Frailty Indices and Nutritional Screening Tools as Predictors of Adverse Outcomes in Hospitalised Older People

THE UNIVERSITY of ADELAIDE

Thesis submitted by

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Bachelor of Applied Science
(Human Movement Studies - Exercise Science) (Hons I)

A thesis submitted for the degree of Doctor of Philosophy

in the

School of Medicine

Faculty of Health Sciences

The University of Adelaide

May 2013

Thesis Declaration

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1. Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People. *Journal of Nutrition Health and Aging.* 2012;16(9):764-7.

2. Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review. *Journal of Nutrition in Gerontology and Geriatrics.* 2012;31(2):97-145.

3. Dent E, Yu S, Visvanathan R, Piantadosi C, Adams R, Lange K, Chapman I. Inflammatory Cytokines and Appetite in Healthy People. *The Journal of Aging Research & Clinical Practice.* 2012;1(1):40-3.

4. Dent E, Chapman I., Piantadosi C, Visvanathan R. Frailty and Functional Decline Indices Predict Poor Outcomes in Hospitalised Older People. Submitted to *Age and Ageing.*

5. Dent E, Chapman I., Piantadosi C, Visvanathan R. Nutritional Screening Tools and Anthropometric Measures Associate with Hospital Discharge Outcomes in Older People. Submitted to *Australasian Journal on Ageing.*

6. Dent E, Chapman I., Piantadosi C, Visvanathan R. Performance of Nutritional 'Performance of Nutritional Screening Tools in Predicting Poor Six Month Outcome in Hospitalised Older People.' Submitted to *Journal of Nutrition Health and Ageing*.

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Keywords

Barthel Index (BI); Mini Nutritional Assessment; Nutritional Assessment; length of stay (LOS); Predictive Value; patient admission; Aged; Aged, 80 and over; older adult; geriatric; cohort study; follow-up; prospective study; nutritional screen; malnutrition; Mini Nutritional Assessment Short Form (MNA-SF); Short Nutritional Assessment Questionnaire; Simplified Nutritional Appetite Questionnaire (SNAQ); Simple Nutritional Assessment Questionnaire (SNAQ); Malnutrition Universal Screening Tool (MUST); Nutritional Risk Screening 2002; Geriatric Nutritional Risk Index (GNRI); Screening Tool; Subjective Global Assessment (SGA); mortality; Activities of Daily Living (ADL); hospital; Katz; Instrumental Activity of Daily Living (IADL); poor discharge outcome; Long-Term Care; Nutrition Index; Nutrition Assessment; Prognosis; Frail Elderly; Hospitalization; functional decline; Incidence; Nutritional Status; Questionnaires; Geriatric Assessment; Quality of Life (QOL); Sensitivity and Specificity; Geriatrics/ methods; ROC Curve; Hand Strength; Inflammation; Appetite; healthy aging; successful aging; vulnerable; vulnerability; disabled person; Fried; Frailty Index; Study of Osteoporotic Fractures (SOF) Index; Frail Elder; Functionally-Impaired Elderly; Elderly, Functionally-Impaired; Functionally Impaired Elderly; Gait Speed; Prevalence; Vulnerability; Geriatric Syndrome.

Abstract

Frailty and malnutrition are two major medical issues influencing the health of older people. This doctoral thesis investigated the predictive ability and discriminatory power of clinically applicable frailty instruments and their malnutrition counterparts - nutritional screening tools (NSTs). The study was prospective and observational by design, and included patients aged ≥ 70 years consecutively admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital, South Australia. Thesis aims were to: (i) identify the prevalence rates of malnutrition and frailty in hospitalised older people and (ii) determine the predictive ability and accuracy of these measurements.

The mean (standard deviation) age of patients was 85.2 (6.4) years; 123 (72 %) were female, n = 172. Malnutrition and frailty prevalence rates were high: malnutrition was found in 53 (31 %) of patients using the Mini Nutritional Assessment (MNA) for classification; and frailty was found in 107 patients (62 %) by the Cardiovascular Health Study (CHS) frailty index.

When looking at nutritional screening tools as predictors of hospital discharge outcomes: the MNA and the MNA-short form (MNA-SF) were associated with length of stay (LOS); the Geriatric Nutritional Risk Index (GNRI) and calf circumference (CC) were associated with functional decline; and mid arm circumference (MAC) was associated with a higher level of care on discharge. At six months post-hospitalisation, malnutrition by the MNA (OR = 3.29) and GNRI (OR = 2.84) was predictive of poor outcome (defined as mortality or admission to high level care). However the discriminative ability of this prediction was inadequate (area under Receiver Operating Characteristic curve ($_{au}$ROC) values were < 0.7).

Regarding frailty, almost all frailty and functional decline indices were predictive of poor outcome (mortality or high level care admission) at both hospital discharge and at six month post-hospitalisation. However when discriminative ability was considered, only the Frailty Index of Cumulative Deficits (FI-CD) and the adapted Katz score of Activities of Daily Living showed adequate values ($_{au}$ROC values of 0.735 and 0.704 respectively). The FI-CD was the only instrument to show adequate discriminatory power in predicting poor six month outcome ($_{au}$ROC = 0.702, P < 0.001).

Malnutrition shares many characteristics with frailty; however the overlap between these two conditions lacks a quantitative foundation. Therefore, this doctoral project also looked at the efficacy of nutritional screening tools as frailty indices in hospitalised older people. An additional focus of this thesis was the association between appetite, body composition and inflammation in healthy people of all ages.

This thesis illustrated the high prevalence rate of both malnutrition and frailty in hospitalised older people. Results highlight the importance of research into the predictive ability of both NSTs and frailty instruments in hospitalised older people. Such knowledge will be of assistance in the areas of gerontology research, clinical practice and public health policy, particularly in the wake of the global expansion of the number of older people. Thesis results may also assist in standardising definitions for both frailty and malnutrition, definitions which are greatly needed in clinical practice and research.

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List of Abbreviations

ADL	Activity of Daily Living
AUC	Area Under Curve
ASPEN	American Society for Parenteral and Enteral Nutrition
BAPEN	British Association of Parenteral and Enteral Nutrition
BMI	Body Mass Index
BI	Barthel Index
CASA	Cytokines, Adiposity, Sarcopenia and Ageing Study
CC	Calf Circumference
CCI	Charlson's Co-morbidity Index
CGA	Comprehensive Geriatric Assessment
CHS	Cardiovascular Health Study (Index)
CI	Confidence Interval
CNTF	Ciliary Neurotrophic Factor
CRP	C-Reactive Protein
CSHA	The Canadian Study of Health and Ageing
DAA	Dieticians Association of Australia
ESPEN	The European Society for Clinical Nutrition and Metabolism
EWGSOP	The European Working Group on Sarcopenia in Older People
FI-CD	Frailty Index of Cumulative Deficits
FI-CGA	Frailty Index Based on Comprehensive Geriatric Assessment
FNA	Full Nutritional Assessment
FRAIL	Fatigue, Resistance, Ambulation, Illness, Loss of Weight (Index)
GDS	Geriatric Depression Scale
GEMU	Geriatric Evaluation and Management Unit
GNRI	Geriatric Nutritional Risk Index
HARP	Hospital Admissions Risk Profile
HPA	Hypothalamic Pituitary Axis
HLC	High Level Care
IADL	Instrumental Activity of Daily Living
IAGG	International Association of Geriatrics and Gerontology
IANA	International Association of Nutrition and Aging
IL-1	Interleukin-1

IL-1β	Interleukin-1β
IL-6	Interleukin-6
IFNγ	Interferon-γ
ISCCWG	International Sarcopenia Consensus Conference Working Group
LASA	The Longitudinal Aging Study Amsterdam
LOS	Length of Stay
MAC	Mid-Arm Circumference
MeSH	Medline Search Heading
MMSE	Mini Mental State Examination
MNA	Mini Nutritional Assessment
MNA-SF	Mini Nutritional Assessment – Short Form
MPI	Multidimensional Prognostic Instrument
MST	Malnutrition Screening Tool
MUST	Malnutrition Universal Screening Tool
NCP	Nutrition Care Process
NPV	Negative Predictive Value
NRI	Nutritional Risk Index
NRS-2002	Nutritional Risk Screening 2002
NST	Nutritional Screening Tool
PPV	Positive Predictive Value
ROC	Receiver Operating Characteristic
SD	Standard Deviation
SGA	Subjective Global Assessment
SHERPA	Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie
SNAQ	Simplified Nutritional Appetite Questionnaire
SOF	Study of Osteoporotic Fractures
SFGG	Society of Geriatrics and Gerontology
TNF-α	Tumour Necrosis Factor-α
TQEH	The Queen Elizabeth Hospital
WHAS	Women's Health and Ageing Study
WHO	World Health Organisation

Publications and Presentations

Publications, papers submitted for publication and conference presentations pertaining to results relating to the thesis are listed below.

Published Journal Articles

Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People. *Journal of Nutrition Health and Aging.* 2012;16(9):764-7. (Printed version in Appendix D; pre-printed version in Chapter 6).

Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review. *Journal of Nutrition in Gerontology and Geriatrics.* 2012;31(2):97-145. (Printed version in Appendix E; pre-printed version in Chapter 5).

Dent E, Yu S, Visvanathan R, Piantadosi C, Adams R, Lange K, Chapman I. Inflammatory Cytokines and Appetite in Healthy People. *The Journal of Aging Research & Clinical Practice.* 2012;1(1):40-3. (Printed version in Appendix F; pre-printed version in Chapter 10).

Published Abstracts

Dent E, Visvanathan R, Piantadosi C, Chapman I. Frailty determinants and discharge outcomes in hospitalised older persons. *Australasian Journal on Ageing*. 2012; Supplement 2:71. (Appendix: Abstract 1)

Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional Status at Admission Predicts Functional Decline in Older South Australians Admitted to a Higher Acuity Geriatric Evaluation and Management Unit. *Australasian Journal on Ageing.* 2012;31,Supplement 1:46. (Appendix: Abstract 2)

Submitted Papers

Dent E, Chapman I., Piantadosi C, Visvanathan R. Frailty and Functional Decline Indices Predict Poor Outcomes in Hospitalised Older People. Submitted for publication (Chapter 9).

Dent E, Chapman I., Piantadosi C, Visvanathan R. Nutritional Screening Tools and Anthropometric Measures Associate with Hospital Discharge Outcomes in Older People. Submitted for publication (Chapter 7).

Dent E, Chapman I., Piantadosi C, Visvanathan R. 'Performance of Nutritional Screening Tools in Predicting Poor Six Month Outcome in Hospitalised Older People.' Submitted for publication (Chapter 8).

Conference Presentations

Frailty and Functional Decline Indices as Predictors of Poor Outcomes in Hospitalised Older People. Oral Presentation accepted to present at The 20th International Association of Gerontology and Geriatrics (IAGG) World Congress of Gerontology and Geriatrics; Seoul, June 23 – 27, 2013 (Appendix: Abstract 3)

'Evaluation of Frailty Indices for the Prediction of Adverse Post-Hospital Outcomes in Older People'. Oral presentation at the Australian Health and Medical Research National Conference; Adelaide, 25 – 29 November 2012. (Appendix: Abstract 4)

'Frailty determinants and discharge outcomes in hospitalised older persons'. Presented at the 45th National Conference of the Australian Association of Gerontology; Brisbane, 20-23 November 2012 (Poster Presentation). (Appendix: Abstract 1)

'Evaluation of Frailty Conceptualisations for the Prediction of Adverse Health Outcomes in Hospitalised Older Persons'. Oral Presentation at The Queen

Elizabeth Hospital Research Day; Adelaide, October 2012. (Appendix: Abstract 5)

'Nutritional Status at Admission Predicts Functional Decline in Older South Australians Admitted to a Higher Acuity Geriatric Evaluation and Management Unit'. Presented at the Australian and New Zealand Society for Geriatric Medicine (ANZSGM) Annual Scientific Meeting; Sydney, 2-6 May 2012 and at the Postgraduate Research Day, The University of Adelaide, 31 August 2012. (Poster Presentation; Appendix: Abstract 2)

'Nutritional Screening Tools as Predictors of Hospital Outcomes in Older Patients'. Oral Presentation at the Australian Society of Medical Research State Conference; Adelaide May 2012. (Appendix: Abstract 6).

'The Mini Nutritional Assessment as a Predictor of Fried's Frailty Classification in Hospitalised Older People'. Oral Presentation at The Queen Elizabeth Hospital Research Day; Adelaide, October 2011. Awarded 'Best Clinical Research Presentation' and 'Runner-up Best Lay-Person Project Abstract'. (Appendix: Abstract 7).

Background

An Ageing Population

We are now living longer than at any previous time in human history. The global population of older people is expanding at such an unprecedented rate, that by 2050, it is projected that one fifth of the world's population will be aged over 60 years (1). The oldest old age bracket (aged 85 years and older) is expanding the fastest (2). With more older people, it is becoming increasingly important to focus on preserving functional independence with age (1, 3).

On the whole, our population is ageing well, at least in developing countries (4, 5). In Australia, 68 % of adults aged 65 years or older classified their health as good or good to excellent according to the Australian Bureau of Statistics in 2004 – 2005 (6). However, living longer increases the risk of developing chronic disease (5). This is especially true in Australia, which has one of the highest growth rates of chronic condition prevalence in the world (2). Risk of disability also increases with age (5). For example, in Australia, disability is found in 15 % of younger adults, 45 % of adults aged 65 – 74 years and 82 % of those aged 85 years and over (6). Mobility also decreases with age, so that by the age of 85 years, up to 95 % of people have lost a degree of their mobility (5).

Although an older person's function tends to decrease with age, older people are extremely heterogeneous with respect to their trajectories of ageing (4, 5, 7). For example, some older people may suffer extended decline, whilst others age well (7). If we are able to predict which individuals will encounter poor outcomes, this will have an enormous impact on prevention, treatment and care given to older people. It must be emphasised that identifying older people at risk of poor outcome is not used to deny older people treatment; instead, it is used to offer appropriate support (8), optimise any medical treatment needed (9, 10) and to prevent unnecessary harm (8, 9).

Major Thesis Topic

Frailty, a core concept in gerontology, can be used to identify older people at risk of poor outcomes (11). Frailty is often linked to malnutrition, which in turn, is also predictive of poor outcomes in older people (12). This doctoral thesis focuses on the ability of clinically applicable frailty measurements (operationalisations) and nutritional screening tools to predict adverse health outcomes in hospitalised older people. The hospital is an important location in which to base this research, as there is a distinct need to translate epidemiological research on frailty and malnutrition into this setting.

1 MALNUTRITION

Chapter 1 presents an introduction to the thesis. It begins by describing what malnutrition is, its aetiology, prevalence and outcomes. Nutritional screening in the hospital setting is then discussed, including an overview of commonly used nutritional screening tools applicable to the hospital setting. Thereafter, this chapter identifies and discusses the literature research gap – the extent to which nutritional screening tools predict adverse outcomes in hospitalised older people. Knowing such information would advance the debate over which nutritional screening tool is best suited for the clinical setting.

1.1 Background

Malnutrition is a geriatric condition (13, 14) affecting up to 10 % of community dwelling older people (15). Malnutrition has no gold standard definition, although the common international consensus is that malnutrition is an inadequate nutritional status associated with adverse clinical outcomes (16). The terms malnutrition and undernutrition are frequently interchanged in the literature, and for the purposes of this thesis, malnutrition will refer to undernutrition rather than over-nutrition (16). Sarcopenia, a concept linked to malnutrition, will also be discussed.

1.2 Aetiology of Malnutrition

Older people are at an increased risk of developing malnutrition (16-23). Table 1-1 provides a list of malnutrition risk factors that increase with ageing. Physiological causes of age-associated malnutrition include appetite loss, swallowing difficulties and early satiation (18, 24). Clinical causes of malnutrition include polypharmacy and hospitalisation (16). Psycho-social causes include depression, dementia, isolation and poverty (16, 20); physical causes of malnutrition include frailty (16, 25) and poor dentition (26, 27).

Age-related malnutrition risk factors can lead to dysfunctional eating patterns, such as slowed eating and eating a non-varied diet (28). Dysfunctional eating results in a reduction of energy and nutrient intake which, if left untreated, manifests as malnutrition (28). Many older people, particularly those who are frail, often have several co-existing risk factors for malnutrition (29). Malnutrition also tends to develop at a much faster rate in older people (30). Of note, around 25 % of malnutrition cases in older people have no known cause (29).

Weight loss attributing to the ageing process is known as the ‘anorexia of ageing’ (31). Anorexia of ageing is highly influenced by inflammatory molecules (18, 32-35). The following section details the role of the inflammatory process in malnutrition.

Table 1-1: Factors Contributing to Malnutrition in Older People

Factors Contributing to Malnutrition in Older People
Physical Changes
Frailty and/or Reduced Function (36-38)
Low Physical Activity (39)
Inability to communicate food needs (40)
Poor Oral Health (22, 27, 41-44) including Xerosomia (dry mouth) (28, 44)
Psychological Changes
Depression (15, 29, 41, 44, 45)
Dementia (37, 46-48)
Confusion (22)
Anxiety (49)
Grief (41, 45)
Several foods are less liked (28, 50)
Lower motivation to eat (28)
Physiological Changes
Lack of Smell (22, 28, 51)
Lack of Taste (22, 28, 51, 52)
Lack of Sight (45)
Dysphagia (Swallowing Difficulty) (16, 22, 37, 51)
Reduced Appetite, including faster and longer satiation (22, 28, 38, 53)
Slower gastric emptying and poorer gut functioning (28, 48, 54, 55) including poorer ghrelin secretion (involved in appetite) (54)
Environmental Changes
Eating and living alone (15, 28, 36)
Poverty (39, 56, 57)
Inadequate Care and Support (15, 28, 57, 58)
Low Education (39)
Communication barriers, including language barriers (40)
Alcohol or Drug Addiction (29)
Clinical Changes
Polypharmacy (29, 44) and Medication issues, including nausea/mal-absorption (22, 46)
Hospitalisation (15)
Co-morbidities and infections (36, 48)
Changes Due to Disease
Endocrine disorder (eg Hyperthyroidism) (29)
More prone to weight change with a reduced ability to recover (22, 29)
Accelerated metabolism (46)
Pain (41)
Constipation (37, 41)
Greater need for protein (eg inflammation) and a reduced ability to use protein (related to insulin resistance) (59)

1.3 Inflammation and Malnutrition

The normal ageing process is accompanied by the shortening of telomeres, DNA damage and cell senescence (60, 61). The longer we live, the more likely were are to accumulate these adverse cellular stressors (62). A major downfall of these stressors is that they can trigger an exaggerated inflammatory response, which can catabolise proteins (59) as well as lead to appetite suppression, and in turn, bring about weight loss (63).

Inflammation is the immune system's localised response to acute infection or illness and is usually accompanied by an acute phase response (64). This acute phase response generates pro-inflammatory cytokines such as Interleukin 1β (IL-1β), IL-6, IL-8, C-Reactive Protein (CRP) and Tumour Necrosis Factor-α (TNF-α) (64, 65). Pro-inflammatory cytokines suspected to play a role in malnutrition development include TNF-α, IL-1β and IL-6 (66). These inflammatory cytokines act both centrally and peripherally (46, 66). Centrally, they act on the hypothalamus and other brain areas where they interfere with appetite by disrupting the regulation of appetite controlling hormones and altering gastric function (33, 63, 66); peripherally they interfere with gastric emptying and motility (66).

Specifically, Il-1β mediates appetite suppression both peripherally and centrally with the assistance of other pro-inflammatory cytokines (63). TNFα also plays a role, but to a lesser extent than Il-1β (63). IL-6 inhibits food intake centrally and one of its family members, ciliary neurotrophic factor (CNTF) is the only cytokine acknowldeged to impact on long term (63). Anti-inflammatory cytokines, such and IL-4 and IL-10 act to down-regulate pro-inflammatory cytokine production (67).

The body's pro-inflammatory response is exaggerated when pathophysiology is induced by both co-morbidities and poor psychosocial conditions (68). In a study

of hospitalised older people by Zamora et al. (2010) (69), malnutrition was found to be closely associated with an exaggerated inflammatory response. An interesting outcome of this study was that patients who were malnourished had a greater incidence of physiological system failure than non-malnourished patients (69). Decline in multiple physiological systems is a common premise in frailty definitions, and is discussed in detail in Chapter 2.

1.4 Malnutrition Prevalence in the Hospital Setting

The prevalence rate of malnutrition in hospitalised older people varies considerably between studies: from 12 – 79 % according to a recent review (70). Much of this difference in prevalence can be attributed to the different nutritional assessment and screening measures used to classify malnutrition. This is evidenced by several comparative studies of nutritional screening tools in hospitalised older people. For example, Drescher et al. (2010) compared the Mini Nutritional Assessment (MNA) and the Nutritional Risk Screening 2002 tools, and found malnutrition prevalence was 22 % and 34 % respectively in their sample of 104 patients (MNA <17 and NRS 2002 moderate to severe malnutrition risk) (71). Baccoro and Sanchez (2009) also found large differences in malnutrition prevalence rates in their study of 150 women, with malnutrition identified by the Subjective Global Assessment (SGA) (rating B + C) and by low BMI being 49 % and 10 % respectively (72). A similar trend was also found by Kyle et al. (2006), who reported that malnutrition prevalence rates by were 44 % with SGA (rating B+C), 28 % by NRS-2002 (moderate to severe malnutrition risk (71)) and 37 % by the MUST (moderate to high risk) (73). Also, Bauer et al. found variation in prevalence rate between nutritional measures (74), with malnutrition by the MNA (<17), SGA (rating B +C), NRS 2002 (moderate to severe malnutrition risk) being 33 %, 45 % and 64% respectively (74).

Other factors contributing to the observed inter-study differences in malnutrition prevalence include the hospital location, the age distribution of patients and the patient characteristics (16). Table 1-2 provides a list of factors influencing the prevalence rate of malnutrition in hospitalised older people.

Malnutrition incidence in older people is higher in the hospital setting than in other settings (16). This high incidence is generally attributed to the common presence of co-morbidities and acute illness found in this population (22). Hospitals themselves can also contribute to declines in nutritional status (16). Table 1-3 outlines factors contributing to nutritional status decline in hospitalised

older people. Older people also have a much higher prevalence of malnutrition than younger people upon hospital admission, ranging from 1.2 – 2.3 times higher in patients aged over 65 years than those younger than 65 years based on several studies using the SGA for malnutrition classification (75-78).

Table 1-2: Factors Influencing Hospital Malnutrition Prevalence in Older People[†]

Factors Influencing Hospital Malnutrition Prevalence (16)
Malnutrition Assessment Method • No reference standard for malnutrition has led to many different nutritional assessment and screening tools used • Cut-off scores to classify malnutrition (eg by BMI) vary considerably Patients 'at risk' of malnutrition misclassified as malnourished • Subjective clinical evaluation used with little reference to nutritional parameters • Lack of consistent identification of malnutrition • Inter-tester differences
Variations in Patient Characteristics • Patients with dementia included/excluded • Surgical and/or medical patients included/excluded • Gender Imbalance. For example, some studies include a high percentage of females (72)
Hospital Location • Country • Neighbourhood location of hospital (eg socio-demographics of the neighbourhood)
Age Distribution of Patients • Patients with older patients included in their dataset tend to have higher malnutrition rates

[†] Table designed incorporating information from Lim (2010) (16)

Table 1-3: Factors Contributing to Decline in Nutritional Status in Hospitalised Older People

Factors Contributing to Decline in Nutritional Status in Hospital
1. Insufficient time to eat meals (22)
2. Inadequate meal service, including no food choice (79)
3. Difficulty in opening food packaging, using cutlery or in reaching food (22)
4. Lack of culturally specific food (15)
5. Unfamiliar environment with foreign sounds, sights and smells (22)
6. Lack of staff to assist at meal times (22, 79)
7. Meal delivery often inflexible and at inconvenient times (22)
8. Disruptions during meal times (80)
9. Lack of awareness of the importance of malnutrition by hospital staff (81)
10. Meals not palatable or lacking in energy requirements (82)
11. Disease (79)
12. Decreased Food Intake (83)
13. Missed meals due to examinations (80)
14. Modified diets prescribed prior to clinical examinations. For example ‘nil by mouth’ or low sodium diets (79) and fasting prior to blood samples collected.
15. Longer length of stay (79, 84, 85)

1.5 Consequences of Malnutrition in Hospitalised Older People

Malnutrition can have dire consequences for hospitalised older adults. A malnourished patient is at an increased risk of many adverse clinical outcomes, including mortality (16, 86-93), infection (94, 95), prolonged length of stay (LOS) (16, 91, 96, 97), functional decline (86, 98) discharge to higher level care (87, 99), falls (100) and rehospitalisation (16, 96, 101). Hospital malnutrition is also costly to the health care system (102, 103). Further details as to malnutrition's influence on mortality, morbidity and health care costs are outlined in the following subsections.

1.5.1 Malnutrition and Mortality

Based on prospective studies, malnutrition in hospitalised older people generally increases mortality risk (16, 86-93, 99, 104). However, not all studies agree. For example, in a recent study of 444 Swedish patients with a heavy disease burden by Vischer et al. (2012) (105), MNA-SF categories were not associated with mortality at discharge, nor at 1 or 4 years follow-up. This lack of a relationship could potentially be due to the high number of co-morbidities overbearing the impact of malnutrition or from the benefits of nutritional care post-hospitalisation (105).

In studies that do show malnutrition contributes to mortality, much variation exists in the actual contribution of malnutrition to mortality risk. This variation can mostly be explained by the differences in nutritional assessment methods used, the differences in follow-up time and the lack of covariates controlled for in several studies and the potential protective effect of nutritional care post-hospitalisation. Section 5.4 (Chapter 5) provides a detailed evaluation of nutritional screening tools (NSTs) as predictors of mortality in older people from all settings, including those who are hospitalised. Of importance, in the limited number of studies in which confounders have been controlled for, malnutrition has been found to consistently associate with mortality (16, 47, 86, 105-110).

1.5.2 Malnutrition and Morbidity

Only a handful of studies have prospectively looked at the influence of malnutrition and functional decline in hospitalised older people in acute care (86, 98, 108) and sub-acute care (96, 111-113). These studies all suggest that malnutrition is associated with a decline in activities of daily living (ADL) both in hospital and post-hospital in older people (86, 98). One study also looked decline in instrumental activities of daily living (IADL) and found malnutrition was not related (86). The extent of functional decline in malnourished patients varied between studies, which could be due to the measure of functional decline used, the country of the population assessed and the degree of intervention patients encountered. The MNA and MNA-SF were used in all identified studies looking at malnutrition and functional decline. Further details about the association with nutritional screening tools and functional decline is outlined in the Systematic Review in Chapter 5 (Section 5.5).

1.5.3 The Financial Burden of Malnutrition

Malnourished patients cost significantly more than non-malnourished patients as highlighted by multiple research studies (77, 102, 103, 114-118). When looking at population studies, these costs are enormous. For example, a recent Irish study found that adult hospital disease-related malnutrition cost over €1.4 million per annum, equating to 10 % of Ireland's national health care budget (114). Moreover, these costs were computed without factoring in the increased daily care cost of malnourished patient (114) which are considerably higher (119). Costs are more for malnourished patients primarily because of increased length of hospital stay (115, 120). Older malnourished people place further financial burdens as they tend to have a higher prevalence of malnutrition than younger people (78).

1.6 Nutritional Screening

Malnutrition in older people is hard to identify (121, 122) and easily missed by clinical staff if nutritional screening is not performed (123, 124). Failing to identify malnutrition will lead to failing to treat (123); an undesirable outcome. Ultimately, to identify malnutrition or risk of malnutrition, a full nutritional assessment should be performed (16) (see Section 1.8). A full assessment involves a comprehensive review of a patient's nutritional status, including medical and dietary history, anthropometric measurements, a physical exam and biomarker measurement (125). Such an assessment, although comprehensive, is not feasible for all patients in the hospital setting due to its costly and time-consuming nature (16).

A more practical option is to use nutritional screening for early identification of malnutrition. Nutritional screening is a relatively fast and inexpensive means of identifying patients who are malnourished or at risk of malnutrition. In the hospital setting, nutritional screening is recommended to be accompanied by both a full nutritional assessment and an appropriate intervention for any patients identified as malnourished or at risk of malnourishment (126, 127). Nutritional screening is therefore a crucial precursor to the Nutrition Care Process (NCP) (128, 129).

Nutritional screening is recommended for routine use in all hospitalised older patients (123, 130). Despite this recommendation, screening does not regularly occur in hospitals. Barriers to nutritional screening are outlined in Table 1-5 and include costs to the health care system (131), the indecision associated with which NST is best to implement (132) and staff shortages (133).

Another potential barrier to nutritional screening is the lack of effectiveness of current nutritional intervention strategies (130). For example, a recent review of older people in primary care facilities found that whilst 3 out of 14 studies (21 %)

reported patients gained weight with nutritional intervention (predominantly oral intervention supplement interventions), 12 out of 16 studies (75 %) reported that there was no effect on physical function with nutritional intervention (134). Similarly, a systematic review of oral nutritional support in older patients discharged from hospital found that whilst all studies found patients gained weight and/or increased their energy intake, mortality rates were not affected by nutritional supplementation in any studies (135). However, despite these findings, a recent randomised control trial in Australia found that if nutritional screening was paired with an early intervention malnutrition care plan in malnourished patients (MNA score < 17), then patient length of stay was reduced from an average of 19.5 to 10.6 days (124).

Currently no reference standard for nutritional screening in older people has been agreed upon for clinical application and accordingly, various nutritional screening tools (NSTs) have been developed. NSTs tend to include body mass index (BMI) (weight/height^2) and a short string of questions regarding recent weight loss, food intake and risk of accelerated nutritional decline due to chronic disease (127). Several recent reviews of NSTs in older people have been conducted, including an evaluation of their validity and reliability (16, 127, 136-138). NSTs suitable for identifying older hospitalised people with malnutrition or risk of malnutrition are described in the next section.

Table 1-4: Characteristics of a Good Nutritional Screening Tool (NST) for Use in Hospitalised Older People.

Characteristics of a Good Nutritional Screening Tool
Tested for Validity in Hospitalised Older People • Criterion Validity – how well the NST compares to either (1) an objective assessment by a professional (138), (2) full nutritional assessment (137, 138) and anthropometric measures (138) (3) MNA or SGA (138) • Construct Validity – how well the NST compares to other NSTs and laboratory values (138) • Content (Face) Validity – includes relevant components (139) • Population specific (137) • Sensitivity and specificity (137)
Tested for Reliability in Hospitalised Older People (137, 140)
Cost Effective (137)
Fast and Easy to Use (137, 140)
Accepted into the Clinical Setting (137) • No laboratory tests needed (16) • Uses routinely collected information (16) • No complex computations (16)
Identify older people with malnutrition or at risk of becoming malnourished (137)
Leads to referral for a Full Nutritional Assessment (126, 127)
Non-invasive (16)
Accepted by patients (16)
Bonus Features
Doubles as a Nutritional Risk Index – that is, predicts nutritional related outcomes (138)

MNA = Mini Nutritional Assessment; SGA = Subjective Global Assessment

Table 1-5: Barriers and Problems with Implementation of Nutritional Screening Tools in the Hospital Setting

Barriers and Problems to Implementation
1. Lack of time and staff to implement the NSTs (133)
2. Health Care Costs (131)
3. Nutritional screening not seen as a important for all patients on admission (141)
4. Not a standard, routine procedure in a patient's hospital admission (142, 143)
5. Discussion over which NST to use can hinder implementation (132)
6. Results of nutritional screening is not always documented in patient charts (130)
7. Patients who do not outwardly look malnourished are often not screened with a NST (133)
8. Most NSTs use BMI computations, which require the often difficult measurement of patient height and weight (133). Moreover, weight and height are commonly not measured in the hospital setting (131)
9. The use of BMI may be masking malnutrition (144)
10. Lack of information on validity and reliability (132)
11. NSTs are validated against many reference standards of malnutrition assessment as there is not one set reference standard for malnutrition assessment/diagnosis (145)
12. Nutritional screening is often not performed with a validated screening tool (146) or is performed with a screening tool not validated in that specific population (133)
13. The common belief by nurses that individual judgement of a patient being underweight is superior to a nutritional screening tool in detecting malnutrition or risk of malnutrition (133)
14. Multiple referral pathways for a full nutritional assessment often can result in a 'verbal' referral rather than a NST being utilised for referral (133)
15. Because nurses report that patients not in the hospital for very long do not need to be screened (133)
16. Limited information for health practitioners on how to implement the NST appropriately (16)
17. Health Care professionals report that there are too many screening tools to choose from, so they choose none (139).
18. Interventions as the result of nutritional screening may not always be beneficial to patients, particularly in the short term (143)

Abbreviations: NST = Nutritional Screening Tool; BMI = Body Mass Index

1.7 Nutritional Screening Tools

A multitude of nutritional screening tools are in existence today. Described in this section are some of the most commonly used nutritional screening tools applicable to the hospital setting. Table 1-6 provides a comparison of selected NSTs including studies looking at their validation and reliability in older people.

1.7.1 The Mini Nutritional Assessment (MNA)

The Mini Nutritional Assessment (MNA) (Appendix 1) is an eighteen question nutritional screening and assessment tool specifically developed for use in older people (147-149). Its methodology is described in detail in Sections 7.2.2.2, 8.2 and 6.2. The MNA has undergone extensive validity and reliability testing, particularly in community based studies, and is popular for use in older people globally (147, 150). Table 1-6 lists validity studies of the MNA, including studies specifically looking at hospitalised older people. From this table it can be seen that there are only a limited number of studies looking at the validity of the MNA in hospitalised older people, with sensitivity and specificity values appearing low overall. Recently, the MNA has also been improved for specificity by using population specific cut-offs for its anthropometric measures of BMI, calf circumference (CC) and mid arm circumference (MAC) (151, 152) but these studies have yet to be applied to acute care geriatric wards. Also evident from Table 1-6 are the mixed results of studies of hospitalised older people looking at the construct validity of MNA, that is, how well it compares against components of a full nutritional assessment.

MNA has many advantages, including identification of malnutrition before severe weight loss occurs (147) and its ability to monitor changes in nutritional status (147). However, the MNA has disadvantages. It includes subjective questions, which are more suited to community-dwelling rather than hospitalised older people (127) and which can result in a lack of inter-tester reliability (125, 153) It can over-diagnose risk of malnutrition in frail, older people (154), perhaps because the MNA itself can also identify frailty (155). (See Table 1-6). Other

disadvantages of the MNA include its lack of ability to predict future malnutrition (154) and its inability to be used in patients with cognitive impairment (16) or in those with enteral feeding (156).

1.7.2 The Mini Nutritional Assessment Short Form (MNA-SF)

The MNA short form (MNA-SF) (157, 158) (see Appendix) comprises six questions from the full MNA, and is described in further detail in Sections 7.2.2.2, 8.2 and 6.2. The MNA-SF is the first step of a two part process: the MNA-SF for screening for malnutrition or risk of malnutrition, followed by referral for MNA assessment (159). The MNA-SF is generally considered to be user friendly in that it takes less than 5 minutes to apply, at least in community dwelling older people (16). It also provides the option of assessing calf circumference (CC) in lieu of the difficult to measure BMI (157). The MNA-SF has a high sensitivity and specificity when compared against the full MNA (157, 160), although this is a form of incorporation bias as the MNA-SF contains questions from the MNA (138). When the MNA-SF has been compared against nutritional assessment or professional assessment of nutritional status in hospitalised older people, it has shown poor specificity (161, 162). Table 1-6 provides an outline of studies validating the MNA-SF against various reference standards. Like the MNA, very few studies have looked at construct validity of the MNA-SF; that is, how well it compares against components of a full nutritional assessment.

1.7.3 The Malnutrition Universal Screening Tool (MUST)

The Malnutrition Universal Screening Tool (MUST) was designed by the British Association for Parenteral and Enteral nutrition (BAPEN) (163). It classifies patients as either at low, medium or high malnutrition risk based on a patient's BMI, history of unintentional weight loss and the probability of future weight loss based on acute disease (163, 164). MUST is a popular screening tool in UK national surveys of malnutrition (165) and has been found to have a similar reliability to the MNA in screening for nutritional risk in geriatric populations (139). When compared to the MNA, MUST has been reported to take less time, and to require less subjectivity by interviewers (139). However, MUST does have

its disadvantages. It was recently found to have a low completion rate (47 % missing data) in a study of hospitalised older people, with the authors of this study rendering it less clinically applicable than other nutritional screening tools (162). MUST also includes BMI which is complicated to measure in older people (see Section 1.9.3) as well as having a BMI cut-off point that has been suggested to be too low for older people (166). Table 1-6 shows validity and reliability studies incorporating MUST. From this table it can be seen that MUST has been found to have a low agreement with both weight loss and BMI (139, 162) and has been found to have low sensitivity (61 %) and specificity (76 %) in a large study of hospitalised older people of all ages (73).

1.7.4 Simplified Nutritional Appetite Questionnaire (SNAQ)

The Simplified Nutritional Appetite Questionnaire (SNAQ) (See Appendix) (167) consists of 4 questions: one each on appetite, taste, satiety and meal frequency (167). Responses to each question are reported on a Likert scale ranging from 'very poor' to 'very good'. A score of 14 or less out of a possible 20 predicts future weight loss in older people (167, 168). SNAQ is advantageous as it is quick and easy to implement and requires no specialist equipment or training of assessors. SNAQ has been validated against weight loss in older people (167). It has also been validated against the MNA in a recent study of hospitalised older people, where it shows modest sensitivity and specificity values of 71 % and 74 % respectively (169). Considerable more work is needed to validate the SNAQ, particularly against components of nutritional assessment (see Table).

1.7.5 Geriatric Nutritional Risk Index (GNRI)

The Geriatric Nutritional Risk Index (GNRI) was recently developed as a nutritional-risk index for older people, based on the 'Nutritional Risk Index' for younger people (170). Since its development, it has also be validated against the MNA, although its agreement is low (kappa = 0.29) (97). The equation for predicting GNRI is as follows:

GNRI = (1.489 x albumin (g/L)) + (41.7 x (weight/WLo))

With WLo = Ideal Weight, using Lorentz equations as described by Boulianne et al. (170):

Men: WLo = *H* -100 – ((*H* - 150)/4)

Women: WLo = *H* - 100 – ((*H* - 150)/2.5)

With H = height in cm; g = grams; L = Litre

GNRI categories are: major risk (scores < 82), moderate risk (scores < 92), low risk (scores 92 to ≤ 98) and no risk (> 9) (170). The GNRI can be considered as a nutritional screening tool, although more validation studies are needed, as evident from reviewing Table 1-6.

1.7.6 Other Nutritional Screening Tools

Multiple other nutritional screening tools exist for older people, including the Malnutrition Universal Screening Tool (163), Malnutrition Screening Tool (171), the Determine Your Health Nutritional Screening Initiative (NSI) checklist (172), the Nutritional Status Score (NSS) (173) and the Rapid Screen (RS) (174).

Table 1-6: Comparisons of Selected Nutritional Screening Tools and Nutritional Risk Indices

Feature	Nutritional Screening Tool				
	MNA (149)	**MNA-SF(158)**	**MUST(163)**	**SNAQ(167)**	**GNRI (170)**
Items Included	Weight Loss BMI and CC Appetite Loss Mobility Stress/Acute Disease Dementia/ Depression Living Situation Drugs Skin Lesions Full Meals Protein Intake Fruits, Vegetables Fluid Intake Mode of Feeding Nutritional Status Health Status MAC	Weight Loss BMI or CC Appetite Loss Mobility Stress/Acute Disease Dementia/Depression	Weight Loss BMI Acute Disease	Appetite Taste Satiety Meal Frequency	Serum Albumin Weight Height
Criterion Validity and Reliability	1. Validated in multiple studies of community dwelling older people where it has shown good sensitivity and specificity against a full nutritional assessment (147, 175). **<u>Hospitalised Older People</u>:** 2.Validated against nutritional assessment by physicians: **Se = 79 %; Sp = 90 %** in 65 patients aged ≥ 65 years. Visvanathan et al. 2004 (174). 3. Validated against nutritional assessment by dieticians: **Se = 57 %; Sp = 69%** in 160 patients aged ≥ 65 years. Azad et al. 1999 (176). 4. Validated against full nutritional assessment: **Se = 77 %; Sp = 36%** in 60 patients aged > 65 years. Thorsdottir et al. 2005.(177).	1. Validated against nutritional assessment by physicians: MNA-SF-BMI: **Se = 89 %; Sp = 82 %,** MNA-SF-CC: **Se = 85 %, Sp = 84 %** in 2032 people aged ≥ 65years; 1346 in residential care, 490 community dwelling, 127 hospitalised, 65 in rehabilitation. Kaiser et al. 2009 (157). 2. Validated against MNA: **Se = 98 %, Sp = 100 %** in 881people (mean aged 76.4 years); with 650 community dwelling, 105 hospitalised, others not defined. Rubenstein et al. 2001 (158). **<u>Hospitalised Older People:</u>** 3. Validated against MNA: **Se = 100 %, Sp = 70 %** in 408 patients aged ≥ 60 years. Cohendy & Rubenstein, 2001 (160). 4. Validated against nutritional assessment by clinical nutritionist: **Se = 100 %, Sp = 38 %** in 69 patients aged ≥ 70 years. Rahnoff et al. 2005 (162). 5. Validated against nutritional assessment (low BMI & weight loss): **Se = 100 %, Sp = 39 %** in 171 patients aged > 60 years. Neelemaat et al. (162) 6. **85 % agreement** with MNA in 444 patients aged ≥ 75 years. Vischer et al. 2012 (105).	1. Validated against SGA: **Se = 61 %. Sp = 76 %** in 995 patients of all ages. Kyle et al. 2006 (73). **<u>Hospitalised Older People:</u>** 2. Validated against SGA: **Se and Sp not reported. Agreement = 92 % (kappa = 0.783)** in 50 patients (mean age 45 years). Stratton et al. 2004 (163). 3. Agreement with MNA (**Kappa = 0.790**) in 531 patients aged ≥ 65 years by Cansado et al. 2009 (139)	1. Validated against MNA: **Se = 71 %, Sp = 74 %** in 175 community/hospitalized and residential care people aged ≥ 65 years. Rolland et al. 2012 (169).	(1) Agreement with MNA **Agreement: kappa = 0.29** in 241 residential care residents. Cereda et al. 2009 (97).

Abbreviations: BMI = Body Mass Index; CC = Calf Circumference; MNA = Mini Nutritional Assessment; MNA-SF = MNA short form; MNA-SF-BMI = MNA-SF with BMI; MNA-SF-CC = MNA-SF with CC substituted for BMI; MUST = Malnutrition Universal Screening Tool; SNAQ = Simplified Nutritional Appetite Questionnaire; GNRI = Geriatric Nutritional Risk Index; Se = sensitivity; Sp = Specificity; MAC = Mid Arm Circumference; n/a = not applicable. 'Patients' refers to hospitalised patients.

Continued...

Table 1-6: Comparisons of Selected Nutritional Screening Tools and Nutritional Risk Indices (continued)

Feature	Nutritional Screening Tool				
	MNA (149)	**MNA-SF(158)**	**MUST(163)**	**SNAQ(167)**	**GNRI (170)**
Construct Validity	**Hospitalised Older People:** 1. Agreement with % Weight Loss (**kappa = 0.293**), BMI (**kappa = 0.063**) and MUST (**Kappa = 0.790**) in 531 patients aged ≥ 65 years (139) 2. No association with BMI or CRP, iron, cholesterol, vitamin D, Albumin, Prealbumin and Haemaglobin showed a weak relationship. 444 patients aged ≥ 75 years. Adjusted for confounders. Vischer et al. 2012 (105). 3. Associated with low BMI and low levels of albumin, serum cholesterol, Vitamin A, Vitamin D. Se and Sp not reported. Univariate analysis in 106 patients aged ≥ 65 years (178). 4. Associated with triceps skinfold thickness, CC and BMI and Mid-Arm muscle circumference. Multivariate analysis in 109 patients aged > 70 years (179). 5. Associated with BMI, arm muscle area, albumin, transferrin, haemoglobin, lymphocyte count, total cholesterol & creatinine in 358 older people (77 % in hospital). Univariate analysis. Mean age = 84.6 years (180)	**Hospitalised Older People:** 1. Associated with weight, BMI, Mid-Arm muscle circumference & grip strength in patients aged 65 – 99 years. Univariate analysis (181).	**Hospitalised Older People:** 1. Agreement with % Weight Loss (**kappa = 0.275**), BMI (**kappa = 0.111**) and MNA (**Kappa = 0.790**) in 531 patients aged ≥ 65 years by Cansado et al. 2009 (139). 2. Associated with weight, BMI, Mid-Arm muscle circumference, grip strength, albumin and pre-albumin in patients aged 65 – 99 years (181). 3. Validated against low BMI and weight loss): **Se = 67 %, Sp = 82 %** in 171 patients aged > 60 years. Neelemaat et al. 2011 (162).	1. Validated against Weight Loss (5 %): **Se = 81 %, Sp = 76%** and Weight Loss (10 %): **Se = 88 and Sp = 84 %** by Wilson et al. 2005 (167); long-term care residents (n=247) and community-dwelling adults (n=352).	1. Associated with BMI, arm muscle area, albumin, transferring & haemoglobin in 358 older people (77 % in hospital). Univariate analysis. Mean age = 84.6 years (180)
BMI cut-off point (kg/m^2)	< 23	< 23	< 20	n/a	Continuous Variable

Abbreviations: BMI = Body Mass Index; CC = Calf Circumference; MNA = Mini Nutritional Assessment; MNA-SF = MNA short form; MNA-SF-BMI = MNA-SF with BMI; MNA-SF-CC = MNA-SF with CC substituted for BMI; MUST = Malnutrition Universal Screening Tool; SNAQ = Simplified Nutritional Appetite Questionnaire; GNRI = Geriatric Nutritional Risk Index; Se = sensitivity; Sp = Specificity; MAC = Mid Arm Circumference; n/a = not applicable. 'Patients' refers to hospitalised patients.

1.8 Nutritional Assessment

Without a gold standard definition or assessment method for malnutrition, a reference standard is often used to diagnose malnutrition. This reference standard is usually a Full Nutritional Assessment (FNA) or an assessment by a trained professional such as a dietician, researcher, nurse or doctor (138, 182). Table 1-7 outlines components commonly used in a full nutritional assessment. Basically, a nutritional assessment includes four main components, summarised as 'ABCD': Anthropometric Measures, Biochemical and laboratory measures, Clinical Methods and Dietary Evaluation Methods (183). Functional capacity is also an important component of a nutritional assessment (16, 184). Other validated reference standards for nutritional assessment in older people include the Subjective Global Assessment (SGA) (184, 185) and the Mini Nutritional Assessment (see 1.7.1) (149, 184).

Table 1-7: Summary of Items Included in a Nutritional Assessment. Modified from Lim (2010) (16)

Anthropometric Measures (16, 186) • Height • Weight: usual weight, ideal weight, BMI, weight loss (absolute and percentage) • Fat and Tissue Measures: calf circumference (CC), mid arm circumference (MAC), triceps skinfold thickness.
Biochemical and Laboratory Measures (16, 186) • Iron: haemoglobin, hematocrit, serum transferrin • Vitamins and Minerals: Vitamin D, Folate • Cholesterol • Plasma Proteins: C-Reactive Protein, serum albumin, serum total protein, retinol binding protein • Total lymphocyte count • Skin test reactivity
Clinical Methods • Physical Exam: detection of signs associated with malnutrition and nutrient deficiency, especially protein-energy deficiency (temporal wasting), oedema, hydration level and micronutritient deficiency (observation of the condition of hair, gyms, nails, bones, skin, eyelids, eyes, muscles and thyroid gland) (186) • Medical History: assessment of any factors which may be inhibiting digestion, absorption or excretion (186)
Dietary Evaluation (16, 186) • 24 hour dietary recall • Food frequency questionnaire • Dietary history across the lifespan • Food diary method • Observed food consumption
Functional Capacity (16) • Grip Strength • Walking Speed

BMI = Body Mass Index

1.8.1 Subjective Global Assessment (SGA)

The Subjective Global Assessment (SGA) (185, 187) is a multidimensional nutritional assessment instrument evaluating: weight loss history, change in dietary intake, persistent gastro-intestinal symptoms (> 2 weeks), functional capacity (optimal, sub-optimal, ambulatory or bedridden), disease diagnosis and its influence on nutritional requirements (none, low, moderate or high stress), physical features of the patient (low subcutaneous fat levels, muscle wasting, ankle and/or sacral oedema and ascites) (185). The SGA has no numerical scoring system, rather it is used by professionals to subjectively classify patients as being well nourished (SGA A), with mild-moderate malnutrition (SGA B) or with severe malnutrition (SGA C) (184, 185). SGA was initially developed for use in people of all ages (185), but has since been validated for use in older hospitalised patients (188-190). However, one downfall of these validation studies is that reference standard the SGA was compared against (anthropometric measure/s with or without biomarkers) falls short of a full nutritional reference standard (16, 138)

The SGA has been endorsed by several organisations, including The American Society for Parenteral and Enteral Nutrition (ASPEN) (191), by The European Society for Clinical Nutrition and Metabolism (ESPEN) (192) and the Dieticians Association of Australia (DAA) (193). However, the SGA is not objective like the MNA, thereby rendering it impractical for intervention and follow-up studies.

1.9 Anthropometric Measures

1.9.1 Weight

Weight assessment is often overlooked in geriatric wards. A recent study of a geriatric ward in Germany found weight was only documented in 54 % of geriatric patients (13). Even nutritional studies of older hospitalised patients have reported not measuring patient weight due to difficulties in assessing. For instance, Stratton and colleagues (91) were only able to weigh 56 % of patients in their study validating the MUST. Additionally, Tsai and colleagues (194) did not measure body weight in any of their long term care subjects, citing a lack of

equipment available as the reason they did not measure weight. Multiple other reasons exist why weight measurement is difficult to perform in older people, including issues such as hearing or vision loss, dementia, incontinence, language barriers, delirium and frailty (16). It could also be that a patient is simply too ill to be weighed (195).

1.9.2 Weight Loss

Weight loss is incorporated as part of many NSTs, including the MNA (148) and MUST (91). Weight loss in older people is associated with many detrimental outcomes (18), including prolonged hospital admissions (139), increased infection risk (95), functional decline (196) and reduced life expectancy (147). A five year follow-up study of the Cardiovascular Health Study (CHS) also reported that weight loss was the best predictor of mortality in older people (197).

1.9.3 Body Mass Index (BMI)

Body Mass Index (weight(kg)/height(m)^2) is an established part of clinical nutrition screening and is often used as a screening tool for malnourishment on hospital admission (16). It is included as part of many NSTs of older people, including the MNA (148) and MUST (91). BMI is quantitative and has the further advantages of being correlated with both fat mass (144) and MNA (198) in older people.

Nevertheless, the use of BMI as a NST in older people is contentious for several reasons: it may not be a sensitive, reliable or valid measure of nutritional status in older people due to inaccuracies in assessing both height and weight (144); it does not correlate with weight loss in geriatric inpatients (139); it is overestimated in those who are well nourished and underestimated in those with risk of malnutrition (198); it is not an indicator of protein-energy malnutrition (16); and its correlation with fat mass is significantly lower in older people compared to younger people (199).

The optimal BMI for older people is also disputed and until this is defined, a broad range of BMI cut-offs for malnutrition detection in older people will exist. Even screening tools do not have standard BMI cut-offs, with the MUST and the MNA having BMI cut-offs of 18.5 kg/m^2 and 20 kg/m^2 respectively. Moreover, the ideal BMI for older people may be significantly higher than the commonly accepted 20-25 kg/m^2 for younger adults (144). This higher optimal BMI may mean BMI cut-offs for malnourishment detection in both the MNA and MUST are currently too low. These low BMI cut-offs may impede diagnoses of malnutrition based on weight loss. For instance, a recent study found many patients with a BMI above 25 kg/m^2 who had unintentional weight loss were not identified as being malnourished (200).

1.9.4 Limb Circumference Measures

Circumference measurements reflect body levels of both lean and fat mass (201). Therefore these measures can be used to assess nutritional status in older people without needing to rely on height or weight measures. Commonly used circumference measures in the hospital setting include mid-arm circumference (MAC) and calf circumference (CC). Both of these measures are included in the MNA, and CC has recently been included in the MNA-SF as an option in lieu of BMI (157). CC and MAC measures are popular with hospital staff as they are simple and easy to measure (16).

CC is measured as the widest girth of the calf; MAC as the mid-point circumference of the upper arm, mid way between the acromion process and lateral epicondyle of the elbow (202). CC has been found to be more accurate at identifying malnutrition than MAC, except in people with end-stage functional decline (203). Despite their advantages, CC and MAC do have limitations. For example, MAC, although correlated with BMI (196) has been found to be a poor marker of malnutrition (204) and CC is highly influenced by common presence of ankle oedema.

1.10 Sarcopenia

Sarcopenia refers to the change in body composition that occurs with ageing, particularly with regards to loss of skeletal muscle mass (205). This muscle mass loss was termed ‘Sarcopenia’ by Rosenburg in 1989; a derivation from the Greek ‘sarx’ meaning ‘flesh’ (muscle) and ‘penia’ meaning ‘loss’ (206). Since then, multiple definitions of sarcopenia have been proposed.

Sarcopenia is a global problem in older people, with epidemiological research reporting that around 50 % of people aged over 75 years of age are affected (207). Sarcopenia is a core component of frailty (208-210), and like both malnutrition and frailty, is a major cause of functional decline, loss of independence and mobility reduction in older people (211).

Although no reference standard definition of sarcopenia yet exists, several advances in the form of consensus definitions have been developed. These definitions do not all agree however. For example, sarcopenia is defined as both muscle mass and strength loss by the European Working Group on Sarcopenia in Older People (EWGSOP) and the ESPEN; as an age-associated loss of muscle mass and function by the International Sarcopenia Consensus Conference Working Group (ISCCWG) (212); and as loss of muscle mass alone (205, 213). Of note, sarcopenia was awarded Medline Seach Heading (MeSH) status in 2010, described as a ‘progressive decline in muscle mass due to ageing which results in decreased functional capacity of muscles’ (214).

1.11 Indices of Nutritional Status and Nutritional Risk

A NST has additional clinical value if it can predict the likelihood of an adverse clinical outcomes occurring (170). However, the ability of a NST to predict adverse clinical outcomes in older people is not yet clearly known (215). Chapter 4 presents a systematic review of NSTs as predictors of adverse outcomes in older people across a variety of settings: community, residential care and acute/sub-

acute hospitalisation. This systematic review identifies several gaps in the literature: (i) very few studies have been conducted in the hospital setting; (ii) the comparative ability of NSTs in outcome prediction is largely un-researched; and (iii) whilst many studies look at predictive ability per se there is a distinct shortage of studies looking at predictive *accuracy*: that is, the ability of NSTs to correctly identify individuals likely to encounter adverse clinical outcomes. Chapters 5 and 6 focus on using nutritional screening tools as predictions of adverse clinical outcomes.

Important to note is the following differentiation: an index of nutritional status, also commonly known as a NST, screens for malnutrition or risk of malnutrition; an index of nutritional risk predicts nutrition related outcomes (170).

The following chapter describes frailty, a concept related to both malnutrition and sarcopenia (216). An outline of the thesis aims and scope is presented in Chapter 3.

2 FRAILTY

'Frailty: Someone who is weak and has tiny muscles'

– Urban Dictionary

This chapter presents the concept of frailty, its various models and operational definitions. It then identifies and discusses the research gap, which is that the predictive ability and discriminatory power of frailty instruments in the hospital setting has received little attention in the literature. This is similar to the research gap of NSTs in the hospital setting from Chapter 1. Knowing such information would advance the debate over which frailty operationalisation definition is the most optimal in the clinical setting.

2.1 Introduction

Amid the rapid global expansion in the number of older people, frailty will become an increasingly important challenge for health and aged care systems worldwide. It is estimated that over a quarter of people older than 85 years are frail, with the greatest frailty burden being found in women (210, 217, 218). Frailty is characterised by a general weakness, thinness and a reduced ability to cope with stressors (210). An individual classified as frail has an elevated risk of mortality (219-225), disability (226-228), falls (221, 222, 229, 230), hospitalisation (228, 231), admission to a nursing home (224, 232, 233) and health care system use (231, 234). Frailty also detracts from quality of life (235, 236).

Research into frailty has shown an unprecedented level of growth over the last two decades (237). However, frailty research is still in its infancy. The underlying pathophysiological pathways leading to frailty are not yet clearly known (238).

Moreover, frailty does not have an international consensus definition, despite multiple reviews highlighting the need for such a definition (8, 238-252). Such a definition is urgently needed for consistent recognition of frailty.

2.2 Frailty Defined

Frailty was first clinically described in the 1970s as older patients needing permanent care (253). By the 1980s, frailty was thought of as a disability caused by chronic disease (254, 255). In 1991, the phrase 'frail elderly' was assigned a Medline Search Heading (MeSH), described as 'older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity' (256). During the 1990s, definitions of frailty inclined towards including measures of dependence on others to perform Activities of Daily Living (ADLs) (257, 258).

In 2001, Fried et al. (210) proposed their landmark frailty phenotype definition, which describes frailty according to its physical, and measureable, components. The following year, Rockwood and Mitnitski released their accumulated deficits model of frailty, which considers not only the physical components of frailty, but also the psycho-social aspects of frailty (259). Both Fried's and Rockwood's frailty models are highly regarded and are in common use today. Fried's phenotypic model has also been expanded to include cognitive frailty, as discussed in Section 2.4.

Nowadays, a plethora of theoretical definitions for frailty exist. By and large, frailty is considered to be a geriatric syndrome (65, 248, 249, 253, 260-263) reflecting multi-system dysfunction (210, 257, 264) and in which individuals are able to dynamically transition between severity states (242, 265, 266). Frailty is associated with an increased risk of adverse outcomes (253). It is different conceptually from ageing, disability, and co-morbidity although it is distinctly

related to these factors. For example, although frailty incidence increases with age, it occurs independently from chronological age (233, 267, 268).

Frailty can occur without disability. For example, in the Cardiovascular Health Study (CHS), only 6 % of those who were frail were also disabled (210). Following from this and other similar observations, frailty has been considered as a pre-disability by several research groups (245, 252, 269, 270). However, disability is often strongly intertwined with frailty (260, 271, 272) and other research groups have used frailty definitions incorporating disability (241, 242, 270, 273-277). Interestingly, the World Health Organisation (WHO) defines disability as a dynamic interaction between a person's health condition and their environment (226). Therefore, frailty could perhaps be an 'unstable disability' as proposed by Woodhouse et al. (1997) (267).

Frailty also occurs without the presence of co-morbidities. For example, in the CHS study, 32 % of frail older people did not have any co-morbidity (210). Conversely, people with one of more co-morbidities may not be frail (278, 279).

Multiple reasons exist as to why it is so difficult to define frailty, including its complex aetiology (65, 280), the independent work of frailty researchers (244, 256) and the inherent difficult in distinguishing frailty from both ageing (281, 282) and disability (260). Regardless of these issues, and perhaps because of them, international consensus groups such as the WHO and the International Association of Geriatrics and Gerontology (IAGG) are currently working on a framework for an internationally accepted frailty definition (9, 252). The most recent consensus for a theoretical definition of frailty is by the Frailty Operative Definition-Consensus Conference (FOD-CC) project who defined frailty 'a multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors' (283).

Nonetheless, what is needed is a now, as recent literature has highlighted, is a translation of frailty measurement into clinical practice (9, 10, 245, 246, 252, 284, 285), the topic of the section 2.5.

2.3 Biological Causative Mechanisms of Frailty

Much debate exists around the biological causative mechanisms underpinning frailty (240, 286). There are multiple biological pathways that can lead to frailty, and many of these are similar to those causing malnutrition (11, 210, 287) and sarcopenia (288). Inflammation is one such pathway, and is well established as a causal factor for frailty (65, 209, 238, 289-301). Pro-inflammatory cytokines can influence frailty directly, for instance by promoting protein degradation (34), or indirectly by metabolic actions on physiological processes (65). The impact of inflammatory cytokines on frailty has also been recently reported to be stronger in women than in men (302).

The biological causative mechanisms of frailty are different from those processes causing the ageing process (303). Frailty occurs when not one, but multiple physiological systems decline (11, 62, 303, 304): the more physiological systems that are in a declined state, the greater the frailty incidence (305). Although, physiological systems do lose their homeostatic reserve with ageing, there is an inherent reserve buffer, suggested to be around 30 %, in which an individual can lose and still function well (306). Frailty results when this threshold is surpassed in multiple physiological systems - so much so that repair mechanisms cannot maintain system homeostasis (303). Pre-frailty (or latent frailty) (303) is thought to be the silent precursor to frailty, and will result in frailty if adverse events, such as acute illness, injury or psychological stress occur (303).

Frailty can also result from undernutrition (303) (11, 210, 287) and from factors associated with undernutrition, such as such as poor appetite (307), poor oral health (308), anaemia (280), vitamin deficiencies (309-311) and endocrine disorders (312, 313). For example, in The Longitudinal Ageing Study Amsterdam

(LASA), incident frailty was linked with low serum levels of 25-hydroxy-vitamin D (25(OH)D) and elevated serum C-Reactive Protein (CRP) levels (314). In the Women's Health and Ageing Study II, the gut-derived hormone, ghrelin was found to be lower in those women classed as frail (315). Glucose and insulin dynamics have also been found to be abnormal in frail older women (316).

Other factors linked with frailty include inactivity, diabetes mellitus, osteopenia, oxidative stress, an imbalance between parasympathetic and sympathetic tone, and polypharmacy (216, 280, 317). Table 2-3 outlines factors associated with frailty in older people.

Table 2-1: Factors Reported to Associate with Increased Frailty Incidence in Older People

Factors Associated with Increased Frailty Incidence in Older People
Psychological Factors
Cognitive Impairment (218)
Depressive Symptoms (218)
Nutritional Factors
Poor Oral Health (308)
Malnutrition (11, 210, 287, 303)
Anaemia (280)
Lower 25-hydroxy-vitamin D (314)
Environmental Factors
Cigarette Smoking (318)
Lower Education (218)
Living Alone (218)
Low Physical Activity (216, 280)
Poverty (319)
Clinical Factors
Polypharmacy (216, 280)
Diseases
Diabetes Mellitus (216, 280)
Endocrine disorders (312, 313)
Impaired cardiac autonomic control (320)
Osteopenia (216, 280)
Factors Resulting From Disease
Glucose and Insulin Abnormalities (316)
Lower ghrelin levels (315)
Inflammation
Oxidative Stress (216, 280)
Cancer (317)
Imbalance between parasympathetic and sympathetic tone (317)

2.4 Cognitive Frailty

Cognitive impairment refers to a decline in cognitive tasks such as remembering, reasoning and planning (321). A bi-directional association occurs between cognitive impairment and frailty (321). As such, there is an emerging debate over whether cognitive impairment should be included in an operational of frailty. That is, in addition to the physical phenotype of frailty proposed by Fried et al. (2001) (210), frailty can also be considered as a cognitive phenotype. Cognitive frailty shows promise as an operational measure of frailty. For example, a recent study of 6030 community dwelling older people reported that adding impaired cognition to the CHS frailty phenotype increased the predictive ability for adverse outcome, particularly 4-year mortality (322). However, cognition has been found to lack association with other aggregate components of frailty, such as depression, energy intake, mobility and physical activity (323). Therefore, based on this finding, Robertson et al. 2013 (321) suggested that frailty and cognitive impairments are perhaps best treated as separate concepts rather than as the same condition.

2.5 Frailty Measurement

Regardless of what definition of frailty is used, to be applied in gerontology research and clinical practice, it first needs to be operationally defined. An operational definition for frailty has been identified as one of ten crucial areas for advancement in frailty research (244). There is currently much debate as to which operational definition of frailty is most suitable for practical application (245, 251, 324). Nonetheless, several advances have been made in identifying what components it should contain. For example, a recent study by Rodriguez-Manas et al. (283) found that although experts disagreed on the details of an operational definition of frailty, there were frequent items identified for inclusion: namely reduced gait speed, mobility, nutritional status, mental health and cognition (283).

These single components of frailty can be used to predict adverse outcomes in older people and their assessment is popular in the clinical setting today (325).

However, in the mid-1990s, it was verified that when these frailty components were grouped together to form combination scores, prediction of adverse clinical outcomes was higher than when components were considered alone (326, 327). Frailty combination scores have been used to operationally define frailty ever since, and a plethora of these operational frailty scores are in current use (328).

Frailty operational scores should fulfil a number of criteria. First and foremost, they should be able to identify frailty. Additional qualities they should have, as identified by Clegg et al. (11) using Bell's (329) disease classification guidelines (329) include:

1. An ability to reliably predict adverse clinical outcomes
2. An ability to reliably predict patient response to potential therapies
3. Be supported by a biological causative theory

In the clinical setting, frailty operationalisations, like nutritional screening tools, should also be quick and easy to apply (245). Table 2-2 outlines qualities a frailty operational score should ideally have.

Table 2-2: Qualities of a Frailty Operational Score

Qualities of a Frailty Operational Score
1. Identifies frailty and pre-frailty
2. Reliably predicts outcomes (11)
3. Reliably predicts patient responses to potential therapies (11)
4. Supported by a Biological Causative Theory (11)
5. Quick and Easy to Apply (245).

Frailty instruments suitable for use in the hospital setting and discussed in this thesis include: the Cardiovascular Health Study (CHS) Index, the Study of Osteoporotic Fractures (SOF) Index, the Frailty Index of Accumulated Deficits (FI-CD), the Frailty Index derived from Comprehensive Geriatric Assessment (CGA) (FI-CGA), and the Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL) Index and the Multidimensional Prognostic Index (MPI) (330).

Although frailty is not the same as disability, functional decline indices can be considered to be frailty instruments (274). Examples including the Katz score of activities of daily living (ADL) (331), Lawton's Instrumental ADL (IADL) scale (332), the Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA) (333) and the Hospital Admissions Risk Profile (HARP) (327). Walking speed and grip strength can also be used in isolation to measure frailty in older people. An outline of frailty operationalisations, functional decline indices and individual markers of frailty is discussed in the following section. Table 2-3 presents a comparison of frailty instruments included in thesis with regards to their clinical operation.

2.5.1 The Cardiovascular Health Study (CHS) Index

The first operational definition of frailty was proposed by Fried et al. (2001) and is often known as the Cardiovascular Health Study (CHS) index from the study it was originally applied to (210). The CHS index considers frailty by its physical characteristics, or 'phenotype', defining the condition as the presence of three or more of: shrinking (unintentional weight loss of 4.5kg or more in the last year), weakness (low grip strength), exhaustion (self reported), slowness (slow walking speed) and low physical activity (210). It has a solid foundation of biological causative theory (210, 334) and has been applied to multiple epidemiological studies where it is predictive of adverse clinical outcomes (222, 311, 335, 336). The CHS index however does not include psycho-social components of frailty. Additionally, a major factor inhibiting its clinical application is its inclusion of measurements not routinely used by clinicians for patient assessment (337) – grip strength, for example.

2.5.2 Study of Osteoporotic Fractures Index

The Study of Osteoporotic Fractures (SOF) frailty index, like the CHS index, considers frailty to be phenotypic in nature (221). It is simpler to apply clinically than the CHS index, as it needs no specialist equipment and only contains three frailty components. To be defined as frail by the SOF criteria, two or more of weight loss (more than 5 % in the last year, either intentional or unintentional), exhaustion (an answer of 'no' to the question 'do you feel full of energy?') and low mobility (inability to perform a chair rise five times) need to be present. The SOF criteria has been found in epidemiological studies to predict falls, disability and premature mortality in both men (229) and women (221) to a similar extent as the CHS index. It also has an underlying biological causative theory (221).

2.5.3 Frailty Index of Accumulative Deficits (FI-CD)

The Frailty Index of Accumulative Deficits (FI-CD) was first proposed by Rockwood and Mitnitski as a way to incorporate the multidimensional nature of frailty into an operational definition (284, 338). The FI-CD is underpinned by biological causative theory (242, 273, 339) and involves the accumulation of 30 or more co-morbidities, symptoms, diseases, disabilities or any deficiency in health with the idea that a greater number of health deficits indicates higher frailty (340). The FI-CD is expressed as a ratio. For instance, if a list of possible health deficits obtainable on a study cohort is 50, a person with 5 of these deficits has a frailty index of 0.1. The exact list of health deficits for inclusion in the FI-CD does not matter other than they should: increase in incidence but not have a ceiling effect with age; be reflective of a range of physiological systems; and be associated with health and not age per se (340). Comprehensive guidelines for creating a FI-CD have recently been provided by Searle et al. 2008 (340). These guidelines also give cut-off points for continuous variables that are used in the index. Section 9.2.3.1 provides further details of FI-CD computation.

The FI-CD has been found to be related to the adverse outcomes of frailty including falls and early mortality (284, 340). Importantly, it is the FI-CD score, rather than type of health deficits included in the FI-CD, that is most predictive of

adverse outcomes (242). An upper limit the FI-CD is believed to exist at around 0.67, beyond which survival is unlikely (341).

The FI-CD can be time consuming to calculate and its mathematical nature, although simple, renders it unpopular clinically (342). However, as highlighted by Jones et al. (343), a FI-CD, when derived from data already collected in a Comprehensive Geriatric Assessment (CGA), can be time-efficient.

2.5.4 Frailty Index Derived From Comprehensive Geriatric Assessment (FI-CGA)

The frailty index derived from Comprehensive Geriatric Assessment (FI-CGA) is simply a FI-CD using data from a CGA. CGA is the global standard clinical assessment for older people, and includes medical, nutritional, functional and psychological assessments by a multidimensional team (11).

The FI-CGA was initially developed as a ten-domain index, with 14 CGA components included (343, 344). It was later expanded out by Rockwood and colleagues (339) to include 52 CGA components. The CGA is used as a clinical standard for frailty assessment and has been found to be highly associated with the FI-CD (343). Scoring is described in Section 9.2.3.2.

2.5.5 Multidimensional Prognostic Instrument (MPI)

The Multidimensional Prognostic Instrument (MPI) was developed as a prognostic tool for hospitalised older patients (330) and has been judged to be a multidimensional frailty instrument, albeit with a simpler nature than the FI-CD (345). The MPI is derived from eight components of the CGA: medication number, IADLs, ADLs, cognitive status, nutritional status by the MNA, risk of developing pressure sores, co-morbidity and living status (330). Problems for each component are classified as either classed as major (1 point), minor (0.5 points)

and none (0 points) (330, 345). Scores are then summed and divided by eight, with scores > 0.66 graded as frailty (330, 345).

2.5.6 Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL) Index

Proposed by the International Association of Nutrition and Ageing (IANA), FRAIL (245, 346) comprises four components of the CHS index, and one component of the FI-CD (337). The FRAIL instrument classifies frailty as three or more of: fatigue (self report), resistance, ambulation (slow walking speed); illness and loss of weight of 5 % or more in the past year (337). FRAIL is judged to be clinically advantageous due to its simple nature and ability to be obtained from data already included in a patient CGA (337).

2.5.7 Functional Decline Indices

Functional decline is defined as 'the loss of independence in self care activities or a deterioration in self care skills' (347). After observing that functional decline is an outcome of frailty, functional decline risk was deemed by de Saint-Hubert et al. in their recent systematic review to approximate frailty (274). Functional decline is known by many terms including: decline in Activities of Daily Living (ADL), status decline and functional impairment (347). Commonly used in the hospital setting to measure functional decline in older people are the Katz Index of Independence in ADL (331) (331) and Lawton and Brody's instrumental ADL (IADL) scale (332). Functional decline indices which can be used as screening tools in the hospital setting include the HARP (327) and the SHERPA (333). The Katz ADL score, Lawton and Brody's IADL scale, HARP and SHERPA are described in the following sections.

2.5.7.1 Katz Score of Activities of Daily Living

The original Katz ADL score (331) considers dependency in six ADLs: bathing, dressing, toileting, transferring, continence, and feeding. Dependency for each

ADL is a two part process. Firstly each ADL is graded according to three categories: no assistance, some assistance and assistance needed. Secondly, these categories are then converted into two categories: either ‘dependent’ or ‘independent’ (331). Since its inception in 1963, the Katz score has been modified dozens of times to include different ADLs and different scoring systems (348). Notably, a recent systematic review of functional decline in hospitalised older people (Buurman et al. 2011), found that only one out of 22 studies referring to the original Katz index, in fact used the original version (348).

The Katz scale is easy to apply, taking around 10 minutes to assess for each hospital patient. It is the most commonly used functional decline assessment measure in hospitalised older people (348) and assessment either by patient self-report of by visual observation have been found to give similar results (349).

2.5.7.2 Lawton’s Instrumental Activities of Daily Living Scale

Lawton’s Instrumental ADL (IADL) scale was developed around the same time as the Katz ADL index and assesses dependency in eight ADLs: phoning, shopping, food preparation, housekeeping, laundry, transportation, medication use and ability to handle finances (332) (see Appendix). Lawton’s IADL scale, like the Katz ADL score, takes around 10 minutes to complete for each hospital patient. Scoring is more accurate if IADLs are assessed by direct observation rather than asking the patient themselves (349). One limitation of Lawton’s IADL is that it is gender biased towards older women, as older men are more likely to be dependent in performing IADLs such as food preparation (350).

2.5.8 Hospital Admissions Risk Profile (HARP)

The Hospital Admissions Risk Profile (HARP) (327) is a weighted mortality risk tool that incorporates three frailty components: age, cognition and IADL (327). Scoring is descibed in Section 2.5.8. It is predictive of functional decline (327, 351) and is therefore considered to be a frailty instrument (274).

2.5.9 Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA)

The Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA) (333) is both a mortality index, and because it contains components underlying frailty, a frailty instrument. It was designed and validated in acutely hospitalised older people (333). SHERPA contains five weighted components: falls in the previous year (no = 0 points, yes = 1 point), MMSE score < 15 (first 21 questions) (no = 0 points, yes = 2 points), bad self perceived health (no = 0 points, yes = 1.5 points), age (years) (< 75 y = 0 points, 75 – 84 = 1.5 points, > 84 = 3 points), impairments in instrumental ADL score (332). Scores > 6/15 correspond to 'high risk of functional decline' (333).

2.5.10 Individual Frailty Measurements

Individual factors underlying frailty can also be used to measure frailty. For example, gait speed is recognised as an indicator of frailty (325, 352-354) and has been found to link closely with adverse health outcomes in older people (353-357). Gait speed is applicable clinically, although problems with measuring out a walking course can be a barrier to its use (262).

Low grip strength can also be used as a single measure of frailty, having been linked with poor mobility (358), longer hospital LOS (359) and disability in older people (360). Interestingly, grip strength has been found to associate with nutritional status in both community dwelling (361) and hospitalised older people (362).

2.5.11 Other Frailty Instruments

Multiple other frailty indices exist in the literature but are beyond the scope of this thesis, including many recently developed such as the: Tilburg Frailty Indicator (270), Groningen Frailty Indicator (GFI) (363), The Edmonton Frail Scale (EFS) (364), the Frailty Instrument of the Survey of Health, Ageing and Retirement in Europe (SHARE-FI) (365, 366), the Clinical Frailty Scale (284), PRISMA-7 (367), the Kihon Check-list (KCL) (368), the Kaigo-Yobo Index (369), the self-

rated Health Deficits Index (370), the Frailty Risk Score (371), and the Self Reported Frailty Score (372).

Table 2-3: Comparisons of Selected Frailty Operational Definitions

Indices	Time Taken (min)	Number of Items	Components	Frailty	Data Extractable from CGA	Special Equipment Required	Assessor Training Required	Valid and Reliable	Geriatric Syndromes Included	Underlying Biological Theory	Frailty's Dynamicity Accounted
Frailty Indices											
CHS(210)	< 10	5	Weight Loss, Low Physical Activity, Exhaustion, Slowness, Weakness	Fraily ≥ 3 items; Pre-frailty 1-2 items; Robust = No Items	x	✓	✓	✓	✓	✓	✓
SOF(221)	< 5	3	Weight Loss, Exhaustion, Unable to Rise from Chair 5times	Fraily ≥ 2 items; Pre-frailty 1 items; Robust = No Items	x	x	x	✓	x	✓	✓
FI-CD(284, 338)	< 10†	30 +	Accumulated health deficits: score of 0 (no deficits) to 1.0 (all deficits)	A continuous score. Cut-off point suggested as Frailty > 0.25 (373)	✓	x	✓	✓	✓	✓	✓
FI-CGA(339, 343, 344)	< 10†	30 +	10 domains, 52 items (originally 14): including ADL, IADL, Co-morbidities, Mood & Cognition	A continuous score. Cut-off point suggested as Frailty > 0.25 (373)	✓	x	✓	✓	✓	✓	✓
MPI(330)	< 10	8	Co-morbidity, Nutrition, Cognition, Medication number, Pressure Sore Risk, Living Status, ADL, IADL	Severe risk (frailty) > 0.66; moderate risk (pre-frailty) 0.34 - 0.66; Robust = Scores < 0.34	✓	x	✓	✓	✓	✓	✓
FRAIL(245)	< 10	5	Fatigue, Resistance, Ambulation, Illness, Loss of Weight	Frailty ≥ 3 items; Pre-frailty 1-2 items; Robust = No Items	✓	x	x	✓	✓	✓	✓
Functional Decline Indices											
Modifed Katz(331)	< 10	7	ADLs: eating, washing, grooming, dressing, toileting, transferring, walking	≥ 1 ADL	✓	x	✓	✓	x	x	x
LB(332)	< 10	8	IADLS: phoning, shopping, food preparation, housekeeping, laundry, transportation , medication use, finances	≥ 3 IADL	✓	x	✓	✓	x	x	x
HARP(327)	< 10	3	Weighted Items: age, cognition, IADL	Scores > 6/15 correspond to 'high risk of functional decline' (231).	✓	x	x	x	✓	x	x
SHERPA(333)	< 10	5	Weighted Items: falls, cognition, bad self perceived health, age, ADL	High Risk of Functional Decline: Scores > 6/15 (231).	✓	x	x	✓	✓	x	✓

† If the Comprehensive Geriatric Assessment (CGA) has already been collected. Abbreviations: CHS = Cardiovascular Health Study Index; SOF = Study of Osteoporotic Fracture (SOF) Index; FI-CD = Frailty Index of Accumulated Deficits; FI-CGA = Frailty Index derived from Comprehensive Geriatric Assessment; MPI = Multidimensional Prognostic Index; FRAIL = Fatigue, Resistance, Ambulation, Illness and Loss of Weight Index; Katz = Adapted Katz Index of Activities of Daily Living (ADL) score; LB = Lawton and Brody's Instrumental ADL (IADL) scale; HARP = Hospital Admissions Risk Profile; SHERPA = The Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie.

2.6 The Predictive Ability of Frailty Instruments

As outlined in Section 2.2, an ideal frailty operationalisation should not only be diagnostic, but should also be predictive of adverse clinical outcomes and be underpinned by biological causative theory (11). The majority of frailty operationalisations in use today claim an underlying biological causative theory. However, the predictive ability of frailty instruments is largely unknown.

Predictive validation has been judged as the most important area to assist in establishing a standard and precise operational frailty definition (340). Moreover, by being predictive of outcomes, a frailty operationalisation will be a valuable tool for patient care (225) and surgical and medical treatment planning (374). However, in spite of these important needs, relatively few epidemiological studies comparing frailty measurements have been conducted (229, 230). In the hospital setting, comparative studies are even scarcer, with only two known studies comparing the predictive ability of frailty measurements (275, 345).

Even hospital-based studies looking at the predictive ability of one frailty instrument are scant, with only two studies identified. Khandelwal et al. (2012) found frailty identified by the CHS index was associated with an increased risk of mortality and a longer length of hospital stay, highlighting that their study was the first of its kind (225). Singh et al. (2012) study of acute geriatric rehabilitation patients in a tertiary hospital found frailty identified by the FI-CD associated with LOS, poor functional gain and poor outcome (admission to residential care or death) (375).

It should be emphasised that the need for an operational measurement of frailty originated in the clinical setting, but its application has mostly been in epidemiological research. There is a definite need to bring back frailty research into the clinical setting, particularly with comparative and risk-prediction studies. This is especially important in the hospital setting in which frailty is common

(376) and a better ability to predict patients at risk of adverse clinical outcomes is urgently required (10, 376). Such knowledge will assist is selecting a standard frailty assessment tool/s for the hospital setting.

Moreover, similar to the literature of Nutritional Screening Tools (see Chapter 1), there is a need to design studies looking at predictive accuracy, rather than solely predictive ability. Chapter 9 looks at the comparative ability of frailty and functional decline indices in predicting poor outcome in hospitalised older people. The following chapter gives an outline and scope for the thesis.

3 Research Aims and Questions

Sections 1.11 and 2.6 identify the thesis literature gap, which is the need for knowledge of the predictive ability of nutritional screening tools and frailty measurements in the hospital setting. Of additional clinical importance is the overlap between malnutrition and frailty, with similarities existing in their consequences, pathological pathways and prevalence rates. Nutritional status has also been judged to be a marker of frailty (12, 150), with the MNA proposed as a measure of frailty (12, 150, 155, 377). However, no studies to date have yet looked at the efficacy of the MNA as a measure of frailty (see Chapter 6).

3.1 Thesis Objectives

This doctoral thesis examined the ability of frailty instruments and nutritional screening tools to predict adverse health outcomes in older people. Main research aims were to:

- Ascertain the prevalence rates of malnutrition and frailty in hospitalised older people as determined by various nutritional screening tools and frailty operational measurements, respectively.
- Determine the predictive ability and accuracy of nutritional screening tools and frailty operationalisations in predicting adverse clinical outcomes in hospitalised older patients. These outcomes are described in detail in section 4.3.

Secondary thesis aims were to:

- Determine the efficacy of two nutritional screening tools, the MNA and MNA-SF, in identifying frailty in the hospital setting.
- Assess the association between appetite, body composition and inflammation in healthy people of all ages.

3.2 Thesis Outline

This thesis addresses the study objectives and research gaps outlined in Section 3.1. Each chapter consists of a research manuscript, either published or submitted for publication. Studies are inter-related, focusing predominantly on the predictive ability of nutritional screening tools and frailty instruments.

Nutritional screening tools have an advantage clinically if they are predictive of adverse clinical outcomes. However, this predictive ability is not clearly known. Chapter 5 addresses this issue, presenting a systematic review of the ability of nutritional screening tools to predict adverse clinical outcomes; 'Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review'. Uncovered in this review was the distinct lack of comparative studies performed in the hospital setting, a setting in which nutritional screening is of utmost importance.

Taking this issue to hand, Chapters 7 and 8 evaluate the ability of nutritional screening tools to predict adverse clinical outcomes in hospitalised older people; 'Nutritional Screening Tools and Anthropometric Measures as Predictors of Hospital Discharge Outcomes in Older People' (Chapter 7) and 'Nutritional Screening Tools and Anthropometric Measures as Predictors of Discharge Outcomes in Older People' (Chapter 8). Chapter 9 continues on the clinimetric research trail, and investigates frailty and functional indices as predictors of poor hospital outcomes; 'Frailty and Functional Decline Indices Predict Poor Outcomes of Hospitalised Older People'. The comparative ability of frailty indices to predict hospital outcomes is largely unknown, and thus Chapter 9 will provide additional information needed to advance a definition of frailty.

As malnutrition and frailty are inter-connected, it has been proposed that the MNA can potentially double both as a nutritional assessment/screening tool and a frailty measurement. Chapter 6 explores this issue quantitatively, and examines

the efficacy of the MNA in identifying frailty in hospitalised older people; ‘Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People’.

Linking the two geriatric conditions of malnutrition and frailty is inflammation. Chapter 10 explores the relationship between inflammation, body composition and appetite in a healthy population across the adult age range; ‘Inflammatory Cytokines and Appetite in Healthy People’. Chapter 11 provides a general discussion and summary of the included research studies.

4 METHODS

This chapter describes the project's methodology, including its location, ethical approval and patient recruitment. There were two study cohorts used for this thesis: (i) a cohort of hospitalised older patients and (ii) a cohort of healthy people from the Cytokines, Adiposity, Sarcopenia and Ageing (CASA) study. Further details of the methods used are described in Sections 6.2, 7.2, 8.2, 9.2 and 10.2.

4.1 Research Location

The setting for this study was the 20-bed Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital, Adelaide, South Australia. The GEMU is a specialised sub-acute hospital ward focusing on the multi-disciplinary rehabilitation of older people with the view to maximising functional independence and discharging patients home where possible (378). GEMU patients have a lower rate of functional decline than their counterparts admitted to general hospital wards, according to a recent systematic review of GEMUs (378). They also have a reduced likelihood of residential care (nursing home) admission one year post-hospitalisation (378).

At the TQEH, patients are generally admitted to the GEMU within a few days of their admission to the Acute Medical Unit. Patients are selected for GEMU admission based on the clinical judgement of hospital geriatricians based on the likelihood of benefiting from the GEMU intervention. Patients selected are those aged over 80 years or those aged over 70 years with geriatric syndromes. All GEMU patients receive a Comprehensive Geriatric Assessment (CGA) by consulting geriatricians during their time in the ward.

4.2 Approval for the Study

The study was approved by the Human Research Ethics Committee at The Queen Elizabeth Hospital: protocol number 2010105. Patients were not offered any reimbursement for their study participation and their usual care was not

influenced by study participation. All patients (or their authorized proxy) gave their informed consent, in accordance with ethical standards from the 2000 Declaration of Helsinki as updated in 2008 (379) and the Australian Government's National Statement on Ethical Conduct in Human Research 2007 (380).

4.3 Clinical Outcome Measures

Clinical outcome measures are important for geriatric medicine, gerontology research and for guiding public health policy. Moreover, outcomes such as admission to high level care are important for the older patient themselves as, on the whole, they prefer not to be placed in high level care. Two outcome time-points were considered for analysing clinical outcomes: hospital discharge and six months post-hospitalisation. Clinical outcome measures were:

Chapter 7:

1. GEMU length of stay (LOS)
2. Functional decline during GEMU stay
3. Discharge to higher level care

Chapter 8:

1. Poor outcome six months after hospital discharge. Poor outcome was defined as a composite measure of mortality and new admission to higher level residential care.

Chapter 9:

1. Poor outcome at hospital discharge (as defined above)
2. Poor outcome at six months after hospital discharge (as defined above)

4.4 Patient Recruitment

Consecutive patients aged ≥ 70 years (or their authorized proxy where applicable) were approached within their first 72 hours of GEMU admission for inclusion in the study. The study period was between October 22, 2010 and December 23, 2011. 427 new patients were admitted to the GEMU during the study period. 172 patients (40.3 %) of these patients were included in the study. The most common reason for study exclusion was the lack of understanding of the consent forms without an authorized proxy to approach for study consent. Table 4-1 outlines reasons for study exclusion.

Table 4-1: Reasons for Study Exclusion

Reason for Exclusion	*n* (%)
1. Dementia or unresolved delirium within 72 hours of GEMU admission without proxy to approach for study consent	77 (18)
2. Language barrier without proxy	67 (16)
3. Declined participation	63 (15)
4. Treating physician advised against patient inclusion: elder abuse, physically aggressive or medically unwell	33 (8)
5. Infectious	11 (3)
5. Missed by researcher	4 (< 1)

4.5 Patient Characteristics and Study Outline

Data collection from the GEMU was performed by the doctoral candidate. Chapters 7 - 9 used the data from the 172 patients recruited from the GEMU. The mean (standard deviation) age of these patients was 85.2 (6.4) years, with 123 (72 %) of these patients female. Details of patient characteristics are found in the Table 4-2 and in the result sections of each chapter. Chapter 6 used the data obtained from the first 100 patients recruited into this study.

Chapter 10 uses data obtained from a different dataset. For this chapter, 180 healthy community dwelling people of all ages (age range 18 – 82 years), were recruited from the North-Western suburbs of Adelaide into the Cytokines, Adiposity, Sarcopenia and Ageing Study (CASA). Telephone numbers from the Electronic White Pages were randomly selected and willing participants aged 18 years and over (with no exclusion criteria) were invited to participate. Further details as to participant recruitment and baseline characteristics for this study are outlined in Chapter 10.

Data were collected during the first 72 hours of GEMU admission. Patient (or proxy) interview was used to obtain socio-demographic and health data, including nutritional status by the Mini Nutritional Assessment (MNA) (147). Patient clinical records were used to obtain CGA items including medications, admission diagnosis, Geriatric Depression Scale-15 (GDS-15) (381), Mini-Mental State Examination (MMSE) (382) and Braden Skin Assessment (383).

Table 4-2: Descriptive Characteristics of Patients on Admission (n=172)

Variable	*n* (%)
Gender (female)	129 (72)
Age Group	
70 -79 years	31 (18)
80-89 years	100 (58)
90-101 years	41 (24)
BMI Category	
< 22 kg/m^2	58 (34)
22 – 30 kg/m^2	75 (44)
> 30 kg/m^2	39 (23)
Calf Circumference (cm)	31.8 (5.0) †
Mid Arm Circumference (cm)	26.1 (4.9) †
Charlson's Co-morbidity Index	3 (Range 0-12)‡
Cognitive Impairment (MMSE Score < 24)	74 (43)
Lives Alone	97 (56)
Polypharmacy (≥ 6 Medications)	131 (76)
Primary GEMU Admission Diagnosis¶	
Chronic Condition	71 (41)
Infection	52 (30)
Injury or Musculoskeletal Condition	28 (16)
Non-musculoskeletal Symptoms	6 (4)
Unclassified	15 (9)

† Mean (SD); ‡ Median (range); ¶ Classifications based on Hastings et al. 2010 (384)
Abbreviations: MMSE = Mini Mental State Examination Score; BMI = Body Mass Index (weight/height^2); GEMU = Geriatric Evaluation and Management Unit

Statement of Authorship

Title of Paper	Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review
Publication Status	⦿ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional screening tools as predictors of mortality, functional decline, and move to higher level care in older people: a systematic review. Journal of Nutrition in Gerontology and Geriatrics. 2012;31(2):97-145.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Contribution to the Paper	Supervised development of the systematic review. Reviewed the section on "admission to high level care" outcomes. Helped to evaluate and edit the manuscript.		
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Contribution to the Paper	Supervised development of the systematic review. Conceived the addition of the mortality section to the paper. Assisted in data interpretation and manuscript evaluation. Helped to evaluate and edit the manuscript (the mortality and functional decline sections) and assisted in preparation of the final draft of the manuscript.		
Signature		Date	MARCH 25, 2013

5 Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review

Published as 'Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional screening tools as predictors of mortality, functional decline, and move to higher level care in older people: a systematic review. *Journal of Nutrition in Gerontology and Geriatrics.* 2012;31(2):97-145.'

This systematic review assessed whether nutritional screening tools (NSTs) predict mortality, functional decline, and move to higher level care in older adults residing in the community or in institutions. In total, 37 prospective studies published between 1999 and 2012 met inclusion criteria and were included in this review. The most commonly used NST in these studies was the Mini Nutritional Assessment (MNA). Comparison of NSTs was limited by variation in follow-up time, lack of uniform definition of functional decline, and biases in many studies. Results of the MNA, MNA-Short Form (MNA-SF) and Geriatric Nutrition Risk Index (GNRI) assessments were significantly associated with subsequent mortality, with good negative predictive power (~0.83), but only modest positive predictive power (PPV~0.32). Both the MNA-SF and MNA results had a low to moderate association with functional decline (PPV~0.34). Move to higher level care was less strongly associated with NST scores (PPV~0.25). Overall, there is evidence that NSTs can predict those at low risk of mortality, functional decline and, to as lesser extent, move to higher level care in older people.

Keywords: Systematic Review, malnutrition, functional decline, mortality, aged, nutritional status, residential care, older persons, nutritional screening tools, sensitivity, specificity.

Erratum: In this review, the word *prediction* has been used to describe the sensitivity, specificity, positive (PPV) and negative (NPV) predictive values of Nutritional Screening Tools. However, rather than the word *prediction*, the term *predictive accuracy* is the correct statistical expression. Prediction refers to the predictive ability (such as odds ratio (OR) and hazard ratio (HR) values), values of which are also reported in this review. The heterogeneity of functional decline measures precluded the performance of a meta-analysis.

5.1 Introduction

Undernutrition is a major health problem in older adults worldwide, with an estimated 22-68% of hospitalised (87, 104) and 9-32% of institutionalised older adults (157, 385) affected. Undernutrition develops when there is a deficiency of energy intake relative to energy expenditure. This often unrecognised, and consequently undetected, condition is associated with increased mortality (87, 88, 386) and has been linked with increased functional dependence in several cross-sectional studies (37, 196, 387-389).

Loss of functional independence results in loss of quality of life (390). In fact, a recent survey of older persons found having better health and physical mobility was the most desired event to improve quality of life (391). Many older people decline in function as the result of one or a combination of chronic conditions such as heart disease, stroke, dementia, injuries from falls, osteoarthritis, diabetes and sight and hearing loss (392). Low muscle strength, a factor related to undernutrition, can compound the functional decline from these conditions (393).

Functional decline refers to the change in function that occurs during two time-points (112) and is generally defined as an increased dependency in Activities of Daily Living (ADL), such as walking or showering. Common scales used to measure ADL include Barthel's Index (BI) (394) and the Katz score (395). Functional decline is also defined as an increased dependency in Instrumental ADL (IADL), which includes components such as shopping, managing finances and cooking (332). Move to higher level care (for example, from the community to a nursing home, or from a nursing home to a hospital) can also indicate functional decline (274). Functional decline is closely associated with hospitalisation rates in older people (352, 396-398). In older populations, functional decline has been found to be a better predictor of mortality and nursing home admission than age, diagnosis and illness severity (112, 399).

The ability to predict those at risk of functional decline would allow for earlier intervention. Many studies have looked at risk factors for functional decline, and there are several systematic reviews of such studies of predictors of functional decline, including examination of both individual predictors (347, 400-402) and screening tools (274, 347, 400, 403). However, few reviews have assessed the ability of nutritional screening tools (NSTs) to predict functional outcome, and only three screening tools identified by one of the systematic reviews (274) had a nutritional component (224, 404, 405).

When single measures of nutritional status, such as body weight or food intake, are combined to form an NST, they may be better predictors of clinical outcomes than single measures. A variety of NSTs have been developed as rapid, easily administered, mass screening tools which aim to identify individuals who are malnourished or at risk of malnourishment, and thus ascertain their necessity for further assessment and interventions (406). Examples of widely used screening tools include the Mini Nutritional Assessment (MNA) (148) and the Malnutrition Universal Screening Tool (MUST) (163). NSTs usually involve a combination of questions regarding appetite, food intake and weight loss, plus or minus simple anthropometric measures such as body weight, Body Mass Index (BMI) (weight/height^2) and limb circumference. These tools are being used increasingly in clinical practice and there are a large and growing number of studies in a variety of settings examining their associations with outcomes such as functional decline and mortality. NSTs are used to screen the nutritional status of older people in settings such as hospitals, the community and in residential care and it would be cost-effective for time-pressured clinicians to use one screening tool to predict those at risk of both undernutrition and functional decline.

There has been limited systematic examination of the ability of NSTs to predict outcomes. A systematic review of six studies by Beck and colleagues (154) looked at the MNA and found it was not a predictor of mortality or move to a nursing home. Their review, however, did not examine functional outcomes, and

excluded many studies due to their lack of sub-classification into the MNA sub-groups.

Thus a systematic review of the ability of NSTs to predict outcomes, particularly functional status, is warranted. The objective of this paper is to review the ability of NSTs to predict mortality, functional decline, and move to a higher level care in older persons, as reported in prospective studies.

5.2 Method of Review

Standard guidelines for reporting systematic reviews were followed (407). For the purposes of this review, a NST was defined as a test that includes a combination of two or more measures or questions related to malnutrition risk, and that categorizes this nutritional risk.

5.2.1 Literature Search and Screening Strategy

The literature search strategy was devised in conjunction with the University of Adelaide research librarian. Databases searched were PubMed, EMBASE and CINAHL. Search limitations were set to 'Human' and 'English'. Age limits were not set so as to include studies potentially using older people in a subset analysis. No date limitations were set. The search involved 4 subsets: older people; study design (prospective; nutritional screening tools; and functional outcome (functional decline, mortality, admittance to higher level care). The complete search strategy is shown in the appendix.

Titles and abstracts were screened by one researcher (ED) and full papers of relevant articles were screened for eligibility using a data extraction form. A priori study inclusion criteria are shown in Table 5-1. The primary literature search was performed during November-December 2011. Emails of updated database searches were sent weekly to the reviewers with the last date of the literature search being 20th January 2012. Components of a 'lateral search' (408) were also performed, including cross-referencing reference lists and tracking citations.

5.2.2 Analysis of Studies

Where possible, data were extracted from published tables or figures. Otherwise, data from the text of the paper were used. The methodological quality of studies was rated using a scale devised in a recent review of frailty and functional decline (402), with a maximum score of 27. Two aspects of each paper were looked at with respect to outcome: (1) association and (2) predictive ability. Association refers to relationship that the NST has on outcome, but does not imply causation

(154). Predictive ability refers to the level that the NST will predict outcome, that is, the number of people who are correctly and incorrectly screened and involves knowing sensitivity and specificity values (123, 136, 154). Sensitivity is the probability a person who is malnourished (or at risk of malnourishment) is screened positive, whereas specificity is the probability that a person who is not malnourished (or at risk) is screened negative (136, 409). It is useful to know predictive ability from a clinical point of view so that older persons at risk of decline can be accurately identified.

In this review, sensitivity and specificity were recorded for those studies reporting these values and computed using contingency tables for other studies where possible. Additionally, positive predictive value (PPV) and negative predictive value (NPV) were also computed. PPV is the proportion of those malnourished (or at risk) who have an adverse outcome, whereas NPV is the proportion of those who are not malnourished (or at risk) who have no adverse outcome (409).

5.2.3 Population Settings

To assess if the location of residence of the older person influenced outcomes, 4 location sub-sets were established:

(1) Acute Hospital – includes Emergency Departments, Medical and Surgical Wards
(2) Sub-Acute Care - Rehabilitation hospitals, Geriatric Evaluation and Management Units
(3) Residential Care (nursing home – low and high level care)
(4) Community (with or without supports)

Table 5-1: Study Inclusion Criteria

Study Inclusion Criteria
Nutritional Screening Tool: incorporates more than one nutritional component and identifies an individual who is malnourished or at risk of malnourishment.
Outcomes include one or more of (1) mortality (2) Higher level of care or nursing home admission (3) functional decline.
Prospective study design
Data reported from an original study (ie not from a review)
Studies incorporating people aged 65 years or older, or outcome results separately reported for those aged 65 years or older.
Article published in peer reviewed journal
Full article not available
Admission functional status included as a covariate or with all patients at baseline with independence in function.

5.3 Results

Details of selection of papers for the review are shown in Figure 5-1. A total of 37 studies were identified. Malnutrition prevalence varied between settings, with malnourishment being more frequent in settings with increased dependency levels: 0-4.9% in community dwelling older persons; 18.6 - 68.0% for those in acute care; 42-47% for sub-acute care and 5.7-39% for residential care.

NSTs used in the identified studies were: the MNA (149), the MNA-short form (SF) (158) MUST (163), the 'Determine Your Nutritional Health' (Nutritional Screening Initiative, NSI) checklist (172), Geriatric Nutritional Risk Index (GNRI) (170), Nutritional Status Score (NSS) (173), Chinese Nutritional Screening Tool (CNS) (410), Birmingham Nutritional Risk (BNR) (411) and the Rapid Screen (RS) (174). Population specific versions of the MNA and the MNA-SF were also identified: the MNA (Chinese Version) (112), the MNA-Taiwanese version 1 (MNA-T1), version 2 (MNA-2) (412) and the short form of version 2 (MNA-T2-SF) (413). One study looked at MNA sub-scores, including the MNA-3, which contains 9 of the possible 30 points of the MNA that specifically assesses appetite and food intake pertaining to assessment of dietetic habits (88). One study looked at the time dependent MNA (MNA-td) which baseline information and data collected at different time-points (113) and another looked at the MNA-Proportional and Objective (104). The total score of NSTs was compared against outcomes in some studies, whereas others compared categories of the screening tools.

MNA categories include malnourished' (M) (scores <17), 'at risk of malnutrition' (AR) (scores 17-23.5) and 'well nourished' (scores 24-30) (WN). MNA-SF categories consisted of (Scores ≤11) and WN (Scores 12-14). For the MUST, GNRI and NSI, categories identified were 'high nutritional risk' (HR), 'moderate nutritional risk' (MR), 'low nutritional risk' (LR).

The quality of studies was similar for those that assessed mortality, functional decline and move to higher level care (means of 22, 22 and 20 respectively). Results are described separately below in three sections according to outcome assessed: mortality, functional decline and move to a higher level care.

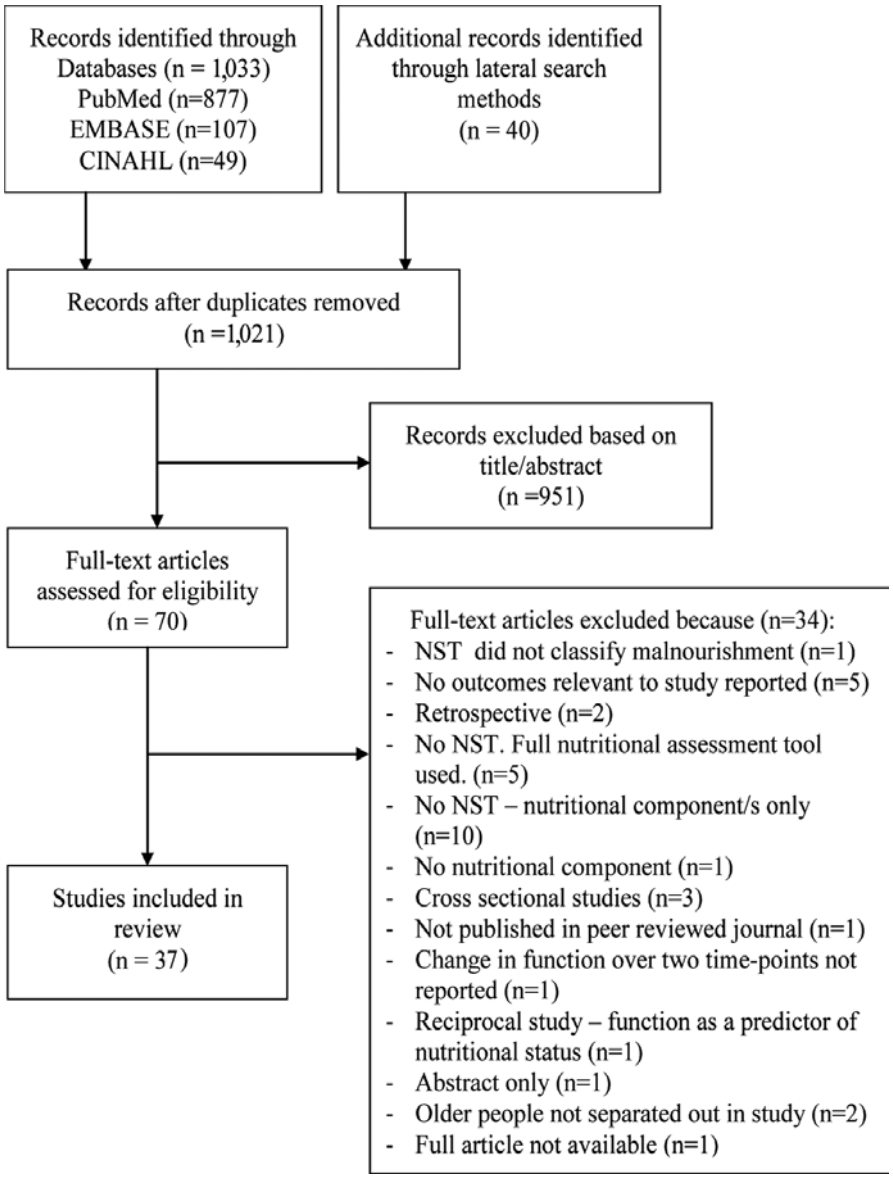

Figure 5-1: Flow Diagram Showing Selection of Final Studies Included in the Review

5.4 Findings from Mortality Papers

28 papers reporting the relationship between NST assessments and subsequent mortality were identified (see Table 5.2, Appendix). Seven studies were performed in the acute hospital setting (86-89, 99, 104, 414), six in sub-acute care (90, 91, 113, 170, 173, 415), seven in residential care (97, 153, 385, 386, 416-418), seven in the community (172, 412, 419-423) and one in both acute and sub-acute settings (424). Eleven studies excluded people with acute and/or chronic illnesses such as cancer and renal failure (97, 113, 153, 170, 386, 416-418, 420, 422, 423), seven excluded those with cognitive impairment and/or dementia (88, 89, 172, 414, 416, 421, 423), six did not mention exclusion criteria (90, 91, 104, 173, 385, 415) and the remaining studies had either limited or no exclusion criteria.

5.4.1 Nutritional Screening Tools Used

Nine studies looked at more than one NST. The most common NST used was the MNA, which was used by 17 studies. Four studies used population-specific versions of the MNA and three used the MNA-SF. Three studies apiece used GNRI, with the MUST, NSS, CNS and BNR all used by one study each (see Table 5.2, Appendix). One study compared both the MNA and population specific versions of the MNA against mortality (412).

5.4.2 Mortality: Outcomes

Follow-up periods ranged from time-to-hospital-discharge (usually < 1 month) to five years, with 1 year being a common follow-up period. Two studies did not use a standardised follow-up period (86, 423). Mortality rates varied from 2.5% to 64% (Appendix: Table 5.3).

5.4.3 Relationship between NST results and Mortality

There was clear evidence of a relationship between NST scores indicating lower levels of nutrition (worse nutrition) and increased mortality at follow-up; a

statistically significant relationship was present in 23 of the 28 studies (see Appendix: Table 5.3). Seven studies reported odds ratio (OR) (26 %) and seven studies (26 %) reported Hazard Ratios (HR) or Risk Ratios (RR).

In those studies reporting odds ratios (ORs), OR values ranged from 5.29 to 30.5 for GNRI severe nutritional risk (values < 82) when compared to those classified as 'no risk', from 6.6 to 30.5 for moderate risk GNRI classification, 0.93 to1.80 for the MNA total score, 2.19 to 2.39 for the MNA (AR) category, 1.35 to 3.03 for the MNA (M) category, and 1.35 for the MNA-SF. Due to the heterogeneity of studies it was difficult to compare different NSTs for the strength of their associations with mortality. Nonetheless, one study compared the MNA and MNA-SF and found the MNA-SF showed the highest association against mortality (90). Additionally, when the GNRI and MNA were directly compared by Cereda et al. (2009) (97), the MNA (M) showed a higher association with mortality than the GNRI (HR). This is in contrast to the overall higher OR values of the GNRI against mortality.

Significant associations between NST measures and mortality were present less often in studies of community-dwelling-older people (3 of 7 studies) than for those in higher levels of care (19 of 20 studies). A significant association was present in 12 of 13 studies with a follow-up period greater than one year, compared, to 11 of 15 with follow up of one year or less. The association between mortality was similar between the MNA and its population-modified versions (MNA-T1 and MNA-T2) according to Tsai et al. (412). Additionally, although there was no comparison within studies, studies using continuous MNA scores appeared to have higher ORs for association with mortality than studies that used MNA categories.

One study (88) looked at the MNA-3 (the subset of questions within the MNA, accounting for 9 of the possible 30 points, that specifically assesses appetite and food intake), and found it showed higher OR values (2.05 vs 1.64 for the MNA-3

and MNA respectively) as well as higher Area Under the Curve (AUC) values (0.755 vs 0.744 respectively) than the full MNA, which also assesses other factors such as quality of life and anthropometric measures. This suggests that appetite and food intake measures may have a particular association with mortality.

All three studies looking at the NSI found no significant association with mortality (172, 419, 423). The NSI tool results are probably therefore not be as closely related to subsequent mortality as are the other tools, particularly the MNA and GNRI. Although 3 studies that used the MNA found no association with mortality (414, 420, 421), there was a significant association in the other 17 studies using the MNA. Two of the 3 'negative' studies involved community-dwelling older people, the setting in which the ability of NSTs to predict mortality appears to be weakest (see above) and in one of those studies the mortality rate was close to zero.

5.4.4 Ability of Nutritional Screening Tool Results to Predict Mortality

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each study, where able to be computed, are shown in Table 5.3 (Appendix). In general, the NPVs are almost always higher than the PPVs, with mean (SD) values of 0.83 (0.18) and 0.32 (0.23) respectively. This is particularly true for studies that used the MNA screening tool, with NPV values often close to 1 whilst PPVs were often low. This indicates that the rate of death during the follow-up period is very low if the person is classified as well-nourished by the NST, but that the majority of people classified as undernourished using the tool, do not die during the study. Due to the variability of the studies, we were not able to determine if the different NSTs differed in their predictive ability for mortality.

5.4.5 Summary of Papers looking at Mortality

Allowing for the great heterogeneity of studies assessed, it is clear that the results of NST assessments of older people are associated with their subsequent mortality rates over periods of up to five years. The tools appear most predictive when used

in more acute settings or higher level of care settings and less so for community-dwelling older people. It is unclear which NST is the best in this regard, possibly the MNA (although that impression may result from its more frequent use in the studies we analysed). The NSI tool did not appear to be able to predict mortality. It is difficult to be conclusive if the MNA or the GNRI is better at predicting mortality. Although the associations observed were significant, often highly, the ability of a score or category on a given NST is at best only moderate, with substantially better negative than positive predictive ability. This is not unexpected given the multiple other factors that contribute to mortality in older people, of which nutritional status is only one. Nevertheless, it appears that the MNA and GNRI can be used to largely rule-out those at low risk of mortality and therefore in less need of further assessment and intervention.

5.5 Findings from Functional Decline Papers

Twelve studies using NSTs and assessing subsequent functional decline were identified (Table 5-4, Appendix). Two studies were conducted in acute settings, four in sub-acute care (96, 111-113), four in the community (172, 413, 419, 420) and two looked at populations in more than one setting (425, 426). There were no papers conducted in the residential care setting. Three studies contained over two thirds women in their dataset (113, 420, 422). A number of studies included in the mortality section of this review and which also looked at function, were excluded from analysis as they did not adjust for baseline function (87, 412, 422). The most common participant exclusion criteria in the studies analysed were acute/chronic illness such as terminal illness or infection (5 studies) (96, 98, 111-113) followed by cognitive impairment/dementia (4 studies) (96, 111, 112, 172). Two studies used the same dataset (425, 426). High participant retention rates (>80 %) were found in all but three studies (172, 419, 420). The mean quality of functional decline studies (22/27) was comparative to a recent systemic review of individual frailty components and their influence on functional decline by Vermeulen et al. (22.5/27) (402). Additionally, the low percentage of papers with high attrition rate in the present review (25 %) was much lower than that of papers identified by Vermeulen et al. (39 %) (402).

5.5.1 Nutritional Screening Tools Used

Five studies assessed more than one screening tool. The most frequently used NST was the MNA (8 studies), with two of these studies using a population version of the MNA (112, 413). Five studies used the MNA-SF. Other NSTs included the NSI checklist (2 studies) (172, 419).

5.5.2 Functional Decline Measures: Outcomes

The methods/tools used to measure change in function varied widely between studies (see Table 5.4 (Appendix). The Barthel Index (BI) was the most frequently used ADL measure and was used in seven studies (58 %). Katz ADL score was used in two studies (17 %), whilst one study combined mortality and functional decline as a composite score (425) and another looked at Physical Functioning Dimension of the Sickness Impact Profile (PDF:SIP) as their measure of functional decline (172). Lee and Tsai (413) used both a functional status ADL and Instrumental Activity of Daily Living (IADL) scores described by Johnson *et al.* (427). IADL decline, using Lawton and Brody's score (332) was reported in one study (86), while two community-based studies looked at utilisation of home care services (419, 420). Most studies used phone call survey for follow-up. The majority of studies looked at changes between two time-points, with only two studies examining functional change over more than two time points (functional trajectory) (112, 113).

The duration of follow-up in the studies varied from time-to-hospital-discharge to up to five years, with six months being a common duration for follow-up. Outcome was reported as OR in five studies (38 %) and as hazard ratio in two studies (15 %). In both of these latter studies, more functional decline occurred in-hospital than post-hospitalisation (112, 113). Functional decline was reported in eight (67 %) of studies, with a prevalence range from 9 – 74%. More IADL decline was observed than ADL decline and the most functional decline occurred in hospital.

5.5.3 Relationship between Nutritional Screening Test (NST) Results and Functional Decline

Nine studies (75 %) showed a significant association between NST scores indicating poor nutrition and subsequent decline in function (86, 96, 98, 112, 113, 172, 413, 419, 425); with five of these showing an association after adjusting for confounders (96, 98, 112, 113, 413), three losing their association after adjustment (86, 172, 425) and one not controlling for confounders (419). One study found a non-significant association between poor nutrition scores and subsequent decline in function (420) while two found no association (111, 426).

The heterogeneity of studies makes it difficult to assess the strength of association between NST scores and functional decline. Nevertheless, significant ORs ranged from 1.07 to 16.19 for ADL decline, with all but one of these studies using the MNA. One study reported a significant OR value of 0.94 for reduced (rather than increased) risk of ADL decline using the MNA (86). All five studies utilising the MNA-SF showed an association with ADL decline. MNA-SF OR values for the two studies that reported it, were 4.25 and in acute care (98) and 1.08 (413) in community older persons, with the latter using MNA-T2-SF. Thus, overall, both MNA and MNA-SF showed a weak to moderate association of with ADL decline. The MNA-SF outperformed the MNA with respect to association with ADL decline when directly compared in the study by Lee and Tsai (2011) (413) but when comparing studies in Table 5.5 (Appendix) the MNA-SF appeared better.

Studies finding no association with functional decline include the two studies using the NonaSantfeliu Study, which a population study is exclusively looking at adults aged over 89 years at baseline and using the MNA-SF (425, 426): Formiga et al. (426)'s paper found no association with BI decline, and Ferrer et al. (425) found no association when controlling for confounders using a composite measure of BI decline and mortality for their outcome measure. Ferrer and colleagues, however, did find an association before confounders were controlled for (425).

Other studies finding no association between nutritional screening tools and ADL outcome include papers by Chen et al., (111), who looked at MNA in sub-acute care populations, and Boult et al. (172) looking at the NSI.

Of the two studies looking at IADL decline, the study by Chang et al. (86) found no association with MNA, and Lee and Tsai (2011) (413) found both the MNA-T2 and MNA-T2-SF showed no association with IADL decline when looking at all older persons, but when looking at those who were disability free at baseline and then who declined in IADL, both MN-T2 and MNA-T2-SF showed significant associations, with OR values of 1.13 and 1.12 respectively.

5.5.4 Ability of Nutritional Screening Tool Results to Predict Functional Decline

Sensitivity, specificity, PPV and NPV for each study, where able to be computed, are shown in Table 5.7 One study reported sensitivity and specificity values for the NSI (172) and two other studies using the MNA (413, 420) provided sufficient data for these values to be computed.

In general for studies assessing ADLs, the NPVs were higher than the PPVs with mean (SD) values of 0.83 (0.10) and 0.34 (0.28) respectively, although these values could not be calculated for the acute care study of Salvi *et al.* (98) where a significant OR of 4.25 was found. The one study which looked at instrumental activities of daily living (IADL) (413), found a high PPV value (0.81) and also a moderately high NPV (0.67). These results suggest that NSTs are good at excluding those at risk of functional decline, but not as good at detecting those at risk of functional decline, particularly if ADLs are assessed.

5.5.5 Summary of Papers Looking at Functional Decline

Allowing for the heterogeneity, limitations and small number of studies assessed, it appears that the results of NST assessments of older people indicate that poorer

nutritional status was associated with an increased rate of subsequent functional decline over periods of up to 5 years. The strength of this relationship was low to moderate. It is not possible to say which NST was the best, although the MNA and MNA-SF provided the most evidence of an association. Additionally, although the associations observed were significant, the ability of a score or category on a given NST to predict declines in ADL was only at best only moderate, with substantially better negative than positive predictive ability. The ability to predict declines in IADL may be better, but there are not enough quality studies to draw firm conclusions in this area.

5.6 Findings from Move to Higher Level Care Papers

Seven studies using nutritional screening tools and assessing subsequent moves to higher level care were identified (Table 5-6, Appendix). Two were conducted in the acute hospital setting (87, 99), three in sub-acute care (91, 96, 174) and two in the community (421, 428). The majority of papers looking at move to a higher level care contained around two thirds women or more (87, 91, 99, 414, 421, 428). Two studies excluded those with acute and/or chronic illnesses (96, 428), three excluded those with cognitive impairment and/or dementia (96, 174, 421) and one did not report exclusion criteria (91).

5.6.1 Nutritional Screening Tools Used

MNA was used in all but one study which used the MUST (91). The MNA-SF (96) and RS (174) were both used in one study apiece together with the MNA. One study compared MNA scores below the median (<25.2) against scores above the median (428).

5.6.2 Move to Higher Level Care: Outcomes

Discharge destination from acute or sub-acute care hospital was the outcome measure used in most studies. The two community-based studies looked at living situation at one year follow-up (421, 428), one with populations receiving

domiciliary services (421)and the other in a population with Alzheimer's dementia (428). OR values were reported in two studies (29 %) (96, 428) and relative risk (RR) was reported in one study (14 %) (421). One study did not specify how many people already in higher level care at baseline returned to higher level care at discharge (91). Overall, five studies (71 %) reported rates of move to higher level care, with rates ranging from 20-32%.

5.6.3 Relationship between Nutritional Screening Test (NST) results and need to move to Higher Level Care

Four studies found a significant association between NSTs and move to a higher level care (96, 99, 174, 428). All four of these studies used the MNA, with one using both the MNA and MNA-SF (96). The OR for move to higher level care was 2.22 for the MNA-SF (M + AR) and 2.29 for the MNA (M + AR) according to Neumann et al. (96) who looked at older persons in sub-acute care. Andrieu and colleagues (428) looked at MNA scores less than the median score (<25.2) and found the age-adjusted OR was 2.19 and age-gender adjusted OR was 2.3 in their study of community residing older persons with Alzheimer's Dementia. The studies by Visvanathan et al. (2004) (174) and Van Nes et al. (2001) (99) also found those with worse malnutrition were more likely to go into higher level care post-discharge from acute and sub-acute care respectively.

Of the three studies finding no association with nutritional screening and move to higher level care, one used the MUST in the sub-acute care setting (91) whilst the two used the MNA; one in the acute care setting (87), the other in the community (174). No studies allowed comparison of the time-dependent association of NSTs and move to higher level care. Overall, when settings were compared, there appeared to be no differences between with respect to the association of MNA or NSTs overall with move to higher level care.

5.6.4 Ability of Nutritional Screening Tool Results to Predict Move to Higher Level Care

Sensitivity, specificity, PPV and NPV, where able to be computed, are shown in Table 5.7 (Appendix). PPV was generally low across all settings, with overall PPV scores lower than NPV (mean (SD) of 0.25 (0.17) and 0.83 (0.15) for PPV and NPV respectively. Two studies allowed comparison of MNA categories; with both revealing the MNA (AR + M) showed higher NPV and around the same PPV than the MNA (M) category (87, 99).

5.6.5 Summary of Papers looking at Move to Higher Level Care

There was a trend for NSTs to be associated with admission to higher level care (4 out of 7 studies). All studies in which there was a significant association used the MNA, with one also including the MNA-SF. As with mortality and functional change, the NPVs of the NSTs for this outcome were substantially higher than their PPVs. Additionally, based on predictive values, it appeared that when the two MNA categories, malnourished (M) and at risk (AR) were combined together, they showed a greater predictive value than the malnourished (M) category. Overall, findings were not influenced by study setting. Of note, it is likely that factors other than nutrition are influencing move to a higher level care. For instance, the presence of dementia, low social support or lack of finances could provide stronger reasons, influencing an older person requiring a higher level care (429)

5.7 Discussion

5.7.1 Major Findings

This review of 37 published studies was undertaken to assess current evidence about the relationship of nutritional screening tool (NST) scores to subsequent mortality, functional decline and move to a higher level care, and the ability of NST scores to predict these outcomes. The studies were conducted in a variety of settings and in several different countries. There were considerable differences between studies in methods used and duration of follow-up, precluding direct comparisons between different NSTs difficult and/or a meta-analysis. Nonetheless, significant associations were identified between poor NST scores indicating worse nutrition and mortality, functional decline and to a lesser extent, move to a higher level care.

With regards to mortality, the strongest association with NST scores tended to be in the most unwell people, that is, for those in acute, sub-acute and residential care rather than those residing in the community. While perhaps not surprising, this does suggest a role for targeted screening. There was no definite difference in the ability of NST scores to predict functional decline across the different population settings, although cross study comparisons, using different versions of the MNA suggested a possibly stronger association between NST scores and decline in IADL scores in the community (413) than acute setting (86).

The most frequently used nutritional tool examined in this review was the MNA. This tool has been validated in a variety of settings, including hospitalised and community welling older people (150). The MNA has also been proposed as the best NST to use in hospitalised older people, because it contains relevant prognostic components (74). Moreover, the MNA contains ADL components (422) and has recently been reported to predict ADL (BI) in a cross-sectional study of older adults (430). However, cross-sectional studies, by their nature, look at associations, not causation or predictive ability (154).

In the present review we examined predictive ability by looking at positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity. Sensitivity and PPV were low in the majority of studies and specificity and NPV generally substantially higher. The low PPVs signify that many older persons identified as being under-nourished are at low risk of the endpoint; death, functional decline or move to a higher level care. Low PPVs were also noted by Beck and colleagues in their systematic review of MNA (154). As with our review, they found that MNA was not highly predictive of adverse outcomes, even though many of their included studies reported a significant relationship with adverse outcome (154). In contrast, specificity and negative predictive ability (the ability to detect those who will not go on to have the adverse outcome) was moderate to high for the outcomes assessed in the papers reviewed. High sensitivity values are essential for screening tests (431) and are dependent on the methodological quality of the papers themselves (274). High specificity values are important for accurately ruling out who is not at risk of poor outcome.

In this review, the most successful NST in significantly associating with and predictive of (at least with respect to negative predictive ability) the outcomes of interest in most studies appeared to be the MNA. The MNA was certainly the most frequently studied NST. The NSI was least predictive of any outcome, perhaps because as outlined by Beck (419), it was validated in US populations but used in European populations. The NSI has not seen much use in the last decade. The GNRI appeared to be closely associated with and good at predicting mortality (at least with negative predictive ability) (97, 170, 417) but its comparison with other outcomes is limited.

There are a number of possible explanations for the relatively low positive predictive ability of NSTs in the studies included in this review. NSTs are generally validated in the general population of older persons, most of whom are community-dwelling, yet the tools are widely used in other settings, such as acute

or sub-acute care (154, 432). It could also be that cut-off scores for nutritional status classification have been selected based on cross sectional studies, rather than clinical outcomes in longitudinal studies (154), and also not on the particular outcomes assessed in this review, namely death, functional decline and move to a higher level care. If the cut-off scores to define undernutrition were set lower than they are for these NSTs the sensitivity and PPV values would likely have been higher. This could also explain why, in the present review, that MNA total score tended to show a higher association with mortality than MNA categories. Additionally, and very likely, factors other than nutritional state, such as acute or chronic illnesses, social situation, and cognitive function, influence the likelihood of the three outcomes assessed (418).

While quite a few studies have examined NSTs and mortality, little has been reported about the ability of NSTs to predict functional decline. If they could, this would be useful as it would allow identification of older persons at greatest risk of functional decline. Identification of these individuals would allow, in conjunction with comprehensive geriatric assessment, appropriate management to be undertaken. The current review has indicated that NSTs do have some use in this area, probably more so for the MNA than for the other tools we assessed. As with mortality the negative predictive power exceeds the positive predictive power, enabling identification of those who do not need further workup and assistance more effectively than it does those who do.

5.7.2 Strengths and Weaknesses of Included Studies

A limitation of this review is that the variety of methods used in the studies assessed, particularly regarding NST used, scoring and sub-categorization of the NSTs, assessment of functional decline and duration of follow-up periods, made it more difficult to draw general conclusions from the results. Sufficient information was not always provided and a number of studies were excluded for this reason. Some studies did not use regression analyses, and some of those that did failed to adequately adjust for influencing confounders. This may have weakened the validity of the results reported.

Another limitation could be that nutrition information collected in the NSTs was not always complete and/or accurate. For example, in a number of studies a proxy for the older person was used to help complete the NST. This could have affected score results. Indeed, Tsai and Ku (2008) (418) found that MNA score was associated with mortality in those older persons who used a proxy, but not in cognitively-normal older persons who did not use a proxy. In most studies looking at functional decline, this outcome was examined between two time points only, rather than over multiple time-points. Change over multiple time-points, known as 'functional trajectory' (112), is a relatively new concept which can allow detection of transient changes in functional status both during hospitalisation and post-hospitalisation, which can often occur (397).

Various biases may also have affected the quality of results assessed. A number of studies did not control for gender in their analysis. Although it is unlikely that gender influenced the MNA score (147), this may not be true for functional outcomes. Espaulella et al. (2007) (113) found the MNA was associated with functional decline in female, but not male older persons. Additionally, many studies reported that excluded participants were more likely to be older and sicker, so selection bias may also have been a factor. Cognition bias was also present in some studies, which included older people with impaired cognition without adjusting for this in the analyses. A further common type of bias was population bias, with many studies excluding patients who could not communicate well (for example, because of poor hearing or sight) and/or looking at one population group (Caucasian or Asian for instance). There were also high levels of self-reporting and recall bias in many studies. While it is possible that these biases may have affected the associations between NST scores and the outcomes reported in these studies, we doubt this would have affected these relationships in any particular direction.

5.7.3 Strengths and Weaknesses of Review Methods

There were limitations with respect to review methods. Only papers in English were chosen, which could have brought bias into the review. Three databases

were searched, and while it is believed that the majority of articles pertaining to this review were in these databases, other papers were almost certainly missed. Only peer-reviewed published articles were included and retrospective studies were excluded to increase the accuracy of studies included. All studies assessed were observational, so no inferences about causation can be made.

5.7.4 Protocol Limitations

This systematic review is comprised of cohort studies of prognosis. Therefore, it would be appropriate to analyse the relative risks, hazard ratios and/or odds ratios. However, this review focused on reporting descriptive measures, such as sensitivity, specificity, PPV and NPV which are important for looking at the accuracy of predictive ability.

5.7.5 Suggestions for Future Research

Further work is needed to clarify and hopefully support our findings, particularly in populations at risk of becoming malnourished. While the Barthel's Index was the most widely used tool for assessment of ADLs in the studies we reviewed (394), allowing some comparison between studies, there is no widely accepted means of assessing functional decline. It would be ideal if there was. Additionally, studies looking at functional decline as a primary rather than a secondary outcome measure and studies undertaken in older people without substantial functional impairment at baseline would also improve the accuracy of studies. Future studies of function would also benefit from a focus on multiple time points (functional trajectory) rather than two time points. Ideally, large scale studies, comparing sensitivity, specificity, PPV and NPV of NSTs against functional decline are needed. Such studies will ensure adequate statistical power to accurately identify which cut-off scores are optimal.

Future studies would ideally ensure the following:

1. Ethics guidelines are adhered to, as older people are a vulnerable population group.
2. A NST appropriate for the population setting is used.

3. The administrator of the assessment, be it the researcher, clinical, nurse, dietician or other health professional, is identified in the report.
4. Inclusion and exclusion criteria are reported.
5. Statistical analyses controls for confounding variables such as age, cognitive impairment, co-morbidities and gender.

It may also be appropriate to consider using composite end-points as recommended by McCusker and colleagues (400), who suggest combining mortality and functional decline in studies with a low incidence of studied outcomes. This would allow a consistent statistical handling of deaths, rather than the range of different methods used currently.

Future research into barriers of implementation to NSTs is also warranted, as is research on the effect, if any, on rates of death, functional decline and move to a higher level care of interventions arising from NST assessments. Randomised clinical trials looking at nutritional and clinical interventions are needed to address the problems identified in the prospective, observational studies reported in this review.

5.7.6 Take Away Points

We conducted a systematic review of nutrition screening tools (NSTs) as predictors of mortality, functional decline, and move to a higher level care in older adults residing in the community or in institutions. The majority of studies used the MNA.

A direct comparison of screening tools was limited by the large variation in follow-up time period, a lack of uniform definition of functional decline, and the biases inherent in many studies, including selection, confounding (such as gender and cognition) and information biases.

There is evidence that NSTs can predict mortality, functional decline and, to as lesser extent, move to a higher level care in populations of older people, although they are better at identifying those at low risk of these outcomes.

Further studies are warranted to establish more clearly whether NSTs can predict functional decline and mortality. Different NST cut-off scores may be required to improve their predictive ability. Standardising outcome measures with respect to functional decline will allow better comparison between research studies.

Author contributions

ED performed the review and wrote the first draft of the manuscript. IC, RV and ED were involved in planning the manuscript. Review of the final draft was performed by IC, RV, CP and ED.

Acknowledgement

We would like to thank Michael Draper, the University of Adelaide research librarian, who helped formulate our literature search strategy.

Statement of Authorship

Title of Paper	Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People
Publication Status	◉ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the mini nutritional assessment to detect frailty in hospitalised older people. Journal of Nutrition Health and Aging. 2012;16(9):764-7.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Contribution to the Paper	Conducted all data collection, performed the statistical analysis, interpreted data and wrote the manuscript. Acted as corresponding author.		
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Contribution to the Paper	Evaluated and edited the manuscript. Supervised the development of the study.		
Signature		Date	MARCH 25, 2013

6 Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People

Published as: 'Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the mini nutritional assessment to detect frailty in hospitalised older people. *Journal of Nutrition Health and Aging.* 2012;16(9):764-7.'

Objectives: The aims of this study were to: (1) determine the prevalence of undernutrition and frailty in hospitalised older patients and (2) evaluate the efficacy of both the Mini-Nutritional Assessment (MNA) screening tool and the MNA short form (MNA-SF) in identifying frailty. **Setting and Participants:** A convenient sample of 100 consecutive patients (75.0 % female) admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital in South Australia. **Measurements:** Frailty status was determined using Fried's frailty criteria and nutritional status by the MNA and MNA-SF. Optimal cut-off scores to predict frailty were determined by Youden's Index, Receiver Operating Characteristic Curves (ROC) and area under curve (AUC). **Results:** Undernutrition was common. Using the MNA, 40.0% of patients were malnourished and 44.0% were at risk of malnutrition. By Fried's classification, 66.0 % were frail, 30.0 % were pre-frail and 4.0 % robust. The MNA had a specificity of 0.912 and a sensitivity of 0.516 in predicting frailty using the recommended cut-off for malnourishment (< 17). The optimal MNA cut-off for frailty screening was <17.5 with a specificity of 0.912 and sensitivity of 0.591. The MNA-SF predicted frailty with specificity and sensitivity values of 0.794 and 0.636 respectively, using the standard cut-off of < 8. The optimal MNA-SF cut-off score for frailty was < 9, with specificity and sensitivity values of 0.765 and 0.803 respectively and was better than the optimum MNA cut-off in predicting frailty (Youden Index 0.568 vs. 0.503).

Conclusion: The quickly and easily administered MNA-SF appears to be a good tool for predicting both undernutrition and frailty in older hospitalised people. Further studies would show whether the MNA-SF could also detect frailty in other populations of older people.

Key words: Aged, frail elderly, undernutrition, screening, predictive value of tests

6.1 Introduction

Undernutrition, with its manifestation of weight loss is common in older populations. This problem is worse in hospitals, with as many as 50 % of hospitalised older people undernourished (147, 433). The Mini-Nutritional Assessment (MNA) is a common nutritional screening tool used to assess nutritional status in older people (150). It takes approximately 10-15 minutes to administer (147) and measures 18 items in 4 components, assessed by asking questions and measuring Body Mass Index (BMI), calf and mid-arm circumference. Older people identified as malnourished by the MNA have an increased risk of in-hospital mortality (88, 99), delayed post-operative wound healing (434), an increased likelihood of nursing home admission (99) and longer lengths of hospital stay (99).

Recently a more easily administered short form (SF) of the MNA, the MNA-SF, has been introduced (157, 158). It comprises BMI measurement and the assessment of the first six of the 18 MNA items, using questions related to food intake, weight loss, mobility, psychological problems and dementia. It takes approximately 4-5 minutes to administer. Its diagnostic accuracy in detecting malnourishment is similar to that of the full MNA (157).

Frailty is also a substantial problem in older people. It is characterised by a general lack of strength and increased susceptibility to disease (256), and is associated with increased mortality (222) and morbidity (228, 245). Frailty is also associated with an increased risk of adverse events occurring during hospitalisation (435) and functional decline post-hospitalisation (228, 436, 437). Identification of frailty in hospitalised older people allows for optimisation of a multidisciplinary subjective global assessment (SGA) to manage frailty and its associated problems both in hospital and post-hospitalisation (438). The Fried's frailty score is often used to identify frailty (222, 228, 233).

While frailty and undernutrition are not the same, older people who are undernourished are more likely to be frail (233), and there is overlap between

these conditions, particularly in hospitalised patients (196). The use of one screening tool for these two common conditions would be of benefit for time-pressured acute care clinicians. The MNA nutritional screening tool has recently been proposed as a possible screening tool for frailty (12, 150) but has not yet been assessed for this use.

In this study, results from an ongoing study of hospitalised older patients were used to (1) determine the prevalence of undernutrition and frailty in hospitalised older patients, and (2) assess whether the MNA and the MNA-SF can be used to identify frailty.

6.2 Methods

Consecutive patients (or their proxy where applicable) were approached within 72 hours of admission to the geriatric evaluation and management unit (GEMU) at The Queen Elizabeth Hospital (TQEH) in Adelaide, Australia. The GEMU generally admits patients a few days after admission for an acute illness. Study exclusion criteria were: unable to comply with the study protocol, a lack of understanding of the consent forms without a proxy, aged <70 years and not wishing to be part of the study. Study participants were recruited as part of a larger study. The study had ethics approval from TQEH Human Research Ethics Committee.

Frailty, MNA and MNA-SF assessments were performed in all subjects by the same investigator (ED). Weight (kg) was measured using a calibrated weigh chair (FVCS-150) to two decimal points. Height was measured to the nearest centimetre using a stadiometer for patients who were able to stand. For other patients, self-reported height was used. Circumference measures were performed using standard anthropometric procedures (439).

Frailty was diagnosed using a modified Fried's frailty criteria, assessing five frailty components – shrinking, weakness, exhaustion, slowness and low physical activity levels. (210). Shrinking and exhaustion were defined as per Fried's original study (210), with shrinking being unintentional weight loss of 4.5kg or more in the last year and exhaustion established by responses to the questions '*I felt that everything I did was an effort'* and '*I could not get going in the last week*'. Weakness was defined as a grip strength <30kg for males and <18 kg for females as per the frailty intervention trial (FIT) (12). Low physical activity was defined as per FIT criteria, which was a 'yes' response to all three of '*did not perform and weight bearing physical activity*', '*spent more than 3 hours per day sitting*' and '*went for a short walk once per month or less*'. Slow walking speed was defined as > 30s to complete 6m or unable to complete 6m as defined by the Elderly Mobility Scale (440). Frailty was defined as the presence of three or more

of the five frailty components; pre-frailty as one or two components; and robust as the absence of all frailty components.

Nutritional Status was determined using the MNA (2, 3) and the MNA-SF (7). MNA scores < 17 out of 30 were classified as 'malnourished', scores 17 – 23.5 as 'at risk of malnourishment' and scores > 23.5 as 'well nourished' (3). For the MNA-SF, scores of 0-7 were designated as 'malnourishment', scores 8-11 'at risk of malnutrition' and scores 12 – 14 as 'well nourished' (7). Body Mass Index (BMI) (weight/height^2) was computed for each patient and so MNA-SF did not use calf circumference measures in lieu of BMI.

6.2.1 Statistical Analysis

Normality of data was assessed using both Kolmogorov-Smirnov tests and histograms. Associations between MNA scores and frailty classifications were determined by Spearman's correlations. The accuracy of MNA and MNA-SF scores in identifying frailty was assessed by Receiver Operating Characteristic Curves (ROCs) and area under curve (AUC) using sensitivity and specificity values for each MNA cut-off point.

The ability of malnourishment classification by MNA and MNA-SF to detect frailty (> 3 criteria) was analysed by calculating MNA's sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for each MNA cut-off point. The maximum Youden Index (YI) (sensitivity + specificity – 1), was computed to determine the most accurate MNA cut-off score to reflect frailty.

Statistical analysis was carried out using PASW Statistics 18 (IBM SPSS Statistics; Chicago, IL) and Microsoft Office Excel 2007 (Microsoft Software, Washington), with statistical significance set at $P < 0.05$.

6.3 Results

Figure 6-1 shows patient recruitment. One hundred consecutive patients were included. Mean (SD) age of patients was 85.2 (6.1) years (range 72 – 98). 75 (75.0 %) of the patients were female. 31 (31.0 %) patients had a proxy assist with data collection. Height was self-reported in 28 (28.0 %). By the MNA, inadequate nutritional health was present in 84 (84.0 %) patients, with malnourishment (score<17) in 40 (40.0 %) and risk of malnutrition (score 17-23.5) in 44 (44.0 %). The MNA and MNA-SF scores were both normally distributed. Using Fried's criteria, 66 (66.0 %) patients were frail, 30 (30.0 %) as pre-frail and 4 (4.0 %) as robust. Table 6-1shows patient characteristics.

Fried's frailty classification was negatively associated with both the MNA ($r = -.479$, $P < 0.001$) and MNA-SF ($r = -.510$, $P < 0.001$). MNA correlated highly with MNA-SF ($r = .868$, $P < 0.001$). Age showed no association with MNA, MNA-SF or frailty status.

Receiver Operating Characteristic curves (ROC) for detection of frailty are shown in Figure 2. The AUC of the ROC demonstrated that both the MNA (0.780, P<0.001) and the MNA-SF (0.802, P<0.001) had good accuracy in identifying frailty, with the MNA-SF outperforming the MNA.

Table 6-2 shows measures of the ability of the MNA and MNA-SF tools to detect frailty at selected cut-off scores. For the MNA, the standard malnourishment cut-off score (<17) showed a high specificity (0.912) but lower sensitivity (0.561). The optimal MNA cut-off score to predict frailty (as determined by the highest YI) was <17.5, with a sensitivity of 0.591 and specificity of 0.912.

For the MNA-SF, the standard malnourishment cut-off point (<8) had a specificity of 0.794 and sensitivity of 0.636. The optimal MNA-SF cut-off score to identify

frailty based on the YI was <9, with a sensitivity of 0.803 and specificity of 0.765. This optimal MNA-SF had a higher sensitivity than that of the optimal MNA cut-off (0.803 vs. 0.591) and was also a better predictor of frailty as indicated by a higher YI (0.568 vs. 0.503).

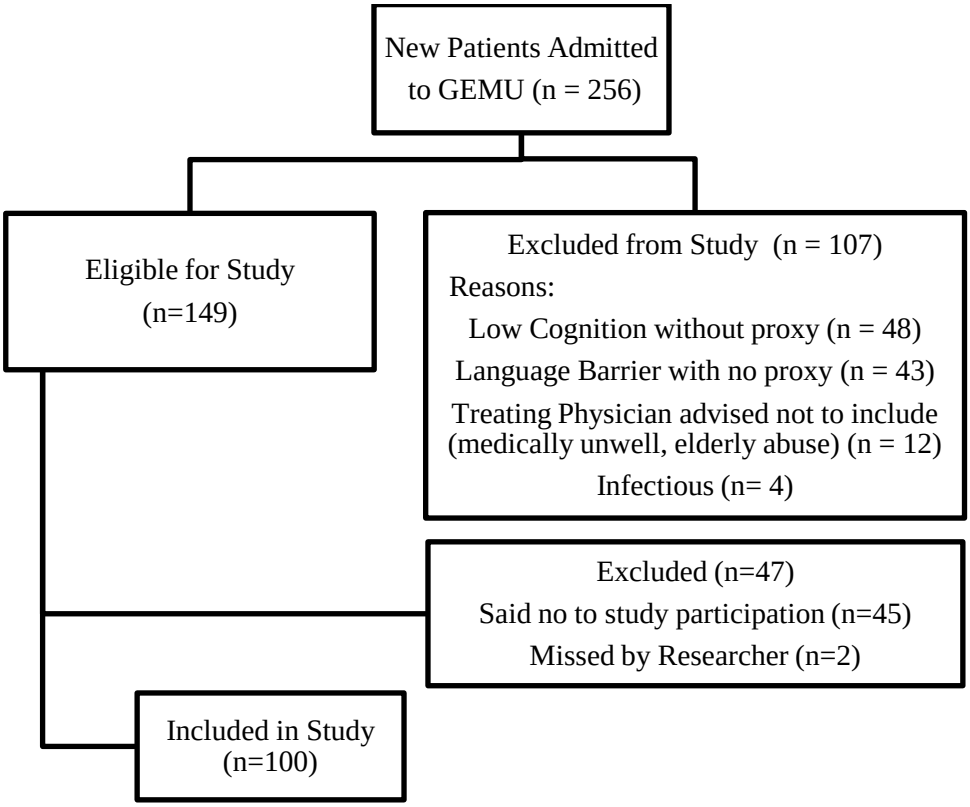

Figure 6-1: Flow Diagram of Patient Recruitment from the Geriatric Evaluation and Management Unit (GEMU)

Table 6-1: Characteristics of Patients for Each Classification by Fried's Frailty Criteria

	Overall (n=100)	Fried Frailty Classification			P
		Frail (n=66)	Pre-frail (n=30)	Robust (n=4)	
Age (years)	85.2 ± 6.1	86 ± 5.9	84.0 ± 6.6	82.5 ± 4.5	0.209
BMI (kg/m^2)	25.8 ± 6.1	25.9 ± 7.2	25.4 ± 5.5	25.5 ± 3.0	0.944
Hospital Days prior GEMU	6.0 ± 8.2	6.6 ± 9.6	4.7 ± 4.0	4.3 ± 3.0	0.539
Days in GEMU	14.8 ± 7.9	15.2 ± 12.7	15.0± 14.5	7.7 ± 1.5	0.627
Gender (Female)	75 (75%)[†]	53 (80.3 %)	19 (63.3 %)	3 (75%)	0.209
Grip Strength (kg)	14.9 ± 6.4	12.9 ± 5.6	18.2 ± 6.1	23.8 ± 4.7	<0.001[⋆]
CC (cm)	31.8 ± 4.9	31.4 ± 5.0	32.0 ± 4.4	34.5 ± 5.0	0.445
MAC (cm)	26.4 ± 4.6	26.2 ± 5.1	26.6 ± 3.3	27.4 ± 4.5	0.853
MNA	18.3 ± 5.0	16.7 ± 5.0	21.1 ± 3.4	23.1 ± 3.3	<0.001[⋆]
MNA-SF	7.8 ± 2.8	6.8 ± 2.6	9.4 ± 2.2	11.5 ± 1.7	<0.001[⋆]

Data are expressed as Mean ± SD. **Abbreviations:** BMI = Body Mass Index; GEMU = Geriatric Evaluation and Management Unit; MAC = Arm Circumference; CC = Calf Circumference; MNA = Mini Nutritional Assessment; MNA-SF = MNA Short Form.

[⋆] Significant differences between groups occur between (i) the Frail and Robust Group and (ii) the Frail and Pre-Frail Group. No significant differences occurred between the pre-frail and robust group.

[†] n (%) for all such values

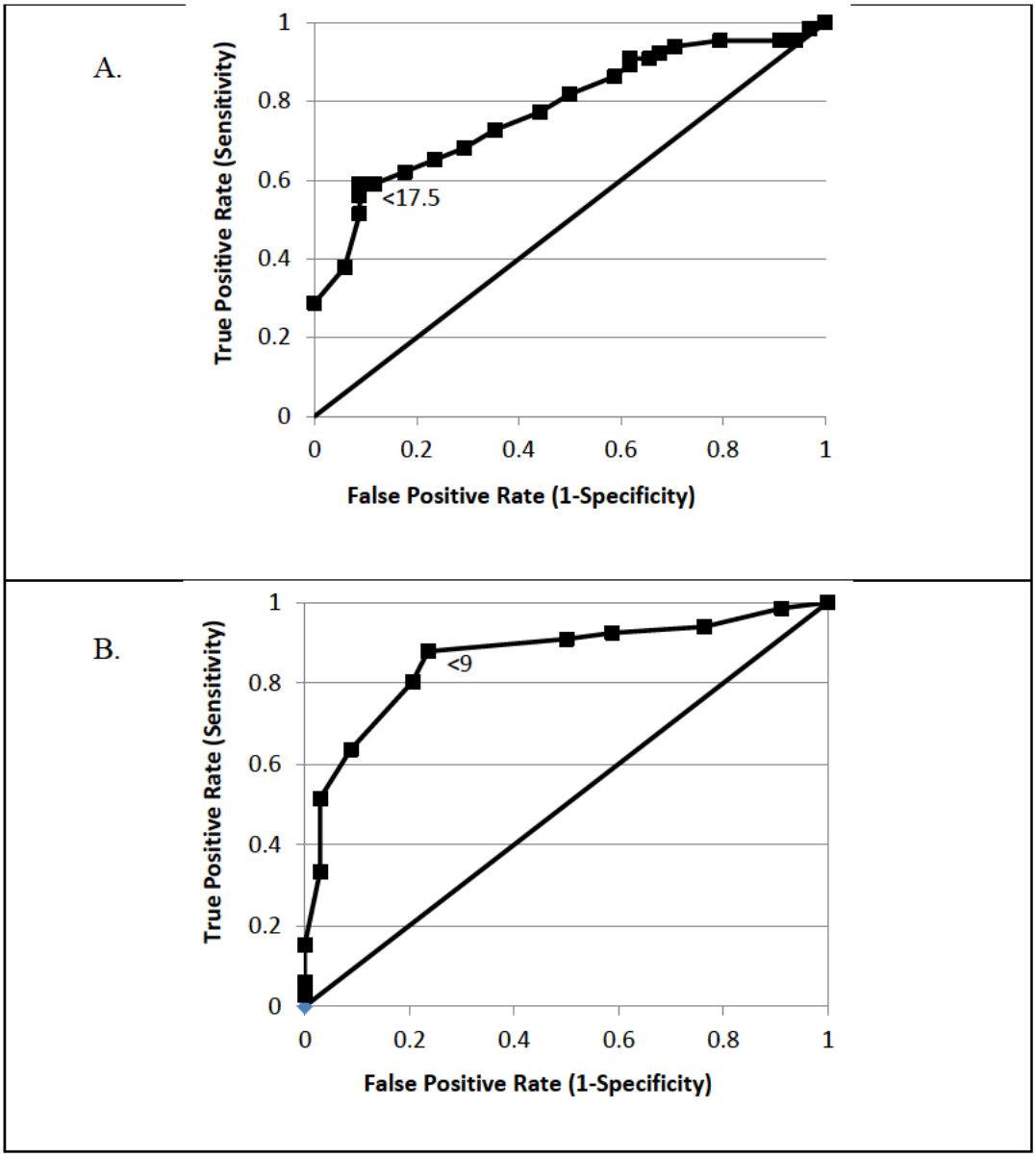

Figure 6-2: Receiver Operating Characteristic Curves for the Identification of Frailty by the (A) Mini-Nutritional Assessment (MNA) Total Score and (B) MNA-SF total Score Using Fried's Frailty Criteria to Classify Frailty. Total Area under Curve (AUC) = 0.780 (P<0.001) for the MNA and 0.802 (P<0.001) for the MNA-SF. Data labels show optimal MNA and MNA cut-off scores.

Table 6-2: Efficacy values of Malnutrition against Frailty Classification by Fried's Criteria Using the MNA and the MNA-SF for Malnourishment Classification (n=100)

	MNA Cut-off Scores						
	< 16.5	**< 17.0**	**< 17.5**	**< 18.0**	**<18.5**	**<19**	**<19.5**
Sensitivity	0.515	0.561	0.591	0.591	0.621	0.652	0.682
Specificity	0.912	0.912	0.912	0.882	0.824	0.765	0.706
PPV	0.919	0.925	0.929	0.907	0.872	0.843	0.818
NPV	0.492	0.517	0.534	0.526	0.528	0.531	0.533
Youden Index	0.427	0.472	0.503	0.473	0.445	0.416	0.388
	MNA-SF Cut-off Scores						
	<6	**<7**	**<8**	**<9**	**<10**	**<11**	**<12**
Sensitivity	0.333	0.515	0.636	0.803	0.879	0.909	0.924
Specificity	0.971	0.912	0.794	0.765	0.500	0.412	0.235
PPV	0.957	0.919	0.857	0.869	0.773	0.750	0.701
NPV	0.429	0.492	0.529	0.667	0.680	0.700	0.615
Youden Index	0.304	0.427	0.430	0.568	0.379	0.321	0.160

Abbreviations: PPV, Positive Predictive Value (the proportion of patients with positive test results that are correctly identified); NPV, Negative Predictive Value (the proportion of subjects with a negative test result that are correctly identified)

6.4 Discussion

The rate of inadequate nutritional health, as assessed by the MNA, was high in our study (84.0%, with 40.0% malnourished and 44.0% at risk of malnourishment). Frailty, as determined by Fried's criteria was also common (66.0 %). The high rates of both conditions is probably not surprising, given the high age of the subjects, the contribution of both frailty (228) and undernutrition (441) to increased risk of hospitalisation in older people and reported substantial rates for both conditions in healthier groups of older people (336, 421).

Our study also found malnourishment, identified by MNA, was significantly associated with frailty status identified by Fried's frailty criteria. Although this finding is probably not surprising, as undernutrition and frailty can contribute to each other, as far as we know this is the first time the link has been reported using validated screening tools for these conditions. Using either the standard cut off score for malnourishment of <17 or the optimal cut-off of <17.5 identified in this study, the MNA score had a high specificity (>90 %) but lower sensitivity (<60 %) in detecting frailty. This high specificity is good as it indicates few false positive results with its associated burdens, including increased costs of further assessments and unnecessary patient stress. Nonetheless, sensitivity should also be high in a good screening tool (fewer false negatives), and this could limit the use of the MNA as a screening tool for frailty.

In contrast, the MNA-SF score had a higher sensitivity than the MNA score: 0.636 at the standard cut-off (<8) and an even higher sensitivity of 0.803 at the optimal identified cut-off score (<9), with a specificity of 0.765 at this cut-off. Based on these values, as well as its higher YI and AUC, the MNA-SF outperforms the MNA score in detecting frailty and appears to be suitable for identifying undernutrition and frailty. It has the added advantage of being quicker and easier to perform compared to the full MNA.

Our results suggest that the MNA-SF, with a cut-off of <9 can be used to identify hospitalised older people at risk of both undernutrition and frailty. More detailed testing, including a complete geriatric assessment and Fried scale testing, can then be undertaken on these undernourished people so that individualised management programs can be implemented. These should target both undernutrition and problems associated with frailty, including reduced muscle strength and falls risk (438) where both conditions are present. If only one of undernutrition and frailty is identified, management could focus more on that issue.

6.4.1 Limitations

Height was self-reported by 28 % of study patients. This could have resulted in an overestimation of height (442) and thus an underestimation of BMI in this subset of patients. This could not have altered those patients BMI scores by more than 1 point, however, which is unlikely to have substantially changed the associations between MNA and frailty scores found in the study. Our finding that frailty was not associated with age could be due to the due to the narrow age range of our study patients with most being octogenarians.

Most subjects (75.0 %) were women. Compared to men, older women are more likely to be underweight (BMI <20 kg/m^2) (443), have higher levels of frailty (210) and report poorer self-reported health in MNA questions than men (444). Similarly, the inclusion of patients with cognitive impairment into our study may have influenced our results, as cognitive impairment has been found to be associated with undernutrition (445) and frailty (322) in older people. Additionally, data collected from a proxy (31.0 % of our patients) could give an information bias. Another possible limitation is that our undernutrition and frailty rates could be overestimated as some patients were recovering from illness, and perhaps more likely to score positive for components such as ‘low mobility’ or ‘exhaustion’.

Our population was clinically unwell compared to community dwelling older people and as such, the Positive Predictive Value (PPV), which is dependent upon condition prevalence, may have been inflated. It is likely that the PPV would be lower in a population of community living older people with lower rates of undernutrition and frailty. Thus, our results may not apply to other groups of older people, and it would be useful to study larger, healthier population groups. It should also be noted that a positive frailty diagnosis by Fried's criteria is limited by its inclusion of only physical attributes of frailty. Frailty is known to be multi-factorial, with psycho-social and cognitive factors also contributing to its features (446).

6.4.2 Conclusion

The MNA-SF appears to be a good tool for predicting both undernutrition and frailty in hospitalised older people.

Statement of Authorship

Title of Paper	Nutritional Screening Tools and Anthropometric Measures as Predictors of Hospital Discharge Outcomes in Older People
Publication Status	○ Published, ○ Accepted for Publication, ◉ Submitted for Publication, ○ Publication style
Publication Details	Submitted to the Australasian Journal on Ageing

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Signature	Date March 25, 2013

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Signature	Date 26/3/13

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Signature	Date 26/3/13

7 Nutritional Screening Tools and Anthropometric Measures Associate with Hospital Discharge Outcomes in Older People

Submitted for publication as: 'Dent E, Chapman I., Piantadosi C, Visvanathan R. Nutritional Screening Tools and Anthropometric Measures as Predictors of Hospital Discharge Outcomes in Older People.' Submitted to *Australasian Journal on Ageing.*

Objectives: To examine the association of nutritional screening tools (NSTs) and anthropometric measures with adverse hospital discharge outcomes in hospitalised older people. **Design:** Longitudinal observational study. **Methods:** Consecutive patients aged ≥ 70 years admitted to a Geriatric Evaluation Management Unit (GEMU) at The Queen Elizabeth Hospital, South Australia were included. Anthropometric measures included calf circumference (CC), Mid-Arm Circumference (MAC) and Body Mass Index (BMI). NSTs studied were: Mini-Nutritional Assessment (MNA), MNA-short form (MNA-SF) using BMI (MNA-SF-BMI) and CC (MNA-SF-CC), Geriatric Nutritional Risk Index (GNRI) and Simplified Nutritional Appetite Questionnaire (SNAQ). ANCOVA and logistic regression analyses were performed to assess the predictive ability of NSTs and anthropometric measures in determining: (1) functional change measured using Barthel's Index (BI), (2) length of GEMU stay (LOS) and (3) discharge to a higher level of care. **Results:** 172 patients were examined; mean (SD) age of patients was 85.2 (6.4) years. Malnutrition according to the MNA, MNA-SF and GNRI occurred in 53 (31 %), 77 (45 %) and 83 (48 %) of patients respectively. Functional change was associated with the GNRI (Beta coefficient (β), 95 % CI = 0.17, 0.001 to 0.33) and CC (β, 95 % CI) = 0.17 (0.01 to 0.33); LOS was associated with the MNA-SF-BMI (β, 95 % CI) = -0.02, -0.003 to -0.004, P = 0.015), the MNA-SF-CC (β, 95 % CI) = -0.02, -0.003 to -0.001, P = 0.039) and the MNA-II (β, 95 % CI) = -0.01, -0.02 to -0.001, P = 0.017. MAC was associated with discharge to higher level of care (OR, 95 % CI) = 0.88, 0.81 to 0.96, P = 0.002). No other variables associated with outcomes. **Conclusion:** In hospitalised older people, admission NSTs and anthropometric measures are associated with outcomes, with different NSTs associated with different outcomes.

Keywords: Aged, 80 and over; Nutritional Assessment; Geriatric Assessment/Methods; Hospitalisation

7.1 Introduction

Malnutrition is common in older persons and associated with functional decline and increased mortality, yet it often goes unrecognised in the hospital setting (13). Screening of hospital patients has therefore been recommended to identity those malnourished or at risk of malnourishment (13). Nutritional Screening Tools (NSTs) offer a fast and easy way to identify these at risk individuals, allowing referral for further nutritional evaluation and management (147, 447).

Several NSTs have been validated for use in hospitalised older persons, including the Mini Nutritional Assessment (MNA) (149), the MNA-short form (MNA-SF) (157) and the Geriatric Nutritional Risk Index (GNRI) (170). The Simplified Nutritional Appetite Questionnaire (SNAQ) has also been validated in older persons to identify those at risk of weight loss (167).

Considerable work has been done to identify which NST is the best in identifying malnutrition (137). Only limited research exists, however, in determining which NST best associates with adverse clinical outcomes in hospitalised older patients (170). An association with adverse outcomes is important for validation of a NST in the clinical setting, particularly when compared to other screening tools (9).

To our knowledge, only three prospective studies have looked at NSTs and functional decline over hospitalisation (86, 98, 112), with mixed results, and none compared NSTs to each other. Additionally, anthropometric measures, such as Body Mass Index (BMI), calf circumference (CC), and mid arm circumference (MAC), have been reported to be associated with functional status (201), but their ability to predict in-hospital outcomes compared to NSTs is unknown. The aim of this study was to compare several NSTs and anthropometric measures in their relationships to discharge outcomes, including change in function, length of stay (LOS), and discharge to higher level of care, among patients in a Geriatric Evaluation and Management Unit (GEMU).

7.2 Methods

7.2.1 Setting and Sample

Consecutively admitted patients aged 70 years or over admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital, Adelaide, Australia (TQEH), from October 22, 2010 to December 23, 2011 were recruited within the first three days of GEMU admission. Informed consent was obtained from patients, or in cases of cognitive impairment, from a family member. The study was approved by the TQEH Human Research Ethics Committee (TQEH) and adhered to the Australian Code for the Responsible Conduct of Research.

The GEMU at TQEH is a higher acuity, specialised geriatric unit providing comprehensive geriatric assessment and multi-disciplinary management, including rehabilitation where appropriate. The majority of patients are identified by the geriatric service in the Acute Medical Unit (short stay < 72 hours), where they have been admitted for management of an acute medical illness, and then transferred to the GEMU. The GEMU aims to undertake comprehensive geriatric assessment and management, to maximise functional independence and discharge patients home where possible. Nutrition management is a key focus.

7.2.2 Assessments

All assessments were completed within 72 hours of a patient's GEMU admission by the same researcher (ED) Function was assessed using Barthel's Index (BI) of Activities of Daily Living (ADL), with a total score of 100 indicating independence in all ADLs (394). Interview data collected included health and lifestyle questions. Information obtained from patient medical records included nutritional blood markers (C-reactive protein (CRP), Lymphocytes, Haemaglobin, Albumin, Cholesterol (total), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), micronutrients (Iron, Folate, Vitamin B12, Vitamin D), medications, Geriatric Depression Scale (GDS-15) (381), cognition using the Mini Mental State Examination (MMSE) (382), and admission diagnosis.

Admission diagnosis was placed into one of five categories: chronic condition, infection, injury or musculoskeletal condition, non-musculoskeletal condition and unclassified (384). Charlson's Co-morbidity Index (CCI) was derived from patient medical records.

7.2.2.1 Anthropometric Measures

Measurements were performed on the right hand side of the body where possible to standardise measurements. CC was measured as the widest calf girth, and MAC measured as the circumference of the upper arm, mid way between the acromion process and the lateral epicondyle of the elbow. Each measurement was performed once (to the nearest 0.1 cm) per patient.

Height was measured with a stadiometer to the nearest 0.5 cm for mobile patients and self-reported height recorded for non-mobile patients. The same calibrated weight chair was used to weigh all mobile patients to the nearest 0.01 kg. For immobile patients, a weigh sling was used. BMI was computed.

7.2.2.2 Mini Nutritional Assessment

The MNA is widely used and contains 18 questions covering four areas (anthropometry, diet, subjective health and overall assessment) (1). It classifies people as 'malnourished' (scores 0-23), 'at risk of malnutrition' (scores 17 - 23.5) or 'well nourished' (scores 24-30) (147). A second MNA version (MNA-II), which excludes BMI, doubles CC score and triples MAC score, was also used (448). The MNA-II was recently validated in Taiwanese older persons and also has a total score of 30 (448). For the purposes of our study, standard CC and MAC cut-offs were used, not Taiwanese specific cut-offs.

Also studied was the MNA-SF, which comprises six MNA questions and can be used with either BMI or CC measures (157), termed the MNA-SF-BMI and

MNA-SF-CC respectively. MNA-SF classifications are: 'malnourished' (scores 0-7), 'at risk of malnutrition' (scores 8-11) and 'well nourished' (scores 8-12) (157). MNA-SF retains MNA's accuracy of nutritional status classification (1).

7.2.2.3 The Geriatric Nutritional Risk Index

The GNRI is both a nutrition-related risk index and NST for use in older persons (97). It is computed as:

GNRI = (1.489 x albumin (g/L)) + (41.7 x (weight/WLo))
With WLo = Ideal Weight, using Lorentz equations as described by Boulianne et al. (170):
Men: WLo = *H* -100 – ((*H* - 150)/4)
Women: WLo = *H* - 100 – ((*H* - 150)/2.5)
With H = height in cm; g = grams; L = Litre

GNRI categories are: major risk (scores < 82), moderate risk (scores < 92), low risk (scores 92 to ≤ 98) and no risk (> 9) (170).

7.2.2.4 Simplified Nutritional Appetite Questionnaire (SNAQ)

The SNAQ is a weight loss prediction tool designed for use in older persons, with scores ≤ 14 / 20 indicating significant risk of at least 5 % weight loss within six months (167). It comprises four questions on appetite and food intake.

7.2.3 Discharge Outcomes

Discharge function was assessed using BI score. Functional decline and improvement were defined as a decrease or increase, respectively, in BI. Other discharge outcomes were GEMU length of stay (LOS) and discharge to a higher level of care. A higher level of care was defined as a move to a destination other than home, which included sub-acute care post-GEMU or move to an address that was not the patient's pre-admission address. Patients who died during

hospitalisation were classified as discharged to higher level care and were excluded from discharge function and LOS analyses.

7.2.4 Statistical Analyses

Normally distributed variables were expressed as means (SD) and non-normally distributed variables as medians (range). Categorical variables were expressed as number and percentage. Paired t-tests were performed to determine the difference between admission and discharge function. The association between NSTs, anthropometric variables, nutritional biomarkers and functional measures at admission were analysed using Spearman's rank correlations.

LOS and functional outcomes were analysed as continuous variables. Their association with each NST was determined using ANCOVAs. Residual plots of regression models were assessed visually for normality, constant variance and outliers. LOS was non-normally distributed and subsequently log transformed. For functional change, BI at discharge controlling for BI at admission was used. Associations between each NST and 'move to higher level of care' were assessed using logistic regression analyses.

All regression models controlled for confounding variables found in previous research to be associated with hospital outcomes: age, gender, CCI, MMSE, Admission BI, and living alone. Due to limited statistical degrees of freedom, no further confounding variables could be included in the logistic regression analyses (move to higher level care). The ANCOVA models additionally controlled for GDS and C-reactive protein (CRP) (a measure of inflammation).

Variables in each regression model were checked for multi-collinearity. All results were analysed using PASW Statistics 18 (IBM SPSS, Chicago, IL) software, with statistical significance set at $P < 0.05$.

7.3 Results

During the study period, 427 new patients aged ≥ 70 years were admitted to the GEMU. Patients were excluded from the study for the following reasons: dementia or unresolved delirium within 72 hours of admission without a proxy (n = 77), did not speak English (with no proxy) (n = 67), treating physician advised against patient inclusion (medically unwell elder-abuse, physically aggressive: n = 33), infectious (n = 11), missed by researcher (n = 4) and did not wish to participate (n = 63).

6-1shows the baseline characteristics of patients recruited (n = 172). The mean (SD) age of patients was 85.2 (6.4 years). Weight, CC and MAC measures were performed for all patients. Height was self-reported in 71 (41 %) patients due to immobility.

The median GEMU LOS for surviving patients was 12 days, with a median of 4 days in hospital before GEMU admission. 129 (75 %) patients had functional improvement, with 76 patients (44 %) showing an improvement in BI of more than 10 %. 28 (16 %) had no change in function and 15 (8 %) had functional decline. 80 (47 %) of patients were discharged to a location other than home and 7 (5 %) died during hospitalisation.

Malnutrition according to the MNA, MNA-SF and GNRI occurred in 53 (31 %), 77 (45 %), and 83 (48 %) patients respectively. Risk of malnutrition, by the MNA, MNA-SF, and GNRI, occurred in 84 (49 %), 67 (39 %) and 24 (14 %) patients respectively. Using the SNAQ, 109 (63 %) patients were classified at risk of weight loss.

Correlations of NSTs scores, anthropometric variables, nutritional biomarkers, micronutrients and functional measures are shown in Table 7-2. All NSTs results were correlated significantly with each other with the exception of GNRI and SNAQ. All NSTs correlated with anthropometric measures with the exception of SNAQ. Regarding functional measures, scores on all long and short versions of

the MNA correlated with admission function, grip strength and MMSE. SNAQ associated with grip strength and GDS. GNRI was not associated with any functional measure. Table 7-3 shows the results of each regression model of individual NSTs against the outcome measures. MNA-II, MNA-SF-BMI and MNA-SF-CC scores associated significantly with length of hospital stay. Both GNRI and CC associated significantly with functional change. MAC was the only variable to show an association with a discharge to higher level care. MNA, BMI and SNAQ showed no association with outcome variables.

Table 7-1: Descriptive Characteristics of Patients on Admission (n=172)

Variable	*n* (%)
Gender (female)	129 (72)
Age Group	
70 -79 years	31 (18)
80-89 years	100 (58)
90-101 years	41 (24)
BMI Category	
< 22 kg/m^2	58 (34)
22 – 30 kg/m^2	75 (44)
> 30 kg/m^2	39 (23)
Calf Circumference (cm)	31.8 (5.0) †
Mid Arm Circumference (cm)	26.1 (4.9) †
Admission function (BI)	58.6 (21.1)†
Charlson's Co-morbidity Index	3 (Range 0-12)‡
Cognitive Impairment (MMSE < 24)	74 (43)
Lives Alone	97(56)
Depressive Risk (GDS score >5)	61 (40)
Polypharmacy (≥ 6 Medications)	131 (76)
Use of Dentures	84 (49)
Problems with Food Supply	
Cooking	96 (56)
Chewing or Swallowing	58 (34)
Cutting	54 (31)
Transportation to Shops	37 (22)
Financial Constraints	18 (11)
Primary GEMU Admission Diagnosis¶	
Chronic Condition	71 (41)
Infection	52 (30)
Injury or Musculoskeletal Condition	28 (16)
Non-musculoskeletal Symptoms	6 (4)
Unclassified	15 (9)

† Mean (SD); ‡ Median (range); ¶ Classifications based on Hastings et al. 2010 (384)
Abbreviations: MMSE = Mini Mental State Examination Score; BMI = Body Mass Index (weight/height^2); GEMU = Geriatric Evaluation and Management Unit

Table 7-2: Spearman's Rank Correlations of Nutritional Screening Tools and Anthropometric Measures with Nutritional and Functional Measures on Admission (n=172)[†]

	Nutritional Screening Tool						Anthropometric Measure		
	MNA	**MNA-II**	**MNA-SF-BMI**	**MNA-SF-CC**	**GNRI**	**SNAQ**	**CC**	**MAC**	**BMI**
Nutritional Screening Tool									
MNA-II	.964***								
MNA-SF-BMI	.893***	.854***							
MNA-SF-CC	.857***	.858***	.912***						
GNRI	.388***	.380***	.383***	.307***					
SNAQ	.418***	.412***	.372***	.338***	.188				
CC	.492***	.512***	.431***	.376***	.671***	.169			
MAC	.366***	.379***	.346***	.334***	.711***	.246	.641***		
BMI	.378***	.357***	.376***	.282***	.854***	.182	.723***	.772***	
Nutritional Biomarkers									
CRP	-.043	-.062	-.046	-.044	-.111	-.137	.006	-.018	.024
Lymph	.162*	.165*	.155*	.152*	.148	.161*	.081	.096	.129
Hb	.134	.135	.180*	.169*	.242**	-.021	.116	.144	.109
Albumin	.190*	.186*	.197*	.172*	.549***	.096	.131	.133	.110
Chol	.002	.015	.043	.045	-.031	.081	-.032	-.041	-.064
HDL	-.106	-.097	-.056	-.058	-.089	-.018	-.149	-.115	-.152
LDL	.113	.131	.122	.132	-.112	.125	.009	-.069	-.065
Micronutrients									
Iron	.105	.087	.104	.106	.270**	.042	.096	.208*	.243**
Folate	.093	.095	.114	.129	-.023	.017	-.083	-.060	-.109
B12	-.107	-.122	-.140	-.139	-.086	-.202*	.047	.023	-.039
Vit D	-.132	-.143	-.119	-.072	.024	-.085	-.020	.012	-.070
Physical and Mental Functional Measures									
BI	.208**	.195*	.151*	.233**	.057	-.013	.097	.082	.028
Grip	.379***	.376***	.321***	.349***	.060	.242**	.179*	.232**	.096
MMSE	.355***	.368***	.306***	.352***	.110	.138	.155*	.202**	.191*
GDS	-.197*	-.192*	-.188*	-.236	.000	-.179*	.001	-.050	.024

* Indicates significance with P < 0.05; ** Indicates significance with P < 0.01; ** Indicates significance with P < 0.001

[†] MNA = Mini-Nutritional Assessment; MNA-II = MNA version II without BMI; MNA-SF = MNA short form: GNRI = Geriatric Nutritional Risk Index; SNAQ = Simplified Appetite Nutritional Questionnaire; CC=calf circumference (cm); MAC = Mid-Arm Circumference (cm); BMI = Body Mass Index; CRP = C-Reactive Protein: Lymph = Lymphocyte; Hb = Haemaglobin; Chol = Cholesterol; HDL = HDL cholesterol; LDL = LDL cholesterol; B12 = Vitamin B-12; Vit D = 25OH-Vitamin D; BI = Barthel Index; Grip = Maximal Grip Strength; MMSe = Mini Mental State Examination; GDS = Geriatric Depression Scale -15

Table 7-3: Association of Nutritional Screening Tools and Anthropometric Measures with Discharge Outcomes[†]

Predictor Variable	Functional Change (BI) (n=165)			Length of GEMU Stay (log(days)) (n=165)			Discharge to High Level Care (n=172)		
	B[‡]	**95% CI**	**P**	**B**	**95% CI**	**P**	**OR**[¶]	**95% CI**	**P**
Nutritional Screening Tool									
MNA	0.38	-0.08 to 0.83	0.119	-0.01	-0.02 to 0.000	0.051	0.95	0.89 to 1.10	0.110
MNA-II	0.31	-0.13 to 0.74	0.168	-0.01	-0.02 to -0.001	0.017	0.96	0.90 to 1.02	0.163
MNA-SF-BMI	0.03	-0.02 to 0.07	0.352	-0.02	-0.03 to -0.004	0.015	0.92	0.83 to 1.02	0.114
MNA-SF-CC	0.37	-0.02 to 0.07	0.329	-0.02	-0.03 to -0.001	0.039	0.95	0.86 to 1.05	0.298
GNRI	0.17	0.01 to 0.33	0.038	-0.002	-0.01 to 0.001	0.233	0.98	0.96 to 1.01	0.164
SNAQ	0.44	-0.3 to 1.16	0.237	0.004	-0.01 to 0.001	0.590	0.98	0.89 to 1.08	0.641
Anthropometric Measure									
CC	0.48	0.02 to 0.93	0.041	-0.003	-0.12 to 0.01	0.466	0.94	0.88 to 1.004	0.064
MAC	0.41	-0.11 to 0.96	0.123	-0.01	-0.02 to 0.003	0.170	0.88	0.81 to 0.96	0.002
BMI	0.23	-0.13 to 0.60	0.208	-0.004	-0.01 to 0.003	0.321	0.96	0.91 to 1.01	0.109

[†]All regression analyses controlling for age, gender, Cognitive Impairment Risk (Mini Mental State Examination), Function (Barthel's Index), Charlson's Comorbitidy Index and Lives Alone. The multiple regression models (LOS and Functional Change) also controlled for Depressive Risk (Geriatric Depression Scale-15) and Inflammation (indicated by C-Reactive Protein levels). Each line represents a separate regression model. CI = Confidence Interval; MNA = Mini-Nutritional Assessment; MNA-II = MNA version II without BMI; MNA-SF = MNA short form: GNRI = Geriatric Nutritional Risk Index; SNAQ = Simplified Appetite Nutritional Questionnaire; CC=calf circumference (cm); MAC = Mid-Arm Circumference (cm): BMI = Body Mass Index; GEMU = Geriatric Evaluation and Management Unit. Bold Indicates Significance (P<0.05)

[‡] *B* = Unstandardised Beta Coefficient

[¶] OR = Odds Ratio

7.4 Discussion

To our knowledge this is the first study to evaluate the use of NSTs and anthropometric measures as predictors of discharge outcomes for older people in a GEMU. Malnutrition rates were high: 31%, 45%, and 48% for the MNA, MNA-SF and GNRI respectively, comparable to those in other studies of hospitalised older persons (111, 147, 170).

Management of GEMU patients involves a balance between providing adequate time for functional rehabilitation and keeping LOS as short as possible, and thus reducing health care costs (378). The median LOS in our study was 12 days, in line with other GEMUs (378). Although we did not find MNA to be associated with LOS, lower scores on the shorter and easier to implement version, the MNA-SF (with BMI), were associated with longer stays. Moreover, the MNA-SF-CC and the MNA-II, in which weight or BMI is not required, also showed a similar association with LOS. These findings have practical implications in the GEMU, as the often considerable burden of weighing frail older people in hospital may possibly be avoided (13).

Lower MAC was the only measure associated with discharge to higher level care, a finding which agrees with previous reports (449). MAC is a measure of both fat and muscle mass and thus possibly indicative of late-stage muscle wastage and impending mortality (201, 450). It is likely that factors other than MAC, including illness and family situation influence discharge destination (447). Our study, however, controlled for a range of covariates that could be influencing discharge destination including cognition, co-morbidity and living alone. No NSTs were associated with discharge to higher level of care, in keeping with the conflicting results of studies as outlined in a recent systematic review (447).

For functional change, lower GNRI and CC measures, indicative of reduced nutritional status, were associated with functional decline as assessed by BI. No

other studies, to our knowledge, have looked at GNRI as a predictor of functional decline. Studies of CC have found it is linked to functional decline in institutionalized older persons (201), possibly because it reflects muscle wastage and an inability to walk (201, 450). In the present study, the GNRI may have shown an association with functional decline for a number of reasons. Firstly, it includes albumin, with lower levels linked to reduced physical function in older persons (451). Secondly, it was originally designed as a prognostic tool (170). Thirdly, in our study it showed high associations with both CC (r = 0.711) and MAC (r = 0.854). Finally, lower GNRI scores were associated with lower iron levels in our study which have been linked with functional decline (452).

Perhaps surprisingly no other measures were associated with functional change. We had expected the MNA score to show an association with function, as it has been found previously to associate with in-hospital functional decline (112), although not functional recovery (111). The MNA-SF score has also been found to be associated with in-hospital functional decline (98). It could be that the MNA and its versions may not have been sensitive enough in detecting functional change during the relatively short hospitalisation period (111).

7.4.1 Strengths and Limitations

This study recruited consecutive patients and eliminated inter-tester bias as one researcher performed all assessments. Many confounding variables were controlled for which improved the generalisability of results to other populations of hospitalised older persons.

The current study was an observational study, so no inference about causation can be made. The sample size was also relatively small. Possible study bias could exist for several reasons, including proxy assistance in patient interview in the cases of cognitive impairment and/or language barrier, self-reported height was used in 41 % of patients due to immobility and CC may have been influenced by oedema. Additionally, “discharge to destination other than home” included

discharges to sub-acute care (rehabilitation). These patients may have returned home after spending time in such a setting, however, at the time of their discharge from the GEMU, they were not deemed functional enough for a direct discharge home.

It should also be noted, that despite 75 % of patients improving in function, many of these patients were not discharged home. Reasons for this lack of discharge home included dementia, and the influence of external factors such as finances and familial wishes. It could also be that this improvement in function was not adequate to return to home immediately at discharge.

7.4.2 Conclusion

In hospitalised older persons, admission NSTs and anthropometric measures are associated with negative outcomes, but different measures are associated with different outcomes. The MNA-SF (using BMI or CC) and MNA-II were associated with LOS. MNA-SF is fast and rapid to implement and MNA-II does not involve the time-consuming measurement of weight. GNRI and CC were associated with functional decline during hospitalisation, perhaps because they reflected greater illness and muscle wastage, respectively. A lower MAC was associated with a greater need for discharge to a higher level of care, possibly because it is an indicator of end-stage decline. The use of a nutritional screening tool to detect both undernutrition and risk of adverse outcomes in hospital will assist time-pressured clinicians. Future research should focus on the predictive ability of NSTs post-hospitalisation and the efficacy of interventions in-hospital.

7.4.3 Key Points

- In hospitalised older people, nutritional screening tools and anthropometric measures are associated with adverse clinical outcomes, such as length of stay, change in physical function and discharge destination.

- Different measures are associated with different outcomes: GNRI and CC were both associated with functional change, MNA-II and MNA-SF were associated with length of hospital stay and MAC was associated with discharge to higher level care.
- The use of a NST to detect both undernutrition and risk of adverse outcomes in hospital could assist time-pressured clinicians.

Statement of Authorship

Title of Paper	Performance of Nutritional Screening Tools in Predicting Poor Six Month Outcome in Hospitalised Older People
Publication Status	○ Published, ○ Accepted for Publication, ⊙ Submitted for Publication, ○ Publication style
Publication Details	Submitted to Australasian Journal on Ageing

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Signature	Date 26/3/13

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Contribution to the Paper	Supervised the development of the research, helped in data interpretation and in editing and evaluating the manuscript.
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Signature	Date 26/3/13

8 Performance of Nutritional Screening Tools in Predicting Poor Six Month Outcome in Hospitalised Older People

Submitted for publication as: 'Dent E, Chapman I., Piantadosi C, Visvanathan R. Performance of Nutritional Screening Tools in Predicting Poor Six Month Outcome in Hospitalised Older People.' Submitted to *Journal of Nutrition Health and Ageing.*

Background/Objectives: Malnutrition is a major problem in hospitalised older people. Many nutrition screening tools are available for malnutrition identification, however little is known about their prognostic ability. This study investigated the prognostic value of three nutritional screening tools.

Design: Prospective, observational study.

Setting: Geriatric Evaluation and Management Unit (GEMU).

Participants: 172 consecutive patients (72 % female; mean (SD) age = 85.2 (6.4) years).

Measurements: Nutritional status was identified using the Geriatric Nutritional Risk Index (GNRI), the Mini Nutritional Assessment (MNA) and the MNA short form (MNA-SF) incorporating either Body Mass Index (BMI) (MNA-SF-BMI) or calf circumference (CC) (MNA-SF-CC). Poor six month outcome was defined as new admission to higher level residential care or mortality at six months post-discharge. Predictive ability of poor outcome was assessed by logistic regression models, adjusting for age, gender and cognition. Predictive accuracy was determined by $_{au}$ROC values, sensitivity, specificity, predictive values (positive and negative) and Youden Index.

Results: Malnutrition was identified by the MNA, MNA-SF-BMI, MNA-SF-CC and GNRI in 31 %, 45 %, 53 % and 48 % of patients respectively. Malnutrition was associated with a higher risk of poor six month outcome when identified by the MNA (OR, 95 % CI = 3.29, 1.17 - 9.23) and the GNRI (OR, 95 % CI = 2.84, 1.31 - 6.19), but not by either MNA-SF version. $_{au}$ROC values for all screening tools lacked discriminative power ($_{au}$ROC values all < 0.7).

Conclusion: Malnutrition was common in GEMU patients. The MNA and GNRI were useful clinical predictors of poor six month outcome, although their accuracy of this prediction was low. Nutritional screening remains a priority in GEMU patients.

Keywords: ROC; Nutritional Status; Aged, 80 and over

8.1 Introduction

Malnutrition, a major problem associated with hospitalisation in older people, has an extensive impact on mortality and morbidity (215). The incidence of malnutrition in hospitalised older people is high, with around 22 – 68% of patients diagnosed, depending on the population studied and the assessment method used (215). Malnutrition, despite this high prevalence, often goes unrecognised in hospitals (13).

Nutritional screening tests are at the forefront of identifying patients with malnutrition. Ideally, identified patients are referred for a full nutritional assessment, which includes diagnosis confirmation, and identification of specific nutritional deficits (147). A nutritional screening tool has additional clinical and research value if it also doubles as an index of nutritional risk and, by definition, is able to predict the probability of an adverse outcome occurring (170). Many nutritional screening tools exist, however, it is not yet clear which one performs best in predicting longer term outcomes in hospitalised older people (215).

Three nutritional screening tools showing promise as indices of nutritional risk are the Mini Nutritional Assessment (MNA) (148), the MNA short form (MNA-SF) (157) and the Geriatric Nutritional Risk Index (97). The MNA is specifically designed for, and extensively validated in older people (147, 148). It includes 18 questions in four domains: subjective assessment, nutritional assessment, anthropometric assessment and general assessment (147). The MNA shows prognostic ability in hospitalised older people (87, 88, 99, 104, 153), although not all studies agree (99, 105). A simpler version of the MNA, the MNA-SF (157) may also have potential as an index of nutritional risk, although studies of its prognostic ability are limited (215).

The Geriatric Nutritional Risk Index (GNRI) was initially developed as a nutrition-related risk index in older people, but has recently been validated as a

nutritional screening tool in its own right (97). The GNRI also shows promise as a predictor of morbidity and mortality in hospitalised older people (170, 453). However, its prognostic ability has only been compared to the MNA in one previous study, and that was conducted in residential care dwelling older people (97).

The aim of this study was to investigate the predictive ability and accuracy of the MNA, MNA-SF and GNRI in determining poor six month outcome in older people hospitalised in a Geriatric Evaluation and Management Unit (GEMU).

8.2 Methods

This was a longitudinal observational study of consecutive patients admitted to the 20-bed GEMU at The Queen Elizabeth Hospital (TQEH), South Australia. Patients were recruited between October 22, 2010 and December 23, 2011. The study was approved by the Human Research Ethics Committee (TQEH) and all patients (or authorised proxy) gave informed consent, in accordance with ethical standards from the 2000 Declaration of Helsinki.

Data were collected from the patient (or proxy) in the first 72 hours of admission. Clinical information from patient records was also collected, including: diagnosis, biomarkers, Braden skin assessment score (383), Barthel's Index of Activities of Daily Living (394), Geriatric Depression Scale (381) and cognition assessment by the Mini Mental State Examination (MMSE) (382). One researcher (ED) collected all data and performed all nutritional screening tool assessments. Patient height was measured to the nearest centimetre using a stadiometer, and for patients unable to stand independently, self-reported height was recorded. Weight was able to be measured in all patients using a calibrated weigh chair (FVCS-150) to two decimal points.

8.2.1 Mini Nutritional Assessment (MNA)

The MNA is scored out of 30, with scores ≥ 24 considered to be well nourished, scores 17 – 23.5 as at risk of malnutrition and scores < 17 as malnourished (147). Inadequate nutrition was defined as either malnutrition or risk of malnutrition (scores < 24).

8.2.2 Mini Nutritional Assessment Short Form (MNA-SF)

The MNA-SF includes six questions of the MNA (157). Two versions of the MNA-SF exist: one including Body Mass Index (weight/height^2) (BMI) (the MNA-SF-BMI) and the other including calf circumference (CC) (MNA-SF-CC). For both MNA-SF versions, scores 0 – 7 points were considered as malnourished;

scores 8-11 as at risk of malnutrition and scores 12 - 14 as well nourished (157). Inadequate nutrition was defined as scores < 12.

8.2.3 Geriatric Nutritional Risk Index (GNRI)

GNRI is computed as follows:

GNRI = (1.489 x albumin (g/L))] + (41.7 x (weight/WLo))
With WLo = Ideal Weight, using Lorentz equations as described by Boulianne et al. (170):
Men: WLo = *H* -100 – ((*H* - 150)/4)
Women: WLo = *H* - 100 – ((*H* - 150)/2.5)
With H = height in cm; g = grams; L = Litre

For the purposes of comparing the GNRI to the three categories of the MNA and MNA-SF, GNRI scores were placed into three categories as described previously (97, 170): severe/moderate risk (scores < 92), low risk (scores 92 – 98) and no risk (scores > 98). Inadequate nutrition was defined as scores ≤ 98.

8.2.4 Outcome

All patients (or proxy) were followed up at six months post-discharge by telephone interview and accessing the South Australian Health Department Open Architecture Clinical Information System system. Poor six month outcome was defined as a composite measure of one or more of the following occurring: (i) death (ii) new admission to a residential care facility or (ii) move from low level care to high level care within a residential care facility. A composite measure was chosen due to the impact of mortality on residential care admission.

8.2.5 Statistics

Statistics were analysed using SPSS for Windows 19.0 (SPSS Inc., Chicago, IL). All statistical tests were two-sided, with P < 0.05 used to indicate statistical

significance. Data are presented as mean (standard deviation) or median (range) for normally and non-normally distributed data respectively. The predictive ability of each nutritional screening tool was determined by logistic regression analyses, both unadjusted and adjusted for age, gender and cognition.

When assessing predictive ability, it is also important to look at the accuracy of each screening tool in correctly identifying patients at risk of poor outcome (154). In this study, predictive accuracy was assessed by sensitivity, specificity, predictive values (positive and negative), Youden Index (sensitivity + specificity – 1) and area under curve of Receiver Operating Characteristic (ROC) curves ($_{au}$ROC). ROC curves were derived from predicted probabilities, and a value > 0.7 was considered to indicate sufficient predictive accuracy (454).

8.3 Results

Of 427 new patients admitted to the GEMU during the study period, 127 were recruited. Exclusion reasons were: language barrier without proxy (n = 67), dementia or unresolved delirium within 72 hours of GEMU admission without proxy (n = 77), treating clinician advised against patient participation (elder abuse, physically aggressive or medically unwell: n = 33), infectious (n = 11), missed by researcher (n = 4) and did not wish to participate (n = 63).

Table 7-1 shows patient admission characteristics. During the six month follow-up period, including the period from the GEMU admission to hospital discharge, 78 patients encountered a poor outcome: 28 (16 %) patients died, 48 (28 %) moved into residential care (low or high level care) and 2 people (1 %) moved from low level to high level care within a residential care facility.

The unadjusted and adjusted odds ratio (OR) values for prediction of poor outcome is shown in Table 8-2. From this table it can be seen that, malnutrition classification at admission by the MNA, MNA-SF-CC, GNRI, but not the MNA-SF-BMI, predicted poor six month outcome. However, after adjustment for age, gender and MMSE score, only MNA and GNRI classified malnutrition retained predictive ability. Risk of malnutrition classification failed to predict poor six month outcome for all screening tools in both unadjusted and adjusted analyses.

Prognostic variables are shown in Table 8-3. From this table is can be seen that both positive and negative predictive values for all screening tool were low-moderate. The MNA showed the highest predictive accuracy overall (indicated by its higher values for $_{au}$ROC and Youden Index). However, the $_{au}$ROC value for all nutritional screening tools, including the MNA, lacked adequate predictive accuracy ($_{au}$ROC values < 7).

Table 8-1: Baseline Characteristics of Patients on Admission (n=172)

Variable	*n* (%)
Gender (Female)	123
Age as of Admission†	85.2 (6.4)
Length of GEMU stay‡	12 (1 – 91)
Length of acute hospital stay before GEMU‡	4 (0-53)
Cognitive Impairment (MMSE < 24/30)	74 (43)
Depression Symptoms (GDS > 5/15)	61 (40)
Admission function (Barthel's Index)	58.6 ± 21.1
Charlson's Co-morbidity Index†	3.0 (2.3)
Medication Number†	9.6 (4.3)
Calf Circumference (cm)†	31.8 (5.0)
Body Mass Index (kg/m^2)†	25.3 (6.5)
Accommodation	
Community Dwelling	151 (88)
Supported Residential Facility	12 (7)
Residential Care (Low Level)	5 (3)
Residential Care (High Level)	2 (1)
Biomarkers‡	
Folate	23.5 (0-1377)
CRP (mg/L)	17.0 (0.5-320.0)
Albumin (g/L)	31.0 (17-41)
Creatinine (μmol/L)	83.5 (4-239)
Lymphocyte	1.29 (0.4-188.0)
Iron Stores (μmol/L)	10.0 (1-201)
Vitamin B12	305 (7-1476)
25OH Vitamin D (nmol/L)	64.0 (14-151)
Haemaglobin (g/L)	120.0 (79-162)

Abbreviations: GEMU = Geriatric Evaluation and Management Unit; MMSE = Mini Mental State Examination; GDS = Geriatric Depression Scale; BI = Barthel's Index of Activities of Daily Living; CRP = C-Reactive Protein

† Mean (Standard Deviation); ‡ Median (Range)

Table 8-2: Odds Ratios for Prediction of Poor Six Month Outcome by Nutritional Screening Tool Assessment on Admission to the Geriatric Evaluation and Management Unit (n =172)†

Nutritional Screening Tool	Poor 6 Month Outcome Unadjusted (n=98)			Poor 6 Month Outcome Adjusted‡ (n=98)		
	OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
MNA						
Malnourishment (Scores < 17)	3.73	1.52 - 9.17	0.004	3.29	1.17 - 9.23	0.024
Risk of Malnutrition (Scores 17 – 23.5)	1.12	0.49 - 2.56	0.786	1.15	0.45 - 2.98	0.769
MNA-SF						
Malnourishment (Scores < 8)	1.78	0.74 – 4.26	0.197	1.51	0.55 - 4.13	0.424
Risk of Malnutrition (Scores 8 - 11)	0.65	0.26 – 1.61	0.354	0.78	0.28 - 2.17	0.640
MNA-SF-CC						
Malnourishment (Scores < 8)	2.60	1.06 – 6.40	0.037	2.54	0.90 - 7.16	0.078
Risk of Malnutrition (Scores 8 - 11)	0.94	0.35 – 2.53	0.944	1.25	0.41 - 3.84	0.701
GNRI						
Severe/Moderate Risk (Scores < 92)	2.21	1.13 - 4.31	0.021	2.84	1.31 - 6.19	0.008
Low Risk (Scores 92 – 98)	1.96	0.76 - 5.06	0.167	1.68	0.55 - 5.14	0.364

† Poor Six Month Outcome = Mortality, new admission to a residential care facility or move from low level care to high level care within a residential care facility.

‡ Adjusted for age, gender and MMSE score

Abbreviations: MNA = Mini Nutritional Assessment; MNA-SF-BMI = Mini Nutritional Assessment Short Form (Body Mass Index version); MNA-SF-CC: MNA-SF (Calf Circumference version); GNRI = Geriatric Nutritional Risk Index; CI= Confidence Interval; OR = Odds Ratio

Bold text indicates significance

Table 8-3: Prognostic Ability of Nutritional Screening Tools as Predictors of Poor Six Month Outcome (n=172)†

Nutritional Screening Tool	Prevalence *n* (%)	Died, *n* (%)		Se	Sp	PPV	NPV	YI	AUC (95 % CI)	P
		Yes	No							
MNA										
Scores < 17 (Mal)	53 (31)	35 (66)	18 (34)	44.9	80.9	66.0	63.9	25.7	0.634 (0.55 – 0.72)	0.003
Scores < 24 (IN)	137 (80)	66 (48)	71 (52)	84.6	24.5	48.2	65.7	9.1		
MNA-SF										
Scores < 8 (Mal)	77 (55)	44 (57)	33 (43)	56.4	64.9	57.1	64.2	21.3	0.610 (0.54 – 0.70)	0.007
Scores < 12 (IN)	144 (84)	66 (46)	78 (54)	84.6	17.0	45.8	57.1	1.6		
MNA-SF-CC										
Scores < 8 (Mal)	92 (53)	52 (57)	40 (44)	66.7	57.4	56.5	67.5	24.1		
Scores < 12 (IN)	145 (84)	69 (48)	76 (52)	88.5	19.1	47.6	66.7	7.6	0.622 (0.54 – 0.71)	0.006
GNRI										
Scores < 92 (Mal)	83 (48)	44 (56)	39 (47)	56.4	58.5	53.0	61.8	14.9	0.592 (0.51 – 0.68)	0.038
Scores ≤ 98 (IN)	107 (62)	56 (52)	51 (48)	71.8	45.7	52.3	66.2	17.5		

† Poor Six Month Outcome = Mortality, new admission to a residential care facility or move from low level care to high level care within a residential care facility. A poor six month outcome occurred in 78 patients.

Abbreviations: MNA = Mini Nutritional Assessment; MNA-SF = Mini Nutritional Assessment Short Form; GNRI = Geriatric Nutritional Risk Index; BMI = Body Mass Index; PPV = Positive Predictive Value; NPV = Negative Predictive Value; Mal = Malnourished; IN = Inadequate Nutrition; Se = Sensitivity; Sp = Specificity; YI = Youden Index

8.4 Discussion

In this study of older people hospitalised in a GEMU, malnutrition was common on admission, ranging from 31 – 48 % depending on the nutritional screening tool used. This high incidence of malnutrition is consistent with previous studies of hospitalised older people (86, 88, 105). This study evaluated the ability of nutritional screening tools to predict a poor six month outcome in GEMU patients. Malnutrition identified by the MNA, MNA-SF-CC, GNRI, but not the MNA-SF-BMI was associated with poor six month outcome. However, after adjustment for confounding variables (age, gender and cognition), only MNA and GNRI maintained their predictive ability. Risk of malnutrition classification failed to predict poor six month outcome for all screening tools.

This is the first study, to our knowledge, to compare the MNA and GNRI with respect to adverse outcomes in hospitalised older people. A previous study comparing MNA and GNRI in residential care residing older people found a malnutrition classification by both screening tools was predictive of mortality, infection and bedsores (97). Their study was inconclusive as to which screening tool performed best, although the GNRI appeared to outperform the MNA when all adverse complications were pooled together (97). In our study, malnutrition identified by the MNA showed higher predictive ability of poor six month outcome than the GNRI (adjusted OR values of 3.29 and 2.84 for MNA and GNRI respectively). This higher predictive ability of the MNA was perhaps because the MNA contained more nutrition-related risk components such as self-reported health, living status and neuropsychological problems than did the GNRI (147) Malnourishment by the MNA is generally considered to be predictive of mortality (87, 99, 104, 153), although not all studies agree (99, 105, 154).

In the present study, risk of malnutrition classification for all nutritional screening tools failed to predict poor six month outcome. This finding does not indicate a person with an ‘at risk’ classification will avoid encountering a poor outcome. It could very well be that GEMU intervention, which includes a Comprehensive

Geriatric Assessment, could have possibly helped prevent a poor outcome (455). Indeed, an 'at risk' classification by the MNA has been found not to be associated with morbidity in hospitalised older people (105), although in community based studies, some studies have found an association (412, 422) whilst others have not (420).

Also in our study, the MNA showed the highest prognostic accuracy in outcome prediction, based on its higher $_{au}$ROC and YI values. However, $_{au}$ROC values for all screening tools, including the MNA, lacked sufficient prognostic accuracy (all $_{au}$ROC values < 0.7). This lack of predictive accuracy disagrees with a study of hospitalised older people in which MNA showed adequate predictive accuracy for mortality prediction ($_{au}$ROC > 0.7) (105). It could perhaps be that our shorter length study and combination measure of mortality and admission to residential care diminished the accuracy of MNA. There are no other studies, to our knowledge, looking at predictive accuracy of nutritional screening tools in hospitalised older people (215).

Study strengths were the inclusion of consecutive patients, the comprehensive admission data and the limited inter-tester bias. This study also recruited many patients with dementia and focused on the oldest old: both areas of growing research interest with the global expansion of the older demographic. Notwithstanding these strengths, our study had limitations. Our sample size was small and there was potential collection bias introduced by the use of a proxy to answer questions for patients with cognitive impairment and/or language barriers. Our analyses also did not account for nutritional support received by patients during and after hospitalisation. A further limitation is that our results only included GEMU patients and future studies should focus on multiple hospital wards with larger sample sizes.

8.4.1 Conclusion

Malnutrition was frequent in GEMU patients. The MNA and GNRI were useful clinical predictors of poor six month outcome, although their accuracy of prediction was low. Nutritional screening remains a priority in GEMU patients.

Statement of Authorship

Title of Paper	7) Frailty and Functional Decline Indices Predict Poor Outcomes of Hospitalised Older People
Publication Status	○ Published, ○ Accepted for Publication, ◉ Submitted for Publication, ○ Publication style
Publication Details	Submitted to Age and Ageing.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate)	Elsa Dent		
Contribution to the Paper	Conducted all data collection, established the study database, performed all statistical analysis, interpreted data, wrote the paper and was corresponding author.		
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Name of Co-Author	Ian Chapman		
Contribution to the Paper	Helped in data interpretation and manuscipt editing. Supervised development of work.		
Signature		Date	March 25, 2013

Name of Co-Author	Cynthia Plantadosi		
Contribution to the Paper	Assisted in study supervision.		
Signature		Date	26/3/13

Name of Co-Author	Renuka Visvanathan		
Contribution to the Paper	Assisted in data interpretation. Helped to evaluate and edit the manuscript. Supervised project development.		
Signature		Date	26/3/13.

9 Frailty and Functional Decline Indices Predict Poor Outcomes in Hospitalised Older People

Submitted as: 'Dent E, Chapman I., Piantadosi C, Visvanathan R. Frailty and Functional Decline Indices Predict Poor Outcomes of Hospitalised Older People.' Submitted to *Age and Ageing.*

Background: Admission to a Geriatric Evaluation and Management Unit (GEMU) can optimise a patient's chance of functional recovery.

Objective: To evaluate the ability of several commonly used frailty and functional decline indices to predict GEMU outcomes, both at discharge and at six months.

Design: A prospective, observational study.

Setting and Participants: Consecutive patients aged 70 years or older admitted to a GEMU.

Methods: Patients were classified as 'frail' or 'at high risk of functional decline' using several different frailty and functional decline instruments. Predictive ability was evaulated using logistic regression and area under receiver operator characteristic (ROC) curves ($_{au}$ROC).

Results: 172 patients (mean age (SD) of 85.2 (6.4) years; 72 % female) were included. Frailty prevalence varied from 24 - 94 % depending on the instrument used. Adequate discriminatory power for discharge outcome was achieved by the frailty index of accumulated deficits (FI-CD) ($_{au}$ROC = 0.735, P < 0.001) and adapted Katz score ($_{au}$ROC = 0.704, P = < 0.001). The FI-CD was the only instrument to show adequate discriminatory power for poor six month outcome ($_{au}$ROC = 0.702, P < 0.001). Negative predictive power (PPV) was generally high for all instruments in predicting poor outcome, however positive predictive power (PPV) was only low-moderate.

Conclusion: Several frailty and functional decline instruments identified GEMU patients at risk of poor discharge and six month outcomes. The FI-CD and the

adapted Katz index showed the highest discriminatory power overall, although further research in a larger group of hospitalised older patients is warranted.

Keywords: Frail Elderly; Geriatric Assessment/Methods; Aged, 80 and over; Prognosis

Key Points:

1. Frailty is common in hospitalised older people.
2. Frailty and functional decline instruments can be used to identify older patients at risk of poor outcomes, both at hospital discharge and at six months post-discharge.
3. The FI-CD showed the highest discriminatory power in predicting poor outcomes at both time-points, followed by the adapted Katz index.

9.1 Introduction

Frailty is a major contributor to morbidity and mortality in older people (245). It is estimated that individuals identified as frail are over twice as likely to encounter adverse health outcomes as their non-frail counterparts (229, 375). Although there is currently no reference standard definition for frailty, it is generally considered to be a multi-factorial condition characterized by a heightened vulnerability to changes in health status (241). Indices developed to identify frailty are generally of two types: phenotypic and multidimensional. Phenotypic indices measure the physical signs of frailty, and include the Cardiovascular Health Study (CHS) index (210) and the simpler Study of Osteoporotic Fractures (SOF) index (221). Multidimensional indices incorporate both the physical and psycho-social components of frailty, and include the frailty index of accumulated deficits based FI-CD (242) and the simper indices: Multidimensional Prognostic Index (MPI) (330), the ten-domain frailty index based on Comprehensive Geriatric Assessment (FI-CGA-10) (343) and FRAIL (Fatigue, Resistance Ambulation, Illness, Loss of Weight) (245). Indices used to measure functional decline can also be considered frailty indices (274); examples include the Katz score of activities of daily living (ADL) (331), Lawton's Instrumental ADL (IADL) scale (332), the Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA) (333) and the Hospital Admissions Risk Profile (HARP) (327).

Hospitalised older people are often frail. Accurate identification of which patients are likely to encounter poor health outcomes is important for discharge care planning and risk assessment for intended surgical or medical treatments (241). As yet, no consensus exists as to which frailty instrument most accurately identifies older hospitalised patients at risk of poor outcomes. The purpose of this study was to evaluate several common frailty and functional decline indices on their ability to predict poor GEMU outcomes, both at discharge and at six months.

9.2 Methods

Between October 22, 2010 and December 23, 2011, consecutive patients aged ≥ 70 years were recruited from the GEMU at the Queen Elizabeth Hospital (TQEH), South Australia. The GEMU is a specialised ward designed to optimise a patient's chance of recovery following acute admission (378). GEMU patients are pre-selected for entry predominantly from TQEH's Acute Medical Unit using the clinical judgement of geriatricians.

All patients (or their authorised proxy) gave their informed consent, in accordance with ethical standards from the 2000 Declaration of Helsinki. The study was approved by the Human Research Ethics Committee (TQEH). Data were collected during the first 72 hours of GEMU admission. Patient (or proxy) interview was used to obtain socio-demographic and health data, including nutritional status by the Mini Nutritional Assessment (MNA) (147). Patient clinical records were used to obtain CGA items including medications, admission diagnosis, Geriatric Depression Scale-15 (GDS-15) (381), Mini-Mental State Examination (MMSE) (382) and Braden Skin Assessment (383).

9.2.1 Single Markers

Single markers of frailty used were grip strength and walking speed. Grip strength was assessed as the maximum of three attempts of the dominant hand using a hand held dyanmometer: low grip strength < 18 kg (women), < 30 kg men (456). Walking speed was meaured over 6 m, with or without the use of a walking aid. Slow walking speed was defined as unable to walk 6 m in 30 seconds (440).

9.2.2 Phenotypic Frailty and Functional Decline Instruments

9.2.2.1 Cardiovascular Health Study (CHS) Index

The CHS index defines frailty as three or more of: shrinking, weakness, exhaustion, slowness and low physical activity (210). Shrinking (unintentional

weight loss of ≥ 4.5 kg in the last year) and exhaustion (self report) were defined as per original CHS criteria (210) Weakness (low grip strength) and low physical activity were applied as per the Frailty Intervention Trial (456). Slow walking speed was defined as above (440).

9.2.2.2 Study of Osteoporotic Fractures (SOF) Index

The SOF index defines frailty as two or more of: weight loss (5 % loss either intentional or unintentional over the last year), self report of low energy and low mobility (unable to rise from a chair five times) (221).

9.2.2.3 Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL)

For our study, the FRAIL index (245) classified frailty as ≥ 3 of: fatigue (self report), resistance (unable to rise from a chair five times), ambulation (slow walking speed); illnesses (≥ 5 illnesses on Charlson's Co-morbidity Index (CCI) (457)) and loss of weight of 5 % or more in the past year.

9.2.3 Multidimensional Indices

9.2.3.1 Frailty Index of Accumulated Deficits (FI-CD)

The FI-CD involves the accumulation of 30 or more co-morbidities, disabilities and health deficiencies (242, 340). The number of deficits is then summed and divided by the total number of deficits (242, 340). For example, if 10 deficits are present in a list of 50, the frailty index is 0.2 (10/50) (340). The present study followed guidelines by Searle et al. (340) to select 50 multidimensional health deficits. Deficits were predominantly obtained from patient CGAs, thus the FI-CD in our study was akin to a CGA frailty index (FI-CGA) (339) (see Table 9-1).

The FI-CD is a continuous score and thus a cut-off point to categorise frailty is arbitrary. A score below 0.2 has been used to define frailty (217), although this

cut-off point possibly distinguishes robust from pre-frail categories (340, 458). Only 11 (6 %) of patients in our study scored < 0.2. Thus, to allow for comparison with other frailty instruments, a score > 0.45 was graded as (373). This cut-off can be clinically considered to be 'severely frail' (284).

9.2.3.2 Frailty Index Based on Comprehensive Geriatric Assessment with Ten Domains (FI-CGA-10)

The CGA was used to construct a ten-domain FI-CGA (termed FI-CGA-10 for this study), based on the FI-CGA definition operationalised by Jones et al. (343, 344) as applied by Pilotto et al. (345). The FI-CGA-10 is distinct from the more comprehensive 52 component FI-CGA described by Rockwood et al. (339). FI-CGA-10 components were: cognition (MMSE), mood and motivation (GDS-15), hearing or sight problem, mobility (6 m walk time), balance (standing ability), bowel function, bladder function, function, ADLs, IADLs, nutritional status (MNA) and social resources (343). Problems for each component were classified as: major (2 points), minor (1 point) and none (0 points) (343). Scores were summed and frailty defined as scores > 13/20 (345).

9.2.3.3 Multidimensional Prognostic Index (MPI)

MPI components include: ADL, IADL, MMSE, CCI, MNA, Braden skin assessment, medication number and living status (330). Problems for each component were classified as: major (1 point), minor (0.5 points) and none (0 points) (330). Scores were summed, divided by eight (330) and scores > 0.66 graded as frailty (345).

9.2.3.4 Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA)

Weighted SHERPA components are: falls in the previous year, MMSE (first 21 questions), bad self-perceived health, age and IADL (333). Scores were summed

and frailty defined as scores > 6/11.5, corresponding with SHERPA's 'high risk of functional decline' (333).

9.2.3.5 Hospital Admissions Risk Profile (HARP)

HARP's weighted components are: age (scored 0-2 points), MMSE-21 (scored 0-1 points) and IADL (scored 0-2 points) (327). Scores ≥ 4 were classified as frailty, equivalent to 'high risk of functional decline' on HARP (327).

9.2.4 Functional Decline and Co-morbidity Indices

9.2.4.1 Activities of Daily Living (ADL)

ADL evaluation instruments included Lawton's IADL scale and an adapted Katz index. For Lawton's scale, frailty was defined as dependency on others to perform ≥ 3 IADLs: telephoning, shopping, food preparation, housekeeping, laundry, transport, medication and finances (332). For the adapted Katz score, frailty was defined as dependency for ≥ 1 of: feeding, washing, grooming, dressing, toileting, transferring from a bed or chair, and walking (459).

9.2.5 Charlson's Co-morbidity Index (CCI)

CCI (457) was used to assess co-morbidity, with scores ≥ 5 chosen as the cut-off to compare against frailty indices, based on FRAIL's 'illness' criteria (245).

9.2.6 Outcomes

A composite outcome measure of 'poor outcome' was defined as one or more of (1) death; (2) admission to a residential care facility; and (3) move from low level care to high level care within residential care. Outcomes were considered both at discharge and at six months follow-up. Six month outcome data were obtained both by telephone (patient or proxy) and accessing the South Australian Health Department Open Architecture Clinical Information System system.

9.2.7 Statistical Analyses

Normally distributed variables were expressed as mean (standard deviation) and non-normally distributed variables as median (range). Bivariate logistic regression analyses controlling for age and gender were used to identify which instruments were most predictive of poor outcomes. Due to the low prevalence of patients classified as "robust" and for comparision purposes, scores for each instrument were dichotomised as "frail" and "not frail" ("pre-frail" or "robust"). Predicted probabilities from regression analyses were used to generate receiver operator characteristic (ROC) curves, with area under curve ($_{au}$ROC) computed to evaluate discriminative ability. Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values and Youden Index (sensitivity + specificity – 1) were also calculated. Statistical tests were based on comparisons of $_{au}$ROC, and the instrument with the largest $_{au}$ROC was considered to be the most accurate; an $_{au}$ROC of 0.7 was set as the threshold for adequate predictive accuracy (454). Bootstrap techniques were used to generate a sample of 1000 $_{au}$ROC for each frailty index. These were used to estimate 95 % confidence intervals and to perform pairwise comparisons between the frailty indexes. Significance was set at an alpha level of 0.001 to control for the increased risk of a Type 1 error associated with performing multiple statistical tests. Analyses were performed using SAS Version 9.3 (SAS Institute Inc., Cary, NC) and SPSS for Windows 19.0 (SPSS Inc., Chicago, IL) with statistical significance set at $P < 0.05$.

Table 9-1: Variables Included in the Frailty Index of Cumulative Deficits (FI-CD)[†]

Deficit Count	Variable
1	Help Bathing
2	Help Dressing
3	Help Transferring From a Bed to Chair and Back
4	Help Walking Around Home
5	Help Eating
6	Help Grooming
7	Help Toileting
8	Help Using Telephone
9	Help Shopping
10	Help Food Preparation
11	Help Housekeeping
12	Help Laundry
13	Help with Transportation
14	Help taking Medications
15	Help with Finances
16	Psychological Stress/Acute Disease in Last 3 Months
17	Previous Myocardial Infarction
18	Chronic Heart Failure
19	Peripheral Vascular Disease
20	Previous Stroke
21	Chronic Obstructive Pulmonary Disease
22	Renal Failure
23	Tumour
24	Diabetes
25	Orthostatic Hypotension
26	Pressure Sore or Skin Ulcer
27	Depression
28	Anxiety
29	Hearing Difficulty
30	Unable to Drive
31	Difficulty Chewing or Swallowing
32	Poor Dentition
33	Self-Reported Poor Health
34	Weight Loss > 4.5 kg in past year
35	Appetite
36	Self Report: "Everything is an effort"
37	Self Report: "Could not get going"
38	Low Physical Activity
39	Lives Alone
40	Low Community Mobility
41	Slow Walking Speed
42	Falls in Previous Year
43	Low Quality of Life
44	Mini Mental State Examination
45	Low Mid-Arm Circumference
46	Low Calf Circumference
47	Low Body Mass Index
48	Grip Strength
49	Low Protein Consumption
50	Self Reported Malnutrition

[†] The present study followed guidelines by Searle et al. (340) to construct the FI-CD, including relevant cut-point cut-offs.

9.3 Results

427 new patients aged ≥ 70 years were admitted to the GEMU during the study period. Study exclusion reasons were: dementia/unresolved delirium within 72 hours of GEMU admission without proxy (n = 77), language barrier without proxy (n = 67), clinician advised against inclusion (elder-abuse, physically aggressive, medically unwell: n = 33), infectious (n = 11), missed by researcher (n = 4) and declined participation (n = 63). Table 9-2 shows admission characteristics of the 172 patients recruited. Frailty prevalence ranged from 24 to 94 % depending on the instrument used.

Results from logistic regression analyses used to assess which frailty instrument was most predictive of poor outcome are shown in Table 9-3. For all instruments, strength of prediction was stronger at discharge than at six month follow-up. Grip strength, adapted Katz index, FI-CD and SOF were most predictive of poor discharge outcome. The FI-CD, SOF, adapted Katz index and grip strength were most predictive of poor outcome at six months. IADL, CHS and SHERPA were also predictive of outcomes both at discharge and at six months. Gait speed was predictive of poor outcome at six months but not at discharge. The simpler multidimensional indices (FRAIL, FI-CGA-10, MPI, HARP) and co-morbidity (CCI) were not predictive of any outcomes.

To assess predictive accuracy, $_{au}$ROC curves were computed (see Table 9-4 and Figure 9-1). Overall, $_{au}$ROC was higher at discharge than at six months. FI-CD showed the highest $_{au}$ROC at both time-points (both $_{au}$ROCs > 0.7). The adapted Katz index showed adequate discriminatory power for poor outcome prediction at discharge, but not at six months. Age lacked discriminatory power for outcome prediction: $_{au}$ROC (discharge) = 0.571, P = 0.195; $_{au}$ROC (six months) = 0.540, P = 0.363. There were statistically significant differences between the $_{au}$ROC values of the majority of frailty instruments, although one notable exception was between the FI-CD and the adapted Katz score in predicting poor discharge outcome (see Table 9-5.

For all instruments, NPV was high for discharge and moderate-high for six month outcomes; PPV was low for discharge and low-moderate for six month outcomes. The FI-CD showed the highest Youden Index value.

Table 9-2: Admission Characteristics of Patients (n = 172)

Variable	Overall *n* (%)
Age	
70 -79 years	31 (18)
80-89 years	100 (58)
90-101 years	41 (24)
Gender (women)	129 (72)
Private Health Insurance	62 (36)
Residing in Residential Care	8 (5)
Education	
Primary School or Less	73 (42)
Junior High School	83 (48)
Senior High School	10 (6)
Tertiary Education	5(3)
Birthplace	
Australia	118 (69)
UK/Europe	53 (31)
Other	1 (1)
English as Primary Language	139 (81)
Medical History	
Polypharmacy (≥ 6 medications)	131 (76)
Hearing Impairment	98 (57)
Lives Alone	97 (56)
Use of Dentures	84 (49)
Cognitive Impairment (MMSE <24)	74 (43)
Depressive Risk (GDS-15 >5)	61 (40)
Malnutrition (MNA < 17)	53 (31)
Falls in the previous year (self-reported)	111 (65)
Hospitalised (any reason) in the last 3 months	50 (29)
Hospital for falls in the previous year	36 (22)
Activities of Daily Living (ADL)	
Dependence Feeding	55 (32)
Dependence Washing	123 (72)
Dependence Grooming	75 (44)
Dependence Dressing	100 (58)
Dependence Toileting	84 (49)
Dependence Transferring	90 (52)
Dependence Walking	67 (39)
Dependence in any ADL (≅ Katz Score for frailty) †	129 (75)
Dependence in > 3 ADL	90 (52)
Dependence in all ADL	29 (17)
Medical Condition	
Chronic Heart Failure	74 (43)
Diabetes	52 (30)
Renal Impairment	37 (22)
Tumour	33 (19)
Previous Myocardial Infarction	31 (18)
Previous Stroke	28 (16)
Pressure Sore or Skin Ulcer	27 (16)
Peripheral Vascular Disease	21 (12)

Continued...

Variable	Overall *n* (%)
CCI (≥ 5 illnesses)	38 (28)
Frailty and Pre-Frailty Prevalence	
FI-CD - Frail (Index > 0.45)	65 (38)
Pre-Frail (Index 0.2 to 0.45)	96 (56)
Robust (Index < 0.2)	11 (6)
CHS - Frail (≥ 3 components)	96 (56)
- Pre-frail (1-2 Components)	64 (7)
- Robust	12 (64)
SOF - Frail (≥ 2 components)	120 (70)
- Pre-frail (1 components)	44 (26)
- Robust	6 (4)
FRAIL - Frail (≥ 3 components)	107 (62)
- Pre-frail (1-2 Components)	62 (36)
- Robust	3 (2)
FI-CGA-10 - Frail (Scores > 13)	45 (26)
- Pre-frail (1-2 Components)	109 (63)
- Robust	18 (11)
SHERPA - High Risk (Score > 6)†	87 (51)
- Moderate Risk (Scores 5 - 6)	41 (24)
- Low or Mild Risk (Scores 0 - 4.5)	43 (25)
MPI -Severe Mortality Risk (Index > 0.66) †	42 (24)
- Moderate Risk (Index 0.34 – 0.66)	125 (73)
- Low Risk (Index ≤ 0.33)	5 (3)
HARP - High ADL Decline Risk (Score ≥ 4)†	43 (25)
- Moderate ADL Decline Risk (Scores 2 or 3)	91 (53)
- Low ADL Decline Risk (Scores 0 or 1)	38 (22)
Lawton IADL - Frail (≥ 3 dependencies in IADL)	98 (57)
Low Grip Strength (< 18 kg F; < 30 kg M)	128 (74)
Slow Walking Speed (> 30 s/ 6 m)	46 (27)
Outcomes	
Length of GEMU stay (days); Median (range)	12 (1-91)
Poor Discharge Outcome	35 (20)
In-Hospital Mortality	7 (5)
New discharge to a Residential Care Facility	26 (15)
New discharge to High to Low Level Care	2 (1)
Poor Six Month Outcome	78 (45)
Mortality (including in-hospital)	28 (16)
Residential Care Admission (including in-hospital)	50 (29)

† Equivalent to frailty for the purposes of this study. **Abbreviations:** FI-CD = Frailty Index of Cumulative Deficits; CHS = Cardiovascular Health Study index (Fried); SOF = Study of Osteoporotic Fractures index; FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight index; FI-CGA-10 = Frailty Index based on Ten Domain Comprehensive Geriatric Assessment; Katz = Adapted Katz index of 7 Activities of Daily Living; SHERPA = Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie index; MPI = Multidimensional Index; HARP = Hospital Admissions Risk Profile; CCI = Charlson's Co-morbidity Index; GEMU = Geriatric Evaluation and Management Unit; MNA = Mini Nutritional Assessment; MMSE = Mini Mental State Examination Score; GDS-15 = Geriatric Depression Scale (15 Item)

Table 9-3: Results of Binary Logistic Regression Analyses Indicating the Contribution of Frailty Instruments to Study Outcomes[†], Controlling for Age and Gender (n =172[‡])

Index	Frailty Prevalence *n* (%)	Poor Discharge Outcome (*n* = 35)			Poor 6 Month Outcome (*n* = 98)		
		OR	95 % CI	P	OR	95 % CI	P
Grip	128 (75)	6.47	1.46 - 28.60	**0.014**	2.65	1.23 - 5.69	**0.013**
Katz	129 (75)	5.55	1.56 - 11.73	**0.008**	3.17	1.45 - 6.91	**0.004**
FI-CD	65 (38)	5.09	2.23 - 11.62	**< 0.001**	4.25	2.18 - 8.31	**< 0.001**
SOF	120 (70)	3.44	1.21 - 9.78	**0.020**	3.26	1.55 - 6.87	**0.002**
Lawton	98 (57)	3.06	1.28 - 7.29	**0.012**	2.21	1.18 - 4.16	**0.014**
CHS	96 (56)	2.98	1.28 - 6.97	**0.012**	2.17	1.15 - 4.09	**0.017**
SHERPA	87 (51)	2.54	1.06 - 6.07	**0.037**	2.54	1.06 - 6.07	**0.037**
Gait Speed	46 (27)	2.18	0.94 - 5.06	0.068	2.06	1.01 - 4.20	**0.046**
HARP	43 (25)	2.04	0.89 - 4.68	0.091	1.91	0.93 - 3.92	0.079
FRAIL	107 (62)	1.81	0.78 - 4.19	0.166	1.68	0.87 - 3.22	0.120
CCI	38 (28)	1.10	0.44 - 2.73	0.847	1.48	0.71 - 3.10	0.295
FI-CGA-10	45 (26)	1.01	0.42 - 2.43	0.976	1.59	0.79 - 3.19	0.195
MPI	42 (24)	0.94	0.38 - 2.33	0.901	1.68	0.83 - 3.42	0.152

[†]Poor Outcome = Mortality, admission to a residential care facility, or move from low level care to high level care within a residential care facility.

[‡] Frail and Not Frail categories were compared, with Not Frail = Pre-Frail or Robust

n=172 for all outcomes, except hospital discharge, where two patients were excluded as they were already residing in high level care at baseline.

OR = Odds Ratio; CI = Confidence Interval; FI-CD = Frailty Index of Cumulative Deficits; CHS = Cardiovascular Health Study index (Fried); SOF = Study of Osteoporotic Fractures index; FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight index; FI-CGA-10 = Frailty Index based on Ten Domain Comprehensive Geriatric Assessment; Katz = Adapted Katz index of 7 Activities of Daily Living; SHERPA = Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie index; MPI = Multidimensional Index; HARP = Hospital Admissions Risk Profile; CCI = Charlson's Co-morbidity Index

Bold indicates significance

Table 9-4: Diagnostic Values for Frailty, Functional Decline and Co-morbidity Indices for the Prediction of Poor Outcomes at Both Discharge and at Six Month Follow-Up[†]

	Poor Discharge Outcome (n=35)								Poor 6 Month Outcome (n=98)							
Index	**$_{au}$ROC**	**P**	**95% CI**	**Se**	**Sp**	**PPV**	**NPV**	**YI**	**$_{au}$ROC**	**P**	**95% CI**	**Se**	**Sp**	**PPV**	**NPV**	**YI**
FI-CD	0.735	< 0.001	0.64 - 0.83	65.7	70.4	36.5	88.8	36.1	**0.702**	< 0.001	0.62 - 0.78	55.1	76.6	66.2	67.3	31.7
Katz	0.704	< 0.001	0.60 - 0.81	91.4	29.6	25.2	93.0	21.1	0.646	0.001	0.56 - 0.73	84.6	33.0	51.2	72.1	17.6
SHERPA	0.697	< 0.001	0.59 - 0.80	74.3	56.3	30.6	89.4	30.6	0.657	< 0.001	0.58 - 0.74	65.4	61.7	58.6	68.2	27.1
Lawton	0.694	0.000	0.59 - 0.80	77.1	48.9	28.1	89.2	26.0	0.635	0.002	0.55 - 0.72	67.9	52.1	54.1	66.2	20.1
Grip	0.690	0.001	0.59 - 0.79	94.3	31.1	26.2	95.5	25.4	0.627	0.004	0.54 - 0.71	84.6	34.0	51.6	72.7	18.7
SOF	0.679	0.001	0.58 - 0.78	85.7	33.6	25.2	90.0	19.3	0.657	< 0.001	0.58 - 0.74	85.7	33.6	25.2	90.0	19.3
CHS	0.675	0.001	0.57 - 0.78	74.3	49.6	27.7	88.2	23.9	0.627	0.004	0.54 - 0.71	65.4	52.1	53.1	64.5	17.5
Gait	0.643	0.009	0.53 - 0.75	37.1	76.3	28.9	82.4	13.4	0.613	0.011	0.53 - 0.70	33.3	78.7	56.5	58.7	12.1
HARP	0.639	0.011	0.53 - 0.75	37.1	79.3	31.7	82.9	16.4	0.600	0.024	0.52 - 0.69	32.1	80.9	58.1	58.9	12.9
FRAIL	0.638	0.012	0.53 - 0.74	71.4	40.7	23.8	84.6	12.2	0.608	0.015	0.52 - 0.69	67.9	42.6	49.5	61.5	10.5
MPI	0.617	0.033	0.50 - 0.73	22.9	76.3	20.0	79.2	-0.8	0.599	0.025	0.51 - 0.68	29.5	79.8	54.8	57.7	9.3
FI-CGA-10	0.617	0.033	0.50 - 0.73	25.7	74.8	20.9	79.5	0.50	0.588	0.047	0.50 - 0.67	30.8	77.7	53.3	57.5	8.4
CCI	0.579	0.074	0.49 - 0.67	25.6	80.9	52.6	56.7	6.50	0.592	0.039	0.51 - 0.68	80.9	52.6	56.7	45.3	<0.1

[†]Poor Outcome = Mortality, admission to a residential care facility, or move from low level care to high level care within the residential facility.

n=172 for all outcomes, except hospital discharge, where two patients were excluded as they were already residing in high level care at baseline.

$_{au}$ROC = Area Under Receiver Operating Characteristic Curve (adjusted for age and gender); CI = Confidence Interval; Se = sensitivity; Sp = Specificity; PPV = Positive Predictive Value; NPV = Negative Predicitive Value; YI = Youden Index; FI-CD = Frailty Index of Cumulative Deficits; CHS = Cardiovascular Health Study index (Fried); SOF = Study of Osteoporotic Fractures index; FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight index; FI-CGA-10 = Frailty Index based on Ten Domain Comprehensive Geriatric Assessment; Katz = Adapted Katz index of 7 Activities of Daily Living; SHERPA = Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie index; MPI = Multidimensional Index; HARP = Hospital Admissions Risk Profile; CCI = Charlson's Co-morbidity Index

Bold indicates adequate discriminatory power ($_{au}$ROC > 0.7)

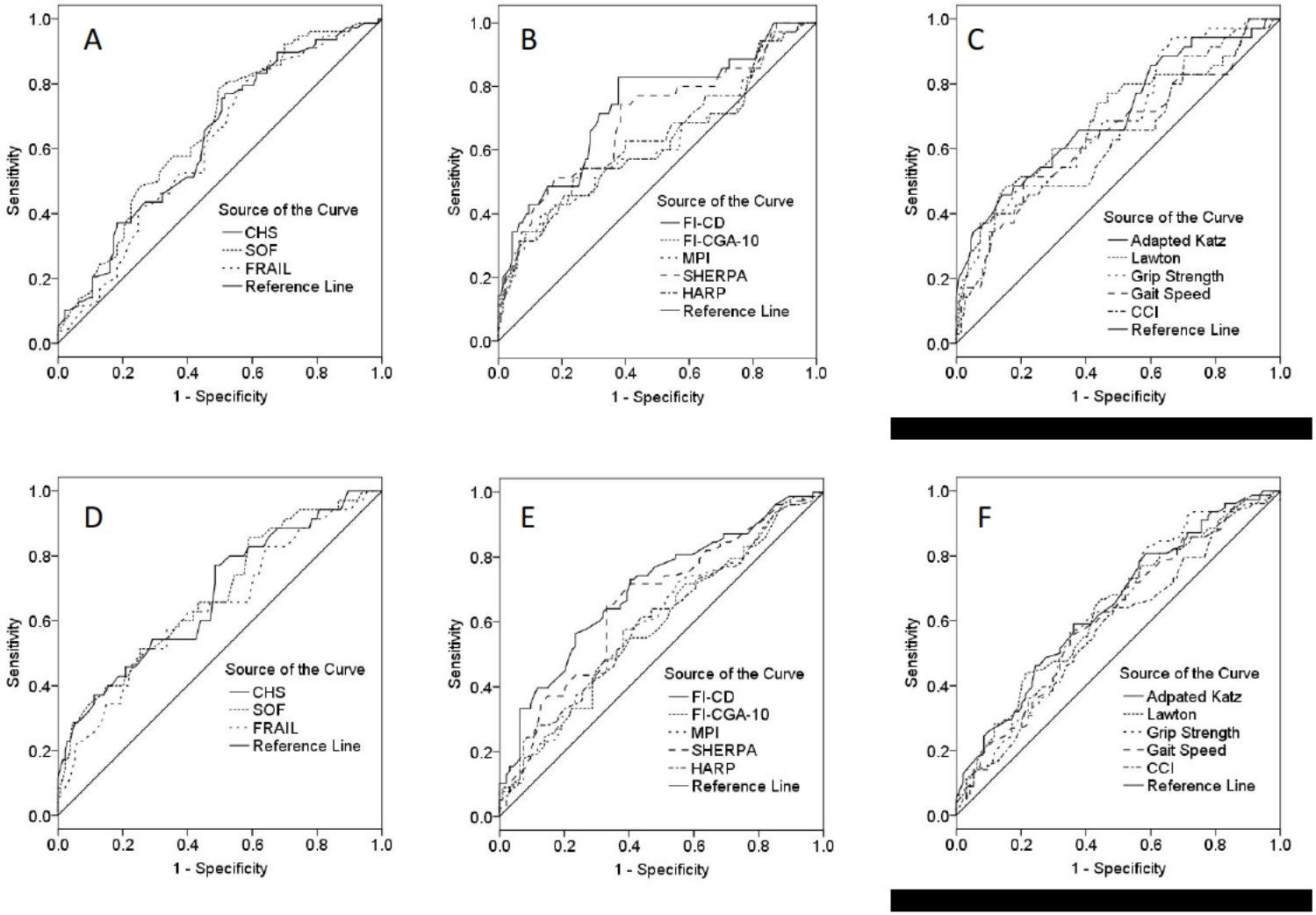

Figure 9-1: Age and Gender Adjusted Receiver Operating Characteristic Curves for Poor Outcome at Discharge (Panels A-C) and at Six Months Post-Discharge (Panels D-F). Poor outcome was considered to be either mortality, admission to a residential care facility or move from low level care to high level care within a residential care facility. Abbreviations: FI-CD = Frailty Index of Cumulative Deficits; CHS = Cardiovascular Health Study index (Fried); SOF = Study of Osteoporotic Fractures index; FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight index; CGA-10 = Frailty Index based on Ten Domain Comprehensive Geriatric Assessment; Lawton = Lawton's scale of Instrumental Activities of Daily Living; Adapted Katz = Adapted Katz score of seven Activities of Daily Living; SHERPA = Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie index; MPI = Multidimensional Index; HARP = Hospital Admissions Risk Profile; CCI = Charlson's Co-morbidity Index

Table 9-5: Contrast Values of Area Under Receiver Operating Characteristic Curves for Poor Outcome at (A) Hospital Discharge and (B) Six Months Post-Discharge in Hospitalised Older People (n = 172).

(A) Hospital Discharge

	Katz ADL	CGA	CCI	FI-CD	FRAIL	CHS	Gait Speed	Grip Strength	IADL	MPI	SOF
Katz ADL	n/a	<0.001	<0.001	0.8618	<0.001	<0.001	<0.002	<0.001	<0.001	<0.001	<0.001
FI-CGA-10	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CCI	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FI-CD	0.8618	<0.001	<0.001	n/a	<0.001	<0.001	0.005	<0.001	<0.001	<0.001	<0.001
FRAIL	<0.001	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CHS	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.8569
Gait Speed	<0.002	<0.001	<0.001	0.005	<0.001	<0.001	n/a	<0.001	0.0133	<0.001	<0.001
Grip Strength	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001
Lawton	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.0133	<0.001	n/a	<0.001	<0.001
MPI	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	<0.001
SOF	<0.001	<0.001	<0.001	<0.001	<0.001	<0.8569	<0.001	<0.001	<0.001	<0.001	n/a

(B) Six Months Post-Hospitalisation

	Katz ADL	CGA	CCI	FI-CD	FRAIL	CHS	Gait Speed	Grip Strength	IADL	MPI	SOF
Katz ADL	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FI-CGA-10	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CCI	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FI-CD	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FRAIL	<0.001	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CHS	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	0.0772	<0.001	0 1727	<0.001	<0.001
Gait Speed	<0.001	<0.001	<0.001	<0.001	<0.001	0.0772	n/a	<0.001	0.0069	<0.001	<0.001
Grip Strength	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	<0.001	<0.001	<0.001
Lawton	<0.001	<0.001	<0.001	<0.001	<0.001	0.1727	0.0069	<0.001	n/a	<0.001	<0.001
MPI	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n/a	<0.001
SOF	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n/a

Abbreviations: FI-CD = Frailty Index of Cumulative Deficits; CHS = Cardiovascular Health Study index (Fried); SOF = Study of Osteoporotic Fractures index; FRAIL = Fatigue, Resistance, Ambulation, Illness, Loss of Weight index; FI-CGA-10 = Frailty Index based on Ten Domain Comprehensive Geriatric Assessment; Lawton= Lawton's scale of Instrumental Activities of Daily Living; Adapted Katz = Adapted Katz score of seven Activities of Daily Living; SHERPA = Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie index; MPI = Multidimensional Index; HARP = Hospital Admissions Risk Profile; CCI = Charlson's Co-morbidity Index

9.4 Discussion

This study found frailty and functional decline instruments identified GEMU patients at increased risk of poor outcomes, both at discharge and six months. Predictive of poor outcome at both time-points were: grip strength, FI-CD, the adapted Katz score, SOF, CHS, SHERPA and Lawton's IADL index. Gait speed was predictive of poor outcome at 6 months but not at discharge. Some indices (FRAIL, FI-CGA-10, MPI and HARP) were not predictive of any study outcomes, perhaps because our study included many severely frail patients. Age and co-morbidity did not predict poor outcomes, which confirms findings from a recent study of older rehabilitation patients (375). As such, age and illnesses per se should not be barriers for rehabilitation access.

The FI-CD showed the strongest discriminatory power for outcome prediction at both discharge ($_{au}$ROC = 0.735) and six months ($_{au}$ROC = 0.702). This good discriminatory ability agrees with a previous epidemiological study looking at mortality prediction (217) and is likely to be the result of the multidimensional nature of the FI-CD (340)FI-CD is also advantageous because it can identify early frailty risk (340, 373).

The adapted Katz index also showed adequate discriminatory power for prediction of poor discharge outcome ($_{au}$ROC = 0.704). Katz is advantageous in a clinical setting due to its fast and simple application (5 minutes per patient) and it can be applied in more general hospital wards where CGAs are not routine. However, the Katz index does not identify early frailty risk or encompass frailty's multidimensional nature.

The phenotypic frailty indices (CHS and SOF), even though predictive of poor outcomes at both time-points, lacked sufficient discriminatory power in their predictions, which agrees with some studies of hospitalised people (229, 269, 345) but not others (229). Also in our study, the MPI showed a low predictive ability,

perhaps unexpectedly, as a recent study of hospitalised older persons found MPI out-performed other frailty instruments (345).

Overall predictive ability in our study was higher at discharge than at six months, which was also found in a recent study of hospitalised older persons (345). NPV was generally high for all instruments in predicting outcomes, which indicates that almost all frail patients were identified. PPV on the other hand was generally only low-moderate, indicating a high number of false positives tests occurred.

Study results should be interpreted with caution as the cut-point for frailty classification by the FI-CD (> 0.45) may have identified more severely frail patients than other instruments. There was also the potential for over-estimation of performance-based frailty components. For example, patients unable to walk due to injury/illness were deemed "low mobility". An additional limitation was the low number of patients classified as "robust", which precluded a comparison of all three frailty categories (frail, pre-frail and robust). Study results may also lack generalisation to other wards as GEMU patients are highly selected prior to their admission. Study strengths included the wide range of indices evaluated, the prospective design and the comprehensive admission dataset.

Future research should focus on the clinical application of frailty instruments in a larger group of patients across multiple ward areas - particularly with regards to practicality (342), detection of frailty change (340) and ability to distinguish pre-frailty from frailty (342).

9.4.1 Conclusion

Frailty and functional decline instruments can be used to identify older hospitalised patients at risk of poor discharge and six month outcomes. The FI-CD and the adapted Katz indices showed the highest discriminatory power overall,

although further research in a larger group of hospitalised older patients is warranted.

Statement of Authorship

Title of Paper	Inflammatory Cytokines and Appetite in Healthy People
Publication Status	⦿ Published, ○ Accepted for Publication, ○ Submitted for Publication, ○ Publication style
Publication Details	Dent E, Yu S, Visvanathan R, Piantadosi C, Adams R, Lange K, Chapman I. Inflammatory Cytokines and Appetite in Healthy People. The Journal of Aging Research & Clinical Practice. 2012;1(1):40-3.

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By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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Contribution to the Paper	Assisted with research supervising.		
Signature		Date	26/3/13

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By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

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10 Inflammatory Cytokines and Appetite in Healthy People

Dent E, Yu S, Visvanathan R, Piantadosi C, Adams R, Lange K, Chapman I. Inflammatory Cytokines and Appetite in Healthy People. *The Journal of Aging Research & Clinical Practice.* 2012;1(1):40-3.

Background and Objectives*:* Inflammation has been associated with reduced appetite and body composition changes in populations with established diseases. However, it is not known if an association exists between appetite, body composition and inflammation in healthy people. *Design:* To explore associations of appetite with markers of inflammation and body composition, data from the Cytokines, Adiposity, Sarcopenia and Ageing (CASA) study was analysed. *Setting:* Western suburbs, Adelaide, Australia.

Participants: 180, population representative, healthy participants, aged 18 – 82 years, were studied.

Measurements*:* Body composition was measured by both Dual X-ray absorbiometry (DXA) and bioelectrical impedance analysis (BIA). Appetite was assessed by the Simplified Nutritional Appetite Questionnaire (SNAQ). Circulating cytokine concentrations were measured. *Results:* Multiple regression analysis showed appetite scores were increased in non-smokers (P = 0.031) and men (P = 0.024), negatively associated with serum levels of the pro-inflammatory IL-1β (β coefficient = - 0.379, P = 0.007), and positively associated with serum levels of the anti-inflammatory cytokine IL-10 (β coefficient = 0.25, P = 0.010). There was no association between appetite and body composition.

Conclusions: Appetite loss may reflect background inflammation even in apparently healthy people, and probably occurs before consequent changes in body composition. Further explorations of longer term appetite changes with respect to inflammation and body composition changes are needed.

Keywords: Appetite, Body Composition, Cytokine, Inflammation

10.1 Introduction

Undernutrition is common among older people, even in developed countries (147, 421, 433, 460), and is associated with serious consequences, including more frequent and prolonged hospital admissions (139) increased infection risk (95), functional decline (196) and reduced life expectancy (147). It is important to identify factors that might predict those older people more likely to lose weight and become under-nourished, so prevention and early treatment measures can be implemented.

Multiple methods have been used to define and diagnose undernutrition in older people, but features commonly seen in this condition are weight loss (particularly muscle loss), reduced body weight, reduced appetite and sometimes cachexia (17). Ageing is associated with decline in appetite and food intake which is probably physiological, but may contribute to the development of pathological anorexia and undernutrition. Indeed, reduced appetite is a reliable predictor of future weight loss in older people; appetite scores obtained from the Simplified Nutritional Appetite Questionnaire (SNAQ) have been found to predict future weight loss in older people (167).

Appetite loss may be caused by inflammation. Inflammation is the immune system's response to an acute infection or illness and is the result of the production of several pro-inflammatory cytokines including interleukin-1 (IL-1), IL-2, IL-6, IL-8, tumour necrosis factor-α (TNF-α) and interferon-γ (IFNγ) (461). These pro-inflammatory cytokines, when persistently elevated, can reduce appetite by actions on the hypothalamus and other neural centres, by altering gastric function and by modifying the regulation of appetite controlling hormones (461). Anti-inflammatory cytokines, such and IL-4 and IL-10 act to down-regulate pro-inflammatory cytokine production (67). An imbalance between pro-inflammatory and anti-inflammatory cytokines is thus thought to lead to the cachexia of many chronic diseases (462).

Ageing itself may be a low-level pro-inflammatory state (463). It might therefore be that the anorexia of ageing is due, at least in part, to increased inflammation. If so, it might be expected that there would be a positive connection between pro-inflammatory markers and reduced appetite even in apparently healthy individuals across the adult age range. Little is known about these possible connections.

This study explored the associations of appetite with markers of inflammation and body composition in healthy adults. It was hypothesised that there would be associations between increased inflammation and reduced appetite even in this group of healthy individuals, but probably not between markers of inflammation and adverse body composition changes, as these are likely to be later effects of undernutrition.

10.2 Methods

10.2.1 Participants

Healthy subjects (ages 18 to 82 years) were recruited from the western suburbs of Adelaide into the Cytokine, Adiposity, Sarcopenia and Ageing Study (CASA). The recruitment methodology is similar to that described for other larger population studies conducted in the same catchment area, the North West Adelaide Health Study (464). Telephone numbers from the Electronic White Pages were randomly selected, and willing subjects, aged 18 or over, with no exclusion criteria, were invited to participate. Subjects able to comply with the study protocol and who reported weight stability over the preceding 3 months were included in the study. Those with confirmed inflammatory diseases, pregnant and those who had been ill in the preceding 3 months or in the 2 weeks following blood sampling, were excluded. This study had ethics approval from the Central Northern Adelaide Health Service Ethics of Human Research Committee and all participants provided written informed consent.

10.2.2 Body Composition Measures

Body composition was assessed by measurement of height; weight; waist circumference; Fat Mass (FM) and Fat Free Mass (FFM) by Dual X-Ray Absorbiometry (DXA) (Lunar PRODIGY whole body scanner; GE Medical Systems, Madison, WI) scan; and Biolectrical Impedence Analysis (BIA) (Quantum II BIA Analyser, RJL system).

10.2.3 Appetite

Participants completed the SNAQ questionnaire, giving one of five responses to four questions regarding appetite, satiety, taste and meal frequency (167). SNAQ gives a score out of 20, with higher scores indicating greater appetite. SNAQ has been found to predict weight loss over a six month period with 81.6 % sensitivity and 84.6 % specificity for people over 60 years of age (167).

10.2.4 Exercise Score

Exercise was assessed using Australian National Health Survey questions (465). Scores for exercise intensity were 3.5 for walking, 5.0 for moderate activity and 7.5 for high intensity activity. Each exercise intensity score was multiplied by minutes per fortnight to give total exercise level. This total level was classified as 'sedentary' (< 100), 'low level' (100 < 1600), 'moderate level' (1600 – 3200 or > 3200 and less than 2 h of vigorous exercise) or 'high level' (> 3200)'.

10.2.5 Data Collection

Fasting blood samples were collected and body composition measured by BIA in the morning, and body composition by DXA was measured either the afternoon of the same day or on another day but within 2 weeks. Plasma samples were stored at –80°C until analysis. Cytokine concentrations were measured using LINCOplex kits. Trace values < 0.08 pg/L for cytokines were recorded as zero values.

10.2.6 Statistical Analysis

SNAQ scores were normally distributed. Other continuous study variables were non-normally distributed and are presented as medians (inter-quartile range). Categorical variables are presented as frequencies. Relationships between the total SNAQ score and the study variables were assessed using Spearman rank correlation tests for non-parametric variables. Cytokines and anthropometric variables were included in a multiple regression analysis along with for age, gender and smoking status. Continuous data were log transformed prior to inclusion in this analysis. Statistical analysis was carried out using SPSS statistical program (17.0, SPSS, Chicago, USA) with statistical significance set at $P < 0.05$.

10.3 Results

180 subjects with complete results were included in the study. Median age was 52 years with a range of 18-82 years. SNAQ total scores ranged from 12-20 (out of 20), with a median score of 17. 15 participants (7.8 %) had low SNAQ scores (defined as ≤ 14). Table 10-1shows baseline subject characteristics.

The results of the univariate regression analysis of the relationship between SNAQ appetite scores and continuous study variables are shown in Table 10-2. Both IL-6 and IL-10 concentrations were positively related to appetite. There were also strong significant associations between concentrations of a number of cytokines, including IL-6 with both IL-1β ($r = .353$, $P < 0.001$) and IL-10 ($r = .410$, $P<0.001$). By multivariate analysis (Table 10-3) non-smokers had higher appetite scores than smokers and men higher scores than women. IL-1β concentrations were negatively and IL-10 concentrations positively associated with appetite. None of the body composition variables showed any association with SNAQ score from either the univariate or multivariate analyses.

Table 10-1: Baseline Participant Characteristics (n=180)

Continuous Variables	Median (Inter-Quartile Range)
Background Variables	
Age (years)	52 (40-62)
SNAQ appetite scores	17.0 (16.0-18.0)
Circulating Cytokine Concentrations	
IL-1β (pg/ml)	0.50 (0.0-1.8)
IL-2 (pg/ml)	1.46 (0.0 - 8.0)
IL-4 (pg/ml)	0.0 (0.0 - 15.8)
IL-6 (pg/ml)	1.95 (0.25-5.9)
IL-10 (pg/ml)	3.9 (0.0-13.8)
TNF-α (pg/ml)	3.5 (1.9 - 5.4)
hs-CRP (mg/L)	1.2 (0.6 - 2.3)
Anthropometric Measures	
BMI (kg/m^2)	25.6 (23.0 - 28.7)
Waist Circumference (cm)	87.2 (76.3 - 96.7)
Total Lean Mass DXA (kg)	44.5 (38.1 - 56.8)
Total Fat DXA (Kg)	24.1 (17.1 - 30.2)
Nutritional Biomarkers	
Haemoglobin (g/L)	140.0 (129.0 - 150.0)
Lymphocyte (g/L)	1.8 (1.6-2.2)
Albumin (g/L)	39.0 (37.0 - 41.0)
Categorical Variables	***n* (%)**
Background Variables	
Gender (Female)	106 (58.9 %)
Smoking Status	19 (10.6%) smokers
Exercise Level	
Sedentary	31 (17.2 %)
Low Level	75 (41.7 %)
Moderate Level	39(21.7 %)
High Level	35(19.4 %)

Abbreviations: SNAQ = Simplified Nutritional Appetite Questionnaire; IL = Interleukin; TNF = Tumor Necrosis Factor alpha; hs-CRP = High Sensitivity C-Reactive Protein; BMI = Body Mass Index ($height/weight^2$); DXA = Dual X-Ray Absorbiometry.

Table 10-2: Univariate Regression Analysis of relationships between total SNAQ appetite score and Continuous Study Variables (n=180)

Variable	R	P
Background Variables		
Age (years)	0.016	0.836
Exercise Score	0.062	0.407
Nutritional Biomarkers		
Haemaglobin (g/L)	0.053	0.463
Lymphocyte (g/L)	0.040	0.585
Albumin (g/L)	0.038	0.601
Cytokines		
IL-1β (pg/ml)	0.033	0.637
IL-2 (pg/mL)	0.034	0.652
IL-4 (pg/mL)	0.041	0.584
IL-6 (pg/mL)	0.153	0.041
IL-10 (pg/mL)	0.210	0.005
TNF-α (pg/mL)	0.089	0.222
hs-CRP (mg/mL)	0.086	0.239
Anthropometric Measures		
BMI (kg/m^2)	0.039	0.599
Waist Circumference (cm)	0.058	0.425
Total Lean Mass DXA (kg)	0.064	0.374
Total Fat DXA (kg)	0.050	0.494

Abbreviations: IL = Interleukin; TNF = Tumor Necrosis Factor alpha; hs-CRP = High Sensitivity C-Reactive Protein; BMI = Body Mass Index ($height/weight^2$); DXA = Dual X-Ray Absorbiometry.

Table 10-3: Multivariate Analysis of relationship between Study Variables and total SNAQ score (n=180)

Variable	β Coefficient	t	P
Background Variables			
Age (years)	0.042	0.472	0.638
Gender	-0.367	-2.287	0.024⋆
Smoking Status	-0.172	-2.176	0.031†
Cytokines			
IL-1β (pg/ml)	-0.379	-2.739	0.007
IL-2 (pg/mL)	0.157	1.018	0.310
IL-4 (pg/mL)	0.057	0.535	0.593
IL-6 (pg/mL)	0.085	0.806	0.422
IL-10 (pg/mL)	0.248	2.598	0.010
TNF-α (pg/mL)	0.035	0.392	0.696
hs-CRP (mg/mL)	-0.165	-1.868	0.064
Anthropometric Measures			
BMI (kg/m^2)	-0.227	-0.971	0.333
Waist Circumference (cm)	0.372	1.739	0.084
Total Lean Mass DXA (kg)	0.281	1.631	0.105
Total Fat DXA (kg)	-0.058	-0.255	0.799
Exercise Score	0.117	1.471	0.143

Abbreviations: SNAQ = Simplified Nutritional Appetite Questionnaire; IL = Interleukin; TNF = Tumor Necrosis Factor alpha; hs-CRP = High Sensitivity C-Reactive Protein; BMI = Body Mass Index (height/weight^2); DXA = Dual X-Ray Absorbiometry.

⋆SNAQ scores higher in men than women.

†SNAQ scores higher in non-smokers than smokers.

10.4 Discussion

In this novel study of appetite in healthy people, appetite as measured by the SNAQ questionnaire was associated negatively with circulating serum levels of IL-1β and positively with IL-10 levels, but was not associated with any measure of body composition or nutritional biomarker – albumin, lymphocyte count and haemoglobin.

The negative association between IL-1β and appetite found in this study is consistent with previous reports in humans with inflammatory conditions such as cancer (466), renal failure (467) eating disorders (468) and depression (469). Our finding is also consistent with the known pro-inflammatory effects of IL-1β and the results of animal studies. In rodents, food intake is suppressed in a dose-dependent manner by IL-1β (461, 470). Additionally, IL-1β knock-out mice are of normal size and weight, but resistant to inflammation-induced weight loss (461). Of interest older mice lose more weight in response to IL-1 administration than young adult mice (471).

The positive association between IL-10 and appetite is consistent with the anti-inflammatory actions of this cytokine. IL-10 is believed to suppress immune responses by inhibiting pro-inflammatory cytokine production (67, 472). For example, IL-10 has been found to be protective against weight loss induced by both pro-inflammatory cytokines (473) and bacteria-mimicked infection (474) in rodent studies.

The finding that IL-6 was associated with appetite in the univariate analysis, but not associated in the multivariate analysis is probably because IL-6 concentrations are significantly associated with those of other cytokines, such as IL-1β and IL-10 which have more powerful effects on appetite. Consistent with the strong association observed between IL-6 and IL-10 concentrations ($r = 0.353$, P

<0.001), IL-6 has been found to up-regulate IL-10 during acute inflammation (475).

In the present study there was no association between appetite and circulating levels of either TNF-α or, CRP. TNF-α is a pro-inflammatory cytokine which has been associated with reduced appetite in patients with chronic diseases such as renal failure (476) and levels of CRP, an inflammatory marker, have been associated with appetite decline in patients with chronic disease (477, 478). The lack of an association with appetite in the present study is perhaps because our subjects were healthy and TNFα and CRP effects on appetite occur later in the pathways of chronic and inflammatory diseases.

Low appetite leads to reduced food intake, which in turn, often results in weight loss (167). Loss of appetite due to inflammation might therefore result in reduced lean tissue stores. We found, however, no such association in our study, a finding supported by a recent study of community elders in Malaysia, where appetite was also not associated with body composition (479).

Our results may provide some insight into the order in which changes leading to undernutrition occur. It is not known if the muscle mass loss that often follows appetite reduction in older people leads to a pro-inflammatory state, or if inflammation leads to reduced appetite and food intake and subsequently to adverse body composition changes. Our findings support the latter sequence, at least in certain circumstances. In apparently healthy people there appears to be already present an association between inflammation and reduced appetite, without adverse effects on body composition, which we postulate would only occur with more prolonged and severe effects on food intake and nutrition.

10.4.1 Limitations

This study was limited by a relatively small sample size. Nevertheless, subjects were randomly chosen from the community and thus reflect the situation in apparently healthy adults. A further limitation is that dietary background was also not assessed in this study and that SNAQ has not yet been validated against objective food intake (480), although it has been shown to predict future weight loss (167). Also Dietary intake was not assessed in this study. Because it is possible that body composition and weight loss may reflect long term nutrition, whereas appetite and inflammation reflect short term nutrition (64), it would be interesting to follow these subjects to assess longer-term relationships between inflammation, appetite, body weight change and nutritional status and we are now planning such a follow-up study.

An additional limitation is that there were a large number of comparisons in this study with only two positive results. It is possible that these positive results are the result of a Type I statistical error. Therefore results from this study should be interpreted with caution and further studies performed to confirm findings.

10.4.2 Conclusion

In summary, the major finding of the present study is that appetite in healthy people is associated with several inflammatory markers but not with any measures of body composition or nutritional bio-markers. Further follow-up is needed to explore the possibility that this may predict future weight loss and increased likelihood of developing undernutrition.

11 Thesis Summary, Limitations and Conclusion

11.1 Summary

With the rapid global increase in the number of older people, it is becoming increasingly important to focus research on conditions affecting this age group. Importantly, if we are able to predict which older individuals are more likely to encounter poor health outcomes, this will have an impact on prevention, treatment and care given to older people. Two common conditions associated with poor outcomes in older people are frailty and malnutrition. This doctoral thesis examined the ability of frailty measurements and Nutritional Screening Tools (NSTs) to predict adverse clinical outcomes in hospitalised older people. The main research project was prospective and observational by design, and included 172 patients aged seventy years or over consecutively admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital, South Australia.

Chapter 5 presented a systematic review of 37 prospective studies examining NSTs as predictors of adverse clinical outcomes in older people across a variety of settings: community, residential care, sub-acute care and hospital. Malnutrition identified by NSTs was found to be associated with mortality in 23 out of 28 studies (82 %), functional decline in 9 out of 12 studies (75 %) and with admission to high level care (nursing home) in 4 out of 7 studies (57 %). NSTs tended to show a good negative predictive power for mortality prediction, meaning that a person identified as well nourished had a high probability of *not* having an increased likelihood of mortality. This finding was particularly true for the Mini Nutritional Assessment (MNA), MNA-short form (MNA-SF) and the Geriatric Nutrition Risk Index (GNRI). However, positive predictive power (precision) was relatively low for these NSTs, indicating that malnourished patients were over-identified for mortality risk. Similar trends were also seen for the outcomes of functional decline and high level care admission. Overall, the systematic review concluded that there is evidence that NSTs are predictive of an increased likelihood of mortality, functional decline and to a lesser extent, admission to high level care. Two major research gaps identified in this review

were: (i) the lack of studies performed in the hospital setting, (ii) the lack of studies comparing nutritional screening tools and (iii) the need to study predictive *accuracy*, which is the ability to correctly identify patients likely to encounter adverse health outcomes.

To address these literature gaps, the work described in Chapters 7 and 8 looked at the predictive ability of NSTs when applied to older people hospitalised in a Geriatric Evaluation and Management Unit (GEMU). In Chapter 7, NSTs were considered as continuous variables. It was found that the MNA-SF and the MNA-II were both predictive of GEMU length of stay (LOS); GNRI and CC were associated with functional decline over hospitalisation; and a lower MAC was associated with discharge to higher level care. In Chapter 8, the malnutrition category of various NSTs was considered as a predictor of poor six month outcome, defined generally as admission to a higher level care facility or mortality. Malnutrition identified by both the MNA (OR = 3.29) and GNRI (OR = 2.84) was associated with poor six month outcome, however the diagnostic ability of these screening tools was too low to be clinical useful ($_{au}$ROC values < 0.7).

No consensus yet exists as to which frailty instrument most accurately predicts older hospitalised patients at risk of poor outcomes. Chapter 9 addressed this issue and looked at poor discharge outcome in the same cohort of hospitalised older people. The Comprehensive Geriatric Assessment (CGA) derived Frailty Index of Accumulated Deficits (FI-CD) showed the highest predictive accuracy at both discharge ($_{au}$ROC = 0.735) and at six months post-discharge ($_{au}$ROC = 0.702). Also an accurate predictor of poor six month outcome (with an $_{au}$ROC value of 0.704), was dependency in one or more of seven ADLs (feeding, washing, grooming, dressing, toileting, transferring from a bed or chair, and walking) as assessed by the adapted Katz index.

Of additional clinical importance is the overlap between malnutrition and frailty. The MNA has been recently proposed as a measure of frailty. To quantitatively

assess this relationship, Chapter 6 examined the ability of the MNA and the MNA-SF to identify frailty as using the Cardiovascular Health Study (CHS) frailty criteria. Results from this study revealed that the MNA showed a high specificity (> 90 %) but a low sensitivity (< 60 %) in identifying frailty, regardless of whether the standard MNA cut-off score for malnutrition (< 17) or its optimal cut-off for frailty as identified from this study (< 17.5) was used. The MNA-SF (using BMI) out-performed the full MNA with respect to sensitivity: 64 % at the standard cut-off point and 80 % at the optimal cut-off point, with 77 % specificity at this cut-off point. Therefore, the MNA-SF can be used to identify frailty. The MNA-SF also has the advantage over the full MNA with respect to its simpler and faster application.

Linking frailty and malnutrition is inflammation. Chapter 10 explored the relationship between inflammation, body composition and appetite in a healthy cohort of 180 adults with ages ranging from 18 – 82 years from the CASA study. Results from this study show that poor appetite identified by the Simplified Nutritional Appetite Questionnaire (SNAQ) was negatively associated with serum levels of the pro-inflammatory IL-1β (β coefficient = - 0.379, P = 0.007) and positively associated with serum levels of the anti-inflammatory cytokine IL-10 (β coefficient = 0.25, P = 0.010). There were no associations between appetite and body composition. Findings from this paper suggested that appetite loss may result from background inflammation, even in healthy people, and therefore possibly occurs before consequent changes in body composition.

11.2 The Importance of Measuring Frailty in Hospitals

Frailty status provides a more accurate quantification of health status in older people than chronological age (210, 481, 482). Frailty measurement is also useful in identifying older people at increased risk of encountering adverse outcomes (481). As such, frailty measures can be used by clinicians to assist with decision making in older patients (482), for example, by optimising any medical treatment needed (9, 10), highlighting care needs of patients (483) and offering targeted

support (8). Importantly, frailty measurement is not used to deny any older people treatment (8, 9).

Frailty is most amenable to responding to interventions in its early stages (286). Older people identified as frail may be beyond nutritional and/or exercise interventions and as such, palliative interventions may be the only management pathway possible (238).

The lack of a standard operational definition for frailty hinders its translation into the clinical setting (484). Even at the GEMU at TQEH, frailty status is not measured operationally, but rather with geriatrician judgement. Although geriatrician judgement is accurate in identifying frailty, it does not allow for a consistent diagnosis of frailty from patient to patient (267, 483, 485). Incorporation of an *operational* frailty measurement into clinical practice will allow for a much needed consistent, standard and precise identification of frailty.

11.3 The Purpose of Nutritional Screening

The purpose of nutritional screening is to identify patients with malnutrition or at risk of developing malnutrition for the referral for a full nutritional assessment and interventions where appropriate (126, 127). Nutritional screening is thus the important pre-cursor step to the cyclic Nutritional Care Process (16), which includes nutritional assessment, nutritional diagnosis, intervention, monitoring and evaluation (129). Nutritional interventions can include protein/calorie supplements, social support at mealtime, physical assist with eating, prescribing orexigenic medications, improving the appeal of the food and enteral/parenteral tube feeding (208). At the GEMU at TQEH, patients identified as malnourished or at risk of malnourishment are referred to the hospital dietician for a full nutritional assessment and subsequent entry to the Nutritional Care Process. All patients in the GEMU at TQEH receive generic nutritional support, such as protected meal times.

11.4 Thesis Limitations

11.4.1 Observational Cohort Study

The project was an analytical study, designed to identify and evaluate NSTs and frailty instruments as predictors of adverse outcomes in hospitalised older people. As such, the project design was an *observational cohort* study (486). Whilst results from an observational study can be used to inform clinical practice, these results cannot be used alone to comment on their effectiveness in clinical practice (486). Results from this thesis should therefore be interpreted with this limitation in mind. Any influence on clinical practice and public health policy would require research into the effectiveness of combined screening and interventions as well as identifying where in the causative pathway screening and interventions would have the most influence.

11.4.2 Selection Bias

Patients in the GEMU are pre-selected for entry from the Acute Medical Unit at TQEH by hospital geriatricians. Decisive factors for GEMU entry include the potential of patients to benefit from the rehabilitative style nature of the ward. This pre-selection limits the generalisation of study results to other settings. Additionally, there is the high likelihood that patients in the GEMU who did not participate in the study were more unwell with higher malnutrition and frailty than study participants. This would likely render an underestimation of the relationship of frailty and malnutrition with adverse hospital outcomes in this study. Therefore, this limitation should be considered when interpreting the results.

11.4.3 Research Protocol

The six month follow-up period was counted as the time from hospital discharge to six months post-discharge. It did not account for the time period between patient assessment and hospital discharge, which was a median of 12 days. This time difference may have impacted on the number of events that occurred, although to a small extent. The comparison of nutritional screening tools and frailty indices would be affected.

Twelve month follow-up was not performed due to time constraints. For instance, baseline data collection took 14 months alone to collect. Another a limiting factor was that, because of the observational nature of the project, it was not possible to track compliance to or influence of any nutritional or physiotherapy interventions both during and after hospitalisation. Nor were any follow-up visits performed to assess function and nutritional status, due to the time and financial restrictions of the project.

A further limitation to the research protocol was that, due to the large amount of data collected at baseline, not all frailty instruments and nutritional screening tools could be included in the study. Frailty scales such as the Edmonton's Frail Scale (364) and Tilburg Frailty Indicator (270) and NSTs such as the Malnutrition Universal Screening Tool (MUST) (163) and the Malnutrition Screening Tool (MST) (171) were not used. Moreover, a full nutritional assessment was not completed due to time constraints. It would have been beneficial to compare the efficacy of NSTs assessed in this thesis against a full nutritional assessment. Nonetheless, the MNA was used instead and it can be used as a nutritional reference standard (147).

Of note, a further limitation of research design is that the project used only one cohort of hospitalised older people which would limit the generalisation of results to other settings.

11.5 Overall Significance and Contribution to Knowledge

This doctoral thesis contributed towards a better knowledge and understanding of the predictive ability of frailty instruments and nutritional screening tools in the hospital setting, with several papers published or submitted for publication. Such knowledge may be useful to guide risk stratification, intervention planning and health forecasting in older people. It must be emphasised that identifying older people at risk of poor outcome is not used to deny older people treatment; instead,

it is used to offer appropriate support (8). Results from this thesis could also be used to assist in standardising definitions for both frailty and malnutrition.

This is the first research to compare the MNA and GNRI with respect to outcomes in hospitalised older people. A previous study comparing MNA and GNRI in residential care residing older people found a malnutrition classification by both screening tools was predictive of mortality, infection and bedsores (97). Their study was inconclusive as to which screening tool performed best, although the GNRI appeared to outperform the MNA when all adverse complications were pooled together (97). In our study, malnutrition identified by the MNA showed higher predictive ability of poor six month outcome than the GNRI (adjusted OR values of 3.29 and 2.84 for MNA and GNRI respectively).

This doctoral thesis project also showed that it is possible to use frailty indices to predict outcomes of hospitalised older people. Only one prior study to date (Pilotto et al. 2012) (345) has compared frailty indices with respect to their ability and accuracy to predict adverse clinical outcomes in the hospital setting (345). In this previous study, the Multidimensional Prognostic Index (MPI) showed a higher ability to predict mortality than other frailty instruments studied. These results are in contrast to those found in this thesis, which found that the FI-CD and the adapted Katz indices both predicted adverse outcome (mortality or admission to high level care) whilst the MPI did not. Differences in our results could be because our study population was different – indeed our population was more unwell than in this previous study. Future research is needed to confirm which frailty instrument is best in predicting poor outcome. Additional research directions are discussed in the following section.

11.6 Future Research Directions

The research presented in this thesis provides a platform for ongoing research. Future studies should focus on the efficacy of interventions both in hospital and

post-hospitalisation. Such interventions could include nutritional supplements, physical activity and medical interventions, with the outcome of these interventions assessed by the change in NST and frailty index scores. Additionally, there is a need to focus on identifying which frailty measurement best predicts which outcome (250). For example, it is not yet known if different frailty instruments predict different outcomes in hospitalised older people, with outcomes including falls, admission to residential care, mortality and hospital readmission.

Importantly, despite the strong link between malnutrition and frailty, frailty indices rarely use malnutrition as one of their components. A research focus on the clinical implementation of frailty indices that include a nutritional component is therefore needed. Moreover, as frailty and malnutrition are both transient processes, incorporating multiple time-point analysis should also be a focus of future research.

11.7 Clinical Practice Recommendations

11.7.1 Nutritional Screening

Without using nutritional screening tools, clinical staff can frequently miss idendifying malnourished older patients (124). Therefore, it is highly recommended that all patients receive nutritional screening on hospital admission (123, 130, 143). Additionally, as older patients are at high risk of weight loss in hospital, nutritional screening should be regularly performed (123, 143). Patients identified as malnourished or at risk of malnourishment should be referred to an appropriate specialist for a full nutritional assessment and an appropriate intervention given (126, 127). Nutritional screening is therefore a crucial precursor to the Nutrition Care Process (NCP) (128, 129).

A requirement of the majority of NSTs considered in this study was that patient weight was required. Although all patients were weighed, the process was

inherently difficult. For example many patients were classified as requiring a ‘two person lift assist’. Compounding the immobility of patients was dementia, delerium, incontinence, hearing loss and poor eyesight. Given these difficulties, it is recommended that a NST for frail, immobile older people in the hospital setting offer an alternative anthropometric measure other than weight.

Results from this thesis show NSTs do predict adverse clinical outcomes in hospital patients, however the prognostic ability of these predictions is low.

11.7.2 Frailty Measurement

Results from this thesis show that frailty operationalisations are predictive of an increased likelihood of adverse clinical outcome in hospitalised older people. Two frailty indices showed adequate prognostic ability: the FI-CD and the adapted Katz score. Of clinical advantage, the FI-CD and adapted Katz score can be derived from a Comprehensive Geraitric Assessment, which is routinely perfomed for each patient in the GEMU. Moreover, both the FI-CD index and the adapted Katz score can be used by clinicans to guide patient management. For example, they can be used to advise whether a patient will tolerate surgery or medical treatment, or if these interventions will cause harm. The FI-CD does take some time to compute, so in the busy hospital setting, the adapted Katz score provides an easy and simple alternative measure of frailty.

11.8 Conclusion

This doctoral thesis highlighted the importance of research into the predictive ability and accuracy of both nutritional screening tools and frailty instruments in hospitalised older people. This research will be of assistance in the areas of gerontology research, clinical practice and public health policy, particularly in the wake of the global expansion of the number of older people.

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APPENDIX A

Table 5-2: Nutritional Screening Tools as Predictors of Mortality in Older People in (i) Acute Hospital (ii) Sub-Acute Care (iii) Residential Care (iv) Community and (v) Composite Settings

Author	Objective (stated by the authors)	n	μ Age; %F	Country	NST	Follow Up	Malnutrition (%)	Mortality (%)	Study Quality
(i) Acute Hospital									
Chang et al. 2010 (86)	Evaluate the outcomes of hospitalised elderly with geriatric syndromes and identify the influencing factors in different hospitals participating in this project across the country.	1008	77; 52	Taiwan	MNA	Not standardised. 380-925 days.	M 29; AR 50	19	24
Gazotti et al. 2000 (87)	Estimate the prevalence of malnutrition in elderly patients hospitalised with an acute illness, as well as to assess the clinical usefulness of standardised nutritional assessment upon admission by means of the MNA scale.	175	80; 65	Belgium	MNA	Discharge	M 22; AR 48	6	16
Kagansky et al. 2005 (88)	To identify risk factors for development of malnutrition in very old hospitalised patients and to evaluate the total MNA score and MNA subscores as predictors of in-hospital and long-term mortality.	414	85; 66	Israel	MNA, sub-scores, MNA-SF	Discharge; 2.7 yr post-discharge	M 49; AR 33	30	25
Persson et al. 2002 (89)	Evaluate the validity of SGA and MNA in geriatric patients against objective nutritional indicators and to assess the ability of these techniques to predict mortality.	83	84; 68	Sweden	MNA	3 yr	M 26; AR 56	NR	25
Donini et al. 2003 (104)	To verify, in a sample of elderly subjects admitted to long term care, the impact of malnutrition according to the MNA, on mortality and on the occurrence of Adverse Clinical Events in a 3-12 month follow-up study.	167	83; 79	Italy	MNA,MNA-P0	Discharge; 3-12 mo with μ 7.5 mo	M 68.0	6	19
Van Nes et al. 2001 (99)	To determine whether the MNA can predict the outcome of hospital stay in older individuals	1319	84; 70	Switzer-land	MNA	Discharge	M 19; AR 60	7	17

Continued...

Vischer et al. 2012 (105)	Verify the agreement between the complete and short versions of the MNA and to examine in more depth the association between the MNA, biological markers and the levels of co-morbidities.	444	85; 74	Sweden	MNA	Discharge, 1 yr, 4 yr	M 26; AR 51	22 1 yr; 51 4 yr	24
(ii) Sub-Acute Care									
Bouillane et al. 2005 (170)	To validate our adaption of NRI (ie GNRI) to elderly patients...to estimate the prevalence of nutrition-related complications in elderly hospitalized patients with the use of the GNRI.	181	84; 78	France	GNRI	6 mo	44 M	15	23
Stratton et al. 2006 (91)	To test the hypothesis that 'MUST' could be undertaken on all admissions to elderly care wards.	150	85; 67	UK	MUST	Discharge, 3 mo, 6 mo	HR 44; MR 17	21 Dis; 30 3 mo; 47 6 mo	21
Espaulella et al. 2007 (113)	To describe the association between the different sociodemographic and medical variables and those obtained through geriatric assessment (ie fixed time variables) as well as the prognostic impact of functional and nutritional variables (ie time-dependent variables), and 6 mo mortality of a cohort of frail elderly patients aged over 75 who were hospitalised for an acute event.	165	84; 69	Spain	MNA	1, 3 & 6 months	NR.	11 1 mo, 23 3mo, 29 6 mo	26
Henderson et al. 2008 (415)	Test whether the MUST and BNR scores were able to predict mortality and length of stay in a cohort of older patients admitted to a specialist Medicine for the Elderly hospital.	115	82; 66	UK	BNR,MUST	2 yrs+ (not standardised)	MUST: HR 35, MR 14, BNS: HR 32, MR 29	67	23
Sancarlo et al. 2011 (90)	Compare the sensitivity of the MPI and m-MPI in stratifying elderly patients into groups at varying risk of short- and long-term mortality.	4088	65+; 52	Italy	MNA, MNA-SF	1, 12 mo	NR.	7 1 mo, 15 6 mo; 19 12mo	25
McMurty & Rosenthal 1995 (173)	To determine if nutritional parameters and discharge setting are associated with mortality in older male veterans on a Geriatric Rehabilitation Unit.	77	77; 0	US	NSS	2 yr	M 42	14 Dis; 39 1 yr, 64 *2* yr	20

Continued...

(iii) Residential Care									
Sharifi et al. 2012 (416)	To develop a practical, easy and non-expensive model for predicting mortality in the elderly residents of KCF (charity foundation).	247	77; 59	Iran	MNA	39 mo	NR	30	20
Kaiser et al. 2009 (153)	To compare the results of two different modes of MNA application in nursing homes: resident interviews vs assessment by nursing staff	200	87; 74	Germany	MNA, MNA-SF	6 mo	Nurse: M 9. AR 54 Resident M 15 AR 53	13	21
Lok et al. 2009 (385)	Provide further validation of the CNS tool by following some of the subjects assessed in the original study in terms of mortality over a 12 month period....to determine whether the CNS cut-off score derived from the first study is able to predict 12 month mortality, and to compare the sensitivity and specificity of the SGA...among Hong Kong population.	515	81; 61	China	CNS	12 mo	M 32	13	18
Chan et al. 2010 (386)	To study the nutritional status of nursing home residents in a multi-racial Asian society and its role in predicting short-term mortality independent of functional status and co-morbidities.	154	77; 52	Singa-pore	MNA	2 yr	M 39	25	24
et al. 2008 (417)	To test the association of this new index (GNRI) with long-term mortality.	245	84; 79	Italy	GNRI	1,2,3 yr	SR 6; MR 24, LR 35	11 1 yr, 30 2 yr, 40 3 yr.	26
Tsai & Ku 2008 (418)	To determine the effectiveness of a modified Mini-Nutritional Assessment (MNA) for assessing the nutritional status and predicting follow-up mortality of instituitionised elderly Taiwanese.	308	80; 59	Taiwan	MNA-T1	6, 12 mo	M 22; AR 59; (self assess). M 14; AR 59 (caregiver	7	22
Cereda et al. 2009 (97)	Investigate ability of the GNRI to assess nutritional status and predict the outcome of home-care resident elderly, when compared to the MNA.	241	60; 61	Italy	MNA, GNRI	6 mo	MNA: M 11; AR 41; GNRI: HR 21; LR 36	3	23

Continued...

(iv) Community									
Beck et al. 1999 (419)	Evaluate the capacity of the 'Determine your nutritional health' checklist (NSI checklist) and 'the MNA' methods to predict nutrition-related health problems.	115	70+: 50	Denmark	MNA (modified); NSI	5 yr	MNA M 79; AR 22. NSI HR 19; 51 MR	24	21
Beck et al. (2001) (420)	To assess the prevalence of old people at risk of undernutrition according to the Mini Nutritional Assessment (MNA), characterise the at risk group with regard to nutritional state, energy intake, and physical and mental functioning, and to assess the consequences of the MNA score over a 6 month period.	61	75; 70	Denmark	MNA	6 mo	M 0: AR 38	3	18
Boult et al. 1999 (172)	To measure the validity of the DETERMINE checklist as a marker for future functional disability, depressive symptoms, and mortality among high-risk older adults.	251	79; 45	US	NSI	12 mo	NR	7	17
Sahyoun et al. 1997 (423)	To evaluate the Nutritional Screening Initiative (NSI) checklist as a screening and awareness/educational tool in an elderly population.	581	NR; 67	US	NSI	Not standardised	HR 21: MR 45	34	23
Saletti et al. (2005) (422)	To evaluate nutritional status and long term outcome in elderly living at home.	353	83; NR	Sweden	MNA	3 yr	M 8; AR 41	35	24
Tsai et al. 2010 (412)	Attempted to use this indicator (long term survivability) to validate the grading ability of the two modified versions of the MNA, MNA-T1 and MNA-T2.	2082	NR; 45	Taiwan	MNA, MNA-T1, MNA-T2MNA-T2	4 yr	M 3	6 1yr, 21 4yr	23
Visvanthan et al. 2003 (421)	To identify predictors and consequences of nutritional risk as determined by the MNA in elderly individuals receiving domiciliary care services.	250	67+; 69	Australia	MNA	1 yr	M 5; AR 38	8	24

Continued...

(v) Composite Settings									
Compan et al. 1999 (424)	To evaluate the difference in the nutritional status of elderly patients hospitalized in different types of care in the same hospital, and to evaluate its relationship with risk factors.	918	83; 67	France	MNA	Discharge	M 26; AR 50	6	17

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; MNA-td = MNA time dependent; MNA-P0 (MNA - Proportional and Objective); MNA-T1 = MNA-Taiwanese version 1, MNA-T2 = MNA-Taiwanese version 2; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; NSI = Nutritional Screening Initiative checklist, GNRI = Geriatric Nutritional Risk Index, HR = High Risk, MR = Moderate Risk; LR = Low Risk; NSS= Nutritional Status Score, CNS = Chinese Nutritional Screening Tool, BNR = Birmingham Nutritional Risk, RS = Rapid Screen; ; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional Risk; LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; BI = Barthel Index; ADL = Activity of Daily Living; IADL = Instrumental Activity of Daily Living; CVD = cardiovascular disease.

Table 5-3: Outcomes and Efficacy Values of Nutritional Screening Tools as Predictors of Mortality in Older People in (i) Acute Hospital (ii) Sub-Acute Care (iii) Residential Care (iv) Community and (v) Composite Settings

Author	Outcome (Results)	NST Categories	Sens	Spec	PPV	NPV
(i) Acute Hospital						
Chang et al. 2010 (86)	Lower MNA total score associated with mortality: OR (95% CI) = 0.93 (0.88-0.98), P=0.009 with gender, age, lives alone, LOS, cognition, depression, BI and IADL used as covariates.	***	***	***	***	***
Gazotti et al. 2000 (87)	Lower Mean (SD) MNA in those who died than those who survived: 20.9(4.8) vs 14.1 (5.6) respectively (P<0.01). Mortality rates different between: M (7 died), AR (4 died) &WN (0 died) (P=0.001).	MNA (M) vs (AR+WN)	0.64	0.81	0.18	0.97
		MNA (IN) vs WN	1.00	0.32	0.09	1.00
Kagansky et al. 2005 (88)	Lower Mean (SD) MNA in those who died than those who survived: 14.9(5.2) vs 18.5(5.5) respectively (P<0.001)). MNA associated with mortality OR (95% CI) = 1.64(1.23-2.17), (P=0.001). MNA-3 (nutrition questions from MNA) OR (95% CI) = 2.05 (1.08-3.91), P=0.028. AUC (MNA) = 0.744 AUC(MNA-3) = 0.755.	***	***	***	***	***
Persson et al. 2002 (89)	MNA(M +AR) associated with mortality: OR (95% CI) = 3.3 (1.11-9.79). Adjusted for age + CVD presence.	***	***	***	***	***
Donini et al. 2003 (104)	Lower mean (SD) MNA score in those who died than those who survived: 10.4 (4) vs 15 (4) respectively (P=0.001). Lower mean (SD) MNA-PO in those who died than those who survived: 0.39 (0.2) vs 0.55 (0.1) respectively (P=0.002).	MNA (M) vs (AR+WN)	0.90	0.34	0.08	0.98
		MNA (M +AR) vs WN	1.00	0.03	0.06	1.00
		MNA-PO (M) vs (AR+WN)	0.90	0.53	0.11	0.99
		MNA-PO (M +AR) vs WN	1.00	0.09	0.07	1.00
Van Nes et al. 2001 (99)	Malnutrition associated with higher mortality: M (11.3% died), AR (6.8% died) and WN (3.7% died) (P=0.01).	MNA (M) vs (AR+WN)	0.30	0.82	0.11	0.94
		MNA (M +AR) vs WN	0.89	0.22	0.08	0.96
Vischer et al. 2012 (105)	MNA-SF categories not associated with mortality at discharge, 1 yr or 4 yr follow-up. M (28.32% died), AR (19.4% died) & WN (20.56% died) (P=NS). MNA (M) against mortality: HR (95% CI) = 1.19 (9.82-1.71), P=0.355 & MNA (AR): 0.96 (0.69-1.32), P=0.786.	1 yr: M vs (AR+WN)	0.33	0.77	0.28	0.80
		1 yr: (M +AR) vs WN	0.77	0.24	0.22	0.79
		4 yr: M vs (AR+WN)	0.28	0.77	0.55	0.51
		4 yr: (M +AR) vs WN	0.76	0.24	0.51	0.50

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(ii) Sub-Acute Care						
Bouillane et al. 2005 (170)	Mortality risk for major risk (GNRI < 82): OR (95% CI) = 29 (95% CI: 5.2, 161.4), P<0.001; For moderate risk (GNRI: 82 to <92): 6.6 (95% CI: 1.3, 33.0), P~0.02 and for low risk (GNRI: 92 to < or =98), 5.6 (95% CI: 1.2, 26.6), P~0.02.	GNRI <82 vs Others	0.29	0.95	0.50	0.88
		GNRI <92 vs Others	0.57	0.72	0.27	0.90
		GNRI <98 vs Others	0.93	0.41	0.23	0.97
Stratton et al. 2006 (91)	Mortality at discharge, 3 and 6 months was sig greater for those with medium to high risk on the MUST when compared to low risk patients (P<0.01). Discharge: M (28.32% died), AR (19.4% died) and WN (20.56% died), P=NS.	Discharge: HR vs (MR+LR)	0.62	0.69	0.52	0.77
		Discharge: (HR +MR) vs LR	0.85	0.56	0.51	0.87
		3mo: HR vs (MR+LR)	0.79	0.64	0.24	0.95
		3mo: (HR +MR) vs LR	0.84	0.46	0.18	0.95
		6mo: HR vs (MR+LR)	0.63	0.63	0.27	0.89
		6mo: (HR +MR) vs LR	0.70	0.45	0.22	0.87
Espaulella et al. 2007 (113)	Low MNA (time dependent) score associated with mortality in multiple regression & bivariate analysis. Adjusted HR (95% CI) for MNA (td) = 0.87(0.81-0.94) & 0.68(0.81-0.93) for unadjusted HR.	***	***	***	***	***
Henderson et al. 2008 (415)	MUST category associated with mortality (log rank test, P=0.022) but BNR category not (log Rank, P=0.35). HR (95% CI) for MUST (MR) = 1.91(0.95-3.83); MUST (HR) = 1.98 (1.15-3.52); BNR (MR) = 1.74(1.01-3.01); BNR (HR) =1.17(0.68-2.05). All HR adjusted for age & gender, P =NR.	MUST: HR vs (MR + LR)	0.38	0.74	0.78	0.33
		MUST (HR + MR) vs LR	0.55	0.67	0.80	0.38
		BNR: HRvs (MR + LR)	0.31	0.68	0.67	0.32
		BNR:(HR + MR) vs LR	0.64	0.46	0.71	0.38
Sancarlo et al. 2011(90)	MNA 1 month mortality OR (1.15, 1.13-1.17) P <0.001 ; MNA 12 month OR 1.14(1.13-1.15); MNA-SF 1 month mortality (1.26, 1.23-1.30) and 12 month MNA-SF OR = 1.35 (1.22-1.27). All P's < 0.001.	***	***	***	***	***
McMurty & Rosenthal 1995 (173)	Low NSS associated with mortality at 2 years (P=0.03) in univarite but not in multivariate analysis (actual numerical results not shown but revealed in Kapler-Meier Curves).	***	***	***	***	***

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(iii) Residential Care						
Sharifi et al. 2012 (416)	Mean MNA score lower in those who died vs those who survived (22.0 vs 23.1 respectively). For MNA total score against mortality, HR (95% CI) = 1.74 (1.19-2.54) unadjusted and 1.72 (1.15-2.57) adjusted, both P's <0.05. For MNA (M), HR (95% CI) = 0.59(0.47-0.74) unadjusted and 0.62 (0.49-0.78) adjusted, both P's NS. For MNA (AR), HR (95% CI) = 2.18 (1.32-3.60) unadjusted and 1.92 (1.15 -3.18) adjusted, both P's <0.05.	***	***	***	***	***
Kaiser et al. 2009 (153)	Malnutrition associated with higher mortality: For nursing-staff assessed MNA, M (33.3% died), AR (9.3% died), WN (3.9% died). For resident-assessed MNA, M (19.0% died), AR (12.3%), WN (0% died), (P<0.05).	Nurse Assessed:M vs (AR+WN)	0.08	0.91	0.06	0.93
		Nurse Assessed: (M + AR) vs WN	0.77	0.38	0.08	0.96
		Resident: M vs (AR+WN)	0.10	0.95	0.14	0.92
		Resident: (M+AR) vs WN	1.00	0.39	0.13	1.00
Lok et al. 2009 (385)	Malnourishment classification by CNS showed higher mortality rate. Logistical regression: CNS score associated with mortality (P<0.001). Specific regression results not reported, but sensitivity/specificity/PPV/NPV values were.	Mortality at 12 mo. Sens/Spec reported in study.	0.61	0.73	0.26	0.92
Chan et al. 2010 (386)	MNA (M) associated with mortality (OR 3.03, 95% CI = 1.43-6.41), P=0.004 but not after adjusting for age, gender, BI, co-morbidity (OR 2.35 (0.83-6.60), P=0.106. MNA-SF <12 not associated with mortality (OR 1.02, 95% CI = 0.10-10.1), P=0.988	***	***	***	***	***
Cereda et al. 2008 (417)	Severe Risk (GNRI <82) associated with mortality OR (95% CI) of 5.29 (1.53-19.57, P=0.0127) when compared with GNRI 'no risk' (GNRI >9.8). Cox regression also found HR (95% CI) = 2.76 (1.89-4.03), P=0.0072 (etc).	1yr mortality GNRI < 82	0.14	0.95	0.29	0.90
		2 yr mortality GNRI < 82	0.10	0.96	0.50	0.71
		3 yr mortality GNRI < 82	0.10	0.97	0.71	0.61
		1yr mortality GNRI < 92	0.46	0.66	0.15	0.91
		2 yr mortality GNRI < 92	0.47	0.70	0.40	0.75
		3 yr mortality GNRI < 92	0.45	0.72	0.52	0.66
		1yr mortality GNRI < 98	0.68	0.28	0.11	0.87
		2 yr mortality GNRI < 98	0.78	0.31	0.33	0.77
		3 yr mortality GNRI < 98	0.76	0.32	0.43	0.66

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Tsai & Ku 2008 (418)	MNA (M) (caregiver assessed) associated with higher 6 & 12 mo mortality than MNA (AR), P<0.01 & MNA (M), P<0.05, (survival curves). MNA (self assessed by cognition normal older people) not associated with mortality. No difference between nutritional groups regarding mortality, regardless of caregiver or patient assessed or patient cognition.	3 mo: MNA M vs (AR + WN) - self assessed, normal cognition	0.33	0.79	0.05	0.97
		3 mo: MNA IN vs WN - self assessed, normal cognition	0.83	0.19	0.04	0.97
Cereda et al. 2009 (97)	MNA (M) associated with mortality (OR, 95% CI) = 38.1, 2.0-607.11, P <0.002. MNA(AR) not associated with mortality (OR, 95% CI) = 6.3 (0.3-2320), P = NS. GNRI < 92 associated with mortality (OR, 95% CI) = 30.5 (1.7-941), P<0.001.	***	***	***	***	***
(iv) Community						
Beck et al. 1999 (419)	MNA (AR) associated with higher mortality (49% died) than MNA(WN) (17% died), P<0.01 (t-test), RR (95% CI) = 0.35 (0.18-0.66), P<0.01. NSI not associated with mortality: RR (95% CI) = 1.45, 0.78-2.71), P=NS. Mortality rates did not significantly differ between NSI categories: HR (36% died) vs LR/MR (23% died), P=NS.	MNA: AR vs WN (none were WN)	0.44	0.86	0.49	0.84
		NSI Checklist: HR vs LT/MR	0.27	0.83	0.36	0.77
Beck et al. 2001 (420)	MNA (AR) not significantly associated with higher mortality (3.3%) than MNA(WN) (0%), P=NS.	MNA: AR vs WN	1.00	0.64	0.09	1.00
Boult et al. 1999 (172)	NSI high nutritional risk not associated with higher mortality (2.8% died) than low nutritional risk (4.4% died), P = 0.30.	***	***	***	***	***
Sahyoun et al. 1997 (423)	NSI score not significantly associated with higher mortality: RR (95% CI) = 1.10 (1.04-1.17), P = 0.05-0.10.	***	***	***	***	***
Saletti et al.2005 (422)	MNA categories associated with mortality: OR (95% CI) = 1.89(1.18-3.01),P=0.007. MNA class associated with mortality: (50% died), AR (40% died), WN (27% died), P<0.05.	MNA (M) vs (AR+WN)	0.11	0.94	0.50	0.67
		MNA (M +AR) vs WN	0.32	0.56	0.33	0.55
Tsai et al. 2010 (412)	MNA (M) and MNA (AR) associated with higher mortality risk (all P's <0.001). HR (95% CI) values against mortality: MNA (M) = 6.59 (4.94-8.79), MNA (AR) = 2.39 (1.99-2.88), MNA-T1(M) = 6.40(4.63-8.85), MNA-T1(AR) = 2.55(2.11-3.08), MNA-T2(M) = 6.79(4.83-9.53), MNA-T2(AR)=2.66(2.20-3.21).	1 yr: MNA (M) vs (AR + WN)	0.19	0.98	0.37	0.95
		1 yr:MNA (M+AR) vs WN	0.56	0.81	0.15	0.97
		1 yr: MNA-T1 M vs (AR + WN)	0.17	0.99	0.46	0.95
		1 yr: MNA-T1 (M=AR) vs WN	0.49	0.86	0.17	0.97

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		1 yr:MNA-T2 M vs (AR + WN)	0.12	0.99	0.39	0.95
		1 yr: MNA-T2 (M+AR) vs WN	0.49	0.87	0.18	0.97
		4 yr: MNA M vs (AR + WN)	0.10	0.99	0.71	0.81
		4 yr: MNA (M+AR) vs WN	0.42	0.85	0.42	0.85
		4 yr: MNA-T4 M vs (AR+WN)	0.07	0.99	0.74	0.80
		4 yr: MNA-T4 (M+AR) vs WN	0.35	0.89	0.46	0.84
		4 yr:MNA-T2 M vs (AR + WN)	0.07	1.00	0.80	0.80
		4 yr: MNA-T2 (M+AR) vs WN	0.35	0.90	0.48	0.84
Visvanthan et al. 2003 (421)	MNA(AR+M) not associated with mortality. Unadjusted RR (95% CI) = 1.11(0.48-2.58), P=0.8096; Adjusted RR (95% CI) = 1.02 (0.44-2.38)	MNA (AR + M) vs (WN)	0.45	0.57	0.08	0.92
(iv) Composite Settings						
Compan et al. 1999 (424)	Lower Mean (SD) MNA in those who died than those who survived: 20.1(0.1) vs 11.8(0.9) respectively for combined mortality (sub-acute + acute care), P = sig. but NR. MNA class associated with mortality: M (16.1% died), AR (2.5% died) & WN (0% died), P= sig. but NR. MNA nutritional status highly correlated with mortality in sub-acute/acute care (P<0.0001) - correlation statistic NR.	MNA (M) vs (AR + WN)	0.79	0.75	0.16	0.98
		MNA (M + AR) vs (WN)	1.00	0.24	0.07	1.00

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; MNA-td = MNA time dependent; MNA-P0 (MNA - Proportional and Objective); MNA-T1 = MNA-Taiwanese version 1, MNA-T2 = MNA-Taiwanese version 2; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; NSI = Nutritional Screening Initiative checklist, GNRI = Geriatric Nutritional Risk Index, HR = High Risk, MR = Moderate Risk; LR = Low Risk; NSS= Nutritional Status Score, CNS = Chinese Nutritional Screening Tool, BNR = Birmingham Nutritional Risk, RS = Rapid Screen; ; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional Risk; LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; BI = Barthel Index; ADL = Activity of Daily Living; IADL = Instrumental Activity of Daily Living; CVD = cardiovascular disease; RR = Relative Risk or Risk Ratio; OR = Odds Ratio; HR=Hazard Ratio.

Table 5-4: Nutritional Screening Tools as Predictors of Functional Decline in Older People in (i) Acute Hospital (ii) Sub-Acute Care and (iii) Community

Author	Objective (stated by the authors)	n	μ Age; % F	Country	NST	Outcome	Follow Up	Malnutrition (%)	Functional Decline (%)	Study Quality
(i) Acute Hospital										
Chang et al. (2010) (86)	Evaluate the outcomes of hospitalised elderly with geriatric syndromes and identify the influencing factors in different hospitals participating in this project across the country.	1008	77; 52	Taiwan	MNA	IADL (Lawton & Brody), ADL (BI)	Not standard-ised (380-925 days)	M 29.3; AR 50.2	ADL 44; IADL 46	24
Salvi et al. (2008) (98)	This study aimed at evaluating whether MNA-SF alone or integrated with albumin is a valid screening tool for (protein-energy) malnutrition and a reliable predictor of functional decline in older patients admitted to an acute medical ward.	275	77; 39	Italy	MNA-SF; MNA-SF + albumin	ADL (BI)	Discharge	M 46	15	24
(ii) Sub-Acute Care										
Chen et al. (2008) (112)	To describe functional trajectory during and 6 months post-hospitalisation and to ascertain the predictors that signal different classes of functional trajectory, using latent class analysis.	241	65+; 46	Taiwan	MNA (Chinese version)	ADL (BI)	Discharge ; 3 & 6 months	NR	Discharge 74; 6 mo 32	22
Chen et al. (2010) (111)	Investigate potential prognostic factors for functional improvement in a GEMU.	117	80; 15	Taiwan	MNA	ADL (BI)	Discharge	NR	54	25

Espaulella et al. (2007) (113)	To describe the association between the different sociodemographic and medical variables and those obtained through geriatric assessment (ie fixed time variables) as well as the prognostic impact of functional and nutritional variables (ie time-dependent variables), and 6 mo mortality of a cohort of frail elderly patients aged over 75 who were hospitalised for an acute event.	165	83; 69	Spain	MNA, MNA time dependent (td)	ADL (BI)	1, 3 & 6 months	NR	NR	26
Neumann et al. 2005) (96)	To assess the nutritional status and outcomes of older adults in rehabilitation.	173	82; 56	Australia	MNA, MNA-SF modified	ADL (BI)	90 days	M 47; AR 47	NR	23
(iii) Community										
Beck et al. (1999) (419)	Evaluate the capacity of the 'Determine your nutritional health' checklist (NSI checklist) and 'the MNA' methods to predict nutrition-related health problems.	115	70+; 50	Denmark	MNA modified NSI	Need of Help (ie home helping, eg cleaning, MOW)	5 yr	MNA: M 78.5; AR 21.6 NSI: HR 19.3, MR 51	NR	21
Beck et al. (2001) (420)	To assess the prevalence of old people at risk of undernutrition according to the Mini Nutritional Assessment (MNA), characterise the at risk group with regard to nutritional state, energy intake, and physical and mental functioning, and to assess the consequences of the MNA score over a 6 month period.	61	75; 70	Denmark	MNA	Start of home care, MOW	6 months	M 0, AR 38,	34	18
Boult et al., 1999 (172)	To measure the validity of the DETERMINE checklist as a marker for future functional disability, depressive symptoms, and mortality among high-risk older adults.	251	79; 45	US	NSI	PDF:SIP	12 months	NR	NR	17

Continued...

Lee & Tsai (2011) (413)	Examine the functional status-predictive ability of the MNA in a large population-based, longitudinal study in Taiwan.	2190	65 +; 47	Taiwan	MNA-T2 modified, MNA-T2-SF	Derived scores: IADL ADL both self reported	4 yrs	M 0.96; AR 10.4	ADL 9 IADL 22	25
Ferrer et al. (2008) (425)	Determine predictors of death or functional decline in basic ADL in this group of oldest old.	135	93; 76	Spain	MNA-SF	Combined ADL (BI) decline >19points + mortality.	2 yr	NR	63	21
Formiga et al. (2007) (426)	Determine predictors of functional decline in nonagenarians' basic ADL after 1 year follow-up.	72	93; 74	Spain	MNA-SF	ADL (BI)	12 months	NR	40	22

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; MNA-td = MNA time dependent; MNA-P0 (MNA - Proportional and Objective); MNA-T1 = MNA-Taiwanese version 1, MNA-T2 = MNA-Taiwanese version 2; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; NSI = Nutritional Screening Initiative checklist, GNRI = Geriatric Nutritional Risk Index, HR = High Risk, MR = Moderate Risk; LR = Low Risk; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional Risk; PDF:SIP – Physical Functioning dimension of the sickness impact profile; LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; BI = Barthel Index; ADL = Activity of Daily Living; IADL = Instrumental Activity of Daily Living.

Table 5-5: Outcome and Efficacy Values of Nutritional Screening Tools as Predictors of Functional Decline in Older People in (i) Acute Hospital (ii) Sub-Acute Care and (iii) Community

Author	Outcome (Results)	Outcome	Sens	Spec	PPV	NPV
(i) Acute Hospital						
Chang et al. (2010) (86)	Lower MNA total score associated with ADL decline, OR (95%CI) =0.94 (0.89-0.99), P=0.01, but not IADL decline OR (95% CI) =1.00 (0.95-1.05) P = 0.98. Adjusted for baseline BI & IADL, gender, age, lives alone, LOS, cognition, depression.	ADL (BI), IADL (L &B)	***	***	***	***
Salvi et al. (2008) (98)	MNA-SF (M + AR) associated with BI Decline. OR (95% CI) = 4.25 (1.83-99), P=0.001. MNA-SF (M +AR), with albumin: OR (95% CI) = 16.19 (4.68-56.03), P<0.001. Analyses adjusted for age, gender, co-morbidity, emergency dept. provenance.	ADL (BI)	***	***	***	***
(ii) Sub-Acute Care						
Chen et al. (2008) (112)	MNA associated with BI decline. Controlled for LOS, gender, surgical diagnosis. OR (95% CI) = 1.68 (1.33-2.13), P<0.005 for good vs poor BI & 1.04 (0.92-1.18) P<0.05 good vs moderate BI. Controlled for LOS, gender, surgical diagnosis.	ADL (BI)	***	***	***	***
Chen et al. (2010) (111)	No sig. difference between total MNA score in functional recovery (FR) group (MNA mean(SD)=20.2(4.2)) and no FR group (MNA mean (SD) = 21.2(6.0), P>0.10 (t-test).	ADL (BI)	***	***	***	***
Espaulella et al. (2007) (113)	MNA(time dependent) associated with BI decline. Adjusted HR (95% CI) for MNA(td) = 0.87(0.81-0.94), & 0.68(0.81-0.93) for unadjusted HR. Both P's <0.05.	ADL (BI)	***	***	***	***
Neumann et al. (2005) (96)	MNA-SF(M + AR) & MNA(M +AR) associated with BI decline (ANCOVAS controlling for baseline ADL & QOL): mean (SD) MNA-SF =86(18) vs MNA-SF(WN) = 97.7(7), P=0.001 MNA(IN) = 85(19) vs MNA(WN) =96(7), P=0.002.	ADL (BI)	***	***	***	***
(iii) Community						
Beck et al. (1999)(419)	Significant association: AR 15% needed help vs 6% WN, P < 0.05 (t-test).	Need of Help	***	***	***	***
Beck et al. (2001)(420)	Non significant association: MNA (AR) non-significantly used more home care than those well nourished (27% 18% respectively), P=NS.	AR vs WN	0.43	0.65	0.39	0.68

Continued...

Boult et al. 1999 (172)	NSI score correlated with 12 month disability (r=0.41, P<0.01), but not associated after controlling for baseline disability, depressive symptoms and health: AOR (95% CI)=1.00 (0.35-2.87), P = NR.	HR vs LR	0.69	0.59	0.13	0.94
Lee & Tsai (2011) (413)	MNA-T2 associated with decline: Excluding people dependent at baseline: OR (95% CI) = 1.07 (1.02-1.13), P=0.009 ADL decline & 1.13 (1.08-1.19), P<0.001 IADL decline. MNA-T2-SF also associated with decline: 1.08 (1.00-1.17), P=0.046 ADL decline & 1.20 (1.12-1.29), P<0.001 for IADL decline. Controlled for sex, age, education, living status, CVD.	ADL: M vs (AR+WN) using MNA-SF-T2	0.02	0.99	0.14	0.91
		ADL: (M + AR) vs WN (MNA-T2	0.26	0.90	0.20	0.93
		IADL: M vs (AR+WN)	0.02	1.00	0.81	0.67
Ferrer et al. (2008) (425)	MNA-SF associated with more decline (BI decline or death): mean (SD) =10.5 (2.5) for those with decline vs 12(2) for those without decline, P=0.0001 (t-test). MNA-SF not significant in multiple regression (actual data/P value NR).	Combined mortality & ADL	***	***	***	***
Formiga et al. (2007) (426)	MNA-SF scores did not sig. differ between those with BI loss > 9 points & those with BI loss < 10 points; mean (SD) of 12.0 (1.8) vs 12.4 (1.1) respectively, P=0.23.	ADL (BI)	***	***	***	***

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; MNA-T1 = MNA-Taiwanese version 1, MNA-T2 = MNA-Taiwanese version 2; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; NSI = Nutritional Screening Initiative checklist, GNRI = Geriatric; HR = High Risk, MR = Moderate Risk; LR = Low Risk; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional Risk; PDF:SIP – Physical Functioning dimension of the sickness impact profile; LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; BI = Barthel Index; ADL = Activity of Daily Living; IADL = Instrumental Activity of Daily Living; RR = Relative Risk or Risk Ratio; OR = Odds Ratio; HR=Hazard Ratio

Table 5-6: Nutritional Screening Tools as Predictors of Move to Higher Level Care in (i) Acute Hospital (ii) Sub-Acute Care and (ii) Community

Author	Objective (stated by the authors)	n	μ Age % F	Country	NST	Higher Level Care	Follow Up	Malnutrition (%)	Moved (%)	Study Quality
(i) Acute Hospital										
Gazotti et al. 2000 (87)	Estimate the prevalence of malnutrition in elderly patients hospitalised with an acute illness, as well as to assess the clinical usefulness of standardised nutritional assessment upon admission by means of the MNA scale.	175	80; 65	Belgium	MNA	Destination other than home (NH or hospital)	Discharge	M 22%; AR 48%	32	15
Van Nes et al. 2001 (99)	To determine whether the MNA can predict the outcome of hospital stay in older individuals.	1319	84; 70	Sweden	MNA	NH admission	Discharge	M 19 AR 60	30	17
(ii) Sub-Acute Care										
Visvanathan et al. 2004 (174)	To determine the prevalence of under-nutrition using brief screening methods and to determine the relation between these results and (1) those of a more standard nutritional assessment and (2) discharge outcomes.	65	>65; 33	Australia	MNA, RS	Poor Discharge outcome =Transfer to Acute Care or Increased Support (eg NH)	Discharge	M +AR: 43	12	17
Stratton et al. 2006 (91)	To test the hypothesis that 'MUST' could be undertaken on all admissions to elderly care wards...	150	85; 67	UK	MUST	Returned home after hospital	Discharge	HR 44; MR 17; LR 42	NR	21
Neumann et al. 2005 (96)	To assess the nutritional status and outcomes of older adults in rehabilitation	173	82; 56	Australia	MNA, MNA-SF modified	Admission to higher level care	Discharge ; 90 days	M 47 AR 47	NR	24

(iii) Community										
Andrieu et al. 2001(428)	To assess the effect of nutritional status on the risk of institutional placement in an elderly population of 318 patients with Alzheimer's disease	318	75; 67	France	MNA	NH admission (including sheltered housing & moving in with care-family)	1 year	M 1; AR 19	20	21
Visvanthan et al. 2003 (421)	To identify predictors and consequences of nutritional risk as determined by the MNA in elderly individuals receiving domiciliary care services.	250	>67; 69	Australia	MNA	Self-Reported: change in living situation (move to more supportive accommodation)	1 yr	M 5 AR 38	34	24

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; HR = High Risk, MR = Moderate Risk; LR = Low Risk; RS= Rapid Screen; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; HC = Higher Level Care.

Table 5-7: Outcomes and Efficacy Values of Nutritional Screening Tools as Predictors of Move to Higher Level Care in Older People in (i) Acute Hospital (ii) Sub-Acute Care and (ii) Community

Author	Outcome (Results)	Outcome	Sens	Spec	PPV	NPV
(i) Acute Hospital						
Gazotti et al. 2000 (87)	No association with destination: MNA mean (SD): 20.3(4.9) vs 21.7 (4.6) for those transferred home vs other destination: respectively, P=0.089.	NH: M vs (AR+WN)	0.21	0.83	0.55	0.53
		NH: (M + AR) vs WN	0.76	0.39	0.54	0.63
Van Nes et al. 2001 (99)	For patients living at home at baseline: M (20.3% NH admission), AR (18.3% NH admission), WN (7.7% NH admission), P<0.001.	NH: M vs (AR+WN)	0.22	0.83	0.20	0.85
		NH: (M + AR) vs WN	0.89	0.22	0.16	0.92
(ii) Sub-Acute Care						
Visvanathan et al. 2004 (174)	MNA (AR) associated with poor discharge outcome: MNA (AR) (50% poor outcome) vs MNA (WN) (21.6% poor outcome), P=0.017. RS categories associated with poor discharge outcome, P=0.004.	NH: (M + AR) vs WN using MNA	0.75	0.25	0.12	0.88
		NH: (M + AR) vs WN using RS	0.63	0.68	0.22	0.93
Stratton et al. 2006 (91)	MUST category not associated with destination (51% of M returned home vs 40% of WN returned home, P=NS.	Did not return home	***	***	***	***
Neumann et al. 2005 (96)	Increased likelihood of NH admission with MNA-SF (IN) OR (95%) CI = 2.22 (1.02-4.82) & MNA (IN) = 2.29(1.09-4.80), P < 0.05.	Higher Level Care	***	***	***	***
(iii) Community						
Andrieu et al. 2001(428)	MNA < 25.2 (median score) associated with NH admission. Age/gender adjusted OR (95% CI) = 2.3 (1,07-5.00), P=0.03. Age-adjusted OR (95% CI) = 2.19 (1.00-4.77), P=0.049.	NH: MNA<25.2 vs MNA ≥25.2	0.71	0.46	0.21	0.88
Visvanthan et al. 2003 (421)	MNA (AR+M) not associated with NH admission. MNA (AR +M) = 12.9% to NH; MNA (WN) = 7.9% to NH. Unadjusted RR (95% CI) = 1.64 (0.74-3.63), P=0.2236; Adjusted RR (95% CI) = 1.32 (0.59-2.95), P=0.493.	Increased Care: (M + AR) vs WN	0.55	0.58	0.11	0.93

Abbreviations: NST = Nutritional Screening Tool; MNA = Mini Nutritional Assessment; MNA-SF = MNA-Short Form; Malnourished (MNA), AR = At Risk of Malnourishment (MNA); WN = Well Nourished (MNA); MUST = Malnutrition Universal Screening Tool; HR = High Risk, MR = Moderate Risk; LR = Low Risk; RS= Rapid Screen; HR = High Nutritional Risk; MR =Moderate Nutritional Risk; LR = Low Nutritional LOS = Length of Stay; NS = Not significant; Dis=Discharge; NR = Not Reported; HC = Higher Level Care; RR = Relative Risk or Risk Ratio; OR = Odds Ratio; HR=Hazard

Appendix B

Abstract 1: **Frailty Determinants and Discharge Outcomes in Hospitalised Older People**

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Objectives: To identify factors associated with frailty in hospitalised older persons and study the discharge outcomes of this condition.

Methods: Consecutive patients admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital (TQEH), South Australia were recruited. Data collected included health and lifestyle factors, nutritional factors, clinical details, socio-demographic data and biomarkers. Frailty was identified on admission using Fried's frailty criteria. Logistic regression analyses were performed to determine factors associated with frailty adjusting for age and gender. Frailty was assessed against GEMU length of stay (LOS) and admission to a nursing home using logistic regression, adjusting for age, gender, cognition and co-morbidity.

Results: 172 patients (age 85.2 ± 6.4 years, 71.5% female) were included. The prevalence of frailty was 56% and was greater in women (60 %) than in men (45 %). 22 patients (13 %) were discharged to a nursing home. Median LOS was 12 days. Factors associated with frailty were: malnutrition assessed by the Mini-Nutritional Assessment (OR (95% CI) = 9.90 (3.62-27.08), P<0.001), dependency in Instrumental Activities of Daily Living (IADL) assessed by Lawton and Brody's scale (OR (95% CI) = 0.78 (0.67-0.90), P<0.001) and number of medications (OR (95% CI) = 1.13 (1.02-1.24) P = 0.13). Frail patients were more likely to be discharged to a nursing home (OR (95% CI) = 3.36 (1.01-10.48), P=0.037) and to have a long LOS (> median LOS) (OR (95% CI) = 2.04 (1.05-3.96, P=0.036).

Conclusions: In older hospitalised persons, frailty on admission was related to malnutrition, pre-admission dependency in IADLs and number of medications. Frail patients were more likely to be admitted into a nursing home and to have a long LOS. Results suggest that systematic screening for frailty should be carried out on admission to hospital to identify patients at risk of poor outcomes.

Poster 1: Frailty Determinants and Discharge Outcomes in Hospitalised Older People

Frailty Risk Factors and Outcomes in Hospitalised Older Persons

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BACKGROUND

- Geriatric Evaluation and Management Units (GEMUs) can optimise a patient's chance of functional recovery[1].
- Very few studies have looked at identifying which older patients will do well during and after rehabiliation[2,3].
- The frailty phenotype, provides a measure of "physiological reserve"[4] and can potentially identify patients likely to do well in a GEMU.

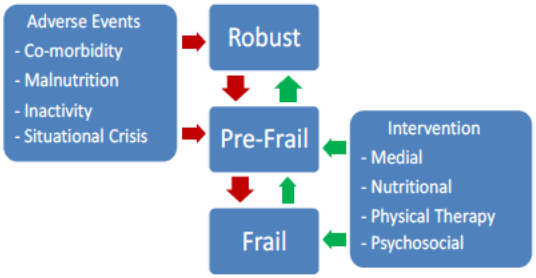


Figure 1: Schematic flow diagram showing the dynamic nature of frailty and the impact of adverse events and interventions. Green arrows indicate potential for improvement in frailty status, whereas red arrows represent detrimental factors

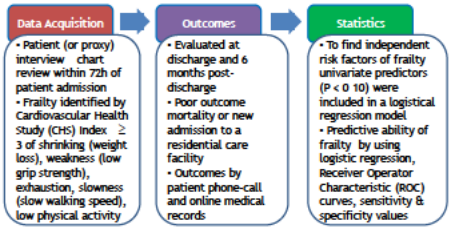
OBJECTIVES

(1) Identify factors associated with frailty on hospital admission

(2) Examine the ability of frailty classification to predict poor outcomes at both discharge and six months post-discharge

METHODS

- A prospective, observational study of consecutive patients aged ≥ 70 years admitted to the GEMU at The Queen Elizabeth Hospital, Adelaide, South Australia.



- Frailty was dichotomised into frail vs "not frail" (pre-frail or robust)
- SPSS Version 19 used for all analyses, with P < 0.05

RESULTS

Table 1: Baseline Characteristics of Patients (n=172)

Variable	n (%)
Age (years)†	85 2 (6 4)
Gender (Female)	123 (72)
Frailty Status	
Frail	96 (56)
Pre-Frail	64 (37)
Robust	12 (7)
Cognitive Impairment (MMSE < 24)	74 (43)
Polypharmacy (≥ 6 Medications)	131 (76)
Malnutrition (MNA < 17)	53 (31)
Poor Outcome (Discharge)	35 (20)
Poor Outcome (6 months)	78 (45)

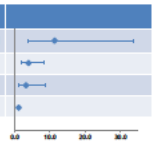
†Mean (SD) ADL = Activities of Daily Living; MMSE = Mini Mental State Examination; MNA = Mini Nutritional Assessment[5]

RESULTS

Table 1: Results of age and gender adjusted multiple regression showing independent risk factors associated with frailty on admission

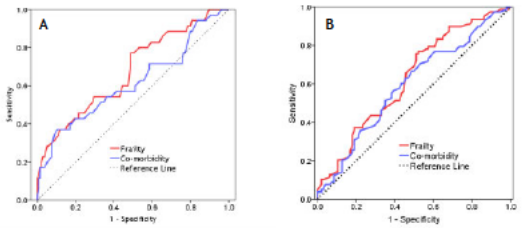
Variable	OR (95 % CI)	P
Malnutrition (MNA)	11 3 (3 7 to 33 9)	< 0 001
Dependency in ≥ 3 IADLs	3 91 (1 8 to 8 5)	0 001
Low QOL (OPQOL)	3 19 (1 2 to 8 8)	0 025
Medication Number	1 12 (1 01 to 1 2)	0 032

OR = Odds Ratio; CI = Confidence Interval MNA = Mini Nutritional Assessment; IADL = Instrumental Activities of Da ly Living; QOL = Quality of Life; OPQOL = Older People's QOL score (lowest quartile)



Tab e 2: Age and gender adjusted odds ratios for prediction of poor outcomes by frailty classification on admission

Outcome	OR (95 % CI)	P	Sensitivity (%)	Specificity (%)
Poor Discharge Outcome	2 98 (1 28 -6 97)	0 012	74 3	49 6
Poor 6 Month Outcome	2 17 (1 15 - 4 09)	0 017	65 4	52 1



Frailty AUC (95 % CI) 0 675 (0 57, 0 78), P 0 001
Co-morbidity AUC (95 % CI) 0 615 (0 51, 0 73), P 0 036

Frailty AUC (95 % CI) 0 627 (0 54, 0 71), P 0 004
Co-morbidity AUC (95 % CI) 0 592 (0 51, 0 68), P 0 039

Figure 2: ROC curves for prediction of poor outcome at (A) discharge and (B) six months follow-up, with frailty identified on admission by the CHS frailty index and Co-morbidity by the Charlson's Co-morbidity Index AUC Area Under Curve

CONCLUSIONS

- Independent risk factors of frailty on admission were malnutrition, dependency in performing ≥ 3 instrumental activities of daily living (IADL), low quality of life and a higher number of medications.
- Patients identified as frail on admission were over twice as likely to encounter poor outcomes as their non-frail counterparts, a finding which supports previous literature[3,6].
- The discriminative ability of these predictions was relatively low (AUC < 0.7). Sensitivity and specificity values were also low, indicating the CHS frailty index is not ideal in identifying patients at risk of poor outcomes.
- Future research should focus on assessing the benefits of longer term community based sub-acute rehabilitation programs, including focusing on patient adherence to nutritional and physical activity interventions[7], as well as medication optimisation.

ACKNOWLEDGEMENTS AND CONTACTS

We wish to thank Kylie Lange, biostatistician, for her guidance on statistical analyses ED was supported from funding from the Clinical Centre for Research Excellence (CCRE); Email elsa.dent@adelaide.edu.au; The Health Observatory http://www.thehealthobservatory.org.au/people/positive-ageing-researchers

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Abstract 2: Nutritional Status at Admission Predicts Functional Outcomes in Older South Australians Admitted to a Higher Acuity Geriatric Evaluation and Management Unit

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Aims: To examine the usage of nutritional screening tools as predictors of discharge clinical outcomes in older persons admitted to a higher acuity Geriatric Evaluation and Management Unit (GEMU).

Methods: Consecutive patients aged ≥ 70 years admitted to the GEMU at the Queen Elizabeth Hospital, South Australia were included in this longitudinal study. Nutritional status was determined using Body Mass Index (BMI), the Mini-Nutritional Assessment (MNA) and the MNA-short form (MNA-SF). Multivariate logistic and multiple linear analyses were performed to measure the association between nutritional status and discharge outcomes including length of stay (LOS), discharge destination, body weight and functional decline (defined as an increased dependency in a modified Katz Activities of Daily Living (ADL) score). Analyses were performed both unadjusted and adjusted for confounding variables.

Results: 150 patients were examined; mean age (SD) of 85.3(6.3) years; 75.0% female. Undernutrition prevalence was: 33.3% (BMI <22.0 kg/m^2), 31.4% (MNA < 17), 44.2% (MNA-SF < 8), Multiple regressions showed both BMI (p=0.026) and MNA (p=0.026) were associated with functional decline after controlling for baseline ADL, but only MNA showed an association after controlling for confounders (p=0.035). No other associations between nutritional status and clinical outcomes existed.

Conclusions The MNA was the best nutritional screening tool in this study for identifying patients at risk of functional decline during hospitalisation. Identification of such patients can guide comprehensive geriatric assessment, which in turn, can guide patient management. Importantly, using one screening tool to detect both undernutrition and risk of functional decline will assist busy clinicians.

Abstract 3: Frailty and Functional Decline Indices as Predictors of Poor Outcomes in Hospitalised Older People

Authors: Elsa Dent[1], Renuka Visvanathan[1,2], Cynthia Piantadosi[1], Ian Chapman[1,3]

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Introduction: Admission to a Geriatric Evaluation and Management Unit (GEMU) can optimise a patient's chance of functional recovery. The aim of this study was to evaluate several common frailty and functional decline indices on their ability to predict poor GEMU outcomes, both at discharge and at six months.

Methods: This was a prospective observational study of consecutive patients aged 70+ years admitted to the GEMU at the Queen Elizabeth Hospital, Adelaide, Australia. Patients were classified as 'frail' or 'at high risk of functional decline' using several different frailty and functional decline indices. The predictive ability of indices was evaluated using logistic regression and area under Receiver Operating Characteristic curves (auROC). A poor outcome was considered as mortality or residential care admission.

Results: 172 patients (mean age 85.2 years; 72% female) were included. Frailty prevalence varied from 24 - 94 % depending on the index used. Several instruments were predictive of poor outcome at both discharge and 6 months. Adequate predictive accuracy for discharge outcome was achieved by the FI-CD (auROC = 0.735, $P < 0.001$) and modified Katz score (auROC = 0.704, $P = < 0.001$). The FI-CD was the only index to show discriminatory power in predicting poor six month outcome (auROC = 0.702, $P < 0.001$).

Conclusion: Frailty and functional decline instruments are a feasible application for identifying GEMU patients at risk of poor discharge and six month outcomes. The FI-CD is best predictor overall, and is recommended for research purposes. Pragmatically, the modified Katz index is the most valuable predictive instrument.

Keywords: Frail Elderly; Geriatric Assessment/Methods; Patient Care Planning; Aged, 80 and over

Abstract 4: Evaluation of Frailty Indices for the Prediction of Adverse Post-Hospital Outcomes in Older Persons

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Background*:* Following hospital discharge, older people are at an increased risk of adverse clinical outcomes. We examined the predictive ability of five frailty indices in identifying patients with increased risk of mortality, emergency rehospitalisation and rehospitalisation due to falls.

Methods: In this prospective study of consecutive patients admitted to a Geriatric Evaluation and Management Unit, we identified frailty using Fried's Index, Study of Osteoporotic Fractures (SOF) Index, Frailty Index of Cumulative Deficits (FI-CD), Multidimensional Prognostic Index (MPI), Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA) and Katz index of Activities of Daily Living (ADL). Logistic regression and area under curve (AUC) of Receiver Operating Characteristic (ROC) curves were analysed, adjusting for age and gender.

Results: 172 patients (mean (SD) age of 85.2 (6.4) years; 72% female) were included. During 6 month follow-up, 28 (16 %) patients died, 92 (53 %) were re-hospitalised for emergencies and 43 (25 %) were re-hospitalised for falls. Frailty identified by all instruments, excluding the MPI, was associated with mortality (odds ratio (OR) values all > 2.50, P < 0.005). Frail patients had a high risk of emergency rehospitalisation, when identified by Fried's Index (OR = 2.47, P = 0.010) and SHERPA (OR = 1.97, P = 0.038). No indices associated with rehospitalisation due to falls. AUC results showed FI-CD had the highest discriminatory power for mortality (AUC= 0.803), followed by SHERPA (AUC = 0.792) and Katz Index (AUC = 0.757). All other AUC values lacked adequate discriminative power for outcome prediction (AUC values < 0.7).

Conclusion: Frailty instruments are a feasible way to identify older patients with an increased likelihood of mortality and rehospitalisation, although not rehospitalisation due to falls. The FI-CD and the simpler to use SHERPA and Katz indices are recommended for prediction of mortality. Our findings can guide patient care and discharge planning.

Keywords: Frail Elderly; Aged; Geriatric Assessment; Aged, 80 and over

Abstract 5: Evaluation of Frailty Conceptualisations for the Prediction of Adverse Health Outcomes in Hospitalised Older Persons

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Rationale: During and after hospitalisation, older people are at an increased risk of adverse clinical outcomes. We examined the predictive ability of five frailty indices in identifying patients with increased risk of: long length of hospital stay (LOS), discharge to residential care (RC), 6 month emergency rehospitalisation and mortality.

Methods: In this prospective study of consecutive patients admitted to a Geriatric Evaluation and Management Unit (GEMU), we identified frailty using Fried's Index, Study of Osteoporotic Fractures (SOF) Index, Frailty Index of Cumulative Deficits (FI-CD), Multidimensional Prognostic Index (MPI) and Katz score. Logistic regression and area under curve (AUC) of Recevier Operating Characteristic (ROC) curves were analysed, adjusting for age and gender.

Results: 172 patients (mean age 85 years; 72% female) were included. Median LOS was 12 days. On discharge, 27 (16 %) patients were admitted to RC. During follow-up, 28 (16 %) patients died and 92 (53 %) were hospitalised for emergencies. Frailty identified by all instruments, excluding the MPI, was associated with mortality (odds ratio values all > 2.50). AUC results showed the FI-CD had the highest discriminatory power for mortality (AUC= 0.803) and RC admission (AUC= 0.712), followed by the Katz index (AUC for mortality and RC admission = 0.757 and 0.693 respectively).

Conclusion: The FI-CD and the simpler to use Katz index are recommended for prediction of adverse outcomes in older hospitalised persons, particularly mortality. Our findings can guide patient care and discharge planning.

Lay Description

During and after hospital discharge, many older patients experience poor health outcomes, such as a long hospital stay, a need for long term care, a return to hospital and death. Our study looked to see if we could predict which patients were more likely to encounter these poor outcomes. To do this, we investigated 5 different types of frailty tests. We studied 172 older patients and found those we identified as frail (in all but one of the frailty tests) were more than twice as likely to die in the 6 months following hospital than a patient who was not frail. Knowing which patients are frail can assist doctors in their care of patients.

Abstract 6: Nutritional Screening Tools and Hospital Discharge Outcomes in Older People

Authors: Elsa Dent[1], Renuka Visvanathan[1,2], Cynthia Piantadosi[1], Ian Chapman[1,3]

1 Department of Medicine, The University of Adelaide, South Australia. 2 Aged and Extended Care Services, The Queen Elizabeth Hospital, Adelaide, South Australia. 3 Department of Medicine, Royal Adelaide Hospital, South Australia.

Background: Malnutrition is common in older people and can influence hospital outcomes.

Aims: To examine the use of nutritional screening tools (NSTs) as predictors of discharge clinical outcomes in older people admitted to a higher acuity Geriatric Evaluation and Management Unit.

Methods: Consecutive patients aged ≥ 70 years admitted to the GEMU at the Queen Elizabeth Hospital, South Australia were included in this longitudinal study. Nutritional status was determined using the Mini-Nutritional Assessment (MNA), MNA-short form (MNA-SF), Malnutrition Universal Screening Tool (MUST) and the Geriatric Nutritional Risk Index (GNRI). Regression analyses were performed to measure the association between nutritional status and discharge outcomes including length of stay (LOS), functional decline (defined as a decrease in Barthel Index (BI) score for Activities of Daily Living (ADL)), and discharge to a higher level of care. All analyses were adjusted for confounding variables.

Results: 172 patients were examined with a mean age (SD) of 85.2 (6.4) years; 71.5% female. Malnutrition according to the MNA, MNA-SF and GNRI occurred in 53(31 %), 77(45 %) and 83(48 %) of patients respectively. For the MUST, all patients were classified as malnourished. NSTs associating with LOS (> than the median of 12 days) were the MNA (OR: 1.09; 95% CI 1.01-1.18; P=0.031) and the MNA-SF (OR 1.19; 95% CI 1.04-1.35; P = 0.012). The MNA was also associated with discharge to higher level care (OR: 0.93; 95% CI 0.86-0.99; P=0.044). No other associations between nutritional status and clinical outcomes existed.

Conclusion: The MNA and MNA-SF were the best NSTs in this study for identifying patients at risk of higher length of stay. Identification of such patients can guide comprehensive geriatric assessment, which in turn, can guide patient management. Importantly, using one screening tool to detect both undernutrition and risk of adverse outcomes in hospital will assist time-pressured clinicians.

Poster 6: Nutritional Screening Tools and Hospital Discharge Outcomes in Older People

Nutritional Screening Tools and Hospital Discharge Outcomes in Older People

E Dent[1], R Visvanathan[1,2], C Piantadosi[1], I Chapman[1,3]

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"Nutritional Status at Admission Predicts Functional Decline in Older South Australians Admitted to a Higher Acuity Geriatric Evaluation and Management Unit"

Introduction

- Knowing which older patients are at increased risk of negative discharge outcomes can guide patient assessment and management.
- Malnutrition is common in hospitalised older people and is associated with mortality and functional decline[1].
- Nutritional Screening Tools (NSTs) are a fast and easy way to screen for malnutrition for referral for further evaluation and management[2].
- Many NSTs have been developed, but limited research exists as to their predictive ability of negative discharge outcomes.

Objective

To compare several popular Nutritional Screening Tools (NSTS) against in-hospital and discharge outcomes.

Methods

Setting and Sample:

- Longitudinal and prospective study
- Consecutive patients aged ≥ 70 years admitted to the Geriatric Evaluation and Management Unit (GEMU) at The Queen Elizabeth Hospital (TQEH), South Australia (see Figure 1).
- Ethics Approval from TQEH Ethics Committee.

Anthropometric Measures:

- Body Mass Index (BMI), Calf Circumference (CC), Mid-Arm Circumference (MAC)

Nutritional Screening Tools:

- Mini-Nutritional Assessment (MNA)[3], Short From MNA (MNA-SF)[4], including versions using BMI, CC and MAC, Malnutrition Universal Screening Tool (MUST)[5] and the Geriatric Nutritional Risk Index (GNRI)[6].

Outcomes:

- Length of Hospital Stay (LOS), Discharge destination other than to home, Discharge Function, defined using Barthel's Index (BI)[7] of Activities of Daily Living (ADL).

Statistics:

- ANCOVAs and bivariate regression analyses
- Confounding Variables controlled for: Admission function (BI), age, gender, Mini Mental State Examination (MMSE)[8], Geriatric Depression Scale-15 (GDS-15)[9] CRP levels, Lives Alone, Charlson's Comorbidity Index (CCI)[10].
- Results analysed using SPSS Version 18, P < 0.05.

Figure 1: Collecting Patient Data in the Geriatric Evaluation and Management Unit

Results

Table 1: Baseline Admission Characteristics of Study Participants (n=172)

Variable	n(%)
Age (years)	85.2 ± 6.4[†]
Gender(female)	129 (71.5)
Low Cognition (MMSE < 24)	74 (43)
Lives Alone	97(56)
Charlson's Comorbidity Index	3 (Range 0-12)[¥]
Depression Symptoms (GDS-15 score >5)	61 (40)[$]
Admission function (BI)	58.6 ± 21.1
Polypharmacy (≥ Medications)	131 (76%)

[†] mean ± SD, and all such values; [¥] Median (range) and all such values; [$] n = 154

Results

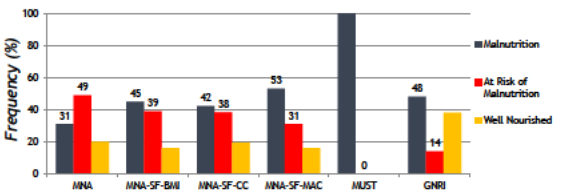

Figure 1: Nutritional Status Classification by Nutritional Screening Tools (n=172)

Discharge Outcomes:

- Median LOS for all patients was 12 days.
- During hospital, 129 (75%) patients showed functional improvement, 28 (16%) showed no change in function and 15 (8%) showed functional decline.
- 80 (46.5%) of patients were discharged to a location other than home.

Clinical Outcomes:

- Poorer nutritional status classified by MNA-SF (BMI) associated with longer LOS: β(95% CI) = -0.19 (-0.08 to 0.10), P=0.027), indicating that for every SD drop in MNA-SF (BMI) score, LOS increased by 0.19 SD (see Table 2).
- Lower MNA-SF (CC) score associated with longer LOS (β (95% CI) = -0.18 (-0.03 to 0.00), P=0.041 (See Table 2).
- Lower GNRI score on admission, indicating poorer nutritional status, was associated with lower discharge function β (95% CI) = 0.13 (0.01 to 0.33), P = 0.043 (See Table 2).

Tab e 2: Nutritional Screening Tools and Their Association with Hospital Discharge Outcomes (n=172)

Predictor Variable	Length of Hospital Stay (days)				Dischargе Function (BI)				Dischargе Other than to Home			
	β*	SE*	95% CI	P	β	SE	95% CI	P	OR	SE	95% CI	P
Nutritional Screening Tool												
MNA	-0 12	0 004	-0 02 to 0 00	0 162	0 11	0 23	-0 08 to 0 83	0 093	0 96	0 03	0 90 to 1 02	0 14
MNA-SF-BMI	-0 19	0 01	-0 08 to 0 10	0.027	0 06	0 40	-0 42 to 1 16	0 320	0 93	0 05	0 84 to 1 04	0 19
MNA-SF-CC	-0 18	0 01	-0 03 to 0 00	0.041	0 07	0 37	-0 37 to 1 10	0 329	0 97	0 05	0 87 to 1 07	0 48
MNA-SF-MAC	-0 16	0 01	-0 02 to 0 00	0 106	0 05	0 36	-0 42 to 0 10	0 418	0 94	0 05	0 85 to 1 03	0 18
MUST	0 02	0 02	-0 03 to -0 04	0 804	-0 4	1 04	-2 63 to 1 49	0 555	0 96	0 14	0 73 to 1 27	0 79
GNRI	0 06	0 002	-0 004 to 0 002	0 450	0 13	0 08	0 01 to 0 33	0.043	0 99	0 01	0 96 to 1 01	0 19

*All regression models controlled for 6 core confounding variables: for age, gender, CCI, MMSE, Admission BI, Lives Alone. The multiple regression models additiona ly controlled for CRP levels and GDS-15. LOS outcomes also controlled for "move not home". β = Standardised Beta Coefficient. SE = Standard Error

Discussion and Conclusions

- In GEMU patients, it is possible to use NSTs to assess risk of adverse discharge outcomes, although no one screening tool is associated with all outcomes.
- Lower MNA-SF (BMI) and MNA-SF (CC) scores, indicating poorer nutritional status, were both associated with longer LOS.
- Lower GNRI scores, indicating poorer nutritional status, was associated with a lower level of function at discharge after adjusting for admission function.

Clinical Implications

- Using one screening tool to detect both malnutrition and risk of adverse outcomes in hospital will assist time-pressured clinicians.

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Acknowledgement and Contacts

We wish to thank Kylie Lange biostat stician for her guidance on statistical analyses. We also wish to thank GEMU staff patients and their families. ED was supported from funding from the Clinical Centre for Research Excellence (CCRE).

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The Health Observatory:

http://www.thehealthobservatory.org.au/people/pos tive-ageing-researchers

Abstract 7: The Mini Nutritional Assessment as a Predictor of Fried's Frailty Classification in Hospitalised Older People

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Malnutrition and frailty are common problems in older people and are both associated with increased mortality and morbidity. This study aimed to: (1) determine the prevalence of malnourishment and frailty in the hospitalised older people and (2) evaluate both the Mini-Nutritional Assessment (MNA) screening tool and the MNA short form (MNA-SF) as predictors of frailty. Setting and Participants: 100 patients (75.0% female) admitted to the Geriatric Evaluation and Management Unit at The Queen Elizabeth Hospital. Measurements: Frailty was identified by Fried's frailty criteria and nutritional status by the MNA and MNA-SF. Optimal cut-off scores to identify frailty were determined by Youden Index, Receiver Operating Characteristic Curves and area under curve (AUC). Results: 40.0% of patients were malnourished and 66.0% were frail. The MNA identified frailty with specificity and sensitivity values of 91.2% and 51.6% respectively using the standard malnourishment cut-off (<17) and with specificity and sensitivity values of 91.2% and 59.1% with the optimal cut-off (<17.5). The MNA-SF predicted frailty with specificity and sensitivity values of 79.4% and 63.6% respectively with its standard cut-off (<8), and with values of 76.5% and 80.3% respectively with its optimal cut-off (<9). The optimal score for the MNA-SF was better in identifying frailty than the optimal MNA score (Youden Index 0.568 vs. 0.503). Conclusion: The MNA-SF can be used to screen both malnourishment and frailty in hospitalised older people. Further studies would show whether it also identifies frailty in other older populations.

Lay Description (100 words)

Malnutrition and frailty are both common, yet often undetected problems in older people. Identifying people with either of these conditions is crucial if interventions are to be implemented to reduce their incidence. Our study assessed how accurate a malnutrition screening tool, the Mini-Nutritional Assessment (MNA) was in identifying frailty. We studied 100 patients (75% female) aged over 70 years at The Queen Elizabeth Hospital and found the MNA was a good identifier of frailty. Thus both malnutrition and frailty could be screened for with the one test, saving both time and resources.

Appendix C

April 10, 2013

Elsa Dent
Department of Medicine
The University of Adelaide, AUSTRALIA 5005
Email: elsa.dent@adelaide.edu.au

Dear Elsa:

Nestlé Nutrition is pleased to grant permission to include the Mini Nutritional Assessment (MNA®) in appendix of your thesis titled "Clinimetrics of Frailty Indices and Nutritional Screening Tools in Hospitalised Older People", to be published online by the University of Adelaide's digital library. To meet copyright requirements, you must comply with the following directions:

1. The MNA® content cannot be altered. The questions and scoring system must be worded exactly as they appear on the attached MNA® form.
2. The Nestlé Nutrition Institute logo must appear as indicated on the attached sample form.
3. The form must include the following statement identifying the trademark owners: ®Société des Produits Nestlé S.A., Vevey, Switzerland, Trademark Owners.
4. The form must include the following copyright statement: © Nestlé, 1994, Revision 2009. N67200 12/99 10M
5. All of the following references must be included:

   Vellas B, Villars H, Abellan G, et al. Overview of the MNA® - Its History and Challenges. *J Nutr Health Aging* 2006;10:456-465.

   Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: Developing the Short-Form Mini Nutritional Assessment (MNA-SF). *J Geront* 2001;56A: M366-377.

   Guigoz Y. The Mini-Nutritional Assessment (MNA®) Review of the Literature - What does it tell us? *J Nutr Health Aging* 2006; 10:466-487.

   Kaiser MJ, Bauer JM, Ramsch C, et al. Validation of the Mini Nutritional Assessment Short-Form (MNA®-SF): A practical tool for identification of nutritional status. *J Nutr Health Aging* 2009; 13:782-788. *(For the MNA-SF only)*

We also strongly encourage you to provide readers with the address of the MNA® website for further information: www.mna-elderly.com. Literature related to the MNA® is regularly updated on this website.

I confirm by this letter that we hold the necessary rights and that no consent is required of any third party to grant such permission.

We are pleased to see the MNA® being included in your thesis and appreciate your interest in validated screening tools.

Best regards.

Jean Zetlaoui, M.D.
Chief Medical Officer
Nestlé Health Science S.A.
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1800 Vevey, Switzerland

Nestlé Nutrition INSTITUTE

Mini Nutritional Assessment MNA®

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers. Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3kg (6.6lbs)
1 = does not know
2 = weight loss between 1 and 3kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F Body Mass Index (BMI) (weight in kg) / (height in m²)
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

Screening score ☐☐
(subtotal max. 14 points)

12 points or greater: Normal – not at risk – no need to complete assessment
11 points or below: Possible malnutrition – continue assessment

Assessment

G Lives independently (not in nursing home or hospital)
1 = yes 0 = no ☐

H Takes more than 3 prescription drugs per day
0 = yes 1 = no ☐

I Pressure sores or skin ulcers
0 = yes 1 = no ☐

J How many full meals does the patient eat daily?
0 = 1 meal
1 = 2 meals
2 = 3 meals ☐

K Selected consumption markers for protein intake
- At least one serving of dairy products (milk, cheese, yoghurt) per day yes ☐ no ☐
- Two or more servings of legumes or eggs per week yes ☐ no ☐
- Meat, fish or poultry every day yes ☐ no ☐

0.0 = if 0 or 1 yes
0.5 = if 2 yes
1.0 = if 3 yes ☐☐

L Consumes two or more servings of fruit or vegetables per day?
0 = no 1 = yes ☐

M How much fluid (water, juice, coffee, tea, milk...) is consumed per day?
0.0 = less than 3 cups
0.5 = 3 to 5 cups
1.0 = more than 5 cups ☐☐

N Mode of feeding
0 = unable to eat without assistance
1 = self-fed with some difficulty
2 = self-fed without any problem ☐

O Self view of nutritional status
0 = views self as being malnourished
1 = is uncertain of nutritional state
2 = views self as having no nutritional problem ☐

P In comparison with other people of the same age, how does the patient consider his / her health status?
0.0 = not as good
0.5 = does not know
1.0 = as good
2.0 = better ☐.☐

Q Mid-arm circumference (MAC) in cm
0.0 = MAC less than 21
0.5 = MAC 21 to 22
1.0 = MAC 22 or greater ☐.☐

R Calf circumference (CC) in cm
0 = CC less than 31
1 = CC 31 or greater ☐

Assessment (max. 16 points) ☐☐.☐
Screening score ☐☐.☐
Total Assessment (max. 30 points) ☐☐.☐

Malnutrition Indicator Score

17 to 23.5 points ☐ at risk of malnutrition
Less than 17 points ☐ malnourished

Ref. Vellas B, Villars H, Abellan G, et al. *Overview of MNA® - Its History and Challenges.* J Nut Health Aging 2006; 10: 456-465.
Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: *Developing the Short-Form Mini Nutritional Assessment (MNA-SF).* J. Geront 2001; 56A: M366-377.
Guigoz Y. The Mini-Nutritional Assessment (MNA®) *Review of the Literature – What does it tell us?* J Nutr Health Aging 2006; 10: 466-487.

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For more information: www.mna-elderly.com

Appendix D

Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People. *Journal of Nutrition Health and Aging.* 2012;16(9):764-7.

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Appendix D

Dent E, Visvanathan R, Piantadosi C, Chapman I. Use of the Mini Nutritional Assessment to Detect Frailty in Hospitalised Older People. Journal of Nutrition Health and Aging. 2012;16(9):764-7. (Pre-printed version in Chapter 6).

Appendix E

Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional Screening Tools as Predictors of Mortality, Functional Decline and Move to Higher Level Care in Older People: A Systematic Review. Journal of Nutrition in Gerontology and Geriatrics. 2012;31(2):97-145. (Pre-printed version in Chapter 5).

Appendix F

Dent E, Yu S, Visvanathan R, Piantadosi C, Adams R, Lange K, Chapman I. Inflammatory Cytokines and Appetite in Healthy People. The Journal of Aging Research & Clinical Practice. 2012;1(1):40-3. (Pre-printed version in Chapter 10).

The following appendix has not been supplied by author:

Appendix G