE CALLS	1st call	2nd call	3rd call	4th call
Scheduled date/time				
Actual call				

FRAILTY – what is it?

Frailty describes the process where our bodies progressively lose our existing reserves. When we are frail, events that are seemingly small such as a minor infection, change in medication or environment can cause major, unexpected changes to our health.

On the left is a picture representation of what it means by being frail. In the following page, you will see that nutrition plays a significant role in reducing frailty.

Reference: Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2001 Mar 1;56(3):M146-57.



APPENDIX 7: CHAPTER 7 INTERVIEW PROTOCOL

INDEPENDENCE STUDY
POST-PROGRAM INTERVIEW PROTOCOL

Instructions

Good morning (afternoon). My name is _____. Thank you for participating. In this interview, I will ask you about your experiences and opinions as a participant in the hospital-to-home support program which you took part in the past 3 months. The purpose is to get your perceptions of your experiences and opinions around this new service.
I must highlight that there are no right or wrong, desirable or undesirable answers. I would like you to feel comfortable with saying what you really think and how you really feel.

Audio recorder instructions

If it is okay with you, I will be recording our conversation. The purpose of this is so that I can get all the details but at the same time be able to carry on an attentive conversation with you. I assure you that all your comments will remain confidential. I will be compiling a report which will contain all participants' comments without any reference to individuals.

Part 1. Introduction – Getting both parties comfortable with the conversation *(keep to 5 minutes)*

- How is a typical day for you like since you were home from the last hospital stay?
- How long has it been since you started participating in this hospital-to-home support program?
- In your opinion, what part of the program has been working well for you?
- What has not been working well for you? What could be different?

Part 2. Open conversation – Seeking stories about their life, work or event about which you are trying to find out?

I will now ask you about your experience on changing your diet

- What are some of the experiences or help that enabled you to keep to the dietary advice and changes within this hospital-to-home program? (*prompts: what stopped you from achieving your diet goals?)*
- Have you had any experiences that prevented you from making the changes to your diet? (*prompts: what stopped you from achieving your diet goals?)*

Thank you for sharing, I will now ask you about your experience on doing home exercises

- I will first ask you about your experience about doing home exercises
- What are some of the experiences or help that enabled you to keep to the exercises with your health care professional? (*prompts: what help you achieve your exercise goals?)*
- Have you had any experiences that prevented you from keeping to the exercises? (*prompts: what stopped you from achieving your exercise goals?)*

Part 3. Clean up – Ask specific questions that have not been addressed, become provocative, or ask standard questions for comparison

- What are some of the factors that helped you stick to the dietary changes and exercises in past 3 months? (prompts: *Like something that helped you eat better and exercising)*
- What are some difficulties that you face when trying to keep to the dietary changes and exercises in past 3 months? (prompts: *Like something that stopped you from eating better and exercising)*

Part 4. Wrap up – Ask if there is anything the respondent would like to add, anything they want you to know

We have come to the end of our questions. I would like to reassure you that all your responses are kept strictly confidential.

Now that you know what the interview was about, and you know what we've been talking about, is there anything else you would like to share that we did not talk about?

Is there anything else that you would like to highlight to me?

Prompts and probes

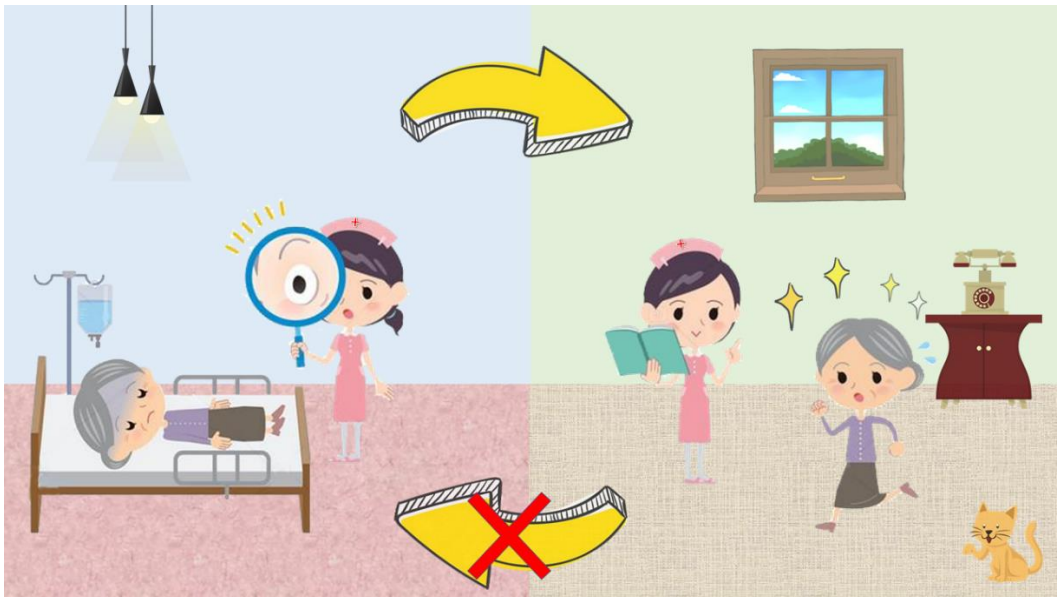
- *Can you explain the situation? What occurred?*
- *How did you respond to that?*
- *What did you do next?*
- *Who was involved?*
- *Was there anything else that you could have done?*
- *How often did it happen?*
- *Who was involved? How did they respond?*
- *How was it resolved?*
- *Was this situation unique? Repeated?*
- *How would you have liked events to have worked?*
- *What do you mean by _____? Can you help me to understand this _____?*

AWARDS AND ACHIEVEMENTS

Best oral presentation

The original research in Chapter Six was showcased in a Three Minute Thesis (3MT®) format at Flinders University in 2021 and given two awards – overall Winner and People's Choice award. The PhD candidate also represented South Australia in the finals of the Asia-pacific 3MT® competition 2021

- Link to video – https://vimeo.com/632502129



2021 Asia-Pacific 3MT® Final - Finalists Announced - Chad Yixian Han (Flinders Uni)

3 Minute Thesis <3MT@gradschool.uq.edu.au>
Tue 12/10/2021 2:30 PM
To: Chad Han <chad.han@flinders.edu.au>
Cc: Dani Milos <dani.milos@flinders.edu.au>; HDR Development <HDR.Development@flinders.edu.au>

1 attachments (618 KB)
2021 Virtual Asia-Pacific 3MT Final Order of Proceedings.pdf;

Dear Chad,

We are delighted to advise that you are one of the nine finalists that have progressed to the 2021 Virtual Asia-Pacific 3MT® Final!

Due to the global COVID-19 pandemic, the Asia-Pacific 3MT competition is once again being held online. The Virtual Asia-Pacific Final will showcase the 9 finalists, who were selected by 2 judging panels and one wildcard entrant from the Semi-Final People's Choice vote, from the 54 entrants this year representing Universities from across Australia, New Zealand, Japan, Hong Kong, Malaysia and Singapore. From everyone in the 3MT team we would like to take the time to acknowledge all the time and effort you put into creating your amazing 3MT presentations, thank you!

The PhD candidate was also invited to present the following:

- Han CY: **Nutritional considerations in older adults 101: Frailty, Malnutrition and Sarcopenia**. *Presented online to a Singapore multidisciplinary clinic, 25 November 2021*.
- Han CY: **INDEPENDENCE: a self-managed hospital-to-home frailty support program.** Presented at the Australian Association of Gerontology South Australian Presentation Evening – Life Disruption and Ageing Well, *24 May 2022.*

REFERENCES

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56.
2. Gobbens R, Luijkx K, Wijnen-Sponselee MT, Schols J. Towards an integral conceptual model of frailty. J Nutr Health Aging. 2010;14(3):175-81.
3. Halil M, Kizilarslanoglu MC, Kuyumcu ME, Yesil Y, Jentoft AC. Cognitive aspects of frailty: mechanisms behind the link between frailty and cognitive impairment. J Nutr Health Aging. 2015;19(3):276-83.
4. Hubbard RE, Maier AB, Hilmer SN, Naganathan V, Etherton-Beer C, Rockwood K. Frailty in the Face of COVID-19. Age Ageing. 2020.
5. Rodríguez-Mañas L, Féart C, Mann G, Viña J, Chatterji S, Chodzko-Zajko W, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci. 2013;68(1):62-7.
6. Al Saedi A, Feehan J, Phu S, Duque G. Current and emerging biomarkers of frailty in the elderly. Clin Interv Aging. 2019;14:389.
7. Sezgin D, Liew A, O'Donovan MR, O'Caoimh R. Pre-frailty as a multi-dimensional construct: A systematic review of definitions in the scientific literature. Geriatr Nurs. 2020;41(2):139-46.
8. Sezgin D, O'Donovan M, Woo J, Bandeen-Roche K, Liotta G, Fairhall N, et al. Early identification of frailty: Developing an international delphi consensus on pre-frailty. Arch Gerontol Geriatr. 2022;99:104586.
9. Zupo R, Castellana F, Bortone I, Griseta C, Sardone R, Lampignano L, et al. Nutritional domains in frailty tools: Working towards an operational definition of nutritional frailty. Ageing Res Rev. 2020;64:101148.
10. Bunt S, Steverink N, Olthof J, Van Der Schans C, Hobbelen J. Social frailty in older adults: a scoping review. Eur J Ageing. 2017;14(3):323-34.
11. O'Caoimh R, Molloy DW, Fitzgerald C, Velsen LV, Cabrita M, Nassabi MH, et al., editors. ICT-supported interventions targeting pre-frailty: Healthcare recommendations from the personalised ICT supported service for independent living and active ageing (PERSSILAA) study. International Conference on Information and Communication Technologies for Ageing Well and e-Health; 2017: Springer.
12. Dent E, Morley J, Cruz-Jentoft A, Woodhouse L, Rodríguez-Mañas L, Fried L, et al. Physical frailty: ICFSR international clinical practice guidelines for identification and management. J Nutr Health Aging. 2019;23(9):771-87.
13. Lang P-O, Michel J-P, Zekry D. Frailty syndrome: a transitional state in a dynamic process. Gerontology. 2009;55(5):539-49.
14. O'Caoimh R, Sezgin D, O'Donovan MR, Molloy DW, Clegg A, Rockwood K, et al. Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies. Age and Ageing. 2021;50(1):96-104.
15. Thompson MQ, Theou O, Karnon J, Adams RJ, Visvanathan R. Frailty prevalence in Australia: Findings from four pooled Australian cohort studies. Australas J Ageing. 2018;37(2):155-8.
16. Veronese N, Custodero C, Cella A, Demurtas J, Zora S, Maggi S, et al. Prevalence of multidimensional frailty and pre-frailty in older people in different settings: A systematic review and meta-analysis. Ageing Res Rev. 2021;72:101498.
17. Doody P, Aunger J, Asamane E, Greig CA, Lord J, Whittaker A. Frailty Levels In Geriatric Hospital paTients (FLIGHT)—the prevalence of frailty among geriatric populations within hospital ward settings: a systematic review protocol. BMJ open. 2019;9(8):e030147.
18. Bryant K, Sorich MJ, Woodman RJ, Mangoni AA. Validation and adaptation of the multidimensional prognostic index in an older Australian cohort. J Clin Med. 2019;8(11):1820.
19. Landi F, Calvani R, Tosato M, Martone AM, Ortolani E, Savera G, et al. Anorexia of aging: risk factors, consequences, and potential treatments. Nutrients. 2016;8(2):69.
20. Kojima G, Taniguchi Y, Kitamura A, Fujiwara Y. Is living alone a risk factor of frailty? A systematic review and meta-analysis. Ageing Res Rev. 2020;59:101048.
21. Vaughan L, Corbin AL, Goveas JS. Depression and frailty in later life: a systematic review.

Clin Interv Aging. 2015;10:1947.
22. Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, Martínez-Velilla N. The relationship between frailty and polypharmacy in older people: a systematic review. Br J Clin Pharmacol. 2018;84(7):1432-44.
23. Midão L, Brochado P, Almada M, Duarte M, Paúl C, Costa E. Frailty status and polypharmacy predict all-cause mortality in community dwelling older adults in Europe. Int J Environ Res. 2021;18(7):3580.
24. Rodriguez-Mañas L, Araujo de Carvalho I, Bhasin S, Bischoff-Ferrari H, Cesari M, Evans W, et al. ICFSR task force perspective on biomarkers for sarcopenia and frailty. J Frailty Aging. 2020;9(1):4-8.
25. Morley JE. Defining undernutrition (malnutrition) in older persons. J Nutr Health Aging; 2018. p. 308-10.
26. Skipper A, Coltman A, Tomesko J, Charney P, Porcari J, Piemonte TA, et al. Adult malnutrition (undernutrition) screening: an evidence analysis center systematic review. J Acad Nutr Diet. 2020;120(4):669-708.
27. Malone A, Hamilton C. The Academy of Nutrition and Dietetics/the American Society for Parenteral and Enteral Nutrition consensus malnutrition characteristics: application in practice. Nutr Clin Pract. 2013;28(6):639-50.
28. Sharma Y, Thompson C, Shari R, Hakendorf P, Miller M. Malnutrition in Acutely Unwell Hospitalized Elderly - "The Skeletons Are Still Rattling in the Hospital Closet". J Nutr Health Aging. 2017;21(10):1210-5.
29. Bistrian BR, Blackburn GL, Vitale J, Cochran D, Naylor J. Prevalence of malnutrition in general medical patients. JAMA. 1976;235(15):1567-70.
30. Gingrich A, Volkert D, Kiesswetter E, Thomanek M, Bach S, Sieber CC, et al. Prevalence and overlap of sarcopenia, frailty, cachexia and malnutrition in older medical inpatients. BMC Geriatr. 2019;19(1):120.
31. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition–an ESPEN consensus statement. Clin Nutr. 2015;34(3):335-40.
32. Laur CV, McNicholl T, Valaitis R, Keller HH. Malnutrition or frailty? Overlap and evidence gaps in the diagnosis and treatment of frailty and malnutrition. Appl Physiol Nutr Metab 2017;42(5):449-58.
33. Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the Mini Nutritional Assessment to detect frailty in hospitalised older people. J Nutr Health Aging. 2012;16(9):764-7.
34. Dorner T, Luger E, Tschinderle J, Stein K, Haider S, Kapan A, et al. Association between nutritional status (MNA®-SF) and frailty (SHARE-FI) in acute hospitalised elderly patients. J Nutr Health Aging. 2014;18(3):264-9.
35. Roy M, Gaudreau P, Payette H. A scoping review of anorexia of aging correlates and their relevance to population health interventions. Appetite. 2016;105:688-99.
36. Xue Q-L. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15.
37. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-62.
38. Cunha AIL, Veronese N, de Melo Borges S, Ricci NA. Frailty as a predictor of adverse outcomes in hospitalized older adults: a systematic review and meta-analysis. Ageing Res Rev. 2019;56:100960.
39. Le Cossec C, Perrine AL, Beltzer N, Fuhrman C, Carcaillon-Bentata L. Pre-Frailty, Frailty, and Multimorbidity: Prevalences and Associated Characteristics from Two French National Surveys. J Nutr Health Aging. 2016;20(8):860-9.
40. Rozzini R, Sabatini T, Cassinadri A, Boffelli S, Ferri M, Barbisoni P, et al. Relationship between functional loss before hospital admission and mortality in elderly persons with medical illness. J Gerontol A Biol Sci Med Sci. 2005;60(9):1180-3.
41. Covinsky KE, Martin GE, Beyth RJ, Justice AC, Sehgal AR, Landefeld CS. The relationship between clinical assessments of nutritional status and adverse outcomes in older hospitalized medical patients. J Am Geriatr Soc. 1999;47(5):532-8.
42. Khandelwal D, Goel A, Kumar U, Gulati V, Narang R, Dey A. Frailty is associated with

longer hospital stay and increased mortality in hospitalized older patients. J Nutr Health Aging. 2012;16(8):732-5.
43. Considine J, Fox K, Plunkett D, Mecner M, M OR, Darzins P. Factors associated with unplanned readmissions in a major Australian health service. Aust Health Rev. 2019;43(1):1-9.
44. Sirven N, Rapp T. The cost of frailty in France. Eur J Health Econ. 2017;18(2):243-53.
45. Bock J-O, König H-H, Brenner H, Haefeli WE, Quinzler R, Matschinger H, et al. Associations of frailty with health care costs–results of the ESTHER cohort study. BMC Health Serv Res. 2016;16(1):128.
46. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet. 2019;394(10206):1365-75.
47. Buckinx F, Rolland Y, Reginster J-Y, Ricour C, Petermans J, Bruyère O. Burden of frailty in the elderly population: perspectives for a public health challenge. Arch Public Health. 2015;73(1):19.
48. Ambagtsheer RC, Beilby J, Dabravolskaj J, Abbasi M, Archibald MM, Dent E. Application of an electronic Frailty Index in Australian primary care: data quality and feasibility assessment. Aging Clin Exp Res. 2019;31(5):653-60.
49. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. Lancet. 2019;394(10206):1376-86.
50. Faller JW, do Nascimento Pereira D, de Souza S, Nampo FK, de Souza Orlandi F, Matumoto S. Instruments for the detection of frailty syndrome in older adults: A systematic review. PLoS One. 2019;14(4).
51. Bruyère O, Buckinx F, Beaudart C, Reginster J-Y, Bauer J, Cederholm T, et al. How clinical practitioners assess frailty in their daily practice: an international survey. Aging Clin Exp Res. 2017;29(5):905-12.
52. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res. 2013;183(1):104-10.
53. Chimukangara M, Helm MC, Frelich MJ, Bosler ME, Rein LE, Szabo A, et al. A 5-item frailty index based on NSQIP data correlates with outcomes following paraesophageal hernia repair. Surg Endosc. 2017;31(6):2509-19.
54. Freiheit EA, Hogan DB, Eliasziw M, Meekes MF, Ghali WA, Partlo LA, et al. Development of a frailty index for patients with coronary artery disease. J Am Geriatr Soc. 2010;58(8):1526-31.
55. Goldstein J, Hubbard R, Moorhouse P, Andrew M. Feasibility of using information derived from a care partner to develop a frailty index based on comprehensive geriatric assessment. J Frailty Aging. 2013;2(1):15-21.
56. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489-95.
57. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing. 2006;35(5):526-9.
58. Hilmer SN, Perera V, Mitchell S, Murnion BP, Dent J, Bajorek B, et al. The assessment of frailty in older people in acute care. Australas J Ageing. 2009;28(4):182-8.
59. Metzelthin SF, Daniëls R, van Rossum E, de Witte L, van den Heuvel WJ, Kempen GI. The psychometric properties of three self-report screening instruments for identifying frail older people in the community. BMC Public Health. 2010;10(1):176.
60. Joseph B, Pandit V, Zangbar B, Kulvatunyou N, Tang A, O'Keeffe T, et al. Validating trauma-specific frailty index for geriatric trauma patients: a prospective analysis. J Am Coll Surg. 2014;219(1):10-7. e1.
61. Toosizadeh N, Mohler J, Najafi B. Assessing upper extremity motion: an innovative method to identify frailty. J Am Geriatr Soc. 2015;63(6):1181-6.
62. Gobbens RJ, van Assen MA, Luijkx KG, Wijnen-Sponselee MT, Schols JM. The Tilburg frailty indicator: psychometric properties. J Am Med Dir Assoc. 2010;11(5):344-55.
63. Graham MM, Galbraith PD, O'Neill D, Rolfson DB, Dando C, Norris CM. Frailty and outcome in elderly patients with acute coronary syndrome. Can J Cardiol. 2013;29(12):1610-5.
64. Keenan LG, O'Brien M, Ryan T, Dunne M, McArdle O. Assessment of older patients with cancer: Edmonton Frail Scale (EFS) as a predictor of adverse outcomes in older patients undergoing radiotherapy. J Geriatr Oncol. 2017;8(3):206-10.

65. Richards SJ, D'Souza J, Pascoe R, Falloon M, Frizelle FA. Prevalence of frailty in a tertiary hospital: A point prevalence observational study. PLoS One. 2019;14(7).
66. Giné-Garriga M, Roqué-Fíguls M, Coll-Planas L, Sitja-Rabert M, Salvà A. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: a systematic review and meta-analysis. Arch Phys Med Rehabil. 2014;95(4):753-69. e3.
67. Ng TP, Feng L, Nyunt MS, Feng L, Niti M, Tan BY, et al. Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal Among Older Adults: A Randomized Controlled Trial. Am J Med. 2015;128(11):1225-36.e1.
68. Hsieh TJ, Su SC, Chen CW, Kang YW, Hu MH, Hsu LL, et al. Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial. Int J Behav Nutr Phys Act. 2019;16(1):119.
69. Lozano-Montoya I, Correa-Perez A, Abraha I, Soiza RL, Cherubini A, O'Mahony D, et al. Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview - the SENATOR Project ONTOP Series. Clin Interv Aging. 2017;12:721-40.
70. Abizanda P, López MD, García VP, Estrella JdD, da Silva González Á, Vilardell NB, et al. Effects of an Oral Nutritional Supplementation Plus Physical Exercise Intervention on the Physical Function, Nutritional Status, and Quality of Life in Frail Institutionalized Older Adults: The ACTIVNES Study. J Am Med Dir Assoc. 2015;16(5):439.e9-.e16.
71. Negm AM, Kennedy CC, Thabane L, Veroniki AA, Adachi JD, Richardson J, et al. Management of Frailty: A Systematic Review and Network Meta-analysis of Randomized Controlled Trials. J Am Med Dir Assoc. 2019;20(10):1190-8.
72. Daly RM, Iuliano S, Fyfe J, Scott D, Kirk B, Thompson M, et al. Screening, Diagnosis and Management of Sarcopenia and Frailty in Hospitalized Older Adults: Recommendations from the Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR) Expert Working Group. J Nutr Health Aging. 2022:1-15.
73. Rasmussen NM, Belqaid K, Lugnet K, Nielsen AL, Rasmussen HH, Beck AM. Effectiveness of multidisciplinary nutritional support in older hospitalised patients: A systematic review and meta-analyses. Clinical nutrition ESPEN. 2018;27:44-52.
74. Wilkinson R, Arensberg ME, Hickson M, Dwyer JT. Frailty Prevention and Treatment: Why Registered Dietitian Nutritionists Need to Take Charge. J Acad Nutr Diet. 2017;117(7):1001-9.
75. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: Cochrane book series. 2008.
76. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006-12.
77. Veritas Health Innovation. Covidence systematic review software. Veritas Health Innovation Melbourne, VIC; 2017.
78. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
79. Farrah K, Young K, Tunis MC, Zhao L. Risk of bias tools in systematic reviews of health interventions: an analysis of PROSPERO-registered protocols. Systematic reviews. 2019;8(1):280.
80. RevMan. Review manager (revman)[computer program]. version 5.3. The Nordic Cochrane Centre, The Cochrane Collaboration Copenhagen, Denmark; 2014.
81. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-60.
82. Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med. 2011;364(13):1218-29.
83. Armamento-Villareal R, Aguirre LE, Qualls C, Villareal DT. Effect of lifestyle intervention on the hormonal profile of frail, obese older men. J Nutr Health Aging. 2016;20(3):334-40.
84. Cameron ID, Fairhall N, Langron C, Lockwood K, Monaghan N, Aggar C, et al. A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial. BMC Med. 2013;11:65.
85. Fairhall N, Sherrington C, Kurrle SE, Lord SR, Lockwood K, Cameron ID. Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people:

randomised controlled trial. BMC Med. 2012;10:120.
86. Fairhall N, Sherrington C, Lord SR, Kurrle SE, Langron C, Lockwood K, et al. Effect of a multifactorial, interdisciplinary intervention on risk factors for falls and fall rate in frail older people: a randomised controlled trial. Age Ageing. 2014;43(5):616-22.
87. Fairhall N, Sherrington C, Kurrle SE, Lord SR, Lockwood K, Howard K, et al. Economic evaluation of a multifactorial, interdisciplinary intervention versus usual care to reduce frailty in frail older people. J Am Med Dir Assoc. 2015;16(1):41-8.
88. Luger E, Dorner TE, Haider S, Kapan A, Lackinger C, Schindler K. Effects of a Home-Based and Volunteer-Administered Physical Training, Nutritional, and Social Support Program on Malnutrition and Frailty in Older Persons: A Randomized Controlled Trial. J Am Med Dir Assoc. 2016;17(7):671.e9-.e16.
89. Haider S, Dorner TE, Luger E, Kapan A, Titze S, Lackinger C, et al. Impact of a Home-Based Physical and Nutritional Intervention Program Conducted by Lay-Volunteers on Handgrip Strength in Prefrail and Frail Older Adults: A Randomized Control Trial. PLoS ONE [Electronic Resource]. 2017;12(1):e0169613.
90. Winzer E, Dorner TE, Grabovac I, Haider S, Kapan A, Lackinger C, et al. Behavior changes by a buddy-style intervention including physical training, and nutritional and social support. Geriatr Gerontol Int. 2019;19(4):323-9.
91. Kapan A, Luger E, Haider S, Titze S, Schindler K, Lackinger C, et al. Fear of falling reduced by a lay led home-based program in frail community-dwelling older adults: A randomised controlled trial. Arch Gerontol Geriatr. 2017;68:25-32.
92. Kapan A, Winzer E, Haider S, Titze S, Schindler K, Lackinger C, et al. Impact of a lay-led home-based intervention programme on quality of life in community-dwelling pre-frail and frail older adults: a randomized controlled trial. BMC Geriatr. 2017;17:1-11.
93. Arrieta H, Astrugue C, Regueme S, Durrieu J, Maillard A, Rieger A, et al. Effects of a physical activity programme to prevent physical performance decline in onco-geriatric patients: a randomized multicentre trial. J Cachexia Sarcopenia Muscle. 2019;10(2):287-97.
94. Niccoli S, Kolobov A, Bon T, Rafilovich S, Munro H, Tanner K, et al. Whey Protein Supplementation Improves Rehabilitation Outcomes in Hospitalized Geriatric Patients: A Double Blinded, Randomized Controlled Trial. J Nutr Gerontol Geriatr. 2017;36(4):149-65.
95. Milte R, Miller MD, Crotty M, Mackintosh S, Thomas S, Cameron ID, et al. Cost-effectiveness of individualized nutrition and exercise therapy for rehabilitation following hip fracture. J Rehabil Med. 2016;48(4):378-85.
96. Singh NA, Quine S, Clemson LM, Williams EJ, Williamson DA, Stavrinos TM, et al. Effects of high-intensity progressive resistance training and targeted multidisciplinary treatment of frailty on mortality and nursing home admissions after hip fracture: a randomized controlled trial. J Am Med Dir Assoc. 2012;13(1):24-30.
97. Blanc-Bisson C, Dechamps A, Gouspillou G, Dehail P, Bourdel-Marchasson I. A randomized controlled trial on early physiotherapy intervention versus usual care in acute car unit for elderly: Potential benefits in light of dietary intakes. J Nutr Health Aging. 2008;12(6):395-9.
98. Miller MD, Crotty M, Whitehead C, Bannerman E, Daniels LA. Nutritional supplementation and resistance training in nutritionally at risk older adults following lower limb fracture: a randomized controlled trial. Clin Rehabil. 2006;20(4):311-23.
99. Rodriguez-Manas L, Laosa O, Vellas B, Paolisso G, Topinkova E, Oliva-Moreno J, et al. Effectiveness of a multimodal intervention in functionally impaired older people with type 2 diabetes mellitus. J Cachexia Sarcopenia Muscle. 2019;10(4):721-33.
100. Azad N, Molnar F, Byszewski A. Lessons learned from a multidisciplinary heart failure clinic for older women: a randomised controlled trial. Age Ageing. 2008;37(3):282-7.
101. Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BMC Geriatr. 2010;10(1):57.
102. Cameron ID. Coordinated multidisciplinary rehabilitation after hip fracture. Disabil Rehabil. 2005;27(18-19):1081-90.
103. Haider S, Grabovac I, Winzer E, Kapan A, Schindler KE, Lackinger C, et al. Change in inflammatory parameters in prefrail and frail persons obtaining physical training and nutritional

support provided by lay volunteers: A randomized controlled trial. PLoS One. 2017;12(10).
104. Thomas SK, Humphreys KJ, Miller MD, Cameron ID, Whitehead C, Kurrle S, et al. Individual nutrition therapy and exercise regime: a controlled trial of injured, vulnerable elderly (INTERACTIVE trial). BMC Geriatr. 2008;8(1):4.
105. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, Cano A, et al. Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults: a systematic review. JBI database of systematic reviews and implementation reports. 2018;16(1):140.
106. De Vries N, Staal J, Van Ravensberg C, Hobbelen J, Rikkert MO, Nijhuis-Van der Sanden M. Outcome instruments to measure frailty: a systematic review. Ageing Res Rev. 2011;10(1):104-14.
107. Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielen E. Effects of multi-domain interventions in (pre) frail elderly on frailty, functional, and cognitive status: a systematic review. Clin interv Aging. 2017;12:873.
108. Tarazona-Santabalbina FJ, Gomez-Cabrera MC, Perez-Ros P, Martinez-Arnau FM, Cabo H, Tsaparas K, et al. A Multicomponent Exercise Intervention that Reverses Frailty and Improves Cognition, Emotion, and Social Networking in the Community-Dwelling Frail Elderly: A Randomized Clinical Trial. J Am Med Dir Assoc. 2016;17(5):426-33.
109. Kim C-O, Lee K-R. Preventive effect of protein-energy supplementation on the functional decline of frail older adults with low socioeconomic status: a community-based randomized controlled study. J Gerontol A Biol Sci Med Sci. 2013;68(3):309-16.
110. Denison HJ, Cooper C, Sayer AA, Robinson SM. Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. Clin Interv Aging. 2015;10:859.
111. Munk T, Tolstrup U, Beck AM, Holst M, Rasmussen HH, Hovhannisyan K, et al. Individualised dietary counselling for nutritionally at-risk older patients following discharge from acute hospital to home: a systematic review and meta-analysis. J Hum Nutr Diet. 2016;29(2):196-208.
112. Beck AM, Kjær S, Hansen BS, Storm RL, Thal-Jantzen K, Bitz C. Follow-up home visits with registered dietitians have a positive effect on the functional and nutritional status of geriatric medical patients after discharge: a randomized controlled trial. Clin Rehabil. 2013;27(6):483-93.
113. Fairhall N, Sherrington C, Cameron ID, Kurrle SE, Lord SR, Lockwood K, et al. A multifactorial intervention for frail older people is more than twice as effective among those who are compliant: complier average causal effect analysis of a randomised trial. J Physiother. 2017;63(1):40-4.
114. Brisswalter J, Collardeau M, René A. Effects of acute physical exercise characteristics on cognitive performance. Sports Med. 2002;32(9):555-66.
115. Klímová B, Vališ M. Nutritional interventions as beneficial strategies to delay cognitive decline in healthy older individuals. Nutrients. 2018;10(7):905.
116. Schättin A, Baur K, Stutz J, Wolf P, de Bruin ED. Effects of physical exercise combined with nutritional supplements on aging brain related structures and functions: a systematic review. Front Aging Neurosci. 2016;8:161.
117. Hardman RJ, Kennedy G, Macpherson H, Scholey AB, Pipingas A. A randomised controlled trial investigating the effects of Mediterranean diet and aerobic exercise on cognition in cognitively healthy older people living independently within aged care facilities: the Lifestyle Intervention in Independent Living Aged Care (LIILAC) study protocol [ACTRN12614001133628]. Nutr J. 2015;14(1):53.
118. Drummond MF, Stoddart GL. Economic analysis and clinical trials. Control Clin Trials. 1984;5(2):115-28.
119. Ruikes FG, Adang EM, Assendelft WJ, Schers HJ, Koopmans RT, Zuidema SU. Cost-effectiveness of a multicomponent primary care program targeting frail elderly people. BMC Fam Pract. 2018;19(1):62.
120. Han CY, Miller M, Yaxley A, Baldwin C, Woodman R, Sharma Y. Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a systematic review and meta-analysis. BMJ Open. 2020;10(12):e040146.
121. Cruz-Jentoft AJ, Woo J. Nutritional interventions to prevent and treat frailty. Curr Opin Clin Nutr Metab Care. 2019;22(3):191-5.
122. Pohju A, Belqaid K, Brandt C, Lugnet K, Nielsen A. Adding a Dietitian to a Danish Liaison-

Team after discharge of geriatric patients at nutritional risk may save health care costs. Aging Sci. 2016;4(159):2.
123. Sun Y, You W, Almeida F, Estabrooks P, Davy B. The effectiveness and cost of lifestyle interventions including nutrition education for diabetes prevention: a systematic review and meta-analysis. J Acad Nutr Diet. 2017;117(3):404-21. e36.
124. Napoli N, Shah K, Waters DL, Sinacore DR, Qualls C, Villareal DT. Effect of weight loss, exercise, or both on cognition and quality of life in obese older adults. Am J Clin Nutr 2014;100(1):189-98.
125. Rydwik E, Lammes E, Frändin K, Akner G. Effects of a physical and nutritional intervention program for frail elderly people over age 75. A randomized controlled pilot treatment trial. Aging Clin Exp Res. 2008;20(2):159-70.
126. Lammes E, Rydwik E, Akner G. Effects of nutritional intervention and physical training on energy intake, resting metabolic rate and body composition in frail elderly. A randomised, controlled pilot study. J Nutr Health Aging. 2012;16(2):162-7.
127. Rydwik E, Frändin K, Akner G. Effects of a physical training and nutritional intervention program in frail elderly people regarding habitual physical activity level and activities of daily living—A randomized controlled pilot study. Arch Gerontol Geriatr. 2010;51(3):283-9.
128. van Lieshout M, Bleijenberg N, Schuurmans M, de Wit N. The Effectiveness of a Proactive Multicomponent Intervention Program on Disability in Independently Living Older People: A Randomized Controlled Trial. J Nutr Health Aging. 2018;22(9):1051-9.
129. Terp R, Jacobsen KO, Kannegaard P, Larsen A-M, Madsen OR, Noiesen E. A nutritional intervention program improves the nutritional status of geriatric patients at nutritional risk—a randomized controlled trial. Clin Rehabil. 2018;32(7):930-41.
130. Pedersen JL, Pedersen PU, Damsgaard E. Early nutritional follow-up after discharge prevents deterioration of ADL functions in malnourished, independent, geriatric patients who live alone–A randomized clinical trial. J Nutr Health Aging. 2016;20(8):845-53.
131. Wu S-Y, Hsu L-L, Hsu C-C, Hsieh T-J, Su S-C, Peng Y-W, et al. Dietary education with customised dishware and food supplements can reduce frailty and improve mental well-being in elderly people: A single-blind randomized controlled study. Asia Pac J Clin Nutr. 2018;27(5):1018.
132. Kwon J, Yoshida Y, Yoshida H, Kim H, Suzuki T, Lee Y. Effects of a combined physical training and nutrition intervention on physical performance and health-related quality of life in prefrail older women living in the community: a randomized controlled trial. J Am Med Dir Assoc. 2015;16(3):263. e1-. e8.
133. Porter Starr KN, Pieper CF, Orenduff MC, McDonald SR, McClure LB, Zhou R, et al. Improved function with enhanced protein intake per meal: a pilot study of weight reduction in frail, obese older adults. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences. 2016;71(10):1369-75.
134. Neelemaat F, Bosmans JE, Thijs A, Seidell JC. Post-discharge nutritional support in malnourished elderly individuals improves functional limitations. J Am Med Dir Assoc. 2011;12(4):295-301.
135. Gray-Donald K, Payette H, Boutier V. Randomized clinical trial of nutritional supplementation shows little effect on functional status among free-living frail elderly. J Nutr. 1995;125(12):2965-71.
136. Johnson S, McLeod B, Gupta S, McLeod K. Impact of a home-based nutrition and exercise intervention in improving functional capacity associated with falls among rural seniors in Canada. Quality in Ageing and Older Adults. 2018.
137. Kicinski M, Springate DA, Kontopantelis E. Publication bias in meta-analyses from the Cochrane Database of Systematic Reviews. Stat Med. 2015;34(20):2781-93.
138. Vasiloglou MF, Fletcher J, Poulia K-A. Challenges and Perspectives in Nutritional Counselling and Nursing: A Narrative Review. J Clin Med. 2019;8(9):1489.
139. Rivera-Torres S, Fahey TD, Rivera MA. Adherence to exercise programs in older adults: informative report. Gerontol Geriatr Med. 2019;5:2333721418823604.
140. Junius-Walker U, Onder G, Soleymani D, Wiese B, Albaina O, Bernabei R, et al. The essence of frailty: a systematic review and qualitative synthesis on frailty concepts and definitions. Eur J Intern Med. 2018;56:3-10.

141. Rockwood K, Howlett SE. Fifteen years of progress in understanding frailty and health in aging. BioMed Central; 2018. p. 1-4.
142. Ligthart-Melis GC, Luiking YC, Kakourou A, Cederholm T, Maier AB, de van der Schueren MA. Frailty, sarcopenia, and malnutrition frequently (co-) occur in hospitalized older adults: a systematic review and meta-analysis. J Am Med Dir Assoc. 2020.
143. Pangman VC, Sloan J, Guse L. An examination of psychometric properties of the mini-mental state examination and the standardized mini-mental state examination: implications for clinical practice. Appl Nurs Res. 2000;13(4):209-13.
144. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.
145. Australia Bureau of Statistics. Sample Size Calculator 2019 [Available from: https://www.abs.gov.au/websitedbs/D3310114.nsf/home/Sample+Size+Calculator.
146. Joosten E, Demuynck M, Detroyer E, Milisen K. Prevalence of frailty and its ability to predict in hospital delirium, falls, and 6-month mortality in hospitalized older patients. BMC geriatrics. 2014;14(1):1-9.
147. Andela RM, Dijkstra A, Slaets JP, Sanderman R. Prevalence of frailty on clinical wards: description and implications. International journal of nursing practice. 2010;16(1):14-9.
148. Chen Y, Almirall-Sánchez A, Mockler D, Adrion E, Domínguez-Vivero C, Romero-Ortuño R. Hospital-associated deconditioning: Not only physical, but also cognitive. Int J Geriatr Psychiatry. 2022.
149. Pilgrim AL, Baylis D, Jameson K, Cooper C, Sayer AA, Robinson S, et al. Measuring appetite with the simplified nutritional appetite questionnaire identifies hospitalised older people at risk of worse health outcomes. J Nutr Health Aging. 2016;20(1):3-7.
150. Zadak Z, Hyspler R, Ticha A, Vlcek J. Polypharmacy and malnutrition. Curr Opin Clin Nutr Metab Care 2013;16(1):50-5.
151. Paul JA, Whittington RA, Baldwin MR. Critical illness and the frailty syndrome: mechanisms and potential therapeutic targets. Anesthesia and analgesia. 2020;130(6):1545.
152. Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment—a review of the evidence and causal mechanisms. Ageing Res Rev. 2013;12(4):840-51.
153. National Institute for Health Care Excellence. Emergency and acute medical care in over 16s: service delivery and organisation: National Institute for Health and Care Excellence (NICE); 2018.
154. Nguyen AT, Nguyen LH, Nguyen TX, Nguyen TTH, Nguyen HTT, Nguyen TN, et al. Frailty prevalence and association with health-related quality of life impairment among rural community-dwelling older adults in Vietnam. Int J Environ Res. 2019;16(20):3869.
155. Eyigor S, Kutsal Y, Duran E, Huner B, Paker N, Durmus B, et al. Frailty prevalence and related factors in the older adult—FrailTURK Project. Age. 2015;37(3):1-13.
156. Dekker-van Weering M, Jansen-Kosterink S, Frazer S, Vollenbroek-Hutten M. User experience, actual use, and effectiveness of an information communication technology-supported home exercise program for pre-frail older adults. Front Med. 2017;4:208.
157. Jadczak AD, Dollard J, Mahajan N, Visvanathan R. The perspectives of pre-frail and frail older people on being advised about exercise: a qualitative study. Fam Pract. 2018;35(3):330-5.
158. Blanco-Reina E, Aguilar-Cano L, García-Merino MR, Ocaña-Riola R, Valdellós J, Bellido-Estévez I, et al. Assessing Prevalence and Factors Related to Frailty in Community-Dwelling Older Adults: A Multinomial Logistic Analysis. J Clin Med. 2021;10(16):3576.
159. Herr M, Robine JM, Pinot J, Arvieu JJ, Ankri J. Polypharmacy and frailty: prevalence, relationship, and impact on mortality in a French sample of 2350 old people. Pharmacoepidemiology and drug safety. 2015;24(6):637-46.
160. Sharma Y, Avina P, Ross E, Horwood C, Hakendorf P, Thompson C. The overlap of frailty and malnutrition in older hospitalised patients: An observational study. Asia Pac J Clin Nutr. 2021;30(3):457-63.
161. Zhao Y, Lin T, Hou L, Zhang M, Peng X, Xie D, et al. Association Between Geriatric Nutritional Risk Index and Frailty in Older Hospitalized Patients. Clin Interv Aging. 2021;16:1241.
162. Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health. 2018;3(7):e323-e32.

163. Verloo H, Goulet C, Morin D, von Gunten A. Association between frailty and delirium in older adult patients discharged from hospital. Clin Interv Aging. 2016;11:55.
164. Chatindiara I, Allen J, Popman A, Patel D, Richter M, Kruger M, et al. Dysphagia risk, low muscle strength and poor cognition predict malnutrition risk in older adults at hospital admission. BMC geriatrics. 2018;18(1):1-8.
165. Parker S, McCue P, Phelps K, McCleod A, Arora S, Nockels K, et al. What is comprehensive geriatric assessment (CGA)? An umbrella review. Age and ageing. 2018;47(1):149-55.
166. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, Cano A, et al. Predicting risk and outcomes for frail older adults: an umbrella review of frailty screening tools. JBI Database Syst Rev Implement Rep. 2017;15(4):1154.
167. Soysal P, Isik AT, Arik F, Kalan U, Eyvaz A, Veronese N. Validity of the mini-nutritional assessment scale for evaluating frailty status in older adults. J Am Med Dir Assoc. 2019;20(2):183-7.
168. Sharma Y, Miller M, Kaambwa B, Shahi R, Hakendorf P, Horwood C, et al. Malnutrition and its association with readmission and death within 7 days and 8–180 days postdischarge in older patients: a prospective observational study. BMJ open. 2017;7(11):e018443.
169. Ottery FD, Isenring E, Kasenic S, DeBolt SP, Sealy M, Jager-Wittenaar H. Patient-generated subjective global assessment: Hanzehogeschool Groningen; 2015.
170. Marshall S, Young A, Bauer J, Isenring E. Malnutrition in geriatric rehabilitation: prevalence, patient outcomes, and criterion validity of the scored patient-generated subjective global assessment and the mini nutritional assessment. J Acad Nutr Diet. 2016;116(5):785-94.
171. Haukoos JS, Lewis RJ. Advanced statistics: bootstrapping confidence intervals for statistics with “difficult” distributions. Acad Emer Med. 2005;12(4):360-5.
172. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biometrical Journal: J Math Biosc. 2005;47(4):458-72.
173. Clayton P. CUTPT: Stata module for empirical estimation of cutpoint for a diagnostic test. 2013.
174. Liu X. Classification accuracy and cut point selection. Stat Med. 2012;31(23):2676-86.
175. Chao C-T, Wang J, Chien K-L. Both pre-frailty and frailty increase healthcare utilization and adverse health outcomes in patients with type 2 diabetes mellitus. Cardiovasc Diabetol. 2018;17(1):1-13.
176. Bollwein J, Volkert D, Diekmann R, Kaiser M, Uter W, Vidal K, et al. Nutritional status according to the mini nutritional assessment (MNA®) and frailty in community dwelling older persons: a close relationship. J Nutr Health Aging. 2013;17(4):351-6.
177. van Kan GA, Rolland Y, Houles M, Gillette-Guyonnet S, Soto M, Vellas B. The assessment of frailty in older adults. Clinics in Geriatr Med. 2010;26(2):275-86.
178. Podsiadlo D, Richardson S. The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142-8.
179. Mertz KH, Reitelseder S, Jensen M, Lindberg J, Hjulmand M, Schucany A, et al. Influence of between-limb asymmetry in muscle mass, strength, and power on functional capacity in healthy older adults. Scand J Med Sci Sports. 2019;29(12):1901-8.
180. Dominguez LJ, Barbagallo M. The relevance of nutrition for the concept of cognitive frailty. Current opinion in clinical nutrition and metabolic care. 2017;20(1):61-8.
181. Pek K, Chew J, Lim JP, Yew S, Tan CN, Yeo A, et al. Social frailty is independently associated with mood, nutrition, physical performance, and physical activity: Insights from a theory-guided approach. Int J Environ Res. 2020;17(12):4239.
182. Lorenzo-López L, López-López R, Maseda A, Buján A, Rodríguez-Villamil JL, Millán-Calenti JC. Changes in frailty status in a community-dwelling cohort of older adults: The VERISAÚDE study. Maturitas. 2019;119:54-60.
183. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Qual Life Res. 2010;19(4):539-49.
184. van de Ree CL, Landers MJ, Kruithof N, de Munter L, Slaets JP, Gosens T, et al. Effect of frailty on quality of life in elderly patients after hip fracture: a longitudinal study. BMJ open. 2019;9(7):e025941.
185. Kistler EA, Nicholas JA, Kates SL, Friedman SM. Frailty and short-term outcomes in patients

with hip fracture. Geriatric orthopaedic surgery & rehabilitation. 2015;6(3):209-14.
186. Lin H-S, Watts J, Peel N, Hubbard R. Frailty and post-operative outcomes in older surgical patients: a systematic review. BMC Geriatr. 2016;16(1):157.
187. Hu F, Jiang C, Shen J, Tang P, Wang Y. Preoperative predictors for mortality following hip fracture surgery: a systematic review and meta-analysis. Injury. 2012;43(6):676-85.
188. Panula J, Pihlajamäki H, Mattila VM, Jaatinen P, Vahlberg T, Aarnio P, et al. Mortality and cause of death in hip fracture patients aged 65 or older-a population-based study. BMC Musculoskelet Disord. 2011;12(1):1-6.
189. Ftouh S, Morga A, Swift C. Management of hip fracture in adults: summary of NICE guidance. BMJ. 2011;342:d3304.
190. Handoll HH, Cameron ID, Mak JC, Finnegan TP. Multidisciplinary rehabilitation for older people with hip fractures. Cochrane Database Syst Rev. 2009(4).
191. Mak JC, Cameron ID, March LM. Evidence-based guidelines for the management of hip fractures in older persons: an update. Med J Aust. 2010;192(1):37-41.
192. Riemen AH, Hutchison JD. The multidisciplinary management of hip fractures in older patients. Orthopaedics and trauma. 2016;30(2):117-22.
193. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Falls prevention over 2 years: a randomized controlled trial in women 80 years and older. Age Ageing. 1999;28(6):513-8.
194. Worsfold C, Simpson JM. Standardisation of a three-metre walking test for elderly people. Physiotherapy. 2001;87(3):125-32.
195. Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. J Gerontol. 1981;36(4):428-34.
196. Bohannon RW. Alternatives for measuring knee extension strength of the elderly at home. Clin Rehabil. 1998;12(5):434-40.
197. Schaubert KL, Bohannon RW. Reliability and validity of three strength measures obtained from community-dwelling elderly persons. J Strength Cond Res. 2005;19(3):717.
198. Langley F. The reliability and validity of the modified Berg Balance Scale: University of South Australia; 2007.
199. McLennan W, McLennan W, Podger AS. National nutrition survey users' guide, 1995: Australian Bureau of Statistics [and] Commonwealth Department of Health and …; 1998.
200. Hawthorne G, Richardson J, Osborne R. The Assessment of Quality of Life (AQoL) instrument: a psychometric measure of health-related quality of life. Qual Life Res. 1999;8(3):209-24.
201. Lane P. Handling drop-out in longitudinal clinical trials: a comparison of the LOCF and MMRM approaches. Pharm Stat. 2008;7(2):93-106.
202. Vickers AJ, Altman DG. Analysing controlled trials with baseline and follow up measurements. BMJ. 2001;323(7321):1123-4.
203. Magaziner J, Mangione KK, Orwig D, Baumgarten M, Magder L, Terrin M, et al. Effect of a multicomponent home-based physical therapy intervention on ambulation after hip fracture in older adults: the CAP randomized clinical trial. JAMA. 2019;322(10):946-56.
204. Mangione KK, Craik RL, Palombaro KM, Tomlinson SS, Hofmann MT. Home-based leg-strengthening exercise improves function 1 year after hip fracture: a randomized controlled study. J Am Geriatr Soc. 2010;58(10):1911-7.
205. Mangione KK, Craik RL, Lopopolo R, Tomlinson JD, Brenneman SK. Predictors of gait speed in patients after hip fracture. Physiother Can. 2008.
206. Mantel A, Trapuzzano A, Chizmar S, Haffke L, Dawson N. An investigation of the predictors of comfortable and fast gait speed in community-dwelling older adults. J Geriatr Phys Ther. 2019;42(4):E62-E8.
207. Ekström H, Elmståhl S. Pain and fractures are independently related to lower walking speed and grip strength: results from the population study “Good Ageing in Skåne”. Acta orthopaedica. 2006;77(6):902-11.
208. Bell JJ, Bauer JD, Capra S, Pulle RC. Multidisciplinary, multi-modal nutritional care in acute hip fracture inpatients–results of a pragmatic intervention. Clin Nutr. 2014;33(6):1101-7.
209. Anbar R, Beloosesky Y, Cohen J, Madar Z, Weiss A, Theilla M, et al. Tight calorie control in geriatric patients following hip fracture decreases complications: a randomized, controlled study. Clin Nutr. 2014;33(1):23-8.

210. Nordström P, Thorngren K-G, Hommel A, Ziden L, Anttila S. Effects of geriatric team rehabilitation after hip fracture: meta-analysis of randomized controlled trials. J Am Med Dir Assoc. 2018;19(10):840-5.
211. Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. Lancet. 2019;393(10188):2312-21.
212. Kashef MA, Giugliano G. Legacy effect of statins: 20-year follow up of the West of Scotland Coronary Prevention Study (WOSCOPS). Glob Cardiol Sci. 2016;2016(4).
213. Volpe M, Cosentino F, Tocci G, Palano F, Paneni F. Antihypertensive therapy in diabetes: the legacy effect and RAAS blockade. Current hypertension reports. 2011;13(4):318-24.
214. Visser M, Fuerst T, Lang T, Salamone L, Harris TB, Health FT, et al. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Journal of applied physiology. 1999;87(4):1513-20.
215. Singh MAF. Exercise, nutrition and managing hip fracture in older persons. Curr Opin Clin Nutr Metab Care. 2014;17(1):12-24.
216. D'Avanzo B, Shaw R, Riva S, Apostolo J, Bobrowicz-Campos E, Kurpas D, et al. Stakeholders' views and experiences of care and interventions for addressing frailty and pre-frailty: a meta-synthesis of qualitative evidence. PloS one. 2017;12(7):e0180127.
217. Robben S, van Kempen J, Heinen M, Zuidema S, Olde Rikkert M, Schers H, et al. Preferences for receiving information among frail older adults and their informal caregivers: a qualitative study. Family Practice. 2012;29(6):742-7.
218. Bindels J, Cox K, Widdershoven G, van Schayck OC, Abma TA. Care for community-dwelling frail older people: a practice nurse perspective. J Clin Nurs. 2014;23(15-16):2313-22.
219. Archibald M, Lawless M, Ambagtsheer RC, Kitson A. Older adults' understandings and perspectives on frailty in community and residential aged care: an interpretive description. BMJ open. 2020;10(3):e035339.
220. Leggo M, Banks M, Isenring E, Stewart L, Tweeddale M. A quality improvement nutrition screening and intervention program available to Home and Community Care eligible clients. Nutr Diet. 2008;65(2):162-7.
221. Charlton KE, Walton K, Moon L, Smith K, McMahon A, Ralph F, et al. "It could probably help someone else but not me": a feasibility study of a snack programme offered to meals on wheels clients. J Nutr Health Aging. 2013;17(4):364-9.
222. Broderick L, McCullagh R, Bantry White E, Savage E, Timmons S. Perceptions, expectations, and informal supports influence exercise activity in frail older adults. SAGE Open. 2015;5(2):2158244015580850.
223. Cavill NA, Foster CE. Enablers and barriers to older people's participation in strength and balance activities: A review of reviews. J Frailty Sarcopenia Falls. 2018;3(2):105.
224. McCullagh R, Darren D, Horgan NF, Timmons S. Factors Associated with Walking in Older Medical Inpatients. Arch Rehabil Res Clin Transl. 2020:100038.
225. Marcucci M, Damanti S, Germini F, Apostolo J, Bobrowicz-Campos E, Gwyther H, et al. Interventions to prevent, delay or reverse frailty in older people: a journey towards clinical guidelines. BMC Med. 2019;17(1):193.
226. Frost R, Kharicha K, Jovicic A, Liljas AE, Iliffe S, Manthorpe J, et al. Identifying acceptable components for home-based health promotion services for older people with mild frailty: A qualitative study. Health Soc Care Community. 2018;26(3):393-403.
227. Ward ME, De Brún A, Beirne D, Conway C, Cunningham U, English A, et al. Using co-design to develop a collective leadership intervention for healthcare teams to improve safety culture. Int J Environ Res. 2018;15(6):1182.
228. O'Donnell D, Shé ÉN, McCarthy M, Thornton S, Doran T, Smith F, et al. Enabling public, patient and practitioner involvement in co-designing frailty pathways in the acute care setting. BMC Health Serv Res. 2019;19(1):1-11.
229. Chun Tie Y, Birks M, Francis K. Grounded theory research: A design framework for novice researchers. SAGE open med. 2019;7:2050312118822927.
230. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care.

2007;19(6):349-57.
231. Han CY, Chan CGB, Lim SL, Zheng X, Woon ZW, Chan YT, et al. Diabetes-related nutrition knowledge and dietary adherence in patients with Type 2 diabetes mellitus: A mixed-methods exploratory study. Proc Singapore Healthc. 2020:2010105820901742.
232. Han CY, Sharma Y, Yaxley A, Baldwin C, Miller M. Use of the Patient-Generated Subjective Global Assessment to Identify Pre-Frailty and Frailty in Hospitalized Older Adults. J Nutr Health Aging. 2021:1-6.
233. Clarke V, Braun V, Hayfield N. Thematic analysis. Qualitative psychology: A practical guide to research methods. 2015;222:248.
234. Jenner B, Flick U, von Kardoff E, Steinke I. A companion to qualitative research: Sage; 2004.
235. Ritchie J, Lewis J, Nicholls CM, Ormston R. Qualitative research practice: A guide for social science students and researchers: sage; 2013.
236. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020;54(24):1451-62.
237. Coker J, Martin M, Simpson R, Lafortune L. Frailty: an in-depth qualitative study exploring the views of community care staff. BMC geriatrics. 2019;19(1):1-12.
238. Gwyther H, Shaw R, Dauden E-AJ, D'Avanzo B, Kurpas D, Bujnowska-Fedak M, et al. Understanding frailty: a qualitative study of European healthcare policy-makers' approaches to frailty screening and management. BMJ open. 2018;8(1):e018653.
239. Chastin SF, Harvey JA, Dall PM, McInally L, Mavroeidi A, Skelton DA. Beyond "# endpjparalysis", tackling sedentary behaviour in health care. AIMS Medical Science. 2019.
240. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community dwelling older people. Nurs Outlook. 2010;58(2):76-86.
241. Dury S, Dierckx E, Van Der Vorst A, Van der Elst M, Fret B, Duppen D, et al. Detecting frail, older adults and identifying their strengths: results of a mixed-methods study. BMC Public Health. 2018;18(1):1-13.
242. Chatindiara I, Sheridan N, Kruger M, Wham C. Eating less the logical thing to do? Vulnerability to malnutrition with advancing age: A qualitative study. Appetite. 2020;146:104502.
243. Bloom I, Lawrence W, Barker M, Baird J, Dennison E, Sayer AA, et al. What influences diet quality in older people? A qualitative study among community-dwelling older adults from the Hertfordshire Cohort Study, UK. Public Health Nutr. 2017;20(15):2685-93.
244. Poveda-López S, Montilla-Herrador J, Gacto-Sánchez M, Romero-Galisteo RP, Lillo-Navarro C. Wishes and perceptions about exercise programs in exercising institutionalized older adults living in long-term care institutions: A qualitative study. Geriatr Nurs. 2022;43:167-74.
245. Alizadeh L, Salehi L. Older people's perspectives on health, physical activity and nutritional behaviors. Health promotion perspectives. 2015;5(4):288.
246. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. BMC Geriatr. 2015;15(1):154.
247. Robertson MC, Devlin N, Gardner MM, Campbell AJ. Effectiveness and economic evaluation of a nurse delivered home exercise programme to prevent falls. 1: Randomised controlled trial. BMJ. 2001;322(7288):697.
248. Brown CJ, Redden DT, Flood KL, Allman RM. The underrecognized epidemic of low mobility during hospitalization of older adults. J Am Geriatr Soc. 2009;57(9):1660-5.
249. Fisher SR, Goodwin JS, Protas EJ, Kuo YF, Graham JE, Ottenbacher KJ, et al. Ambulatory activity of older adults hospitalized with acute medical illness. J Am Geriatr Soc. 2011;59(1):91-5.
250. Battersby M, Harris M, Smith D, Reed R, Woodman R. A pragmatic randomized controlled trial of the Flinders Program of chronic condition management in community health care services. Patient Educ Couns. 2015;98(11):1367-75.
251. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687.
252. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346.

253. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. bmj. 2016;355.
254. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189-98.
255. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharmaceutical Statistics: The Journal of Applied Statistics in the Pharmaceutical Industry. 2005;4(4):287-91.
256. Serra-Prat M, Sist X, Domenich R, Jurado L, Saiz A, Roces A, et al. Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. Age and ageing. 2017;46(3):401-7.
257. Billingham SA, Whitehead AL, Julious SA. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. BMC medical research methodology. 2013;13(1):1-6.
258. Pedersen MM, Petersen J, Beyer N, Damkjaer L, Bandholm T. Supervised progressive cross-continuum strength training compared with usual care in older medical patients: study protocol for a randomized controlled trial (the STAND-Cph trial). Trials [Electronic Resource]. 2016;17:176.
259. Alix E, Berrut G, Boré M, Bouthier-Quintard F, Buia JM, Chlala A, et al. Energy requirements in hospitalized elderly people. J Am Geriatr Soc. 2007;55(7):1085-9.
260. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. 2013;14(8):542-59.
261. Gopinath B, Russell J, Flood VM, Burlutsky G, Mitchell P. Adherence to dietary guidelines positively affects quality of life and functional status of older adults. J Acad Nutr Diet. 2014;114(2):220-9.
262. Robertson MC, Campbell AJ, Gardner MM, Devlin N. Preventing injuries in older people by preventing falls: A meta-analysis of individual-level data. J Am Geriatr Soc. 2002;50(5):905-11.
263. Langley J, Wolstenholme D, Cooke J. 'Collective making'as knowledge mobilisation: the contribution of participatory design in the co-creation of knowledge in healthcare. BMC Health serv Res. 2018;18(1):1-10.
264. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994;49(2):M85-M94.
265. Thomas J, Isenring E, Kellett E. Nutritional status and length of stay in patients admitted to an Acute Assessment Unit. J Hum Nutr Diet. 2007;20(4):320-8.
266. Incalzi RA, Cesari M, Pedone C, Carbonin P. Construct validity of the 15-item geriatric depression scale in older medical inpatients. J Geriatr Psychiatry Neurol. 2003;16(1):23-8.
267. Oppe M, Devlin NJ, Szende A. EQ-5D value sets: inventory, comparative review and user guide: Springer; 2007.
268. Sager MA, Rudberg MA, Jalaluddin M, Franke T, Inouye SK, Landefeld CS, et al. Hospital admission risk profile (HARP): identifying older patients at risk for functional decline following acute medical illness and hospitalization. J Am Geriatr Soc. 1996;44(3):251-7.
269. Gupta SK. Intention-to-treat concept: a review. Perspect Clin Res. 2011;2(3):109.
270. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Trials. 2010;11(1):32.
271. Boyd CM, Landefeld CS, Counsell SR, Palmer RM, Fortinsky RH, Kresevic D, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. J Am Geriatr Soc. 2008;56(12):2171-9.
272. Kümmel J, Kramer A, Giboin L-S, Gruber M. Specificity of balance training in healthy individuals: a systematic review and meta-analysis. Sports Med. 2016;46(9):1261-71.
273. Lopez P, Pinto RS, Radaelli R, Rech A, Grazioli R, Izquierdo M, et al. Benefits of resistance training in physically frail elderly: a systematic review. Aging Clin Exp Res. 2018;30(8):889-99.
274. Hestevik CH, Molin M, Debesay J, Bergland A, Bye A. Older patients' and their family caregivers' perceptions of food, meals and nutritional care in the transition between hospital and home care: a qualitative study. BMC nutrition. 2020;6(1):1-13.
275. Catalan-Matamoros D, Gomez-Conesa A, Stubbs B, Vancampfort D. Exercise improves depressive symptoms in older adults: an umbrella review of systematic reviews and meta-analyses.

Psychiatry Res. 2016;244:202-9.
276. Lang UE, Beglinger C, Schweinfurth N, Walter M, Borgwardt S. Nutritional aspects of depression. Cell Physiol Biochem. 2015;37(3):1029-43.
277. van Rijckevorsel-Scheele J, Willems RC, Roelofs PD, Koppelaar E, Gobbens RJ, Goumans MJ. Effects of health care interventions on quality of life among frail elderly: a systematized review. Clin Interv Aging. 2019;14:643.
278. Haraldstad K, Wahl A, Andenæs R, Andersen JR, Andersen MH, Beisland E, et al. A systematic review of quality of life research in medicine and health sciences. Qual Life Res. 2019;28(10):2641-50.
279. Davis-Ajami ML, Chang P-S, Wu J. Hospital readmission and mortality associations to frailty in hospitalized patients with coronary heart disease. Aging and Health Research. 2021;1(4):100042.
280. Harris R, Dyson E. Recruitment of frail older people to research: lessons learnt through experience. J Adv Nurs. 2001;36(5):643-51.
281. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The challenge of patient adherence. Ther Clin Risk Manag. 2005;1(3):189.
282. Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. Implemen Sci. 2017;12(1):1-18.
283. Travers J, Romero-Ortuno R, Bailey J, Cooney M-T. Delaying and reversing frailty: a systematic review of primary care interventions. Br J Gen Prac. 2019;69(678):e61-e9.
284. Sabaté E. Adherence to long-term therapies: evidence for action: World Health Organization; 2003.
285. Gourlan M, Bernard P, Bortolon C, Romain AJ, Lareyre O, Carayol M, et al. Efficacy of theory-based interventions to promote physical activity. A meta-analysis of randomised controlled trials. Health Psychol Rev. 2016;10(1):50-66.
286. Peat G, Fylan B, Marques I, Raynor DK, Breen L, Olaniyan J, et al. Barriers and facilitators of successful deprescribing as described by older patients living with frailty, their informal carers and clinicians: a qualitative interview study. BMJ open. 2022;12(3):e054279.
287. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. Implementation science. 2012;7(1):1-17.
288. McGowan LJ, Powell R, French DP. How can use of the Theoretical Domains Framework be optimized in qualitative research? A rapid systematic review. Br J Health Psychol. 2020;25(3):677-94.
289. Damush TM, Perkins SM, Mikesky AE, Roberts M, O'Dea J. Motivational factors influencing older adults diagnosed with knee osteoarthritis to join and maintain an exercise program. J Aging Phys Act. 2005;13(1):45-60.
290. Moynihan P, Mulvaney C, Adamson A, Seal C, Steen N, Mathers J, et al. The nutrition knowledge of older adults living in sheltered housing accommodation. J Hum Nutr Diet. 2007;20(5):446-58.
291. van der Zanden LD, van Kleef E, de Wijk RA, van Trijp HC. Knowledge, perceptions and preferences of elderly regarding protein-enriched functional food. Appetite. 2014;80:16-22.
292. Cohen-Mansfield J, Marx MS, Biddison JR, Guralnik JM. Socio-environmental exercise preferences among older adults. Prev Med. 2004;38(6):804-11.
293. Gonzalez BCS, Jirovec MM. Elderly Mexican women's perceptions of exercise and conflicting role responsibilities. Int J Nurs Stud. 2001;38(1):45-9.
294. Hardy S, Grogan S. Preventing disability through exercise: investigating older adults' influences and motivations to engage in physical activity. J Health Psychol. 2009;14(7):1036-46.
295. Weeks LE, Profit S, Campbell B, Graham H, Chircop A, Sheppard-LeMoine D. Participation in physical activity: influences reported by seniors in the community and in long-term care facilities. J Gerontol Nurs. 2008;34(7):36-43.
296. Åhlund K, Öberg B, Ekerstad N, Bäck M. A balance between meaningfulness and risk of harm–frail elderly patients' perceptions of physical activity and exercise–an interview study. BMC geriatrics. 2020;20(1):1-9.
297. Franco MR, Tong A, Howard K, Sherrington C, Ferreira PH, Pinto RZ, et al. Older people's perspectives on participation in physical activity: a systematic review and thematic synthesis of qualitative literature. Br J Sports Med. 2015;49(19):1268-76.

298. Melillo KD, Futrell M, Williamson E, Chamberlain C, Bourque AM, MacDonnell M, et al. Perceptions of physical fitness and exercise activity among older adults. J Adv Nurs. 1996;23(3):542-7.
299. De Groot GCL, Fagerström L. Older adults' motivating factors and barriers to exercise to prevent falls. Scand J Occup Ther. 2011;18(2):153-60.
300. Hubner S, Boron JB, Koehler K. The Effects of Exercise on Appetite in Older Adults: A Systematic Review and Meta-Analysis. Front Nutr. 2021;8.
301. Whitehead S, Lavelle K. Older breast cancer survivors' views and preferences for physical activity. Qual Health Res. 2009;19(7):894-906.
302. Wilcox S, Bopp M, Oberrecht L, Kammermann SK, McElmurray CT. Psychosocial and perceived environmental correlates of physical activity in rural and older African American and white women. J Gerontol B Psychol Sci Soc Sci. 2003;58(6):P329-P37.
303. Resnick B. Geriatric rehabilitation: The influence of efficacy beliefs and motivation. Rehab Nurs. 2002;27(4):152-9.
304. Cousins SOB. A self-referent thinking model: How older adults may talk themselves out of being physically active. Health Promot Pract. 2003;4(4):439-48.
305. Dunlop DD, Manheim LM, Yelin EH, Song J, Chang RW. The costs of arthritis. Arthritis Care Res. 2003;49(1):101-13.
306. Laguna L, Mingioni M, Maitre I, Vanwymelbeke V, Pirttijärvi T, Artigas M, et al. Perception of difficulties encountered in eating process from European elderlies' perspective. J Texture Stud. 2016;47(4):342-52.
307. Edfors E, Westergren A. Home-living elderly people's views on food and meals. J Aging Res. 2012;2012.
308. Petroka K, Campbell-Bussiere R, Dychtwald DK, Milliron B-J. Barriers and facilitators to healthy eating and disease self-management among older adults residing in subsidized housing. Nutr Health. 2017;23(3):167-75.
309. Sahyoun NR, Vaudin A. Home-delivered meals and nutrition status among older adults. Nutr Clin Pract. 2014;29(4):459-65.
310. Heesch KC, Brown DR, Blanton CJ. Perceived barriers to exercise and stage of exercise adoption in older women of different racial/ethnic groups. Women Health. 2000;30(4):61-76.
311. Schneider JK, Eveker A, Bronder DR, Meiner SE, Binder EF. Exercise Training Program for Older Adults Incentives and Disincentives for Participation. SLACK Incorporated Thorofare, NJ; 2003. p. 21-31.
312. Baert V, Gorus E, Mets T, Geerts C, Bautmans I. Motivators and barriers for physical activity in the oldest old: a systematic review. Ageing Res Rev. 2011;10(4):464-74.
313. Chan CB, Ryan DA. Assessing the effects of weather conditions on physical activity participation using objective measures. Int J Environ Res. 2009;6(10):2639-54.
314. Burgess E, Hassmén P, Pumpa KL. Determinants of adherence to lifestyle intervention in adults with obesity: a systematic review. Clin Obes. 2017;7(3):123-35.
315. de Castro JM. Age-related changes in the social, psychological, and temporal influences on food intake in free-living, healthy, adult humans. J Gerontol A Biol Sci. 2002;57(6):M368-M77.
316. Abbott RA, Whear R, Thompson-Coon J, Ukoumunne OC, Rogers M, Bethel A, et al. Effectiveness of mealtime interventions on nutritional outcomes for the elderly living in residential care: a systematic review and meta-analysis. Ageing Res Rev. 2013;12(4):967-81.
317. Govindaraju T, Owen AJ, McCaffery TA. Past, present and future influences of diet among older adults–A scoping review. Ageing Res Rev. 2022:101600.
318. Tolkacheva N, Van Groenou MB, De Boer A, Van Tilburg T. The impact of informal care-giving networks on adult children's care-giver burden. Ageing Soc. 2011;31(1):34-51.
319. Asamane EA, Greig CA, Aunger JA, Thompson JL. Perceptions and factors influencing eating Behaviours and physical function in community-dwelling ethnically diverse older adults: a longitudinal qualitative study. Nutrients. 2019;11(6):1224.
320. Sladdin I, Ball L, Gillespie BM, Chaboyer W. A comparison of patients' and dietitians' perceptions of patient-centred care: A cross-sectional survey. Health Expect. 2019;22(3):457-64.
321. Forkan R, Pumper B, Smyth N, Wirkkala H, Ciol MA, Shumway-Cook A. Exercise adherence following physical therapy intervention in older adults with impaired balance. Phys Ther.

2006;86(3):401-10.
322. Miller KJ, Mesagno C, McLaren S, Grace F, Yates M, Gomez R. Exercise, mood, self-efficacy, and social support as predictors of depressive symptoms in older adults: Direct and interaction effects. Front Psychol. 2019:2145.
323. Cummings SM, Cooper RL, Cassie KM. Motivational interviewing to affect behavioral change in older adults. Res Soc Work Pract. 2009;19(2):195-204.
324. Azizan A, Justine M, Kuan CS. Effects of a behavioral program on exercise adherence and exercise self-efficacy in community-dwelling older persons. Curr Gerontol Geriatr Res. 2013;2013.
325. Aira M, Kauhanen J, Larivaara P, Rautio P. Factors influencing inquiry about patients' alcohol consumption by primary health care physicians: qualitative semi-structured interview study. Fam Pract. 2003;20(3):270-5.
326. Chew-Graham CA, May CR, Perry MS. Qualitative research and the problem of judgement: lessons from interviewing fellow professionals. Fam Pract. 2002;19(3):285-9.
327. Andersson SJ, Troein M, Lindberg G. Conceptions of depressive disorder and its treatment among 17 Swedish GPs. A qualitative interview study. Fam Pract. 2001;18(1):64-70.
328. Geelen SJG, van Dijk-Huisman HC, de Bie RA, Veenhof C, Engelbert R, van der Schaaf M, et al. Barriers and enablers to physical activity in patients during hospital stay: a scoping review. Systemat Rev. 2021;10(1):1-13.
329. Rezaei-Shahsavarloo Z, Atashzadeh-Shoorideh F, Gobbens RJ, Ebadi A, Ghaedamini Harouni G. The impact of interventions on management of frailty in hospitalized frail older adults: a systematic review and meta-analysis. BMC Geriatr. 2020;20(1):1-17.
330. Han CY, Sharma Y, Yaxley A, Baldwin C, Miller M. Use of the patient-generated subjective global assessment to identify pre-frailty and frailty in hospitalized older adults. J Nutr Health Aging. 2021;25(10):1229-34.
331. Han CY, Crotty M, Thomas S, Cameron ID, Whitehead C, Kurrle S, et al. Effect of Individual Nutrition Therapy and Exercise Regime on Gait Speed, Physical Function, Strength and Balance, Body Composition, Energy and Protein, in Injured, Vulnerable Elderly: A Multisite Randomized Controlled Trial (INTERACTIVE). Nutrients. 2021;13(9):3182.
332. Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. Age Ageing. 2016;45(3):353-60.
333. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391(10132):1775-82.
334. de Morton NA, Davidson M, Keating JL. The de Morton Mobility Index (DEMMI): an essential health index for an ageing world. Health and quality of life outcomes. 2008;6(1):1-15.
335. Auld R, Loppacher T, Rose S, Milat A, Penna A. Translational Research Grants Scheme (TRGS): a new approach to strengthening health system research capacity. Public Health Res Pract. 2018;28(3):2831818.
336. Haji Ali Afzali H, Karnon J, Theou O, Beilby J, Cesari M, Visvanathan R. Structuring a conceptual model for cost-effectiveness analysis of frailty interventions. PLoS One. 2019;14(9):e0222049.
337. Bauer MS, Kirchner J. Implementation science: What is it and why should I care? Psychiatry research. 2020;283:112376.