Nutritional frailty:
Prevalence, screening and management

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Dedication

I dedicate this thesis to my loving parents, Visva and Vas and my brother Thava who have always been there for me.

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List of figures and tables

Publications and awards arising from thesis

Articles

Visvanathan R, Chen R, Garcia M, Horowitz M, Chapman I. The effects of drinks made from simple sugars on blood pressure in healthy older people**. British Journal of Nutrition** 2004 (In Press)

Visvanathan R, Zaiton A, Sherina S, Yunus A. The nutritional status of 1081 older residents of publicly funded shelter homes in Peninsular Malaysia. **European Journal of Clinical Nutrition** 2004 November [advanced online access].

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Chapman I & Visvanathan R. Under-nutrition In Older People Is Far Too Common. Council Of The Ageing (COTA) 50 Something Extra Newsletter, South Australia June/July 2004.

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Visvanathan R. Malnutrition in older people: a serious growing global problem! **J Postgrad Med** 2003; 49(4): 352-360.

Visvanathan R, MacIntosh C, Callary M, Penhall R, Horowitz M, Chapman I. The Nutritional Status of 250 Older Australian Recipients of Domiciliary Care Services, and its Association with Outcomes at 12 months. **J Am Geriatr Soc** 2003; 51:1007-1011.

Zaiton A, Cugadasan T, Visvanathan R. Good oral health, consumption of fruits and vegetables and family support is associated with a reduced risk of being underweight amongst the older residents of publicly funded shelter homes in Peninsular Malaysia. In review with the **Australasian Journal of Ageing** 2004.

Visvanathan R, Hammond A, Wishart J, Horowitz M, Chapman I. Fasting plasma ghrelin levels in under-nourished and well-nourished older people are comparable. In review with the **Neurobiology of Ageing** 2004

Abstracts

Visvanathan R, MacIntosh C, Callary M et. al. The Nutritional Status of 250 Older Recipients of Domiciliary Care Services Living at Home in Adelaide, and its Association with Outcomes at 12 Months. Int Med J 2003; 33: A26

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Visvanathan R, Chen R, Garcia M, Horowitz M, Chapman I. The effects of 50g carbohydrate containing drinks with carrying glycemic indices and content on post-ingestion blood pressure in healthy older people. Int Med J 2004 (In Press)

Visvanathan R, Zaiton A, Sherina S, Yunus A. The nutritional status of 1081 older residents of publicly funded shelter homes in Peninsular Malaysia. Age Ageing 2004 (In Press)

Visvanathan R, Penhall R, Chapman I. Screening For Under-nutrition in Older People-A Hampstead Centre Perspective. Int Med J (In Press) 2004.

Visvanathan R. Nutritional frailty. Proceedings of the Symposium on the Dynamic Processes in Aging, Canberra 2003

Prizes or awards related to thesis

RM Gibson Prize- best advance trainee platform presentation- Australian Annual Geriatric Scientific Meeting, June 2002 in Darwin. Title: The nutritional status of 250 domiciliary care recipients in Australia and its relation to outcomes.

Emerging Australian Researcher's Traveling Scholarship–to attend the Symposium on the Dynamic Processes in Aging, Canberra 2003. Title: Nutritional Frailty.

Professor John Chalmers Prize- Best Physician Trainee platform presentation at the 2003-South Australian Royal Australian College of Physicians Scientific Meeting. Title: Screening For Under-nutrition in Older People- A Hampstead Centre Perspective.

Pfizer Advance Trainees Awards Finalist (South Australian Representative)- Annual Scientific Meeting of the Royal Australasian College of Physicians, Canberra May 2004

International Postgraduate Research Scholarship- 2003-2005- Awarded by the Department of Education, Training and Youth Affairs, Australia

University of Adelaide Postgraduate Scholarship- 2003-2005

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution (except in part the study described in Chapter 6 which was also submitted by Dr Caroline Macintosh as part of her PhD thesis) and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Signed …….

Date ……

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Dr Caroline MacIntosh and Dr Mandy Callary conducted the baseline survey in the study described in Chapter 6.

The staff (nursing and interns) of the Hampstead Rehabilitation Centre assisted with data collection in the study described in Chapter 7.

Ms Angela Hammond assisted with data collection in the study described in Chapter 8.

Ms Judith Wishart conducted the plasma ghrelin assays reported in Chapter 8.

Dr Richard Chen assisted with data collection in the studies described in Chapters 9 and 10.

Ms Marian Garcia assisted with data collection in the study described in Chapter 10.

Mr Justin Lokhorst assisted with the statistical analyses of the studies described in Chapters 5 and 8 and Ms Kirstyn Wilson assisted with the statistical analyses of the study described in Chapter 6.

Abstract

Nutritional frailty refers to the downward spiral of increasing frailty that may occur in old age as a result of rapid, unintentional loss of body weight and sarcopenia. In the studies described in this thesis, the prevalence of under-nutrition was high and these under-nourished older people were more likely to be hospitalized, spend longer in hospital, be admitted to facilities with increased level of care, fall and report weight loss. Also, medical and emotional well-being, good oral and dental health and access to nutritious food were all shown to be associated with better nutritional health.

Screening for under-nutrition is important. The 'DETERMINE Your Nutritional Health Checklist' was found to be a simple awareness tool that could be easily used to increase knowledge in carers and older people. The rapid screen, in which an older person is classified as under-nourished if they have: 1) body mass index < 22 kg/m^2 and/or 2) unintentional weight loss > 7.5% in the previous 3 months, was found to be simple and highly specific and suitable for use in facilities with financial, time and staffing constraints. The Mini Nutritional Assessment tool with its better sensitivity and specificity may be better in resource rich settings as results from this tool can guide management.

In one of the studies, fasting plasma ghrelin levels in under-nourished older people were comparable to that in nourished older people, not higher as in previous studies (in other states of negative energy balance) and this may indicate a failure in energy homeostasis. Relatively reduced ghrelin levels in under-nourished older people may contribute to the development and/or progression of the anorexia of ageing and this requires further evaluation.

Many frail older people are at risk of post-prandial hypotension and its many adverse health effects. Dietary carbohydrate manipulation by substituting sucrose with fructose may be beneficial in reducing the post-prandial blood pressure fall in older people.

In conclusion, nutritional frailty is prevalent and has many adverse health consequences. Early detection and systematic intervention may help reduce morbidity.

Nutritional frailty:
Prevalence, screening and management

Chapter 1

Nutritional frailty - A brief introduction to an important clinical problem affecting many older people

Frailty is a clinical syndrome that can be viewed as a multidimensional construct consisting of a complex interplay of a person's assets and deficits, including health and illness, attitudes, practices and resources, and dependence on others (Rockwood *et al*., 1994; Rockwood *et al*., 1996; Wells *et al*., 2003). Frailty involves a spiralling decline in non-homeostatic, self sustained cyclic processes where initial impairments and limitations precipitate further decline (Ferrucci *et al*., 2002). Geriatric syndromes such as malnutrition, falls, delirium and incontinence may be possible markers of frailty (Rockwood *et al*., 1994; Wells *et al*., 2003).

Nutritional frailty (Figure 1.1) is the disability that occurs in old age due to rapid, unintentional loss of body weight and sarcopenia (Bales & Ritchie, 2002). The term 'anorexia of ageing' refers to the decline in energy intake and appetite that occurs with progressive ageing (Morley, 1997; Wurtman *et al.*, 1988). This reduction in energy intake often exceeds the decrease in energy expenditure that occurs with normal physiological ageing, so body weight is unintentionally lost (Forbes & Reina, 1970). When body weight decreases in older people, lean body tissue is thought to be lost disproportionately (sarcopenia) (Chapman, 2004; Forbes & Reina, 1970). A complex interaction exists between unintentional weight loss, sarcopenia and the numerous health, physical, social and psychological insults that occur with increasing age, and this in turn can result in physical frailty and its undesirable outcomes which include nursing home placements, falls, malnutrition, immobilization and increased dependency and eventually death (Bales & Ritchie, 2002; de Jong, 2000).

Older adults comprise a heterogeneous group, ranging from the very robust to very frail individuals (Bales & Ritchie, 2002). With increasing age, there is a decreasing margin of homeostatic reserve and an increasing likelihood of experiencing numerous assaults to the homeostatic balance (Bales & Ritchie, 2002). For example, ageing may be associated with an impaired homeostatic regulation of feeding (Chapman, 2004). When 17 young and older men were underfed in one study by 3.17MJ/day (approximately 750 kcal/day) for 21 days, both groups lost weight (Roberts *et al.*, 1994). When the men were permitted to eat as much as they wanted after the underfeeding period, younger men ate more than at baseline and regained their weight (Roberts *et al.*, 1994). In contrast to this, the older men continued to under-eat and so did not regain the weight lost during the underfeeding period (Roberts *et al.*, 1994). Therefore, it is likely that after a significant insult (i.e. surgery), older people are more likely than younger adults to become or remain under-nourished and take longer to regain weight (Chapman, 2004).

Population ageing is a worldwide phenomenon. If anything, population ageing is more rapid in developing than in developed countries. For example, the population of Malaysia (a rapidly developing, newly industrialized country) is progressively ageing with a significant increase in life expectancy seen between 1980 and 2000; males from 66.4 years to 70.2 years and females from 70.5 years to 75.0 years (Ministry of Health Malaysia, 2003). Similarly, the proportion of the Australian population aged 65 years and over is expected to increase from 12% in 1999 to 24 - 27% in 2051, at which point 1.3 million Australians or 5% of the total Australian population will be over the age of 85 years (Australian Bureau Statistics, 2003).

As nations age, compression of morbidity will become a more important goal as the number of years spent living healthily is a more important marker of successful ageing than chronological age per se. In 1999, Australia was ranked second in the world for this indicator with an estimated average (Australian Institute of Health and Welfare, 2002)

healthy life expectancy of 73.2 years at birth (Mathers *et al.*, 2001) and a total life expectancy at birth of 79.8 years in 2000. To maintain this, if not improve on it, the management of common syndromes affecting elderly people such as under-nutrition and falls should be prioritized both in developed (for example Australia) and rapidly developing countries (for example Malaysia).

For most, an ideal life is one that is vigorous and vital over the life span with a terminal collapse of physical and mental function limited to a short period (Fries, 2000). Unfortunately, with the human ageing process, when not prematurely stopped by trauma or disease, there is a progression towards multiple organ frailty (Fries, 1989; Fries, 2000; Gruenberg, 1977). Therapeutic interventions should be directed towards easily treatable causes with the goals of preventing functional decline and morbidity (i.e. falls, malnutrition) and optimizing overall quality of life.

In view of this, the studies in this thesis have targeted two nutrition-related disorders, under-nutrition and post-prandial hypotension, which are commonly associated with ageing syndromes (i.e. frailty and falls). These studies have focused on: 1) determining the prevalence, predictors and consequences of the major geriatric syndrome, under-nutrition [chapters 5-7], 2) identifying nutritional screening and assessment measures that would enable therapeutic targeting [chapters 5-7]; 3) investigating the effects of nutritional status on ghrelin, an orexigenic hormone possibly involved in the pathogenesis and/or progression of the anorexia of ageing [chapters 8]; and 4) evaluating the use of dietary carbohydrate manipulation in the management of post-prandial hypotension [PPH] in older people [chapters 9 & 10]. The possible impact of the results of these studies on clinical practice and future research is discussed in the final chapter [chapter 11].

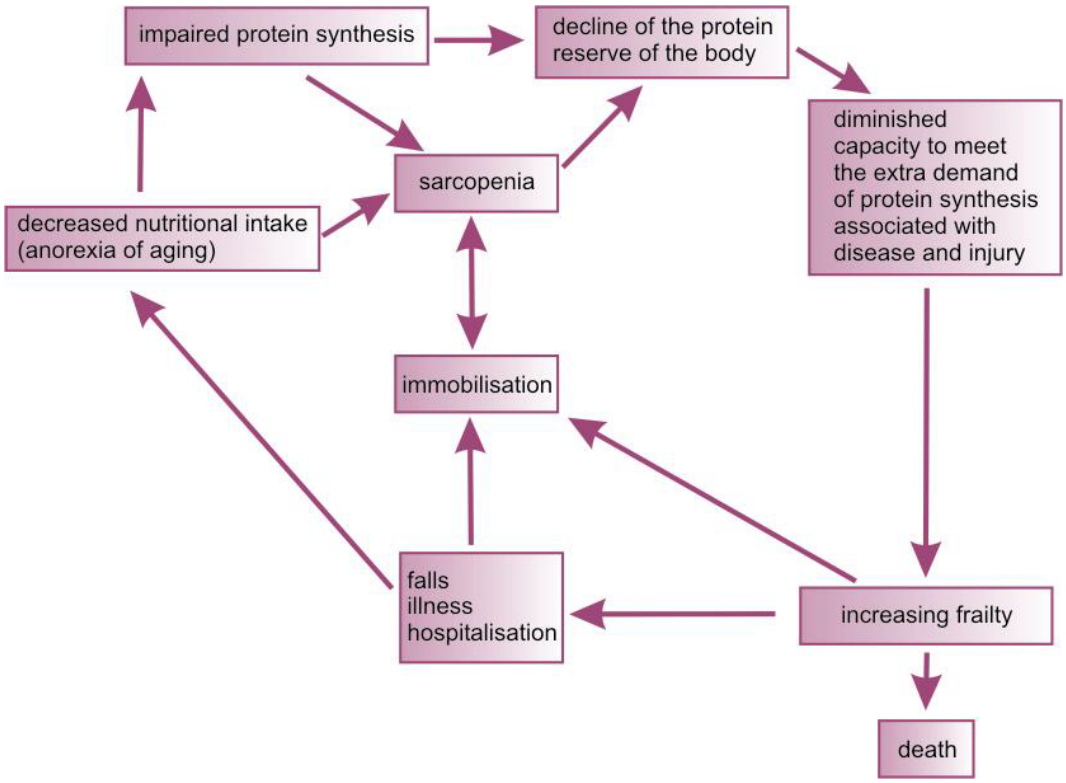


Figure 1.1 The downward spiral to increasing frailty and eventual death.

Chapter 2

Under-nutrition in older people – Prevalence, consequences and pathophysiology

2.1 Introduction

In this chapter, the prevalence of under-nutrition, as determined by the Mini Nutritional Assessment (MNA), in various clinical settings is detailed. The prevalence of under-nutrition in the community (domiciliary care recipients) and in a sub-acute care facility in South Australia was determined using the MNA, in the studies described in Chapter 6 and 7 of this thesis. In these same studies, the adverse consequences of under-nutrition in older people were also determined. Commonly seen adverse health outcomes in older people associated with impaired nutritional intake and status is also described in this chapter. It is said that under-nutrition in older people is due to physiological (Anorexia of Ageing and Sarcopenia) and non-physiological causes and these are briefly described in this chapter (MacIntosh *et al.*, 2000). The studies described in Chapters 5 and 6 evaluated whether there were independent associations between some of the non-physiological factors which are discussed in this chapter (i.e. depression, illnesses) and impaired nutritional status in a group of older people. Ghrelin, an orexigenic gut hormone, may possibly play a role in the pathogenesis and/or progression of the physiological anorexia of ageing. The study described in Chapter 8 was performed to investigate if there were differences in fasting plasma ghrelin levels between under-nourished and well-nourished community dwelling older people ($\geq$ 65 years).

2.2 The prevalence of under-nutrition in older people

There is no gold standard for the diagnosis of under-nutrition and as a result the prevalence figures quoted in the literature vary widely depending on the diagnostic method chosen. To enable clear comparisons (table 2.1), the prevalence figures quoted below are from studies that have used the MNA (see 3.6.1, Appendix 1) as the preferred method to assess nutritional risk. Consistent with this clinical concept of nutritional frailty, the prevalence of under-nutrition increases as frailty and physical dependence increases. On average, the prevalence of nutritional risk is approximately 45% in the community (de Groot *et al.*, 1998), 45-51% in domiciliary care or home-care recipients (Soini *et al.*, 2004; Visvanathan *et al.*, 2003), 50-82% in hospitalized elderly (Barone *et al.*, 2003; Persson *et al.*, 2002) and between 84-100% in institutionalized elderly (Saletti *et al.*, 2000). In every setting, for every malnourished individual (MNA <17), there are many more individuals at-risk of malnutrition (MNA 17-23.5). Screening for and early management of nutritional risk is clearly warranted given the high prevalence of under-nutrition as shown here. The studies described in chapter 5-7 were designed to evaluate the prevalence of under-nutrition amongst 1) older residents of shelter homes in Peninsular Malaysia, 2) domiciliary care recipients in Adelaide, South Australia and 3) sub-acute care patients in Adelaide, South Australia. At the time of these studies, the prevalence of under-nutrition in older people in these settings in Australia and Malaysia was not known.

Table 2.1 Prevalence of malnutrition by the level of care

Clinical Setting	Prevalence (%)-	Under-nourished	Total
	(MNA<17)	(MNA 17-23.5)	%
Community			
European community (healthy)(de Groot *et al.*, 1998)	1	44	45
Elderly home-care rural Finland(Soini *et al.*, 2004)	3	48	51
Hospitals: Acute			
Australian acute hospital(Barone *et al.*, 2003)	20	30	50
Swiss acute hospital(Van Nes *et al.*, 2001)	18.6	60	78.6
Swedish acute geriatric unit(Persson *et al.*, 2002)	26.5	55.9	82.4
Hospitals: Sub-acute			
American sub-acute care(Thomas *et al.*, 2002)	28.8	62.5	91.3
Low Level Care			
Swedish Old People's Home (Hostel)(Saletti *et al.*, 2000)	33	51	84
High Level Care			
Group Living- Demented- Sweden(Saletti *et al.*, 2000)	38	57	95
Swedish Nursing Home(Saletti *et al.*, 2000)	71	29	100
MNA < 17- malnourished MNA 17-23.5- at-risk of malnutrition			

2.3 The health and economic consequences of under-nutrition in older people

Under-nutrition is associated with negative health outcomes and increased financial burden to the individual, families and the community at large. The studies described in Chapters 6 and 7 were performed in South Australia to evaluate the effects of under-nutrition on health in frail older people receiving domiciliary care services and also older people admitted to a sub-acute care facility.

2.3.1 Economic costs

It has been stated that people with gastrointestinal-, respiratory- and neurological disease-related malnutrition have a 6% higher general practitioner consultation rate, are given 9% more prescriptions and have a 26% higher hospital admission rate than people who are well-nourished (Martyn *et al.*, 1998). The King's Fund (UK) has previously estimated that up to 266 million pounds (1992 figures) could be saved each year if malnourished hospitalized patients were given appropriate nutritional intervention (Lennard Jones, 1992). It has also been postulated that the direct cost of malnutrition in the United Kingdom was in excess of 1 million pounds per average Parliamentary constituency per year (Malnutrition Advisory Group). In addition, there would also be added indirect costs as a result of social care, lost workdays, and disability benefits (Malnutrition Advisory Group). It is likely that under-nutrition in the elderly result in similar increases in costs in other developed countries such as Australia.

2.3.2 Health consequences

Under-nutrition in older people is associated with many undesirable health consequences which impact on overall quality of life, increase morbidity and eventually may result in death. Below, some of the more common adverse consequences are briefly described. Where possible, examples using the Mini Nutritional Assessment (MNA) are provided.

Mortality

The Survey in Europe on Nutrition and the Elderly, a Concerted Action [SENECA] studies were part of a large longitudinal study spanning Europe whereby older people were assessed in 1989 (n=2586, born between 1913 and 1918), 1993 (n=1273) and 1999 (n=843) (de Groot & van Staveren, 2002). In the SENECA study, subjects with nourished MNA scores (MNA $\geq$ 24) had significantly lower mortality (OR: 0.35, 95% CI 0.18-0.66) compared to subjects at nutritional risk (MNA < 24) (Beck *et al.*, 1999). Similarly, in their study of 83 consecutive acute geriatric patients, Persson and colleagues reported that nutritional risk (MNA <24) was associated with an OR of 3.3 (95% CI 1.11-9.79) for death within 3 years in comparison to nourished scores (MNA $\geq$ 24) (Persson *et al.*, 2002). In a study of 175 acutely admitted elderly patients, Gazzotti and colleagues found that the MNA scores in survivors were significantly higher than the MNA scores in non-survivors (20.9 vs. 14.1; P <0.001) (Gazzotti *et al.*, 2000). Therefore, there appears to be a strong association between under-nutrition in older people as defined by the MNA and increased mortality.

Geriatric failure to thrive

Under-nutrition in older people may result in a 'geriatric failure to thrive'. The accepted definition for this syndrome includes several parameters pertaining to nutritional status in the older person: weight loss > 5% of baseline weight, decreased appetite, poor nutrition, impaired immune status and low cholesterol levels (Institute of Medicine (U.S.) & Committee on a National Research Agenda on Ageing, 1991).

Impaired social functioning or institutionalization

Previous studies have shown that under-nourished older people are at increased risk of declining physical health and placement in residence with increased level of care (i.e. nursing homes or hostels). For example, in a study of hospitalized elderly subjects, it was found that of the 908 patients who had previously been living independently at home prior

to admission, 32 (20.3%) of 158 subjects with a score < 17 (malnourished) were discharged to a nursing home compared to 16 (7.7%) of 208 subjects with a score of ≥ 24 (nourished [P<0.001]) (Van Nes *et al.*, 2001).

Increased health care utilization and hospitalization

Under-nourished older people experience more frequent and prolonged hospitalizations. Thomas and colleagues studied 837 consecutively admitted elderly patients to a sub-acute care facility in the United States and found that malnourished patients (MNA <17) spent 11 days more (P= 0.007) than at-risk patients (MNA 17-23.5) in hospital (Thomas *et al.*, 2002). Similarly, another study of 1319 hospitalized elderly patients found that subjects scoring < 17 on the MNA (malnourished) spent 42.0 days in hospital in comparison to the 30.5 days spent by those scoring ≥ 24 on the MNA (nourished; P<0.0002) (Van Nes *et al.*, 2001). In a study of 94 patients older than 65 years attending general practice clinics in Denmark, there was increased trend towards greater utilization of meals on wheels (39% vs. 8%), home-care assistance for cleaning (52% vs. 26%) and shopping (48% vs. 18%) by under-nourished patients (MNA 17-23.5) in comparison to nourished patients (MNA ≥ 24) (Beck *et al.*, 1999).

Decreased immunity, increased risk of infections, pressure sores and delayed wound healing

Under-nourished older people have impaired immunity and are at increased risk of infections. Timely management may be beneficial. For example, a study of 3012 patients (mean age 73.3 ± 12 [SD] years) hospitalized following an acute cerebral-vascular event found that those who were under-nourished on admission were more likely to suffer infections and other complications than nourished patients [pneumonia- 21% vs. 12%; P=0.0001, other infections 21% vs. 15%; P = 0.0005, pressure sores 4% vs. 1%; P=0.010] (FOOD Trial Collaboration, 2003). Similarly, in another study, following transtibial

amputation, under-nourished patients receiving nutritional supplementation (91.3%) experienced greater (P=0.01) wound healing success than the non-supplemented (55.6%) control group (Eneroth *et al.*, 1997).

Poorer post-operative outcomes

In a study of 87 post-hip fracture patients, patients with low albumin and total lymphocyte counts, two indicators of under-nutrition, were 2.9 times more likely to have a length of stay greater than two weeks (p = 0.03), 3.9 times more likely to die within one year after surgery (p = 0.02), and 4.6 times less likely to recover their pre-fracture level of independence in basic activities of daily living than in patients with normal values (p < 0.01) (Koval *et al.*, 1999).

Falls

Under-nourished older people are at risk of sarcopenia and falls. Nutritional supplementation may possibly be beneficial in reducing this falls risk. A recent meta-analysis found that lower extremity weakness was associated with an increased risk of falls (OR1.76; 95%CI 1.31-2.37), recurrent falls (OR 3.06; 95% CI 1.86-5.04) and injurious falls (OR 1.52; 95% CI 1.05-2.20) (Moreland *et al.*, 2004). The prevalence of sarcopenia (see 2.3.2) is thought to be as high as 30% in people aged 60 years and older (Doherty, 2003). By the seventh and eighth decade of life, maximal voluntary contractile strength may be decreased, on average, by 20-40% for both men and women in proximal and distal muscles (Doherty, 2003). In a recent intervention trial, 85 subjects with a diagnosis of chronic obstructive airways disease were randomized to receive either a 570 kcal carbohydrate rich supplement or a non-nutritive placebo daily for 7 weeks. A positive correlation between changes in carbohydrate intake and incremental shuttle walk test was seen (r=0.337; P= 0.01) (Steiner *et al.*, 2003). There was also a trend toward increased handgrip (0.64kg vs. – 0.05; P=0.06) and quadriceps strength (17.4 N vs. 3.6 N; P=0.068) in supplemented subjects in comparison to non-supplemented subjects) (Steiner *et al.*, 2003).

2.4 The pathophysiology of under-nutrition in older people

Broadly speaking, the pathophysiology of under-nutrition can be classified into physiological (anorexia of ageing and sarcopenia) and non-physiological causes and these are discussed below with brief examples given.

2.4.1 The anorexia of ageing

The anorexia of ageing describes the physiological decrease in appetite and food intake that accompanies normal ageing and which may result in undesirable weight loss. In the cross-sectional 3rd National Health and Nutrition Examination Survey [NHANES (III)] study from the United States of America, an average decline in energy intake between the ages of 20 and 80 years, of 1321 cal/day (1.32 kcal/day) in men and 629 cal/day (0.63 kcal/day) in women was seen (Briefel *et al.*, 1995). Similarly, in the SENECA [Survey in Europe on Nutrition and the Elderly, a Concerted Action] longitudinal study of older people, over the first 4 years of follow-up, the average energy intake in men declined by 0.6 MJ/day (142.9 kcal/day) and in women by 0.4 MJ/day (95.2 kcal/day) (de Groot *et al.*, 2000). In these same studies, over a period of 10 years, 23% of men and 27% of women had lost 5 kg of their initial body weight (de Groot & van Staveren, 2002). Over the 4-year follow-up period, a weight loss of more than 5 kg was predictive of reduced survival (de Groot & van Staveren, 2002). There was also strong evidence that older people were at an increased risk of reduced energy and nutrient intake (de Groot & van Staveren, 2002).

Although weight loss and decreased nutrient intake may accompany normal ageing, perhaps secondary to decreased physical activity and energy demands, this effect may be undesirable. The control of feeding involves complex interactions between the cortex, limbic system and the midbrain, in addition to peripheral inputs from the organs transducing taste and smell (Table 2.2), the gut, adipose tissue and the endocrine system. The effects of ghrelin, an orexigenic gut hormone on appetite and food intake are described in greater detail, as plasma ghrelin levels were measured in the study described in Chapter 8 which

was performed to investigate if differences existed in fasting plasma ghrelin levels between under-nourished and well-nourished community dwelling older people. Ghrelin is thought to play a role in meal initiation and ghrelin infusions have been shown to increase food intake in certain groups of people and may possibly be of benefit in the management of the Anorexia of Ageing (Cummings *et al.*, 2004; Neary *et al.*, 2004).

Table 2.2 An overview of the central and peripheral mechanisms involved in the regulation of appetite (MacIntosh *et al.*, 2000)

Central satiety system	Corticotrophin–releasing factor, serotonin, insulin, cholecystokinin (CCK), insulin
Central feeding drive mediators	neuropeptide Y, noradrenaline, opioids, orexins (ghrelin), galanin
Peripheral satiety system	Stomach: gastric distension, gastric emptying Small intestine gastrointestinal hormones: insulin, CCK, amylin, peptide YY, glucagonlike peptide-1, ghrelin Small intestine motility Plasma nutrient levels: amino acids, monosaccharides, fatty acids Fat stores: leptin, tumour necrosis factor α Cytokines: Interleukin-6

Ghrelin

Ghrelin, an endogenous ligand for the growth hormone secretagogoue receptor (GHS-R), has recently been purified from the human stomach and found to release more growth hormone synergistically, than growth hormone releasing hormone (GHRH)(Arvat *et al.*, 2000; Kojima *et al.*, 1999). Ghrelin is present in the hypothalamus but is mainly produced in the fundus of the stomach and reaches brain centers via the bloodstream (Tschop *et al.*, 2000; Ukkola, 2003). Ghrelin stimulates lactotroph and corticotroph secretion, has orexigenic activity, modulates energy balance via the influence on glucose metabolism and insulin secretion, and also regulates gastric motility and acid secretion through vagal mediation (Arvat *et al.*, 2001; Muccioli *et al.*, 2002; Takaya *et al.*, 2000).

Ghrelin is thought to play an important role in meal initiation and so perhaps the exogenous administration of ghrelin may stimulate increased food intake (Cummings *et al.*, 2004). In one study, 6 young adults (mean age 21.2 $\pm$ 1.2 [SD] years, BMI 21.3 $\pm$ 1.8 kg/m^2) were deprived of all visual and auditory time cues (Cummings *et al.*, 2004). Following a

standardized dinner, usual breakfast and an unrestricted lunch, subjects were asked to eat only when hungry (study meal - ad libitum). Plasma ghrelin was measured frequently (every 5 minutes) for 10 hours following lunch. Subjects were only permitted to leave after 10pm. In this study, there was a pre-prandial rise in plasma ghrelin levels just before the study meal in 5 subjects. The temporal profiles of mean ghrelin levels and subjective hunger scores overlapped closely and in at least 4 subjects, the rise in pre-prandial ghrelin levels slightly preceded the increase in hunger scores. A high ghrelin level was also associated with a high hunger score in 5 subjects. Therefore, it is likely that ghrelin is associated with meal initiation. In this study also, there was no significant association between the energy intake at lunch and the test meal, anthropometric measures (BMI, fat mass, % fat, fat-free mass) and the area under the ghrelin curve.

Two recent studies have shown that ghrelin infusion in humans can increase energy intake at meals. In a recent cross-over study of 7 patients with a diagnosis of metastatic cancer (mean weight loss 13% compared to pre-cancer weight, mean BMI 22.6kg/m^2), ghrelin (5pmol/kg.min) and saline were infused on two separate study days one and a half hours after a standardized breakfast and for 90 minutes before a buffet lunch (Neary *et al.*, 2004). The infusion continued during the buffet lunch. In that study, a marked increase (31 $\pm$ 7%; P=0.005) in energy intake was seen on the ghrelin day in comparison to the saline day. Therefore, it would appear that exogenous ghrelin administration is able to stimulate oral intake and so may be beneficial in the management of under-nutrition. Similarly, in another earlier randomized blinded cross-over study in nine non-obese young adult Caucasian volunteers (five male, age 21-32 years, BMI 19-26.8 kg/m^2), ghrelin (5 pmol/kg/min) or saline was infused intravenously for 270 minutes (Wren *et al.*, 2001). At 120 minutes post commencement of infusion, subjects ate a breakfast (1550 kJ/369 kcal). Subjects were then offered a buffet lunch at 240 minutes post commencement of the infusion. In this study, there was an increase in energy intake (mean increase 28 + 3.9 [SEM]%, approximately 306 kcal, P<0.001) at the buffet lunch on the ghrelin infusion day.

States of negative energy balance may be associated with increased ghrelin levels. Voluntary weight loss following an exercise program (3 months) and an energy-deficit diet was followed by a significant compensatory increase in fasting plasma ghrelin levels in one study (Leidy *et al.*, 2004). In that study of 22 healthy young people (age 18-30 years) with BMI between 18 and 25 kg/m^2, subjects were randomized to three study groups: 1) weight-stable exercisers (exercises but body weight did not change significantly), 2) weight-loss exercisers (exercised and lost a significant amount of weight), and 3) control group (no exercise, weight maintenance diet) (Leidy *et al.*, 2004). This study found that ghrelin concentrations increased significantly from pre- to post-intervention (770 $\pm$ 296 [SD] to 1322 $\pm$ 664 pmol/l) in the weight lost exercisers but did not change significantly in the controls (403 $\pm$ 102 to 466 $\pm$161 pmol/l) or weight-stable exercisers (744 $\pm$ 399 to 646 $\pm$ 263 pmol/l) (Leidy *et al.*, 2004). In this study also, the change in fasting plasma ghrelin levels occurred after weight loss had occurred (Leidy *et al.*, 2004). Changes in plasma ghrelin levels were significantly correlated with changes in body weight in the exercising group ($r = -0.607$; $P<0.05$). The authors of this study suggested that in an attempt to maintain energy homeostasis, plasma ghrelin levels may be reduced in response to positive energy balance states (i.e. voluntary weight gain) to promote a reduction in food intake, but increased in response to negative energy balance states (i.e. voluntary weight loss) to promote an increase in food intake (Leidy *et al.*, 2004). Similarly, other studies have also shown that fasting plasma ghrelin concentrations decrease with weight gain in patients with anorexia nervosa and increase with weight loss in patients with obesity (Hansen *et al.*, 2002; Otto *et al.*, 2001).

Concurring with this, it has been previously demonstrated in humans (age 16-39 years) that mean fasting plasma ghrelin levels in subjects with Anorexia Nervosa and obesity were higher (630 $\pm$ 32 pg/ml, $P<0.05$) and lower (136 $\pm$ 18 pg/ml, $P<0.05$) respectively than that in normal weight young people (245 $\pm$ 35 pg/ml) (Rigamonti *et al.*, 2002). It may be that in these disease states, a new theoretical set-point for plasma ghrelin levels may have been reestablished at higher or lower levels in response to either a chronic negative energy balance or chronic positive energy balance state respectively (Leidy *et al.*, 2004).

Similarly, increased fasting ghrelin levels may also be seen in under-nourished older people who may have been exposed to prolonged periods of negative energy balance. This is supported by the findings of a recent small study in Adelaide (Sturm *et al.*, 2003). In their study, Sturm and colleagues classified the older women in their study as being under-nourished if they had a BMI $\leq$ 18.5kg/m^2 and/or at least two of the following risk factors: (a) a food intake < 1000 kcal/day (on a 3-day food diary); (b) serum albumin concentration < 30g/L; > 10% weight loss > 10% in the previous 6 months (Sturm *et al.*, 2003). In their study, they found that older under-nourished women (Table 2.3) had higher fasting plasma ghrelin levels that nourished older women (1320 $\pm$ 348 [SEM] pg/ml vs. 552 $\pm$ 132 pg/ml; P<0.1) (Sturm *et al.*, 2003). It is not clear if ghrelin levels were increased in under-nourished, older women, because of marked ghrelin resistance, increased concentrations of bio-inactive ghrelin or due to a compensatory response of plasma ghrelin to under-nutrition (similar to that seen when healthy young subjects exercised and lost weight in the study described earlier) (Leidy *et al.*, 2004). This is the only study to date that has explored the effects of nutritional status on fasting plasma ghrelin levels in older people. To confirm these results, and to investigate the effects of nutritional status on plasma ghrelin levels in men, the study described in Chapter 8 was performed.

Some but not all studies (as discussed above- (Cummings *et al.*, 2004)) have suggested that differences in lean and fat mass are associated with differences in fasting plasma ghrelin levels. For instance, in a recent study of 50 men and women with chronic obstructive airways disease (COAD) (age range 41-83 years), fasting plasma ghrelin levels were found to negatively correlate with fat-free mass (lean body mass) measured using bioelectrical impedance [r=-0.49; P<0.05] in a subset of 16 subjects (Itoh *et al.*, 2004). In this same study, fasting plasma ghrelin levels correlated negatively with the body mass index (BMI) [r=-0.38; P<0.01] (Itoh *et al.*, 2004). Fasting plasma ghrelin levels were significantly higher in underweight subjects than in normal weight subjects with COAD (272 $\pm$ 20 fmol/L vs. 195 $\pm$ 11 fmol/L; P<0.01) (Itoh *et al.*, 2004). In another larger study of 852 healthy Swedish

men (58 year olds), fasting plasma ghrelin levels were inversely associated with several measures indicating obesity and abdominal obesity [waist circumference: r=-0.46, P<0.001; waist to hip ratio: r= - 0.38, P<0.01; body fat: r= -0.53, P<0.01] (Fagerberg *et al.*, 2003). In this study, following multiple regression analysis, body fatness was found to be the strongest determinant of circulating ghrelin (Fagerberg *et al.*, 2003).

It is not clear as to what the effect of age is on plasma Ghrelin levels. In a small study of 60 volunteers (age range 19-64 years, BMI range 20-64 kg/m^2) where plasma ghrelin was measured frequently over 24 hours (standardized meals provided), multiple linear regression analysis found that age, weight, BMI, % fat, fat mass and lean mass were all not independently associated with the fasting plasma ghrelin levels (Purnell *et al.*, 2003). In contrast to this, two other small studies have reported that circulating ghrelin concentrations were 20% and 35% lower in healthy older people when compared to younger adults (Table 1.1) (Rigamonti *et al.*, 2002; Sturm *et al.*, 2003). In one study, Ghrelin levels were significantly (P<0.05) lower in older normal weight people (158 $\pm$ 29 [SEM] pg/ml) than younger normal weight people (245 $\pm$ 35 pg/ml) (Rigamonti *et al.*, 2002). In a second study, Ghrelin levels were non-significantly lower in healthy older people (552 $\pm$ 132 [SEM] pg/ml) than in younger nourished older people (664 $\pm$ 83 pg/ml)(Sturm *et al.*, 2003). In contrast to this, in a third study in 10 healthy people (age 29-1-63.7 years, BMI 22.0-30.0 kg/m^2), a multivariate regression analysis with 24-hour area under the curve (AUC) ghrelin as the dependant variable and age, BMI and total calories ingested over 24 hours as the independent variables found that age was the only variable that correlated significantly with ghrelin levels (P=0.045) (Cummings *et al.*, 2001). Age correlated positively with the 24-hour AUC ghrelin values (r= 0.701, P=0.022) (Cummings *et al.*, 2001). A limitation of these studies was that differences in body composition measurements (i.e. free fat mass and body fat mass), factors that may affect plasma ghrelin levels, were not adjusted for (Itoh *et al.*, 2004).

It is also not clear if fasting plasma ghrelin levels are different in men and women. Greenman and colleagues recently found in their small study of 24 healthy adults (13 men, mean age 55.3 ± 2.9 [SEM] years, range 26-74 years) that fasting plasma ghrelin levels were significantly higher in women compared to men (794 ± 198 [SEM] pg/ml vs. 397 ± 72 pg/ml; P=0.04) (Greenman *et al.*, 2004). This study had not adjusted for differences in waist/hip ratios [men 0.95 ± 0.03 [SEM] vs. female 0.79 ± 0.002]. As previously discussed, increased body fat may affect plasma ghrelin levels (Fagerberg *et al.*, 2003; Greenman *et al.*, 2004). In contrast to this study, in another study of 60 volunteers (described earlier), no significant differences were found between gender and ghrelin levels ([AUC] 417 ± 247 vs. 362 ± 290 pg/ml; P=0.19)(Purnell *et al.*, 2003).

Table 2.3 The relationship between plasma ghrelin, nutritional status and age.

[mean ± SEM]	Mean Age (year)	Body Mass Index (kg/m^2)	Fasting Ghrelin Levels (pg/ml)
(Rigamonti *et al.*, 2002)			
Healthy Old (n=7)	79.8 + 2.1	25.0 ± 1.7	158 ± 29
Healthy Young (n=12)	33.4 + 1.0	21.2 ± 0.9	245 ± 35
(Sturm *et al.*, 2003) - all women			
Old Under-nourished (n=8)	80.4 ± 2.6	16.9 ± 0.57	1320 ± 348
Old Nourished (n=8)	77.0 + 0.9	23.7 ± 0.8	552 ± 132
Young Nourished (n=8)	22.0 + 1.3	20.5 ± 0.4	664 ± 83

2.4.2 Sarcopenia and older people

Rosenberg coined the term sarcopenia in 1989 from a Greek word that means 'poverty of flesh' (Rosenberg, 1997). Sarcopenia refers to the decline in muscle mass and strength that may occur with healthy ageing and is thought to be both a process and an outcome (Roubenoff & Hughes, 2000). Changes in muscle, decreasing anabolic hormones, decreasing physical activity, impaired oral intake and changes in the cytokine system contribute to sarcopenia (Figure 2.1).

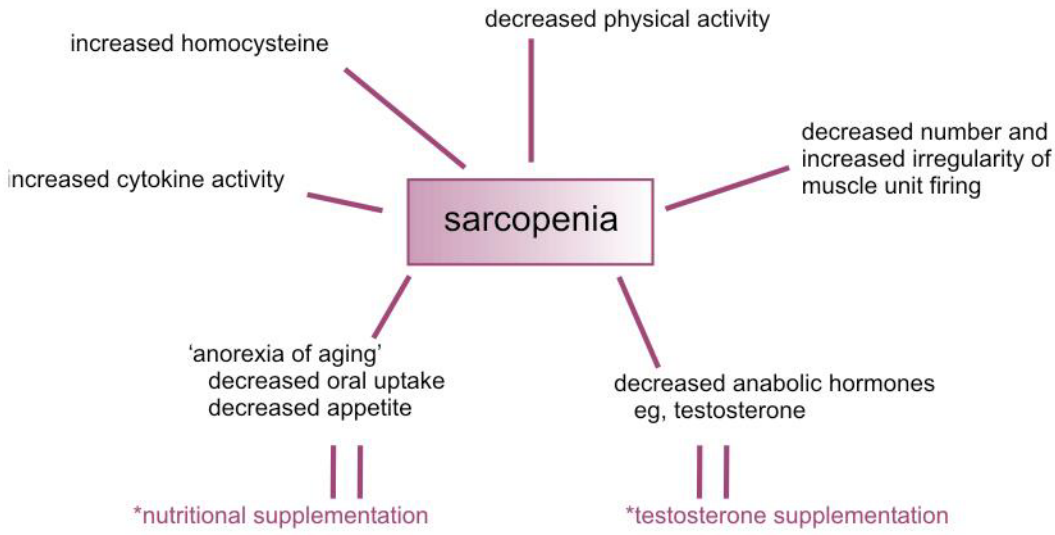


Figure 2.1 The multifactorial origin of sarcopenia [*possible interventions]

2.4.3 Non-physiological causes of under-nutrition in older people

Non-physiological factors (Table 2.4) are important in the pathophysiology of under-nutrition in older people. Brief important examples are discussed below. The studies described in Chapter 5 and 6 aimed to determine what non-physiological factors were associated with a poor nutritional status in South Australia (domiciliary care recipients) and Malaysia (shelter care residents).

Cognitive impairment

Older people with cognitive impairment are at increased risk of under-nutrition. In an observational study of 32 residents of a long term care facility with a confirmed diagnosis of Alzheimer's disease(AD), BMI was negatively associated with the baseline Neuropsychiatric Inventory: Nursing Home Version [NPI-NH] total score (r=-0.52, P <0.01), suggesting that subjects with low BMIs were more likely to have a higher frequency and severity of behavioral problems (White *et al.*, 2004). In another study, 21 consecutive days of investigator-weighed food intake collections were conducted on 25 subjects with likely AD residing at a home for the aged in Canada (Young & Greenwood, 2001). In that study, approximately 88% of participants did not meet targeted energy needs and so it was concluded that people with cognitive impairment were at significant risk of weight loss and under-nutrition (Young & Greenwood, 2001).

Depression

In one study which looked at 837 elderly patient admitted consecutively to a sub-acute care facility in the United States of America, the Geriatric Depression Scale score in malnourished patients (Mini Nutritional Assessment [MNA] <17; Maximum 30) were worse than in patients at-risk of malnutrition (17-23.5 on the MNA) [12.2 $\pm$ 6.4 [SD] vs. 8.7 $\pm$ 5.8; P=0.05] (Thomas *et al.*, 2002). The diagnosis of depression may be associated with reduced nutritional intake and treatment of depression may improve the nutritional status of older people (Kazes *et al.*, 1994). In another study, some under-nourished subjects (n=381) as per the DETERMINE Your Nutritional Health Checklist received lunch only (5 days/week) through an Elderly Nutrition Program in the United States of America whilst others received two meals per day for 5 days (breakfast and lunch; n=167) (Gollub & Weddle, 2004). This difference had occurred as a result of financial constraints to the program (Gollub & Weddle, 2004). The combined meals (lunch and breakfast) supplied two thirds of the recommended daily dietary intake (RDI) whilst lunch alone only provided

one third of the RDI (Gollub & Weddle, 2004). Subjects on the combined meals (6.26 ± 3.52) had less depressive symptoms based on a modified Geriatric Depression Scale (max score 16) than subjects on only one meal per day (7.45 ± 4.16; P=0.03) after at least 6 months of supplementation (Gollub & Weddle, 2004).

Social isolation

Older people who live alone are less likely to eat properly and are also likely to be at risk of under-nutrition. For example in an age-, sex- and race- matched study comparing 58 recently widowed women to 58 married women in Israel, weight loss was significantly higher in the widowed women in comparison to the control group (Shahar *et al.*, 2001). It may have been because, widowed women ate more meals alone, ate more commercial meals per week and fewer snacks and homemade meals and enjoyed eating less than married women (Shahar *et al.*, 2001).

Poverty

Being poor is also a risk factor for under-nutrition in older people. For example, a large cross-sectional survey conducted in the United States of America (n=709), found that an annual income of less than $USD 10000 (OR 4.12; 95% CI 1.98-8.58) and a reduction in food stamps (OR 2.02; 95% CI 1.23-3.32) were predictors of food insecurity (Nelson *et al.*, 1998).

Polypharmacy

Many drugs have adverse effects that can impair nutritional intake (table 2.4) and so polypharmacy is likely to put older people at risk of under-nutrition. In the same study described above, drug use (OR 2.11; 95% CI 1.66-5.08) was also a strong independent predictor of food insecurity (Nelson *et al.*, 1998).

Medical illnesses

Many acute and chronic illnesses are associated with reduced oral intake. For example, an elderly person who has suffered a stroke may have limited oral intake due to dysphagia. A person with severe chronic obstructive disease may suffer from malnutrition as they may be too breathless to eat, may have increased metabolic needs, may be depressed and may also have difficulty shopping and preparing their own meals. Older, under-nourished people, with other co-morbidities (medical illnesses) are more likely to experience adverse health outcome (i.e. death) than healthier older people. In one study, the odds of death in patients with concurrent protein energy malnutrition (PEM) and congestive heart failure were 36.2 (95% CI 6.7 – 196), relative to patients with neither congestion nor PEM (Cederholm *et al.*, 1995).

Poor dentition and oral disease

Nutritional status is also influenced by oral health. In a study on 51 subjects (mean age 83.7 years) in Finland, dry mouth and eating problems (subjective assessment) were found to be significantly associated to lower MNA scores ($p = 0.049$ and $p = 0.015$, respectively) (Soini *et al.*, 2003). Complimentary to this, subjects with natural functioning dentition had higher BMI scores ($p = 0.049$) (Soini *et al.*, 2003).

Table 2.4 The many well-known non-physiological causes of under-nutrition in the elderly (Chapman, 2004; MacIntosh *et al.*, 2000).

Non-physiological causes of anorexia in older persons
Social factors
poverty
inability to shop
inability to prepare and cook meals
inability to feed oneself
living alone, social isolation, or lack of social –support network
failure to cater to ethnic food preferences
Psychological factors
alcoholism
bereavement
depression
dementia or Alzheimer's disease
cholesterol phobia
Medical factors (mediated through anorexia, early satiation, malabsorption, increased metabolism, cytokine-mediated and impaired functional status)
cancer
alcoholism
cardiac failure
chronic obstructive airways disease
infection
dysphagia
rheumatoid arthritis
Parkinson's disease
hypermetabolism (e.g., hyperthyroidism)
malabsorption syndromes
gastrointestinal symptoms: dyspepsia, atrophic gastritis, vomiting, diarrhoea,
constipation
poor dentition
medications
nausea/vomiting – antibiotics, opiates, digoxin, theophylline, non-steroidal anti-inflammatory agents (nsa
anorexia- antibiotics, digoxin
hypogeusia- metronidazole, calcium channel blockers, angiotensin –converting enzyme inhibitors (acei), metformin
early satiety- anticholinergic drugs, sympathomimetic agents
reduced feeding ability- sedatives, opiates, psychotropic agents
dysphagia –potassium supplements, NSAIDs, biphosphonates, prednisolone
constipation- opiates, iron supplements, diuretics
diarrhoea- laxatives, antibiotics
hypermetabolism- thyroxine, ephedrine

Chapter 3

Screening for and diagnosing under-nutrition in older people

3.1 Introduction

A number of techniques have been used to determine nutritional status in older people. However, there is no consensus about the best way to diagnose protein energy malnutrition (PEM), or screen for those at risk of under-nutrition. In-depth assessment of nutritional status usually involves some combination of: 1) dietary intake evaluation, 2) anthropometric measures, 3) laboratory markers, and 4) body composition analysis. It is unlikely that the use of a single measure can adequately screen or diagnose PEM. It is more likely that a combination of methods, preferably tailored to the individual person's needs, is required to diagnose under-nutrition. For this reason, in the study described in Chapter 7, several measures were combined to form the Standard Nutritional Assessment (SNA, Table 7.1) grid. The benefits and limitations of some of these assessment methods are discussed here. Nutritional screening for use in the community at-large, needs to be cheap, quick, easily administered, reliable, sensitive and specific. In this Chapter also, the benefits and limitation of some commonly used nutritional screening tools, including those utilized and assessed by the author in the studies described in Chapters 5-8, are addressed.

3.2 Assessment of dietary intake

Best performed by trained dietitians are four methods to obtain information regarding food habits and food consumption: 1) food records (diaries), 2) the 24-hour recall method, 3) the Food Frequency Questionnaire (FFQ) and 4) diet histories (Omran & Morley, 2000a). No one method has been established as clearly superior (Omran & Morley, 2000a). The 24-hour recall method and food diaries are discussed here as they were used to estimate food intake in the study described in Chapter 8.

3.2.1 The 24 hour recall method

The 24-hour recall method requires participants to recall the type and portion size of the food consumed in the preceding 24 hours. It's accuracy may be affected by short-term memory difficulties, which are more common in elderly than younger subjects (Omran & Morley, 2000a). The best results are often obtained when this is performed by professionals trained in dietetics, as they are able to prompt subjects to estimate portion size accurately and ask probing questions regarding commonly used snacks to refresh the subject's memory [multiple pass] (Omran & Morley, 2000a). Another limitation of this method is that it does not allow for day-to-day variations in food intake (Omran & Morley, 2000a). For example, in a study of 587 adults, the food intake varied significantly over the week with the greatest intake of meat, carbohydrate and alcohol occurring over the weekend (Jula *et al.*, 1999).

Validity studies comparing this method to food records have shown mixed results highlighting the limitations of this dietary evaluation method (Omran & Morley, 2000a). In one study, there was a weak correlation between 24-hour urine nitrogen excretion (gold standard) and dietary nitrogen as estimated from the 24-hour food recall method and the FFQ, in the order of 0.01 to 0.5 (Bingham *et al.*, 1995). The 7 day food diary and weighed records were found to be more accurate than the 24-hour food recall method (Bingham *et*

al., 1995). Similar findings were seen in a more recent study, when weighed records had the highest correlation [r=0.78-0.87] with biological variables (eg. urine nitrogen excretion), whilst the 24-hour recall and the food frequency questionnaire recorded the lowest [r=0.10-0.27] correlation with biological variables (Bingham *et al.*, 1997).

The 24-hour recall method was used to assess food intake in a group of older under-nourished people who were enrolling into an intervention study and the results derived were also used in the study described in Chapter 8. That randomized control intervention trial involved the administration of many different (some lengthy) assessment tools at baseline, 6 and 12 months. The 24-hour recall method, which is the quickest method of food intake estimation, was chosen to be used in that study despite it's limitations because of it's simplicity. Investigators recorded the details of all food and beverage items consumed over the preceding 24-hour period based on interviews conducted with the subject's in their own homes. Subjects were asked to estimate portion size using measure cups or spoon measures. Subjects were also asked for recipes used for meals as well as the method of cooking of foods. Individual food items recorded were entered into and the dietary energy intake (kJ) was calculated using a computer software program Foodworks version 3.1 (Xyris Software, Australia, Pty Ltd).

3.2.2 Food diaries (records)

Motivated and literate subjects are expected to record all food and beverages consumed in type and amount, estimated by weight, for a period of time (Omran & Morley, 2000a). This method has several advantages. In their study, Bingham and colleagues found that there was a strong correlation of 0.87 between 24 hour urine nitrogen excretion and dietary nitrogen estimated from 7 day weighed food records (Bingham *et al.*, 1995). Other advantages of this method are that it takes into account day-to-day variation in food intake and it's limited dependence on recall (memory) (Omran & Morley, 2000a). Recording food intake over a shorter period (i.e. 3 days) may have better accuracy than food records over a longer period (i.e. 7 days). In one study of 587 adults where it was clearly shown that food intake varied

over the week (i.e. greater intake on weekends compared to weekdays), there was a very strong correlation between the shorter 5-day food record and the 7-day food record (r=0.96-0.98) (Jula *et al.*, 1999). It has also been previously shown that the accuracy of food records decline in the later part of a week (5th, 6th and 7th days) and so shorter periods of record (5 days or less) may be preferable (Gersovitz *et al.*, 1978; Omran & Morley, 2000a). It has been proposed that the 3-day food record method may have a lower error rate. In a study comparing the 24-hour recall method, 3-day food diary and 5-day food frequency method to observed intake, in 58 girls aged 9 and 10 years, the 3-day food diary recorded the lowest percentage of absolute error (12-22%) in comparison to the 24-hour recall (19-39%) and the 5-day food frequency method (20-33%) (Crawford *et al.*, 1994).

The 3 day diary was used in the study described in Chapter 8 to assess the food intake of healthy nourished volunteers because it was shorter than the 7-day food diary and so, less taxing on the volunteers encouraging better compliance with record keeping. We had opted to use the 3-day food diary as we were fairly certain that these healthier older people would be able to reliably complete the diary as opposed to the frail older people in the intervention study who were asked to complete a 24 hour food recall record instead. The 3-day food diary would more accurately reflect food intake than the 24-hour food recall diary. Subjects were asked to record, in a diary that was provided, the details (including weight) of all food and beverage items consumed over 3 days. When it was impractical to weigh the foods or beverages, subjects were asked to estimate portion size using measure cups or spoon measures. Subjects were also asked to record recipes used for meals as well as the method of cooking of foods in the diary. Individual food items recorded were entered into and the dietary energy intake (kJ) was calculated using a computer software program Foodworks version 3.1 (Xyris Software, Australia, Pty Ltd).

The main disadvantages of this method is that it is cumbersome and time consuming for the subject and also it requires some training in terms of estimating portion size (Omran & Morley, 2000a).

3.3 Anthropometric measurements

In this section, the use of the body mass index (BMI), as an anthropometric measure to predict nutritional risk is discussed. Also, we discuss the use of unintentional change in weight over time as a predictor of change in nutritional status. Weight measurement is the most basic anthropometric measure available and serial monitoring of weight change is very simple to perform. These 2 measures (low BMI and unintentional weight loss over time) have been shown to strongly predict the mortality and morbidity risk within various settings (Bo *et al.*, 2003; Maurer *et al.*, 2002; Somes *et al.*, 2002). These 2 measures were used in the studies described in Chapters 5-8 to screen or diagnose nutritional risk. Detailed description of other anthropometric measures are described elsewhere (Omran & Morley, 2000a).

3.3.1 Body Mass Index (BMI)

BMI (kg/m^2) is calculated by dividing body weight (kg) by height^2 (m^2). BMI estimation is frequently performed in clinical practice but has several limitations and these are discussed below. Nevertheless, it remains one of the cheapest and easiest method of screening for under-nutrition in older people and so should be utilized. Healthy BMI ranges are likely to vary with age, sex and ethnicity and as yet there is no consensus as to the best normative values for various population groups. However, there is strong evidence that a reduced BMI in an older person is associated with increased mortality and morbidity and this is discussed below (Bo *et al.*, 2003; Maurer *et al.*, 2002; Somes *et al.*, 2002). The BMI was estimated in the studies described in Chapter 6 - 8 as part of the Mini Nutritional Assessment (MNA-Appendix 1), Standard Nutritional Assessment (SNA-Table 7.1) and rapid screen. The BMI was also used as an objective comparator for the evaluation of the translated 'DETERMINE Your Nutritional Health Checklist' (NHC) in the study described in Chapter 5.

As stated earlier, at present there is no consensus on the best cut-off values to be used for the diagnosis of under-nutrition in older people, especially in Australia and Malaysia. The

Nutrition Screening Initiative (NSI) had previously defined that the normal BMI for the American population is between 22 and 27kg/m^2 (Committee on Diet and Health *et al.*, 1989). The Nutrition Screening Initiative was a collaborative effort of the American Dietetic Association, the American Academy of Family Practitioners, and the National Council on the Ageing Inc to aid in the evaluation of the nutritional status of older persons in the United States of America (The Nutrition Screening Initiative, 1994). As the composition of the Australian population is very similar to the American population, we elected to us a lower cut-off value of 22 kg/m^2 in the SNA and rapid screen, similar to the NSI, to define nutritional risk in the study described in Chapters 7 and 8. In keeping with this, in an Australian study comparing the MNA to the Subjective Global Assessment, the authors similarly recommended that the BMI range for healthy older adults should be 22-27 kg/m^2 (Barone *et al.*, 2003; Bartlett, 1998). This lower cut-off (BMI < 22kg/m^2) has also been associated with poorer health outcomes. In their prospective cohort study of 586 hospitalized patients ($\geq$ 3days), Sullivan et. al. found that the adjusted relative risk of a life threatening complication for a BMI < 22kg/m^2 (15.4%) was 7.1 (95% CI 2.0-25.7) in comparison to BMI $\geq$ 22 kg/m^2 (4%) (Sullivan *et al.*, 2002). Similar cut-off values have been used in other studies (Barone *et al.*, 2003; Sullivan *et al.*, 2002).

This normal range is likely to vary as the ethnicity of the study population changes. Several studies have shown that Asian populations have a higher body fat percent at similar BMI, compared with Caucasian/European populations (Deurenberg *et al.*, 2002; Ministry of Health Malaysia, 2003; Wang *et al.*, 1994). For this reason, in Malaysia, the healthy BMI range for adult Malaysians has been determined to be between 18.5 and 22.9 kg/m^2 (Ministry of Health Malaysia, 2003). Therefore, when a Malaysian population was studied in Chapter 5, a lower cut-off value of <18.5 kg/m^2 was used to define nutritional risk (Ministry of Health Malaysia, 2003).

There is good evidence to support the fact that a low BMI in an older person is associated with increased mortality and morbidity (Bo *et al.*, 2003; Maurer *et al.*, 2002; Somes *et al.*,

2002). In a restrospective study reviewing complication rates in a population of older patients (n=1448, >75 years older) admitted for cardiac surgery in the United States, subjects with BMI < 23kg/m^2 had a higher risk of experiencing serious post-operative complications (Maurer *et al.*, 2002). In the large Systolic Hypertension in the Elderly Program (SHEP), 4736 participants 60 years and older were studied and those with a BMI values less than 23.6 kg/m^2 had a 35% increased odds of mortality in comparison to those with BMI between 23.6 (inclusive) and 28 kg/m^2 (Somes *et al.*, 2002).

The result of recent large studies (i.e. SHEP trial) contradict previously held beliefs that a U-shaped curve model of survival to BMI (i.e. Framingham study) exists (Harris *et al.*, 1988; Somes *et al.*, 2002). These new studies suggest that an increased BMI in older people is not associated with increased risk of death (Stevens *et al.*, 1998). For instance, in the SHEP trial, the lowest mortality rates (6%) were seen at the highest BMI quintiles (BMI $\geq$ 31.0 kg/m^2) and the highest mortality rate (9.4%) was seen when the BMI values were < 23.6 kg/m^2 (Somes *et al.*, 2002). In another large study of over 320,00 people followed for 12 years, Stevens and colleagues found that increasing BMIs was not associated with increased mortality in older age groups (men $\geq$ 85 years, female $\geq$ 75 years) (Stevens *et al.*, 1998). Similarly, in another study of 4208 people (age $\geq$ 65 years), Taylor and Ostbye found that BMI and mortality had a 'reverse-J' relationship for both men and women with the highest mortality rate found among persons who were very light (<18.5kg/m^2) and the lowest mortality being found in those with a BMI between 30 and 34.9 regardless of age (Taylor & Ostbye, 2001). This relationship was totally reversed when the BMI at age 50 was analyzed (Taylor & Ostbye, 2001). Therefore, BMIs commonly associated with being over-weight or obese in middle age may actually be protective in older people and this requires further study as this may have public health policy implications in ageing nations, especially with increasing awareness with regards to the dangers of obesity in younger age groups. Misconception amongst older people that being thin is healthy may need to be addressed sooner rather than later.

3.3.2 Unintentional weight loss

Unintentional weight loss occurs frequently in the elderly, and the loss of body weight is disproportionately lean body mass (sarcopenia), as opposed to fat mass (Liu *et al.*, 2002; MacIntosh *et al.*, 2000; Somes *et al.*, 2002; Wedick *et al.*, 2002). The unintentional loss of body weight is strongly associated with an increased risk of mortality (Liu *et al.*, 2002; Somes *et al.*, 2002; Wedick *et al.*, 2002). In one study looking at patients discharged from hospital, weight loss > 10% of their body weight in the 12 months before discharge was strongly associated with mortality at 12 months after discharge [RR of 2.31 (95% CI 1.35-3.94)] (Liu *et al.*, 2002). In fact, in the large SHEP trial (Systolic Hypertension in The Elderly Program), it was shown that after adjustment for baseline BMI and covariates, a weight loss of >1.6 kg/year was associated with increased mortality with an odds ratio of 4.9 (95% CI: 3.5-6.8) in comparison to the reference group (i.e. weight change –0.7 to 0.5 kg/year) (Somes *et al.*, 2002). A 'U' shaped curve was also seen (Figure 1 and 2) with the extremes of weight change being associated with the highest mortality (Somes *et al.*, 2002). The combination of weight loss and a low BMI put subjects at greatly increased risk of death (Somes *et al.*, 2002).

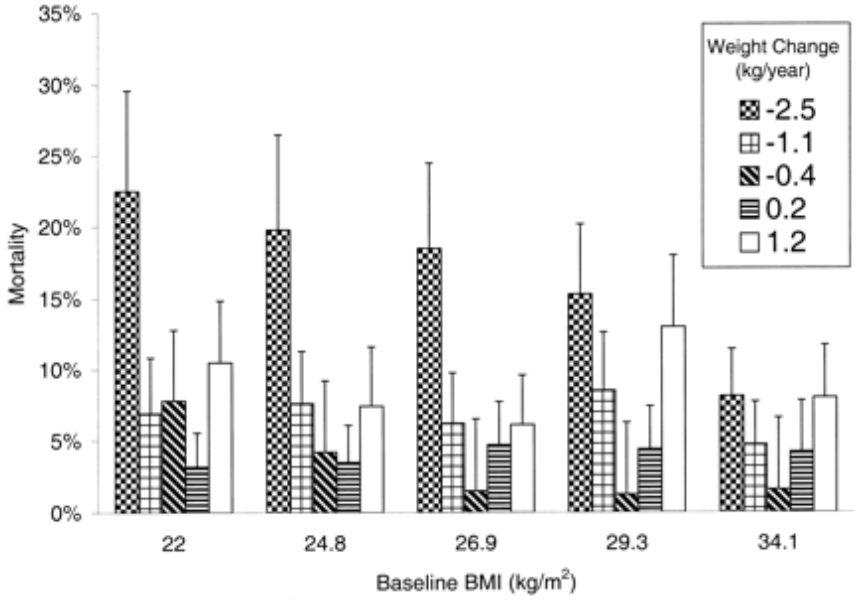


Figure 3.1 Mortality risk by baseline body mass index (BMI) and average annualized weight change (quintile medians displayed), Systolic Hypertension in the Elderly Program, 1984–1990. The error bars represent 95% confidence intervals (Somes *et al.*, 2002). [Reproduced with permission]

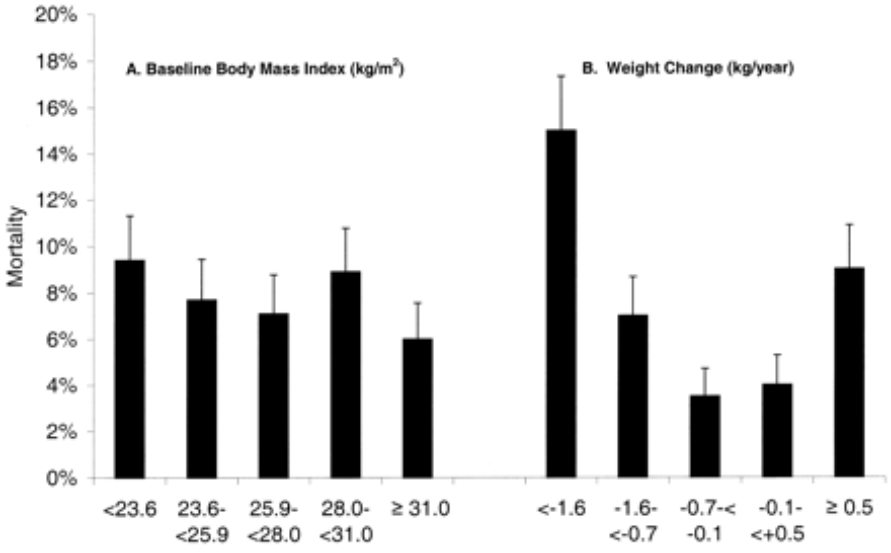


Figure 3.2 Mortality risk by baseline body mass index (A) and by average annualized weight change (B), Systolic Hypertension in the Elderly Program, 1984–1990. The error bars represent 95% confidence intervals (Somes *et al.*, 2002). [Reproduced with permission]

3.4 Laboratory markers of under-nutrition

Laboratory markers potentially provide an objective method of defining nutritional risk. The use of only one specific marker is unlikely to provide a satisfactory diagnosis in all older people as each of these marker has potential limitations. There are many laboratory markers that that may reflect protein energy malnutrition and these include: serum proteins (albumin, pre-albumin), urine creatinine, immune function parameters (total lymphocyte count), serum cholesterol and haemoglobin (Omran & Morley, 2000b). Serum albumin, total lymphocyte count and total serum cholesterol were used as part of the standard nutritional assessment (SNA- Table 7.1, described in 7.3.1), which was devised for use as the in-depth nutritional assessment comparator for the study described in the study described in Chapter 7, and so these are described below. These markers were also selected because they are performed frequently in clinical practice for evaluation of other common medical complaints. There is evidence for their utility and this is described here. Detailed description of other laboratory measures are available elsewhere (Omran & Morley, 2000b).

3.4.1 Albumin

Albumin has a long circulating half-life of approximately 18 days (Omran & Morley, 2000b; Rothschild *et al.*, 1972). Serum levels of albumin reflect the net balance of hepatic synthesis (12-15 g/d), plasma distribution, and protein loss. Over 60% of albumin is present in the extravascular pool and can be mobilized into the intravascular space in periods of stress due to surgery or infection. With ageingageingageing, there may be a small decline in serum albumin of up to 0.8g/l per decade after the age of 60 years, although this is not certain (Omran & Morley, 2000b; Rall *et al.*, 1995). Serum albumin levels often decrease acutely following hospitalization for an illness and this is thought to be due to release of cytokines and/or the adoption of the recumbent position for prolonged periods (Omran & Morley, 2000b). Cytokines are produced during and participate in inflammatory processes and are the chief stimulators of the production of many acute-phase proteins (e.g.

fibrinogen) (Gabay & Kushner, 1999). It is not clear what functional advantages may arise from decreases in plasma concentrations of negative acute-phase proteins (i.e. albumin) (Gabay & Kushner, 1999). Possibly, there may be a need to divert available amino acids to the production of other more necessary acute-phase proteins for host defense (Gabay & Kushner, 1999). Chronic alteration in serum albumin levels can also occur with diseases that reduce hepatic production of albumin (i.e. cirrhosis or heart failure) and diseases that increase peripheral protein loss (i.e. nephrotic syndrome). For this reason, the use of serum albumin levels alone to diagnose under-nutrition is not recommended.

Nevertheless, as many studies have shown a strong relationship between hypoalbuminemia and increased mortality, most in-depth assessment of nutritional status include an assessment of serum albumin levels (Omran & Morley, 2000b). For review see Omran and Morley (Omran & Morley, 2000b). In the MacArthur Research Network on Successful Ageing Community Study, subjects who were hypoalbuminemic (≤ 38g/l) [normal serum cholesterol levels] had an adjusted relative risk (RR) 1.84 (95% CI 0.80-4.29) of dying within 3 years and an adjusted RR of 1.33 (95% CI 0.77-2.30) of dying within 7 years compared with those with normal serum albumin values (Reuben *et al.*, 1999). This association with increased risk of mortality was amplified when subjects were both hypoalbuminemic (≤ 38g/l) and hypocholesterolemic (≤ 4.33 mmol/l). Subjects who were both hypoalbuminemic and hypocholesterolemic had an adjusted RR of 3.62 (95% CI 1.07-12.20) of dying within 3 years and an adjusted RR of 3.52 (95%CI 1.39-8.96) of dying within 7 years when compared to subjects with normal serum and cholesterol values (Reuben *et al.*, 1999). This large cohort study of 1192 community dwelling older people (age 70-79 years) with good physical and cognitive function was conducted over a period of 7 years (Reuben *et al.*, 1999). 937 subjects had blood chemistries performed in 1988 and had follow-up dates in 1991 and 1995 (Reuben *et al.*, 1999). In another study, pre-operative hypoalbuminemia (<25g/l) was associated with increased risk of death and was also an independent predictor of post-operative (cardio-thoracic) complications (Engelman *et al.*,

1999). Operative mortality was highest in those with concomitant hypoalbuminemia and low BMI (<20kg/m^2) (Engelman *et al.*, 1999). The exact serum albumin cut-off value that should be used in older people has not been clearly defined and varying cut-off values have been used in various studies with the most common value being < 35 g/l (Azad *et al.*, 1999; Engelman *et al.*, 1999; Reuben *et al.*, 1999; Reuben *et al.*, 1997; Thomas *et al.*, 2002).

3.4.2 Total Lymphocyte Count (TLC)

Malnutrition is not only a major risk factor for infection, but because of an increase in metabolic demand and its duration, infection is also an important cause of malnutrition (Gavazzi & Krause, 2002). There is still no consensus as to what happens to the TLC with ageing (Omran & Morley, 2000b) (Krause *et al.*, 1999; Mazari & Lesourd, 1998). TLC may decrease at times of stress and with tumors, sepsis and steroid use (Omran & Morley, 2000b). Total plasma lymphocyte count (TLC) decreases with progressive malnutrition and correlates with mortality and morbidity in hospitalized patients (Omran & Morley, 2000b). Under-nutrition in older people results in decreased lymphocyte proliferation and impaired cell-mediated immunity (Lesourd, 1997). TLC have been used in many studies as a nutritional markers often in combination with other anthropometric, dietary and biochemical markers (Azad *et al.*, 1999; Millen *et al.*, 2001; Sungurtekin *et al.*, 2004). Up to a four-fold increase in mortality has been reported with a TLC of less than 1500/mm^3 (Omran & Morley, 2000b; Seltzer *et al.*, 1979). In another study, a pre-operative lymphocyte count of less than 1500/mm^3 was associated with a three times higher frequency of healing complications post knee or hip replacement surgery (Marin *et al.*, 2002). Based on these literature evidence, a cut-off value of TLC < 1500/ mm^3 was chosen as one of the parameter indicating an impaired nutritional status in the SNA (Table 7.1) which was used in Chapter 7.

3.4.3 Total cholesterol

Total plasma cholesterol concentrations increase with age in healthy individuals, reaching a peak between the sixth and ninth decades and decreasing afterwards (Omran & Morley, 2000b; Tietz *et al.*, 1992). It is unclear if low total serum cholesterol is a marker of poor nutrient intake (Noel *et al.*, 1991; Omran & Morley, 2000b; Sullivan *et al.*, 1999) or a nonspecific feature of poor health status (Goichot *et al.*, 1995; Rosenthal *et al.*, 1998). Low cholesterol values (e.g. <4.2 mmol/l [$\pm$ hypoalbuminemia, $\pm$ low BMI]) have been shown to be associated with increased mortality and morbidity (e.g. functional decline) in older people in hospitals (Noel *et al.*, 1991; Onder *et al.*, 2003; Sullivan *et al.*, 1999), nursing homes (Verdery & Goldberg, 1991) and community settings (Casiglia *et al.*, 2003; Reuben *et al.*, 1999; Schalk *et al.*, 2004) in many studies. For example, in a recent longitudinal study of 3282 elderly subject older than 65 years conducted in Italy, overall mortality was higher with lower total serum cholesterol and this association was particularly evident in women and amplified by the co-existence of a low BMI (Casiglia *et al.*, 2003). Total cholesterol had a protective role in women ($P = 0.0001$) (Casiglia *et al.*, 2003). In women, there was –0.2% risk reduction for every mmol/l total serum cholesterol increase (Casiglia *et al.*, 2003). In that study also, men and women with total cholesterol levels < 4.66 mmol/l and BMIs < 25 kg/m^2 had an increased relative risk for overall mortality of 1.38 and 1.39 respectively in comparison to men and women with total cholesterol levels $\geq$ 4.66 mmol/l and BMIs $\geq$ 25kg/m^2. A decrease in cholesterol levels after admission to hospital was associated with more complications and increased length of stay in another study (Noel *et al.*, 1991). A larger Italian study (Italian Longitudinal Study on Ageing) found that subjects with higher serum total cholesterols (> 4.9mmol/l) were at lower risk of mortality than those with lower serum cholesterol levels even after adjustment for multiple confounders such as pre-existing medical illnesses and frailty markers (Brescianini *et al.*, 2003). Interestingly, most subjects with very low serum total cholesterol levels were not on cholesterol lowering medications (Brescianini *et al.*, 2003). In their study using a detailed nutritional grid to

evaluate various nutritional screening tools, Azad et. al. included serum cholesterol measurements and used a cut-off value of $\leq$ 4.15 mmol/l as a marker of under-nutrition (Azad *et al.*, 1999). Based on this study, we arbitrarily opted to use a lower cut-off value of $\leq$ 4.15 mmol/l as an indicator of malnutrition in the SNA (Table 7.1) which we devised for use in the study described in Chapter 7 (Azad *et al.*, 1999).

3.5 Body composition assessment

3.5.1 Background

Weight loss can be due to either a loss of body fat mass or fat free mass or a combination of both (Omran & Morley, 2000a). There are good reasons for including objective measurements of fat free mass (FFM) and body fat mass (BFM) in the nutritional assessment of older people (Kyle *et al.*, 2001c). Age-related loss of muscle mass and muscle strength or sarcopenia is common in the elderly and is associated with disability, loss of independence and morbidity (Baumgartner *et al.*, 1998). Nutritional depletion in older people may be missed as weight stability may mask sarcopenia (Gallagher *et al.*, 2000). Older subjects are known to have lower FFM and appendicular skeletal muscle mass (ASMM) and higher body fat than younger people (Haapanen *et al.*, 1997; Kyle *et al.*, 2004; Kyle *et al.*, 2001a; Williamson *et al.*, 1991).

3.5.2 Methods for estimating body composition

Several methods exist for estimating body fat (FM) and fat free mass (FFM). For instance, the use of triceps skinfold (TSF; measured by a caliper) and the measurement of the mid arm circumference (MAC; using a flexible tape) provides an approximate assessment of fat stores and muscle mass (Omran & Morley, 2000a). Bioelectrical impedance (BIA) on the other hand is a non-invasive method to determine body composition based on the resistance of FFM to a high frequency, low – amplitude, alternating electric current that is inexpensive, safe, quick and highly reliable (Omran & Morley, 2000a). Computed Tomography (CT) has the ability to visualize subcutaneous and intra-abdominal fat whilst Magnetic Resonance Imageing (MRI) has the ability to also provide accurate information regarding fat distribution and muscular changes with age (Omran & Morley, 2000a). Dual energy X-ray absorptiometry (DEXA) is also an important, non-invasive, method for quantifying changes in bone and soft tissue with age (Omran & Morley, 2000a). The underwater weight remains the gold standard against which all other measures are validated

(Omran & Morley, 2000a). DEXA was used in the study described in Chapter 8 to estimate FFM and FM. Therefore, this method is described in greater detail here. Omran and colleagues have discussed the other methods for assessing body composition in their published review (Omran & Morley, 2000a).

The dual energy X-ray absorptiometry method

Dual energy X-ray absorptiometry (DEXA), bioelectrical impedance analysis (BIA) and air displacement plethysmography are frequently used, mainly in research settings, as non-invasive methods for estimation of body composition, and are said to have similar accuracy (Kyle *et al.*, 2002a).

In Chapter 8, DEXA (Norland TM densitometer XR36, Norland Medical Systems, Fort Atkinson, Wisconsin, USA) was used to assess FFM and FM at baseline in under-nourished and healthy older people. The DEXA method involves subjects lying supine on a scanning bed with minimal clothing whilst a low dose x-ray scans their body. Individuals are scanned at 130mm/s using a scan resolution of 6.5 x 13mm for approximately 20 minutes. The Norland XR36 DEXA which uses version Revision 3.9.4 software, defines the head region as the area from the top of the head to the bottom of the cervical vertebra; the trunk region from the top of the clavicle bone to the bottom of the pubic bone; the abdominal region from the bottom of the rib cage to the bottom of the pubic bone. The leg region is defined as the area from the spinal line of the femur bone to the tip of the distal phalanx bone of the foot. The arm region on the other hand is defined as the area from the top of the humerus bone to the tip of the distal phalanx bone of the hand. The left and right leg and arms are analyzed separately, and then both masses are summed to calculate the total mass of the legs and arms, respectively. Total fat and lean mass were calculated as the sum of all these respective components.

DEXA directly measures percentages of fat and lean soft tissue and compares the ratio of photon attenuation and low and high energy beams (Rst) to experimental ratio values of fat and lean soft tissue, established by calibration with phantoms equivalent to 100% fat and 100% lean soft tissue (Blake, 1999; Genton *et al.*, 2002). DEXA measurements are quick, non-invasive, precise and largely operator independent (Genton *et al.*, 2002). They deliver a radiation exposure of 2 to 5 microSv, which is low in comparison to background radiation of 5 to 7 microSv (Genton *et al.*, 2002; Madden & Morgan, 1997).

Limitations of the DEXA method

Several limitations with DEXA arise from the need to make certain assumptions: 1) there is the same amount of fat over bone as over neighbouring bone-free tissue; 2) that designed calibration phantoms correct for beam hardening [increased tissue thickness interferes with Rst estimation]- may not be true in very obese individuals; and 3) that there is constant hydration and electrolyte content of lean soft tissue (Genton *et al.*, 2002). Changes in body positioning on the examination table may also affect body composition measurements by DEXA.

A recent Australian study compared DEXA-derived [NorlandXR36] skeletal muscle mass (SMM) values [1.333 (total arm and leg skeletal mass)] with those calculated by a nuclear method (TBK) from total body potassium (TBK) and total body nitrogen (TBN) using an equation (SMM= [0.188 x TBK] + [0.00183 X TBN]) in 75 older Australian (aged 51-84 years) and found that the DEXA could be used confidently (men r=0.83, women r=0.87; $P<0.0001$ for both) to estimate SMM in older people (Hansen *et al.*, 1999; Wang *et al.*, 1996). DEXA measurements, however, were found to underestimate FFM estimates in older women in comparison to FFM determined by TBK (37.4kg vs. 41.1kg; $P<0.01$), possibly because of software modeling inaccuracies in defining truncal fat (Hansen *et al.*, 1999). It is thought that in individuals with increased upper body adipose tissue (i.e. obese older people), DEXA may underestimate % body fat (Clasey *et al.*, 1999). Therefore, caution was recommended when interpreting these values in older women (Hansen *et al.*, 1999).

In another study comparing % body fat mass (FM) estimation by DEXA against a 4-compartment model (validated against neutron-activation analysis), the mean difference between % fat estimated by DEXA and the 4-comp model ranged from 0.9-4.5%, with the largest difference seen in younger women (mean difference –4.5%; P<0.01) (Clasey *et al.*, 1999). The fact that DEXA assumes constant hydration state for the FFM of all individuals may have contributed significantly to the large individual errors in the estimation of % fat by DEXA in this study (Clasey *et al.*, 1999). Therefore, changes in the hydration status of older people may possibly affect body composition results (Clasey *et al.*, 1999).

Changes in body positioning on the examination table may also affect body composition measurements by DEXA due to subtle changes in regional tissue depth and fat distribution (Lambrinoudaki *et al.*, 1998). In one study, the DEXA estimated (fan beam mode) mean fat tissue mass (FTM) and mean lean tissue mass (LTM) with the head excluded, was significantly different in the prone and supine position (FTM supine vs. prone, 25.129 $\pm$ 10.445 vs. 24.030 $\pm$ 10.388 kg, P=.0001; LTM supine vs. prone, 37.309 $\pm$ 9.357 vs. 38.246 $\pm$ 9.150 kg, P=.0001) (Lambrinoudaki *et al.*, 1998).

3.5.3 Body composition and nutritional status

The inclusion of body composition analysis may aid the assessment of nutritional risk in older people. In their study of 995 patients admitted consecutively to a hospital in Switzerland, Kyle et al. found that 73% of patients with a BMI < 20kg/m^2 and 31% of patients with a BMI between 20 and 25kg/m^2 fell below the 10th percentile for FFM [BIA assessment] (Kyle *et al.*, 2001c). The use of a BMI cut-off value of < 20kg/m^2 (17.3%) or a serum albumin value < 35g/l (14.9%) as a marker of under-nutrition under-estimated the percentage of patients who had a very low FFM (31%). FFM was also significantly lower in severely under-nourished (by subjective global assessment) patients and moderately undernourished female patients and body fat was significantly higher in well- nourished patients in comparison to healthy aged-matched volunteers (Kyle *et al.*, 2002c).

3.5.4 Population percentile distributions

Percentile distributions for FFM have been formulated for use in countries such as Switzerland (Caucasian population) and Japan (Japanese population) (Ito *et al.*, 2001; Kyle *et al.*, 2002a; Kyle *et al.*, 2001b). Percentile ranks such as the 10^{th} and the 90^{th} percentiles can be used to define nutritional depletion and obesity (Kyle *et al.*, 2003). Body composition is known to vary with age, sex and population specifics (Craig *et al.*, 2001; Kyle *et al.*, 2002a; Molarius & Seidell, 1998). It can be expected that over time, the population distribution will change (ethnicity, lifestyle etc.) and with this, reassessment of cut-off values must be made (Kyle *et al.*, 2002a). Unfortunately, presently, there are no known normative data for use in an Australian population.

3.5.5 Height adjusted body composition measures may be better

It has been suggested that height-normalized indices of body composition (adjusted for $height^2$ - kg/m^2) should be used in preference to other measurements in the assessment of nutritional status (Kyle *et al.*, 2003; VanItallie *et al.*, 1990). The fat free mass index (FFMI) and the body fat mass index (BFMI) have the advantage of being height adjusted (VanItallie *et al.*, 1990). FFM values decline in men and women from 50 years of age onwards (Ito *et al.*, 2001). It is thought that this decrease in FFM is partly caused by the shorter height of older individuals (Ito *et al.*, 2001; Kyle *et al.*, 2001b). In contrast to this, the FFMI is said to be stable until the ages of 75 years before declining thereafter (Kyle *et al.*, 2003; Schutz *et al.*, 2002). In the First National Health and Nutrition Examination Survey (NHANES1) which was conducted in the United States between 1971 and 1975, baseline height measurements (n=14,407) revealed that 70-74 year olds were shorter than the 40-59 year olds by an average of 4.2 cm, an absolute difference of 2.6% (Opotowsky *et al.*, 2003). Therefore, height adjusted body composition measures can be advantageous.

3.5.6 Poor body composition measures are associated with increased morbidity

Reduced amounts of lean mass have been associated with increased risk of prolonged hospitalization (Kyle *et al.*, 2002b). A significant association between the length of hospitalization and low FFMI and very high BFMI was seen when 1762 patients were evaluated upon admission to hospitals in Geneva and Berlin and compared to healthy volunteers who were selected from a database of Geneva volunteers (Kyle *et al.*, 2002b). In another Swiss age-matched study of 995 patients (age 15-98 years) hospitalized for medical and surgical reasons, low FFM values (< 17.4 kg in men and < 15.0 in women) were noted in 37% and 55.6% of patients who were hospitalized for 1-2 and >12 days respectively. In that study, severe nutritional depletion as assessed by a low FFM was associated with an increased length of hospitalization (low FFM [<17.4 kg (men) and < 15.0 kg (women)] vs. normal/high FFM [2.5-8.2kg (men) and 4.9-11.8kg (women)] = 8.7 days vs. 4.3 days, P <0.001) (Pichard *et al.*, 2004).

3.6 Nutritional screening tools

Several nutritional screening tools exist to identify elderly people at risk of the negative health consequences of under-nutrition, so they can then be targeted for suitable interventions. All these tools have strengths and weaknesses. This section focuses on the Mini Nutritional Assessment (MNA- Appendix 1) and the 'DETERMINE Your Nutritional Health Checklist' [NHC- Appendix 2] for the reasons given below.

The Mini Nutritional Assessment (MNA) and the Australian Nutritional Screening Index (ANSI) have been used to screen older people for nutritional risk in several recent Australian studies. The ANSI was developed based on the 'DETERMINE Your Nutritional Health Checklist' (NHC). Of the two screening instruments, the MNA has been most extensively validated for use in the elderly in various settings, has been used widely overseas, and shown to accurately identify under-nourished older people at-risk of negative health outcomes. The MNA (Appendix 1) was used in the studies described in Chapters 6 and 7 to determine the prevalence and consequences of under-nutrition in older people in the community and a sub-acute care facility in Adelaide, South Australia, and in the study described in Chapter 8 as a means of defining the study population suitable for intervention. To the best of our knowledge, the MNA had not been previously compared to a more in-depth nutritional assessment in Australia. Therefore, in the study described in chapter 7, the results of the MNA were also compared to those of a more in-depth nutritional assessment (SNA- Table 7.1), which combined several parameters previously described in Sections 3.3 and 3.4.

The 'DETERMINE Your Nutritional Health Checklist' (NHC-Appendix 2), on the other hand, is a self-reporting nutritional tool that has been used for nutritional screening in many large European and American studies. It is a simple, short questionnaire, although it has not been as widely validated as the MNA and is probably not as effective as the MNA in screening for under-nutrition. Nevertheless, it has the advantage of simplicity and for that

reason was translated into Bahasa Malaysia, the national language of Malaysia and used in Chapter 5 to determine the prevalence of under-nutrition in older people residing in publicly funded shelter homes in Peninsular Malaysia.

3.6.1 Mini nutritional assessment

The MNA (Appendix 1), which was developed and validated for use in older adults in the early 1990s, is easily administered within 15 minutes with no biochemical investigations (Guigoz *et al.*, 1994). It has been used in various settings with ease and has been shown to accurately identify older people at-risk of increased mortality and morbidity (Persson *et al.*, 2002; Thomas *et al.*, 2002). The MNA has a reported sensitivity of 96%, specificity of 98% and predictive value of 97% for malnutrition, when compared to the nutritional status determined by physicians using anthropometric, clinical biochemistry and dietary parameters (Vellas *et al.*, 1999). It contains 18 items grouped into four main sections: anthropometric assessment (weight, height and weight loss); general assessment (lifestyle, medication use, and mobility); dietary assessment (number of meals, food and fluid intake, and autonomy of feeding); and subjective assessment (self-perception of health and nutrition status). Each response has a numerical value, which contributes to a final score (maximum =30). These questions can be completed by a carer if the older person is unable to answer them due to speech, hearing or cognitive impairment (5). Subjects scoring 17 or less are classified as malnourished whilst those scoring between 17 and 23.5 are at-risk of malnutrition and should be further investigated (Guigoz *et al.*, 1994). Subjects scoring 24 or more are classified as nourished.

To simplify things, a Short-form Mini Nutritional Assessment was developed subsequently (MNA-SF- Appendix 1) (Guigoz *et al.*, 2002; Rubenstein *et al.*, 2001). The MNA-SF consists of 6 questions and has a maximum score of 14. It takes approximately 3 minutes to administer but still requires some anthropometric measurements to be made (height and weight). A screening score of 11 or less suggests a risk for under-nutrition and the full

MNA should then be completed. This 2-step screening method was found to predict the absence of malnutrition (i.e. a score ≥ 17 on the MNA) with a sensitivity of 100% and negative predictive value of 100% (Cohendy *et al.*, 2001). It has also been shown that subjects scoring 11 or less on the MNA-SF (i.e. risky nutritional status) were at increased risk of mortality compared to nourished subjects (score ≥12)(Persson *et al.*, 2002). The MNA-SF's ability to predict the absence of risk for malnutrition (i.e. MNA score ≥ 24) was not as good with a sensitivity of 86% and a negative predictive value of 93% (Cohendy *et al.*, 2001; Guigoz *et al.*, 2002). The use of this 2-step process can save considerable time especially in settings with low prevalence of under-nutrition (i.e. community). The use of the MNA-SF in settings with an expected high prevalence of under-nutrition (i.e. nursing homes) is probably less useful, as more often the full MNA will still be required (Guigoz *et al.*, 2002; Murphy *et al.*, 2000). In such circumstances, it would be better to perform the MNA in all patients rather than complicate any screening process by a 2-tiered system.

3.6.2 The DETERMINE Your Nutritional Health checklist

The 'DETERMINE Your Nutritional Health Checklist' (NHC- Appendix 2), which is widely used in North America, was designed to enhance the older persons' understanding of the determinants of nutritional well-being and to promote the consideration of nutritional problems by health professionals (Dwyer, 1994; Posner *et al.*, 1993). Those identified by the checklist as being at-risk of under-nutrition are prompted to seek further evaluation by their medical practitioners. The NHC is a simple questionnaire of 10 statements on a single page requiring yes/no answers (Omran & Morley, 2000a). These statements represent different common risk factors for malnutrition and are scored in relation to their importance (Omran & Morley, 2000a). The statements cover: a) dietary assessment [questions related to the number of meals, autonomy in food preparation, food and alcohol intake], b) general assessment [questions related to medical condition, medications, oral health and weight loss] and c) social assessment [questions related to economic hardship and reduced social

contact] (Omran & Morley, 2000a). Older adults scoring 6 or more (out of a maximum of 21) are thought to be at high risk of under-nutrition and require further medical and nutritional evaluation. Those scoring between 3 and 5 should be aware that they are possibly at-risk of under-nutrition and require advice on improving their dietary habits. Those scoring less than 3 are said to be well-nourished.

The NHC also has the added advantage over many other screening methods (i.e. the MNA) in that it does not involve anthropometric or biochemical measurements. It can therefore be used as a self-administered tool, with the subject answering the questions themselves without assistance. However, when used as a screening instrument, it has been shown to have poor sensitivities (75%, 25%, 52%) and specificities (54%, 52%, 51%) when compared to other markers of under-nutrition such as weight loss ($\geq$10%), hypoalbuminemia (<30g/l) and lymphopenia (< 1500/ml)(de Groot *et al.*, 1998). For this reason, it has been strongly recommended that the NHC should only be used as an awareness tool and not as a screening tool (de Groot *et al.*, 1998). Despite this limitation, in the SENECA studies [longitudinal study- Survey in Europe of Nutrition in the Elderly, a Concerted Action], subjects identified as being at-risk of nutrition (score $\geq$ 6, 33%) in 1988 using this scale were at significantly greater risk than nourished subjects (score < 6, 26% [P<0.001]) of experiencing acute illnesses in the 6 months leading up to the follow-up survey in 1993 than nourished subjects (Beck *et al.*, 1999). The NHC was able to identify population groups that were at risk of adverse health outcomes and so its use can still be recommended in settings where resources to administer screening tools is severely limited and its use is intended as a guide to stimulate interest in nutritional status and prompt further screening.

Chapter 4

Post-prandial hypotension – Prevalence, consequences and pathophysiology

4.1 Introduction

Post-prandial hypotension (PPH) is generally defined as a decrease in systolic blood pressure (BP) of 20 mmHg or more within 2 hours of the start of a meal, or a decrease in systolic BP to less than 90 mmHg after a meal, especially when the systolic BP before that meal was greater than 100 mmHg (Jansen & Lipsitz, 1995). The fall in systolic BP often reaches a nadir between 30 and 60 minutes (Lipsitz et al., 1983). It is possible, however, to have symptomatic PPH with BP values which do not meet this arbitrary definition, and it is also common for older people to be asymptomatic when this definition is fulfilled (Jansen & Lipsitz, 1995). Therefore, the value of this definition is uncertain (Jansen & Lipsitz, 1995). Nevertheless, as this is currently the definition of choice, the studies described in Chapters 9 and 10 use this definition.

PPH was first documented as a clinical problem in 1977 (Jansen & Lipsitz, 1995; Seyer-Hansen, 1977). In 1983, Lipsitz and colleagues documented that older people (mean age 87 years) were at increased risk of experiencing PPH than younger subjects (mean age 24 years) (Lipsitz *et al.*, 1983). PPH is now clearly accepted as a common disorder affecting older people (see 4.2) and although most times it is asymptomatic, it can result in falls, syncope and other medical complications (see 4.3) contributing to the development of frailty in older people (Jansen & Lipsitz, 1995). The etiology of PPH has not been clearly defined but may possibly involve the gastrointestinal, endocrine, nervous and vascular system (Jansen & Lipsitz, 1995). Dietary manipulation in symptomatic older people may be a simple, safe, cost-effective, non-pharmacological management measure and this is investigated in the studies described in Chapters 9 and 10.

4.2 Prevalence of post-prandial hypotension in older people

PPH occurs more commonly in older and hypertensive people than in healthy (normotensive) younger people. For example, in one study, after a glucose load (75g glucose/300ml water), mean arterial BP decreased significantly ($P<0.01$) by 17 mmHg in the elderly hypertensive group (n=10, mean age 75 $\pm$ 1 [SEM] years), 6 mmHg in the elderly normotensive group (n=10, mean age 75 $\pm$ 2 years), 7 mmHg in the young (n=10, mean age 44 $\pm$ 2 years) hypertensive group, but did not fall in the young (n=10, mean age 28 $\pm$ 1years) normotensive group (Jansen *et al.*, 1987).

The prevalence of PPH in elderly people in different studies has been reported to be between 20-45 % (Table 4.1) (Aronow & Ahn, 1994; Grodzicki *et al.*, 1998; Le Couteur *et al.*, 2003; Puisieux *et al.*, 2002; Vaitkevicius *et al.*, 1991). Most often, these elderly people with PPH are asymptomatic (Aronow & Ahn, 1994; Grodzicki *et al.*, 1998; Le Couteur *et al.*, 2003; Puisieux *et al.*, 2002; Vaitkevicius *et al.*, 1991). The Cardiovascular Health Study, a large prospective cohort study (n=5888), found that systolic BP measurements immediately after a meal, at 0-, 1-, 2-, 3- and 4-hours were 133.7, 129.9, 132.1, 134.9 and 136.2 mmHg respectively (Smith *et al.*, 2003). Therefore, it is apparent that in many older people, BP decreases following a meal, but not low enough to meet the definition of PPH. Of note, the prevalence of symptomatic PPH is said to be much lower than asymptomatic PPH and in one simple study using mail out questionnaires (n=1611), only 2.6-2.7% of respondents reported symptoms such as faintness, weakness and dizziness within one hour of a meal (Cohen *et al.*, 1998). Therefore, it is likely that the extent of symptomatic PPH is considerably lower than that of asymptomatic PPH.

Table 4.1 The reported prevalence of post-prandial hypotension in older people in different clinical settings.

Setting	Description	Prevalence
Nursing Home (Vaitkevicius et al., 1991)	113 residents. Mean age 78 ± 9 [SD] years. Blood pressure measurements were made whilst patient was sitting. Diet content: 65% carbohydrate and 650kcal in total.	≥ 20 mmHg systolic blood pressure drop seen in 36% (n=41) following lunch.
Nursing Home (Aronow & Ahn, 1994)	499 residents, ambulatory and wheelchair bound. Mean age 80 ± 9 [SD] years. Residents ate usual lunch. Blood pressure measurements were made whilst patient was sitting.	24% of subjects (n=118) subjects experienced a blood pressure fall ≥ 20 mmHg following lunch.
Hostel (Le Couteur et al., 2003)	179 subjects from 8 aged care hostels. Mean age 83.2 ± 7.0 [SD] years. Resident's own usual breakfast. Blood pressure measurements made with subject sitting, followed by standing (1 and 3 minutes) and walking.	A decline in systolic blood pressure to ≥ 20 mmHg occurred in 38% following breakfast, 44% after standing for 1 or 3 minutes and in 41% with walking.
Acute and rehabilitation units (Puisieux et al., 2002)	126 inpatients. Mean age 81.4 ± 7.9 [SD] years. Seated position. Test meal: Coffee 10g, Milk 19g, 3 slices of bread (90g), Marmelade 30g and natural yoghurt 125g [Carbohydrate was 75% of total calories].	A decline in systolic blood pressure to ≥ 20 mmHg occurred in between 38 – 42% following breakfast and in 32% following lunch.
Community (Grodzicki et al., 1998)	530 patients (median age 70 years) with isolated systolic hypertension. Ambulatory blood pressure monitoring. Subject's usual meals.	In 24.1% of subjects, a fall in systolic blood pressure ≥ 16 mmHg was seen.
Community (Cohen et al., 1998)	1611 respondents to a questionnaire asking if subjects experienced faintness, weakness and dizziness after a meal.	2.7% of men and 2.6% of women described experiencing such symptoms.

4.3 Clinical presentations associated with post-prandial hypotension (PPH) in older people

PPH has been associated with syncope, cerebrovascular accidents (stroke), falls and even death. In what is probably the largest prospective study to date, 118 (24%) of 499 ambulatory or wheelchair-bound residents of a long-term care facility in the United States of America (mean age 80 $\pm$ 9 [SD]) were shown to have PPH at baseline (i.e. post-prandial systolic BP fall of 20 mmHg or more) (Aronow & Ahn, 1994). Residents with a history of syncope in the preceding 6 months had a mean maximal post-prandial decrease in systolic BP of 24 $\pm$ 5 [SD] mmHg, compared to 14 $\pm$ 5 mmHg in residents with no history of syncope ($P<0.0001$), whilst residents with a history of falls in the preceding 6 months had a mean maximal fall in post-prandial systolic BP of 21 $\pm$ 5 mmHg, compared to the mean of 13 $\pm$ 4 mmHgmmHg in residents with no history of falls ($P<0.0001$) (Aronow & Ahn, 1994). These subjects were then followed up for an average of 29 $\pm$ 10 [SD] months. In the follow-up period, the maximum decrease in post-prandial systolic BP was 20 $\pm$ 5 [SD] mmHg in residents who experienced falls, compared to 12 $\pm$ 4 mmHg in those that had not fallen ($P<0.001$), 23 $\pm$ 5 mmHg in subjects with syncope, compared to 14 $\pm$ 5 mmHg in those without syncope ($P<0.001$), 18 $\pm$ 6 mmHg in those with coronary events, compared to 14 $\pm$ 5 mmHg in those without coronary events ($P<0.001$), 21 $\pm$ 6 mmHg in those with stroke compared to 15 $\pm$ 5 mmHg in those without stroke ($P<0.001$) and 17 $\pm$ 6 mmHg in those who died compared to 15 $\pm$ 5 mmHg in those who were still alive ($P<0.001$) (Aronow & Ahn, 1997). In this study, the maximal decrease in post-prandial systolic BP at baseline was found to be an independent risk factor ($P<0.001$) for mortality, falls, syncope, new coronary events and new cerebrovascular accidents (Aronow & Ahn, 1997).

4.4 Factors affecting post-prandial blood pressure

The reported prevalence of PPH varies widely from study to study (Table 4.1). To some extent these differences are due to the variations in the definition chosen to define PPH, the posture of the subject, the temperature of the meal, intra-individual variability, the timing of the studies and the health status of the subjects (Jansen & Lipsitz, 1995; O'Mara & Lyons, 2002). Nutrient delivery, meal composition, and cardiovascular and hormonal factors have also been shown to influence the severity of PPH (Jansen & Hoefnagels, 1989; Jansen *et al.*, 1988; Jansen *et al.*, 1990; O'Donovan *et al.*, 2002; O'Donovan *et al.*, 2004). The exact mechanisms leading to the development of PPH are still a mystery but are most likely multi-factorial.

The effect of meal composition on post-prandial blood pressure is discussed in more detail below, as the effects of carbohydrate drinks with varying glycaemic effects (or indices) and nutrient content on post-ingestion blood pressure were investigated in the studies described in Chapters 9 and 10. Other factors affecting post-prandial BP have been extensively reviewed elsewhere (Jansen & Lipsitz, 1995; O'Mara & Lyons, 2002).

4.4.1 What normally happens after a meal?

Splanchnic blood pooling following meal ingestion results in reduced systemic vascular resistance, but it is thought to not be the sole cause of PPH (Jansen & Lipsitz, 1995). For instance, it has been shown that bowel blood volume increases by approximately 20% after a meal in both healthy young and old people (Jansen & Lipsitz, 1995; Lipsitz *et al.*, 1993). It has also been shown that the increase in superior mesenteric arterial blood flow velocity after a high-carbohydrate meal is similar in both healthy young and elderly subjects and yet we know that PPH is more common in older people compared to younger people (Jansen & Lipsitz, 1995; Lipsitz *et al.*, 1993; Sidery *et al.*, 1993).

Accompanying splanchnic blood pooling, there is usually an increase in cardiac output and heart rate (Fagan *et al.*, 1986; Jansen & Lipsitz, 1995; Lipsitz *et al.*, 1993). Sympathetic nervous system activity also increases following a meal, as indicated by increases in heart rate, plasma noradrenaline levels and muscle recorded microneurographic readings (Fagius & Berne, 1994; Jansen & Hoefnagels, 1989; Jansen & Lipsitz, 1995; Jansen *et al.*, 1987). Plasma renin activity is also increased following meal ingestion (de Mey *et al.*, 1987; Jansen & Lipsitz, 1995). In older people, any one of these compensatory responses may be impaired. It is possible that with failure of some of these processes in older people, blood pressure homeostasis fails and PPH develops.

4.4.2 Nutrient content of a meal

The meal composition is an important determinant of the degree of post-prandial BP decrease. Ingestion of carbohydrates, particularly glucose and to a lesser degree starch but not fructose or xylose, lowers BP more than ingestion of water (Heseltine et al., 1991a; Jansen et al., 1990; Jansen et al., 1987; Mathias et al., 1989; Robinson TG, 1995). The effect of fat and protein ingestion on post-prandial BP is not clearly defined, with some studies showing a fall in post-prandial BP and others not (Hoeldtke et al., 1985; Jansen et al., 1990; Potter et al., 1989). Strikingly, no study has documented the effect of sucrose (table sugar) on post-prandial BP, despite sucrose being used more often in drinks and food than glucose. The study described in Chapter 10 evaluated the effects of 50g carbohydrate drinks with varying nutrient content (glucose, sucrose and fructose) on post-prandial BP in 10 healthy older people and for the first time, the effect of sucrose ingestion on post ingestion blood pressure was defined.

4.4.3 Nutrient amount or meal size

Reducing the carbohydrate content in a meal or the meal size may reduce the duration, symptoms and severity of PPH in healthy older people. In a randomized cross-over study involving twelve elderly patients ($\geq$ 70 years) with a confirmed diagnosis of PPH receiving

low (25g)-, normal (65g)- and high (125g)- carbohydrate meals, the fall in systolic BP was of significantly smaller magnitude ($P<0.05$ between groups) and shorter duration ($P<0.01$ between groups) [SBP 28 $\pm$ 5 [SEM] mmHg; time 18 $\pm$ 6 minutes] after the smallest (25g) carbohydrate meal in contrast to the other two meals [65g carbohydrate meal: SBP 39.7 $\pm$ 7 mmHg, time 37 $\pm$ 7 minutes; 125g carbohydrate meal: SBP 40 $\pm$ 5 mmHg, time 43 $\pm$ 6 minutes] (Vloet *et al.*, 2001). In this same study, the number of reported adverse effects increased with increasing carbohydrate amounts. Following the low carbohydrate meal, seven of the twelve subjects reported feeling sleepy but none felt unwell, whilst eleven out of twelve subjects felt unwell after the normal- and high- carbohydrate meals. After the normal- carbohydrate meal seven subjects felt sleepy and some also reported feeling nauseous, dizzy or restless. Following the high carbohydrate meal, two patients felt dizzy, one very sleepy, one had chest pain, two described blurred vision and three had reduced consciousness. These symptoms were related to hypotensive periods, where systolic BP had declined by 20 mmHg or more (Vloet *et al.*, 2001).

In another study, seven subjects with primary autonomic failure consumed either three large meals or six smaller meals of identical total calorie content. Systolic and diastolic BP 30 minutes after the meal was lower following the large meals than the smaller meals (lying: systolic BP 131 $\pm$ 5.1 [SEM] vs. 151 $\pm$ 3.8 mmHg, $P = 0.005$, diastolic BP 76 $\pm$ 3.4 vs. 90 $\pm$ 3.0 mmHg, $P = 0.02$; sitting: systolic BP 109 $\pm$ 5.7 vs. 124 $\pm$ 5.0 mmHg [not significant], diastolic BP 66 $\pm$ 3.9 vs. 78 $\pm$ 3.7 mmHg, $P = 0.07$; standing: systolic BP 89 $\pm$ 5.1 vs. 103 $\pm$ 6.4 mmHg [not significant], diastolic BP 50 $\pm$ 3.5 vs. 66 $\pm$ 5.1 mmHg, $P = 0.06$) (Puvi-Rajasingham & Mathias, 1996). Therefore, splitting larger meals into smaller but more frequent meals is likely to be of benefit in reducing the post-prandial BP decreases in symptomatic older people with PPH.

4.4.4 Meal composition

The addition of guar, a naturally occurring, non-absorbed, gel-forming carbohydrate of vegetable origin, to a meal has been shown to attenuate the fall in post-prandial BP following a glucose drink in healthy older people (Jones *et al.*, 2001). This may be due to a combination of delayed gastric emptying and reduced nutrient absorption or contact in the duodenum (Jones *et al.*, 2001; O'Donovan *et al.*, 2004). In one study looking at the effects on systolic BP measurements of intra-duodenal glucose infusions (3 kcal min^{-1}) with and without guar added, the fall in systolic BP measurements was reduced on the day with guar in comparison to the control day and it was thought that the reduction in the rate of luminal glucose exposure (or reduced glucose absorption) resulting from the addition of guar to the glucose drink was the cause of this (O'Donovan *et al.*, 2004).

The glycaemic index is a surrogate marker for the glycaemic effect of a drink. Per gram of carbohydrate, foods with a high glycaemic index (GI) produce a higher peak in postprandial blood glucose and a greater overall blood glucose reponse during the first two hours after consumption than foods with a low GI (Foster-Powell *et al.*, 2002). The addition of 14.5 g of guar to a 50g glucose drink reduces its GI from 100 (arbitrarily designated) to 62 (Foster-Powell *et al.*, 2002). Perhaps, by lowering the GI (or it's glycaemic effect) of the glucose drink by adding guar, the post-ingestion fall in BP usually seen after a pure glucose drink may be reduced (Jones *et al.*, 2001). If so, using the increasingly available published tables of glycaemic index of foods as a guide, people with PPH might be able to choose drinks or meals with lower GIs and these would be a simple non-pharmacological intervention measure (Foster-Powell *et al.*, 2002). With this in mind, the study described in Chapter 9 was performed to investigate the effects of 50g carbohydrate drinks with varying glycaemic effects (low GI [<55] vs. intermediate GI [55-69] vs. high GI [≥70]) on post-ingestion BP.

4.5 Management options for older people with postprandial hypotension

As with all medical syndromes, management strategies for PPH can be broadly divided into non-pharmacological and pharmacological options. In older people, it is usually better to maximize the use of non-pharmacological interventions in preference to pharmacological measures to avoid drug interactions and polypharmacy. Drug interactions and polypharmacy are common in older people and are responsible for significant morbidity and mortality in older people (Juurlink *et al.*, 2003; Onder *et al.*, 2003a).

4.5.1 Non-pharmacological management options for older people with postprandial hypotension

Changing the meal composition and meal size

Reducing the meal size (see 4.4.3) and the amount (see 4.4.3) or type of carbohydrate (see 4.4.2) in a meal may be beneficial in the management of PPH. The addition of guar to a meal may also be beneficial but this option is less appealing as guar is not very palatable. However, the future design of a more palatable agent along the same principle may be beneficial. The studies described in Chapters 9 and 10 were designed to evaluate two simple, practical, non-pharmacological management strategies involving dietary manipulation (varying the glycaemic effect or varying the carbohydrate nutrient type) that could be used to manage PPH in symptomatic older people.

Walking after a meal

Walking after a meal is effective in ameliorating the fall in BP following meal ingestion but this effect disappears once the person stops walking. In a study of fourteen elderly nursing home residents with confirmed PPH, on the control day, subjects remained seated for 60 minutes following the meal (Oberman *et al.*, 1999). On the intervention day, following a 20 minute rest post-meal, subjects walked at their own pace for 10 minutes. On the intervention day, mean arterial BP increased by 18 $\pm$ 4 mmHg from pre-exercise values

with walking. In contrast to this, mean arterial BP continued to decline on the control day where the subject remained seated during the same 10 minute period. On the intervention day, 10 minutes after walking, at rest and sitting, the mean arterial BP declined to be similar to that seen on the control day during this same period. Therefore, this treatment modality is perhaps not practical, as postprandial blood pressure decrease in sufferers of PPH can last more than one hour and older people are unlikely to be able or likely to walk for such a long time (Smith *et al.*, 2003).

Drinking water with a meal

In some studies, water ingestion (at least 500 ml) has been associated with a transient increase in blood pressure (Jordan *et al.*, 2000; Shannon *et al.*, 2002). In one study involving 11 healthy older subjects (mean age 57 $\pm$ 2.2 [SEM] years), water (480 ml) ingestion was associated with a 11 $\pm$ 2.4 [SEM] mmHg increase in systolic BP approximately 35 minutes after water ingestion. In another study of 9 healthy subjects (age 26-57 years), water ingestion was associated with significant increases in multi-unit bursts (muscle sympathetic nerve activity; MSNA) and single-unit impulses (s-MSNA). Accompanying this was also increased calf vascular resistance and plasma noradrenaline levels. Therefore, it is thought that the pressor effect of water is mediated through sympathetic activation. The efficacy of water in preventing PPH has not been assessed.

4.5.2 Pharmacological management options for older people with postprandial hypotension

The use of Octreotide (somostatin analogue) in the treatment of PPH

The efficacy of Octreotide (somatostatin analogue) in the management of symptomatic PPH in older adults has not been studied. However, its efficacy in preventing the reduction in postprandial BP in normal and hypertensive elderly people has previously been demonstrated (Jansen *et al.*, 1988; Jansen *et al.*, 1989). In one randomized double-blind controlled study, on the placebo study day, mean arterial pressure fell ($P<0.001$) by 15 $\pm$ 1

[SEM] mmHg in hypertensive older people and by 7 ± 2 mmHg in normotensive elderly people on the placebo study day (Jansen *et al.*, 1988). This fall in mean arterial BP was ameliorated when Octreotide was administered on the treatment day (Jansen *et al.*, 1988). The exact mechanism by which Octreotide exerts its effect is not known but is thought to possibly involve suppression of vasoactive gut peptides, reduce post-meal increase in splanchnic blood flow, increase cardiac output and increase peripheral vascular resistance (i.e. reduced forearm blood flow) (Hoeldtke *et al.*, 1991; Jansen *et al.*, 1989; Kooner *et al.*, 1989). Treatment with Octreotide is expensive and requires subcutaneous administration. It can also cause diarrhoea and is painful.

Other agents

Smaller studies have investigated the use of other agents such as caffeine, vasopressin, indomethacin, cimentidine, diphenhydramine, cimentidine, dihydroergotamine, denopamine and midodrine (Jansen & Lipsitz, 1995). The efficacy of caffeine has not been confirmed and results of various studies have been conflicting (Heseltine *et al.*, 1991b; Lipsitz *et al.*, 1994). The efficacy of vasopressin in treating older people with PPH is yet to be proven although some benefits have been shown in patients (n=4) with Shy-Drager syndrome and confirmed PPH (Hakusui *et al.*, 1991). In a study of six patients with autonomic failure, indomethacin was shown to ameliorate the hypotensive effect of a meal (Jansen & Lipsitz, 1995; Robertson *et al.*, 1981). Also, in another study in subjects with autonomic failure, the combination of denopamine (beta 1 adrenergic agonist) and midodrine (alpha 1 adrenergic agonist) attenuated the fall in postprandial BP (Hirayama *et al.*, 1993; Jansen & Lipsitz, 1995). The other medications have not been found to be efficacious in preventing PPH, especially in older people (Jansen & Lipsitz, 1995).

Chapter 5

The nutritional status of 1081 elderly people residing in publicly funded shelter homes in Peninsular Malaysia

5.1 Summary

Under-nutrition in older people is common and frequently overlooked. At the time of this study, there was no published information on the nutritional status of elderly Malaysians residing in publicly funded shelter care facilities. Therefore, the aim of this study was to determine the: 1) prevalence of under-nutrition as determined by the 'DETERMINE Your Nutritional Health Checklist' (NHC- Appendix 2); and 2) factors independently associated with under-nutrition amongst the older residents of these publicly funded shelter homes in Peninsular Malaysia. 1081 elderly people over the age of 60 years were surveyed using questionnaires determining baseline demographics, nutritional and cognitive status, physical function and psychological well-being.

In this study, 41.4% (n=447) of subjects were nourished [NHC score <3], 32.1% (n=347) at moderate risk [score between 3 and 5] of under-nutrition and 26.6% (n=287) were at high risk of under-nutrition [score>5] according to the NHC. A large proportion of subjects were underweight with 14.3 % of subjects recording a low body mass index (BMI) < 18.5 kg/m^2. The residential geriatric depression score [GDS-12R] (Relative Risk [RR] = 1.03 [95% CI 1.01-1.05]; P =0.002) and the number of illnesses (RR = 1.14 [95% CI 1.07-1.21]; P< 0.001) were found to be independently associated with nutritional risk (NHC score > 3). Having no family (RR 1.80 [95%CI 1.26-2.57), P<0.001) and negative responses to statement 3 [I eat few fruits or vegetables or milk products] (RR 0.78 [95% CI 0.57-1.07]; P=0.013) and statement 5 [I have tooth or mouth problems that make it hard for me to eat] (RR 0.57 [95%CI 0.42-0.77]; P=0.023) of the 'DETERMINE Your Nutritional Health Checklist' were independently associated with low BMIs (<18.5 kg/m^2). Using a BMI <

18.5 kg/m^2 as an objective marker for nutritional risk, the NHC was shown to have a sensitivity of 66.4% (95% CI 58.0-74.2%), specificity of 42.7% (95% CI 39.3-46.1%), positive predictive value of 16.2% (95% CI 13.3-19.5%) and a negative predictive value of 88.4% (95% CI 84.9- 91.4%). As a result of this study, it was determined that many elderly people residing in publicly funded shelter homes in Malaysia may be at-risk of under-nutrition and were underweight. The NHC is better used as an awareness tool rather than as a screening tool.

5.2 Introduction

Malaysia has enjoyed economic prosperity and improvements in health care delivery over the past 20 years. With increasing affluence and community expectations, the need for improved overall health and quality of life now governs many national health care policies. Before policies can be formulated and interventions devised, the extent of any problem should be clearly defined.

The nine 'Rumah Seri Kenangan' in this study are publicly funded shelter homes for the elderly and admission to these institutions is voluntary. The aims of these homes are to provide adequate care and support in the form of medical and rehabilitative services and counseling to older people who lack family and financial support. Presently, the extent of nutritional risk amongst elderly Malaysians residing in these shelter homes is not known.

Whilst the 'Rumah Seri Kenangan' is different to a nursing home in that its residents are generally less dependent, it is still likely that the prevalence of under-nutrition will be high, as these elderly people have often lived an impoverished and lonely life prior to admission. Both social isolation and poverty are known to be associated with nutritional risk in older people (Visvanathan, 2003; Walker & Beauchene, 1991). It is also probable that a large percentage of the residents residing in these facilities would have originated from rural villages. With industrialization and with the disappearance of extended family network systems, the displacement of older people from rural villages to urban shelters is very likely. A very recent Malaysian study had found that almost 38.5% of elderly people residing in rural areas in Malaysia had Body Mass Indices (BMIs) < 18.5 kg/m^2(Suzana *et al.*, 2002). Therefore, it is postulated that a large proportion of older people in these shelter homes may be at-risk of under-nutrition, especially with rural to urban displacement. Remedial strategies may need to be devised to improve their nutritional health. Protein energy malnutrition in older people is known to be associated with prolonged hospitalization, increased complications, institutionalization and death, whilst adequate treatment has been shown to reduce mortality and complications (Milne *et al.*, 2002; Persson *et al.*, 2002; Visvanathan, 2003; Visvanathan *et al.*, 2003; Walker & Beauchene, 1991).

As with the rest of the world, the population of Malaysia is progressively ageing with a significant increase in life expectancy seen between 1980 and 2000; males from 66.4 years to 70.2 years and females from 70.5 years to 75.0 years (Ministry of Health Malaysia, 2003). It is expected that the prevalence of under-nutrition in older people and its many negative health consequences will increase and result in increasing individual and community health care costs over the next few decades. Therefore, the aim of this study was to determine: 1) the prevalence of under-nutrition; and 2) the factors associated with under-nutrition amongst the older residents of these publicly funded shelter homes in Peninsular Malaysia.

5.3 Method

5.3.1 Study population

A total of nine publicly funded shelter homes ('Rumah Seri Kenangan') were visited in Peninsular Malaysia between March and September 2002. Residents who were 60 years and older and had resided in these homes for at least three months were invited to participate in this study. Out of a total of 1341 residents, only 1126 were eligible for the study. 45 (4%) residents did not participate due to poor health, severe dementia or intercurrent illnesses. Informed consent was obtained from all 1081 subjects and/or their carers. The study was approved by the Department of Social Welfare, Malaysia and ethics approval was obtained from the University Putra Malaysia. This study was funded by a grant to Dr Zaiton Ahmad from the University Putra Malaysia. The author and her collaborator, Dr Zaiton Ahmad from the University Putra Malaysia designed this study to meet its study objectives (described earlier). All questionnaires described below were translated into 'Bahasa Malaysia', the official written and spoken language of Malaysia, by Dr Zaiton Ahmad and it's accuracy was verified by the author (Appendix 3). Two research assistants (trained by Dr Zaiton Ahmad) administered all questionnaires and made all measurements. The author was primarily responsible for the analysis of the results (with statistical assistance from Mr Justin Lokhurst, Department of Public Health, University of Adelaide) and the authorship of the two papers related to this chapter.

5.3.2 Baseline Patient Characteristics

Nutritional status

1) The 'DETERMINE Your Nutritional Health Checklist' (NHC) [Appendix 2] has been described in detail in 3.6.2. In this study, subjects scoring 3 or more were considered to be at nutritional risk (AR) [3-5 moderate risk, $\geq$ 6 high risk].

2) The BMI can be used as an anthropometric measure of nutritional status. Body weight and height were measured and the body mass index (BMI) calculated (weight in kg/[height in m]^2). It has been suggested that adult Malaysians with a BMI < 18.5 kg/m^2 are underweight [under-nourished] and this was discussed in 3.3.1 (Ministry of Health Malaysia, 2003). The reason for this lower healthy BMI range [18.5 and 22.9 kg/m^2] in adult Malaysians compared to Caucasian populations is because Asian people have a higher body fat percent at a similar BMI in comparison to Caucasian/European populations (Deurenberg *et al.*, 2002; Ministry of Health Malaysia, 2003; Wang *et al.*, 1994). To the best of our knowledge, at present, there are no clear guidelines in Malaysia defining the healthy BMI range for older people based on life expectancy or other similar end-points. Similar cut-off values (i.e. < 18.5 kg/m^2) have also been used in other Malaysian research studies involving older people (Shahar *et al.*, 1999a; Suzana *et al.*, 2002). Weight was measured using the same portable weighing scale (TANITA weighing scale) in light clothing (without shoes) to the nearest 0.1kg. Height (SECA bodymeter) was measured whilst the patient was standing to the nearest 0.5cm.

Cognition

The Elderly Cognitive Assessment Questionnaire (ECAQ - Appendix 4) was used to evaluate cognitive status and was developed specifically for use among elderly people in developing countries (Kua & Ko, 1992). The questionnaire consists of 10 items grouped under 3 categories: memory (3 items), orientation (6 items) and memory recall (1 item). Out of a maximum score of 10, subjects were classified in this study as experiencing probable (< 5), borderline (5-6) and no (>6) cognitive impairment.

Physical Function

The 10-item modified Barthel Index (Appendix 5) was used to determine ability to independently perform activities of daily living (ADL) and it has a maximum score of 20 (Wade & Collin, 1988). Subjects were classified according to their scores; 'moderate to very severe disability' ($\leq$14), 'mild disability' (15 to 19) and ' fully independent' (20).

Depression

The 12 question Geriatric Depression Scale for people in residential care facilities (GDS-12R- Appendix 6) was used to diagnose depression in this study (Sutcliffe *et al.*, 2000). It was developed from the 15-item Geriatric Depression Scale (GDS-15) by excluding items that were found to be poor identifiers of depression in nursing and residential home populations (Sutcliffe *et al.*, 2000). The 3 items excluded were the questions pertaining to: 1) the preference of going out rather than staying home; 2) the feeling of having more problems with memory than other people; and 3) the feeling that most people were better off than them (Sutcliffe *et al.*, 2000). In this study, subjects scoring 5 and above (maximum score of 12) were said to be at high risk of experiencing clinically relevant depression (Sutcliffe *et al.*, 2000).

Others

Frequency of visits from family/friends and the presence of social support were also determined. History was obtained from the subject, staff members and clinical records.

5.3.3 Statistical analysis

Log-binomial regression univariate analyses of subject's clinical characteristic based on impaired nutritional status (NHC score $\geq$ 3) and low BMI (< 18.5 kg/m^2) were performed. The potential predictors of an impaired nutritional state [NHC score $\geq$ 3](P<0.10 by univariate analysis) were included into a log-binomial regression multivariate analysis

adjusting for age, sex and BMI, yielding factors independently associated with nutritional risk as indicated by a NHC score $\geq$ 3. Similarly, the potential predictors of low BMI ($P \leq 0.12$ by univariate analysis) were included into a log-binomial regression multivariate analysis adjusting for age and sex. Using a BMI cut-off of < 18.5 kg/m^2 as an objective marker of under-nutrition, the sensitivity, specificity, positive and negative predictive value (PPV and NPV) of the NHC for identifying older people at-risk of under-nutrition were calculated. Sensitivity was defined as the proportion of subjects who were objectively under-nourished (BMI < 18.5 kg/m^2) who were classified as under-nourished by the NHC ($\geq$ 3). The specificity was defined as the proportion of subjects who were objectively nourished (BMI $\geq$ 18.5 kg/m^2) who were classified as nourished by the NHC (< 3). The PPV was defined as the proportion of subjects screening positive (under-nourished- $\geq$3) on the NHC that was actually underweight (BMI < 18.5 kg/m^2). The NPV was defined as the proportion of subjects screening negative (nourished- $\leq$3) on the NHC that was not underweight (BMI $\geq$ 18.5 kg/m^2). SAS was the software program used (SAS Institute, inc, Cary, NC). P values < 0.05 were considered to be statistically significant.

5.4 Results

The socio-demographic characteristics of the study population are shown in Table 5.1. Most subjects had minimal (33%) or had not received any (64%) formal education. Of special note was that 73% of subjects were generally independent with their activities of daily living. However, many (86%) scored poorly on the ECAQ scale indicating risk of cognitive impairment and almost two thirds (79%) of subjects were at risk of depression. The BMI was not determined in 102 people as 93 were too physically dependent and a further nine people declined. 42% of subjects reported having no medical illnesses. Approximately 9% of subjects had diabetes, 14% hypertension, 6% asthma, 8% ischaemic heart disease, 2% cerebrovascular disease and 4% osteoarthritis. According to clinical records, 32% of subjects were on 3 or more medications.

The response of the residents to each of the statements comprising the NHC is shown in Table 5.2. A little more than a third of respondents reported eating few fruits, vegetables or milk products, suffering from some form oral or dental troubles or not having sufficient money to buy the food they required. Very few people reported drinking too much alcohol (<1%), consuming 3 or more prescription medications (8.0%) or loosing weight unintentionally (<4%). Consistent with the result of the Barthel Index (almost 9% severely dependant), only 3.5% of respondents stated that they were physically unable to shop, cook or feed themselves.

Table 5.3 shows the results of the univariate log-binomial regression analysis of subjects' clinical characteristics, based on the NHC score of ≥ 3. Subjects were grouped as nourished (41.4%) and at-risk of under-nutrition [AR] (58.6%). Eight parameters were potentially associated with ($P<0.10$) higher scores on the NHC (≥ 3) and being AR. These included lower level of education, rural origin, fewer visits from family or friends, worse scores on the ECAQ, the GDS-12R and the modified 10-item Barthel Index, increasing number of medications and reported illnesses. When these parameters were further evaluated by a log-

binomial regression multivariate analysis [adjusted for age, sex and BMI], the GDS-12R score (Relative Risk [RR] = 1.03 [95% Confidence Interval (CI) 1.01-1.05]; P =0.002) and the number of illnesses (RR = 1.14 [95% CI 1.07-1.21]; P< 0.001) were found to be independently associated with higher NHC scores [AR].

Table 5.4 shows the results of the univariate log-binomial regression analysis of subjects' clinical characteristics, based on the baseline BMI. Subjects were grouped as not underweight (BMI $\geq$ 18.5 kg/m^2) and underweight (BMI < 18.5 kg/m^2). Fifteen parameters were potentially associated with (P$\leq$0.12) being underweight and having a low BMI. These included, female gender, lack of education, no family, no visits from friends and family, negative responses to statements 1-3, 5, 6, 8-10 of the NHC (Table 5.2), being on less than 3 medications and the number of medical illness. All these parameters were further evaluated by multivariate analysis [adjusted for age and sex] except: 1) the nutritional score and nutritional status derived from the NHC as individual statements from the NHC were included into the analysis; 2) sex as the analyses was adjusted for this; and 3) statement 8 on the NHC as the number of medications determined using the medical records was more accurate and this was included into the analysis instead. The multivariate analysis (adjusted for age and sex) revealed that having no family (RR 1.80 [95%CI 1.26-2.57), P<0.001) and negative responses to statement 3 [I eat few fruits or vegetables or milk products] (RR 0.78 [95% CI 0.57-1.07]; P=0.013) and statement 5 [I have tooth or mouth problems that make it hard for me to eat] (RR 0.57 [95%CI 0.42-0.77]; P=0.023) of the NHC were independently associated with a lower BMI.

When the scoring on the NHC was compared to an objective marker for under-nutrition (BMI < 18.5 kg/m^2), the sensitivity was 66.4% (95% CI 58.0-74.2%), specificity was 42.7% (95% CI 39.3-46.1%), PPV was 16.2% (95%CI 13.3-19.5%) and the NPV was 88.4% (95% CI 84.9-91.4%).

5.5 Discussion

A high proportion of elderly people living in these shelter homes in Peninsular Malaysia were at risk of being under-nourished or developing under-nutrition. The 'DETERMINE Your Nutritional Health Checklist' [NHC] identified more than half of the elderly people in this study as being at-risk of under-nutrition (25% high risk - Table 5.1). Approximately 14% of these elderly residents were clearly underweight with a BMI < 18.5 kg/m^2. It is important to note that this low BMI cut-off value had been selected with the aim of targeting obesity amongst adult Malaysians (Ministry of Health Malaysia, 2003). However, there is strong evidence that increasing adiposity and BMI in older people is not as strongly associated with increased mortality as in younger people (Somes *et al.*, 2002; Taylor & Ostbye, 2001). Instead, loss of lean body mass (sarcopenia) is associated with significant morbidity (Bales & Ritchie, 2002; Janssen *et al.*, 2004). Therefore, it can be argued that when attempting to diagnose and treat under-nutrition and prevent its many adverse consequences in older people, it may be prudent to choose a slightly higher BMI cut-off value (e.g. under-nourished < 20 kg/m^2) and there is some local evidence supporting this (Suriah AR, 1998). In their study of 344 older Malay (one racial group) village residents, the mean BMI was 23.5 $\pm$ 4.49 [SD- standard deviation] kg/m^2 in the 60-69 year age group, 22.30 $\pm$ 4.34 [SD] kg/m^2 in the 70-79 year age group and 21.52 $\pm$ 4.32 [SD] kg/m^2 in the 80-89 year age group (differences between group not significant)(Suriah AR, 1998). The authors of this paper had suggested that the lower cut-off for a normal BMI should be 20 kg/m^2 but unfortunately had not quantified the proportion of older people in their study who were underweight (i.e. BMI < 20 kg/m^2) (Suriah AR, 1998). In this study, we found that almost one third of respondents had a BMI of less than 20 kg/m^2. There is a need to define the lower cut-off for under-nutrition in older people in Malaysia based on life expectancy or similar end-points.

To the best of our knowledge, no study has previously examined the nutritional status of elderly people living in publicly funded shelter care facilities such as this, especially in Malaysia. Such shelter care facilities provide care to destitute elderly people who lack financial and family support but are physically quite healthy. Consistent with this, subjects in this study were mostly independent (>70%) with their activities of daily living. Also, slightly more than 60% of respondents reported having no kin. Often seen in developing economies is a displacement of rural people to urban shelters as exhibited in this study whereby 81% of subjects were originally from rural communities. Consistent with the rural origin of the study population, there is also a high proportion of people with only primary education or less (90%). Therefore, a large proportion of residents in these shelter homes, originated from rural villages, were poorly educated and at-risk of under-nutrition. The results of this study are supported by those by Shahar et al. who also found that rural Malaysians were at high risk of under-nutrition (39 %) and unemployment with no steady financial support (60%) and were also often uneducated (48%) (Shahar *et al.*, 2001). Interestingly, far fewer older people in this study had BMIs < 18.5 kg/m^2 than in the study by Suzana et al. [14.30% vs. 38.5%] (Suzana *et al.*, 2002). We do not have information about their BMIs on arrival at the shelter but possibly, once there, the provision of regular and nutritious meals improved nutritional status increasing body weight. This needs further confirmatory investigation. Nevertheless, these studies highlight the fact that these displaced, isolated, poor and often illiterate people are at risk of being or becoming under-nourished.

When looking at the responses to individual questions making up the NHC (Table 5.2), the following questions received the most positive responses (approximately one third of respondents); 1) eating few fruits, vegetables or milk products, 2) having oral or dental problems and 3) not having enough money to buy food. Between 15 to 20% of respondents also reported having an illness that changed the type of food eaten, eating fewer than two meals per day and eating alone most of the time. Once again, similar findings were found in

2 smaller Malaysian studies in rural regions whereby chewing difficulties were reported frequently (43%), poverty was found to be an independent predictor of being underweight (< 18.5kg/m^2) and decreased fruit intake and less than 3 meals per day were independent predictors of dietary inadequacies (Shahar *et al.*, 1999b; Suzana *et al.*, 2002). These dietary, economic and health factors are known to be associated with poor nutritional status and similarly high responses to these questions were seen in other studies using the checklist (de Groot *et al.*, 1998; Sahyoun *et al.*, 1997). Interestingly, less than 1% of respondents reported consuming more than 3 standard drinks of alcohol per day and this is most likely due to cultural and religious beliefs that prohibit social drinking, especially in women. As an awareness tool, the responses of an individual person to the NHC provides us with clues as to what non-physiological factors may be contributing to the older person's poor nutritional status and appropriate corrective measures may be instituted accordingly (i.e., ensuring 3 full meals are eaten per day).

In this study, the GDS-12R score was found to be independently associated with nutritional risk as identified by the NHC (score $\geq$ 3). Depression is known to be associated with poor nutritional status and depressed older people are at an increased risk of mortality and morbidity (Luukinen *et al.*, 2003; Visvanathan *et al.*, 2003). It has also been recently shown that anti-depressant therapy may promote weight gain or prevent weight loss in elderly people (Thomas *et al.*, 2003). A high proportion of elderly people residing in these facilities appear to be at-risk of depression (65%) and it is important that potential stressors (i.e. lack of visitation) are sought and treatment plans instituted to prevent further decline in health and social wellbeing. Emotional and mental health are often neglected but they are strong determinants of one's ability to live life to the fullest.

In this study also, the number of medical illnesses was strongly associated with nutritional risk. For every additional illness suffered, there was a 14% increase in relative risk of being at-risk of under-nutrition (NHC score $\geq$ 3). Gastrointestinal disease, malabsorption

syndromes, acute and chronic infections, cancer, hypermetabolism (i.e., hyperthyroidism), rheumatoid arthritis and many other diseases are associated with anorexia, micronutrient deficiencies and increasing energy requirement, which may result in an impaired nutritional status (Katelaris *et al.*, 1993; Kerstetter *et al.*, 1992; Morley, 1997; Roubenoff, 1993; Visvanathan, 2003).

Attention to oral and dental health in older people is very important in older people but unfortunately access to dental care is sometimes difficult. Consistent with the results of many other studies, this study found that residents reporting no oral or dental health troubles were less likely to be underweight. In another study on 51 subjects (mean age 83.7 years) in Finland, dry mouth and eating problems (subjective assessment) were found to be significantly associated to lower MNA scores ($p = 0.049$ and $p = 0.015$, respectively) (Soini *et al.*, 2003). Older people who are poor, isolated and frail (as in this study) are less likely to access dental services. In a recent study conducted in New South Wales, Australia, being edentulous was associated with being older, having no private dental insurance, being female, leaving school at less than 15 years of age, being poor, not owning a home, living in a rural area, and being unable to travel alone (Ringland *et al.*, 2004).

Regular consumption of fruit and vegetables is said to be associated with a reduced risk of cancer, cardiovascular disease, stroke, Alzheimer disease, cataracts, and some of the functional declines associated with aging (Liu, 2003). Therefore, not surprisingly, the World Health Organization recommends adequate consumption of fruits, vegetables and milk products (Wahlqvist *et al.*, 2002). Older people in this study who reported eating fruits, vegetables or milk products were more likely to be nourished and so not surprisingly were less likely to be underweight. Encouraging older people to consume fruits, vegetables and milk products should be strongly encouraged.

Older people in these shelter homes often had no independent income and were dependent on support from family or outside agencies. Often, these people had lived alone for quite some time, dependent on the help of others prior to admission to these shelter facilities. Therefore, it was not surprising that older people without families were at increased risk of having a low BMI. This group of older people are at high risk of developing under-nutrition and its many adverse consequences. Targeting this group of elderly people early using community support services is likely to be beneficial.

This study has several limitations. The NHC was designed for use in North America as an awareness tool. Similar to many other nutritional screening tools (i.e. Mini Nutritional Assessment), at the time of this study it had not been validated for use in Asia. When compared to an objective marker for under-nutrition (BMI < 18.5 kg/m^2), not surprisingly, a low sensitivity (66.4%), specificity (42.7%) and positive predictive value (16.2%), but very good negative predictive value (88.4%) was seen. We had elected to use the NHC instead of other screening tools (i.e. Mini Nutritional Assessment) for logistical reasons, given its simplicity (i.e. biochemical and anthropometric measures not required). Azad and colleagues had compared the NHC to a more detailed nutritional assessment including objective markers in Canadian hospitals and similarly found that the sensitivity of this awareness tool was 54.4% whilst its specificity was 61.3% (Azad *et al.*, 1999). Another European community study comparing the NHC to a BMI < 20 kg/m^2 reported a sensitivity of 59% and a specificity of 53% (de Groot *et al.*, 1998). Given the similarities in these values, it would appear that the response to the NHC in our population (South East Asian) was comparable to the responses seen in western populations. It's excellent negative predictive value of almost 90% is reassuring as older people classified as nourished (< 3) on the NHC are unlikely to be at nutritional risk. Older people scoring $\geq$ 3 on the NHC should be prompted to improve their dietary practices or consult their medical practitioners for further evaluation. The NHC may be used as an awareness tool in Malaysia for these reasons. It should not be used as a nutritional screening tool in Malaysia given its poor

sensitivity and positive predictive value. Further studies are required to identify a suitable nutritional screening tool that can be easily and reliably administered to a multicultural Malaysian population. Also, almost 76% of the residents surveyed in this study were identified as being cognitively impaired. This high prevalence of cognitive impairment may impair the accuracy of responses to the questionnaires. Scores on cognitive assessment tools are influenced negatively by low educational background (De Yebenes *et al.*, 2003). It should be noted that at least 64% of participants were uneducated and a further 32.7% had only received primary educations and this may account somewhat for the high prevalence of low ECAQ scores seen in this study.

In conclusion, there is a high risk of under-nutrition in residence of these shelter homes in Peninsular Malaysia. There is a need for a simple, cost-effective and validated nutritional screening tool that can be used to evaluate older people in countries such as Malaysia and further efforts to develop this is urgently required. The NHC should be used mainly as an awareness tool and not as a screening tool. Under-nutrition is a clinical syndrome with many physiological and non-physiological causes. Several well-established non-physiological causes of under-nutrition, like depression and medical illnesses, were positively identified in this study, and measures should be instituted to manage these conditions appropriately. Attention to oral health is important and the provision of nutritious food in such facilities should not be under-valued. Older people who lack family support are at high risk of developing under-nutrition and its adverse consequences and so targeting this population group early (perhaps with community support services) may be beneficial.

Table 5.1 Characteristics of the 1081 elderly people residing in the shelter homes in Peninsular Malaysia

	Male	Female	Total
Number (%)	633(58.6)	448(41.4)	1081
Age*			
60-74	418(66.4)	302(68.2)	720
75-84	174(27.6)	113(25.5)	287
>85	38(6.0)	28(6.3)	66
Ethnicity			
Malay	249(39.3)	231(51.6)	480
Chinese	213(33.7)	116(25.9)	329
Indian	171(27.0)	97(21.7)	268
Others	0(0)	4(0.9)	4
Education			
None	362(57.2)	331(73.9)	693
Primary	248(39.2)	105(23.4)	353
Secondary or more	23(3.6)	12(2.7)	35
Origin			
Urban	118(18.6)	86(19.2)	204
Rural	515(81.4)	362(80.8)	877
Family Relationships			
[Remove this line across all columns]	377(59.6)	290(64.7)	667
None	49(7.7)	22(4.9)	71
Siblings	158(25.0)	108(24.1)	266
Children	49(7.7)	28(6.3)	77
Others			
Nutritional Status			
Nourished	260(41.1)	187(41.7)	447
Moderate of Under-nutrition (UN)	219(34.6)	128(28.6)	347
High-risk of (UN)	154(24.3)	133(29.7)	287
Body Mass Index [BMI] (kg/m^2)+			
<18.5	59(10.3)	81(20.0)	140
[18.5-19.99]	[115(22.8)]	[63(15.5)]	[178]
>23	131(22.9)	110(27.1)	241
18.5-22.9	383(66.8)	215(53.0)	598
Mood±			
Normal	109(21.2)	79(20.7)	188
At-risk of depression	405(78.8)	302(79.3)	707
Cognitive State			
Normal	44(9.8)	113(17.9)	157
Borderline Cognitive Impairment (CI)	67(10.6)	40(8.9)	107
CI	453(71.6)	44(81.3)	817
Physical Function			
Independent	463(73.1)	322(72.1)	786
Mildly dependent	123(19.4)	79(17.6)	202
Moderate-severe dependence	47(7.4)	46(10.3)	93

* 8 missing data for age + 102 missing data for BMI

± 186 missing data for geriatric depression score

Table 5.2 Number of people responding with a 'Yes' to each of the questions in the 'DETERMINE Your Nutritional Health Checklist'.

Statement No.	Statements: 'DETERMINE Your Nutritional Health Checklist' [Points]	Number (%) of residents with positive response ('Yes')
1	I have an illness or condition that made me change the kind and/or amount of food that I eat [2]	202 (18.7)
2	I eat fewer than two meals per day [3]	175 (16.2)
3	I eat few fruits or vegetables or milk products [2]	381 (35.3)
4	I have 3 or more drinks of beer, liquor or wine almost every day [2]	5 (0.5)
5	I have tooth or mouth problems that make it hard for me to eat [2]	374 (34.6)
6	I don't always have enough money to buy the food I need [4]	342 (31.6)
7	I eat alone most of the time [1]	160 (14.8)
8	I take 3 or more different prescribed or over-the-counter drugs a day [1]	86 (8.0)
9	Without wanting to, I have lost or gained 10 pounds in the last 6 months [2]	36 (3.3)
10	I am not always physically able to shop, cook and/or feed myself [2]	38 (3.5)

Table 5.3 Descriptive statistics of patients' baseline clinical characteristics and log–binomial regression univariate analysis of subjects' clinical characteristics based on the ' DETERMINE your nutritional health checklist' [NHC] score

	At-Risk of Under-nutrition (NHC ≥ 3)	Nourished (NHC < 3)	Relative Risk (95% CI)	P-value
N (%)	634 (58.6)	447 (41.4)		
Age (years): mean (95% CI)	72.1 (71.4-72.7)	71.4 (70.8-72.1)	1.00 (1.00-1.01)	0.164
Female: n (%)	261 (41.2)	187 (41.8)	0.99 (0.89-1.09)	0.827
BMI (kg/m^2): mean (95% CI)	21.6 (21.2-21.9)	21.4 (21.1-21.8)	1.00 (0.99-1.02)	0.597
No Education: n (%)	392 (61.8)	301 (67.3)	0.91 (0.82-1.00)	0.058
Rural Origin: n (%)	503 (79.3)	374 (83.7)	0.89 (0.79-1.00)	0.059
No Family: n (%)	395 (62.3)	272 (60.9)	1.03 (0.92-1.14)	0.630
No visit: n (%)	501 (79.0)	372 (83.2)	0.90 (0.80-1.01)	0.070
ECAQ score: mean (95% CI)	2.8 (2.5- 3.0)	2.3 (2.0- 2.6)	1.02 (1.00-1.03)	0.014
No CI: n (%)	93 (14.7)	64 (14.3)	1.01 (0.88-1.16)	0.871
GDS score: mean (95% CI)	7.5 (7.3- 7.8)	7.0 (6.7- 7.3)	1.03 (1.01-1.05)	0.007
Not at risk of depression: n (%)	112 (20.4)	76 (22.0)	0.96 (0.84-1.10)	0.559
Barthel score: mean (95% CI)	18.4 (18.1-18.7)	18.8 (18.6-19.1)	0.99 (0.97-1.00)	0.027
Moderately-severely dependent: n (%)	59 (9.3)	34 (7.6)	1.09 (0.93-1.28)	0.300
No difficulty eating: n (%)	616 (97.2)	434 (97.1)	1.01 (0.75-1.37)	0.947
No past history fall: n (%)	397 (62.6)	285 (63.8)	0.98 (0.88-1.09)	0.701
Medications ≥ 3: n (%)	222 (35.0)	124 (27.7)	1.14 (1.03-1.27)	0.009
Number of illness: mean (95% CI)	0.9 (0.8- 1.0)	0.7 (0.7- 0.8)	1.09 (1.04-1.14)	<0.001
Presence of any illness: n (%)	373 (58.8)	252 (56.4)	1.04 (0.94-1.15)	0.423
Illness < 2: n (%)	498 (78.5)	380 (85.0)	0.85 (0.76-0.95)	0.004

Table 5.4 Descriptive statistics of patients' baseline clinical characteristics and log–binomial regression univariate analysis of subjects' clinical characteristics based on the subject's weight as determined by body mass index (BMI- Underweight= <18.5kg/m^2)

	BMI < 18.5 kg/m^2	BMI ≥ 18.5 kg/m^2	RR (95% CI)	P-value
Number (n) (%)	140 (14.3)	839 (85.7)		
Age (years): mean (95% CI)	72.4 (71.0-73.7)	71.6 (71.1-72.1)	1.01 (0.99-1.03)	0.275
Female: n (%)	81 (57.9)	325 (38.7)	1.94 (1.42-2.64)	<0.001
No Education: n (%)	96 (68.6)	514 (61.3)	1.42 (1.00-2.03)	0.051
Rural Origin: n (%)	115 (82.1)	679 (80.9)	1.07 (0.72-1.60)	0.735
No Family: n (%)	104 (74.3)	499 (59.5)	1.80 (1.26-2.57)	0.001
No visits: n (%)	119 (85.0)	665 (79.3)	1.41 (0.91-2.18)	0.1234
Nourished as per NHC: n (%)	47 (33.6)	358 (42.7)	0.72 (0.52-0.99)	0.0454
NHC Score: mean (95% CI)	4.7 (4.1- 5.3)	3.7 (3.5- 3.9)	1.08 (1.04-1.13)	0.0003
S1- Negative response: n (%)	97 (69.3)	699 (83.3)	0.52 (0.38-0.71)	<0.001
S2- Negative response: n (%)	103 (73.6)	731 (87.1)	0.48 (0.35-0.67)	<0.001
S3- Negative response: n (%)	83 (59.3)	554 (66.0)	0.78 (0.57-1.07)	0.120
S4- Negative response: n (%)	139 (99.3)	835 (99.5)	0.71 (0.12-4.15)	0.707
S5- Negative response: n (%)	72 (51.4)	565 (67.3)	0.57 (0.42-0.77)	<0.001
S6- Negative response: n (%)	105 (75.0)	553 (65.9)	1.46 (1.02-2.09)	0.037
S7- Negative response: n (%)	117 (83.6)	736 (87.7)	0.75 (0.50-1.13)	0.168
S8- Negative response: n (%)	120 (85.7)	784 (93.4)	0.50 (0.33-0.75)	<0.001
S9- Negative response: n (%)	128 (91.4)	815 (97.1)	0.41 (0.25-0.66)	<0.001
S10- Negative response: n (%)	134 (95.7)	822 (98.0)	0.54 (0.27-1.09)	0.084
No Cognitive Impairment: n (%)	17 (12.1)	133 (15.9)	0.76 (0.47-1.23)	0.268
ECAQ score: mean (95% CI)	2.4 (1.9- 2.8)	2.8 (2.6- 3.0)	0.96 (0.91-1.02)	0.161
GDS score: mean (95% CI)	7.1 (6.6- 7.6)	7.2 (7.0- 7.4)	0.99 (0.93-1.04)	0.642
Not Depressed: n (%)	31 (24.2)	152 (21.7)	1.13 (0.78-1.63)	0.523
Barthel score: mean (95% CI)	19.2 (18.8-19.6)	19.3 (19.2-19.4)	0.98 (0.92-1.05)	0.622
Moderately-severely dependent: n (%)	6 (4.3)	23 (2.7)	1.47 (0.71-3.04)	0.304
No past history fall: n (%)	94 (67.1)	507 (60.4)	1.29 (0.93-1.78)	0.134
Medications < 3: n (%)	55 (39.3)	246 (29.3)	1.46 (1.07-1.99)	0.018
Number of illness: mean (95% CI)	0.9 (0.8- 1.0)	0.7 (0.7- 0.8)	1.19 (1.01-1.39)	0.036

NHC- 'DETERMINE Your Nutritional Health Checklist', GDS- Geriatric Depression Scale, ECAQ- Elderly Cognitive Assessment Questionnaire; S1-10- Statements in the NHC- see method

Chapter 6

The nutritional status of 250 older Australian recipients of domiciliary care services, and its association with outcomes at 12 months

6.1 Summary

It is thought that the prevalence of under-nutrition increases with increasing frailty and so it was hypothesized that elderly recipients of domiciliary care services in South Australia may be at nutritional risk. Therefore, the aim of this study was to identify predictors and consequences of nutritional risk, as determined by the Mini Nutritional Assessment (MNA), among older recipients of South Australian domiciliary care services living at home. The prevalence of under-nutrition was determined based on the Mini Nutritional Assessment (MNA) scores. Factors independently associated with low MNA scores (<24) at baseline were also identified. One year later, at follow-up, the consequences of these low scores in 250 domiciliary care clients (age 67-99, 173 women) were assessed. Letters suggesting nutritional intervention were sent to the general practitioners of subjects who were not well nourished following the initial interview at baseline. At baseline, 56.8% were well nourished (MNA $\geq$ 24), 38.4% at-risk of malnutrition (MNA 17-23.5) and 4.8% malnourished (MNA < 17) [43.2% not well nourished (NWN)]. Independent factors associated with low MNA scores (<24) were living alone, the Physical and Mental Component Scale of the 36-Item Short Form Health Survey (SF-36). Follow-up information was obtained for 240 subjects (96%). In the ensuing year not well-nourished subjects were more likely than well-nourished subjects to have been admitted to hospital (RR 1.51, 95%CI 1.07-2.14), have two or more emergency hospital admissions (2.96,1.15-7.59), spend more than 4 weeks in hospital (3.22, 1.29-8.07), fall (1.65, 1.13-2.41) and report weight loss (2.63, 1.67-4.15). In this study, the MNA identified a large number of subjects with impaired nutrition who did significantly worse than well-nourished subjects during the following year. Studies are needed to determine if nutritional or other interventions in people with low MNA scores can improve clinical outcomes.

6.2 Introduction

The decline in body weight after the age of 60 years is disproportionately that of lean body tissue, i.e., sarcopenia , and this has adverse effects (Evans & Campbell, 1993). In a recent, large study of community-dwelling people aged 65 years or older in the United States of America, weight loss in excess of 5% body weight over 3 years occurred in 17% and was associated with a significant increase in mortality of some 70%, irrespective of the initial weight (Newman *et al.*, 2001). Studies in both the United States and Australia have established that up to 15% of community-dwelling and home-bound elderly, between 23 and 62%, of hospitalized patients, and up to 85% of nursing-home residents suffer from protein energy malnutrition, with an associated increase in morbidity and mortality (MacIntosh *et al.*, 2000; Morley, 1996).

Domiciliary care services help elderly people with moderate or severe functional limitations remain at home. In South Australia, approximately 10% of persons over the age of 65 years receive publicly funded in-home care, such as domiciliary care (ie. the provision of equipment, assistance with personal care) or home-delivered meals (Australian Bureau Statistics, 1995; Payette *et al.*, 1995). The 'functionally dependant' elderly may be at increased risk for malnutrition and should perhaps be targeted for screening, treatment and prevention of malnutrition (Beck *et al.*, 2001; Payette *et al.*, 1995).

The major aims of this study were to identify factors associated with and the consequences of nutritional risk as determined by the Mini Nutritional Assessment (MNA), in elderly individuals receiving domiciliary care services.

6.3 Materials and methods

6.3.1 Study population

Contact details of all clients (n=1295) who registered with the Eastern Domiciliary Care Service in Adelaide over an eight month period were obtained with the permission of the Research Ethics Committee of the Royal Adelaide Hospital (RAH). Subjects younger than 65 years (16.2%), non-English speaking (7.9%) and with the diagnosis of dementia (11.2%) were excluded. The 838 remaining subjects were sent an information sheet inviting them to participate. The 250 participating subjects gave informed consent and were interviewed at home by either Dr Caroline MacIntosh or Dr Mandy Callary.

6.3.2 Baseline patient characteristics

The Mini Nutritional Assessment (MNA- Appendix 1) was used to assess nutritional status in this study and is described in detail in 3.6.1.

The Standardized Mini Mental State Examination (SMMSE- Appendix 7) which consists of 11 tasks was used to assess cognitive impairment or dementia (Folstein *et al.*, 1975). Cognitive status was classified as intact (score≥24); moderately impaired (17-23) or demented (<17). Score range was 0-30. All subjects in this study scored ≥ 24 (Folstein *et al.*, 1975).

The 30 question Geriatric Depression Scale (GDS 30 – Appendix 8) was used to diagnose depression. It focuses on the cognitive aspects of a depressive illness and consists of a series of 30 questions in a simple 'yes/no' format (Yesavage *et al.*, 1982). A score ≥11 indicates depression (Yesavage *et al.*, 1982).

The 36-Item Short Form Health Survey (SF-36- Appendix 9) was used to assess health status and quality of life. The SF-36 is a multi-item scale which assesses 8 health concepts: 1) limitations in physical functioning because of health problems (SF-36 PF); 2) role

limitations due to physical problems (SF-36 RP); 3) bodily pain (SF-36 BP); 4) role limitation due to emotional problems (SF-36 RE); 5) general mental health (SF-36 MH); 6) limitations in social functioning (SF-36 SF) 7) vitality (SF-36 VT); and 8) general health perceptions (SF-36 PCS). From the 8 health concepts an overall score for physical (SF-36 PCS) (0-100) and mental (SF-36 MCS) (0-100) health status can be calculated (Ware & Sherbourne, 1992).

Age, body weight, height, body mass index (BMI), smoking status, the amount of formal care (hours/month), receipt of 'Meals on Wheels' (MOW), number of medications used per day, hospital admissions within the last 12 months, were recorded. History was obtained from the subject supplemented by review of Domiciliary Care case files, to determine the presence of medical disorders, such as cardiovascular and respiratory disorders, depression and Parkinson's disease.

6.3.3 Intervention

A letter was sent to the general practitioner of all subjects identified as being malnourished or at-risk of malnutrition alerting them to this finding and suggesting further nutritional assessment and/or intervention. In addition, subjects classified as malnourished were offered a referral to a clinical dietitian at the Royal Adelaide Hospital.

6.3.4 Prospective survey

Twelve to fifteen months after the initial interview, subjects were contacted by telephone by the author to obtain information about changes in their living situation, hospital admissions and their duration, the occurrence of nutritional intervention, subjective weight loss and falls over the 12-month period following initial contact. Some subjects (16%) were contacted 13 to 15 months after baseline. However, efforts were made to ensure that information only pertaining to the 12 months following baseline contact was obtained and analyzed.

6.3.5 Statistical analysis

As the number of malnourished subjects (MNA<17) was small, subjects were re-grouped as either well nourished (N) or not well nourished (NWN =MNA <24) for statistical analyses. Chi square and t-tests were used to compare the participants to those who elected not to participate. Log-binomial regression univariate analysis of subjects' clinical characteristics based on low baseline MNA scores (<24) was performed. The potential predictors of low MNA scores derived (P<0.15 by univariate analysis) were included into a log-binomial regression multivariate analysis yielding independent predictors of low MNA scores (ie. MNA <24). The number of medications, BMI and GDS scores were not included into the multivariate analysis, as these factors contributed 2, 3 and 2 points on the MNA, respectively, and were accordingly expected to be a determinant of nutritional status. Log-regression binomial univariate analysis of 12-month outcomes based on baseline MNA scores was then performed whilst correcting for age and living status as confounders. SAS was the software program used. P values < 0.05 were considered to be statistically significant.

6.4 Results

Although Dr Caroline MacIntosh had described some of the baseline results in her PhD thesis, the baseline results presented here have been re-analysed using different statistical methods. Furthermore, new information regarding health outcomes is presented here.

Of the 838 domiciliary care clients contacted, 250 (29.8%) agreed to take part. 77 men and 173 women were assessed and formed the baseline population. The majority of subjects were Caucasian (98.8%), with the rest either Oriental, Indian or of Aboriginal descent (0.4% each).

Compared to those subjects who did not participate in the study (n=588), participating subjects were more likely to be living alone (53.60% vs. 45.44%; P=0.03) and younger (mean 79.45 (CI 78.63-80.27) vs. 80.63 (80.05-81.20); P=0.03). There was no significant difference with regards to gender (P=0.15).

Table 6.1 shows the results of the univariate log-binomial regression analysis of subjects' clinical characteristics, based on baseline MNA scores of <24. Subjects were grouped as well nourished (N 56.8%) and not well nourished (NWN 43.2%). 21 parameters were identified as potential predictors (P<0.15) of a low MNA score (< 24). These included age, Body Mass Index (BMI), living alone, number of medications, receipt of formal care, receipt of 'Meals on Wheels', number of hospital admission days in the preceding 12 months, cardiovascular disorders, gastrointestinal disorders, diabetes, respiratory disorders, Geriatric Depression Scale (GDS) scores and several quality of life domains. The factors found to be independently associated with nutritional risk derived by multivariate analysis were 1) living alone, 2) the Physical Component Scale score (SF-36 PCS) and 3) the Mental Component Scale score (SF-36 MCS) of the 36-Item Short Form Health Survey (SF-36); a low score on these scales was associated with low MNA scores (<24).

244 (97.6%) subjects were successfully re-contacted at 12-15 months. 6 could not be contacted (1 N, 5 NWN). 4 subjects declined further participation (3 N, 1 NWN). Of the 240 subjects re-analyzed, 138 (57.5%) were N at baseline, while 102 (42.5%) were NWN. Table 6.2 shows the results of the log-binomial regression analysis of the 12 month outcomes based on low MNA scores at baseline (< 24), corrected for age and living status, which were likely confounders. 20 subjects had died since the initial assessment (9 NWN vs. 11 N, RR 1.02, 95% CI 0.44-2.38, P=0.96). NWN subjects were more likely to have been admitted to hospital (42 NWN vs. 37 N, RR 1.51, 95% CI 1.07-2.14, P=0.02), particularly as an emergency admission (35 NWN vs. 24 N, RR 1.94, 95% CI 1.24-3.03, P<0.01), to have 2 or more emergency admissions (13 NWN vs. 6 N, RR 2.96, 95% CI 1.15-7.59, P=0.02), to spend more than 4 weeks in hospital (15 NWN vs. 6 N, RR 3.22, 95% CI 1.29-8.07, P=0.01), to report weight loss (41 NWN vs. 21 N, RR 2.63, 95% CI 1.67-4.15, P<0.001) and fall (39 NWN vs. 33 N, RR 1.65, 95% CI 1.13-2.41, P<0.001) compared to N subjects over a 12 month period (Table 6.2). Subjective reports of nutritional intervention were infrequent (11 NWN) and therefore no statistical analysis of this outcome was undertaken. An impact on study outcome was unlikely as only 11 out of 93 subjects reported receiving nutritional intervention.

6.5 Discussion

This study revealed a high prevalence of malnutrition amongst 'functionally dependant' community dwelling elders. Living alone, and score on the Physical Component Scale (SF-36 PCS) and the Mental Component Scale (SF-36 MCS) of the 36-Item Short Form Health Survey (SF-36) were found to be independently associated with an impaired nutritional status. The MNA, an easily administered, validated screening tool was able to identify subjects (not well nourished (NWN)) who experienced increased hospitalization frequency and duration, falls and subjective weight loss over a 12 month period.

As classified by the MNA, 38.4% of subjects in this study were at-risk of malnutrition and 4.8% were malnourished. Our findings are consistent with those of two recent studies that used the MNA to screen similar population groups. In a study of 61 patients presenting to general practitioners in Denmark, 38% were classified as at-risk of malnutrition and none as malnourished (Beck *et al.*, 2001). In a Spanish study of 3,460 community-dwelling subjects older than 65 years, 3.3% were classified by the MNA as malnourished and 40% at-risk of malnutrition (Ramon & Subira, 2001; The Spanish Geriatric Oral Health Research Group, 2001).

Subjects with MNA scores <24 (not well nourished) were significantly more likely to perform substantially and significantly worse than subjects scoring > 24 (well nourished) during the following year. These results are consistent with that of a Danish general practice study (Beck *et al.*, 2001), which reported a hospitalization rate among at-risk patients twice that of the well nourished, although the increase was not significant. It therefore appears that subsets of under-nourished community dwelling older people at-risk of adverse consequences can be identified relatively easy, and could be selectively targeted for intervention. Home-based services such as domiciliary care could play an important role in screening and systematically delivering intensive nutritional supplements or other interventions to elders in their homes. Protein energy supplementation has previously been

shown to be of benefit in more severely malnourished older populations, such as people in hospital or nursing homes (Bourdel-Marchasson *et al.*, 2000; Lauque *et al.*, 2000; Potter *et al.*, 2001). Little is known about the benefits, if any, and the most appropriate form of intervention, in more marginally under-nourished community dwelling older people such as those in this study.

This study had several potential limitations. There may have been a selection bias in the choice of the sample population, as 70.2% of eligible subjects declined participation. Participating subjects were younger and more likely to be living alone. Individuals who were non-English speaking, without access to an interpreter or had been clinically diagnosed with dementia were specifically excluded for logistical reasons. The majority of subjects in this study were Caucasians. Medical information was provided by the subject and supplemented by review of the Domiciliary Care Service case-file, which may be incomplete. The data obtained at follow-up was dependent on the subject's ability to recollect events over the previous 12 months, thus also introducing a possible reporting bias. Some strengths of the study were the relatively high follow-up rate (96%), and limited potential for inter-observer bias.

In conclusion, almost half of community dwelling older recipients of domiciliary care services in this study were malnourished or at-risk of malnutrition and this was associated with a poorer outcome. These findings are consistent with a high rate of under nutrition among older people in developed countries, even among those living relatively independently. To be effective, interventions may need to target elders directly in their homes. Community organizations such as domiciliary care could be instrumental in delivering such care. There is need both to develop effective intervention strategies for these at-risk elderly, and to determine how best to implement them. Studies are needed to determine if nutritional or other interventions in patients with low MNA scores can improve clinical outcomes.

Table 6.1 <u>Baseline Data:-</u> Descriptive statistics of patients' baseline clinical characteristics and log–binomial regression analysis of subjects' clinical characteristics based on a low baseline Mini Nutritional Assessment score of <24.

	#Not-Well-Nourished (MNA <24)	#Nourished (MNA >24)	*RR (95% CI)	*P-value
Total Subjects (%)	**108 (43.2)**	**142 (56.8)**		
Gender-Female (%)	78 (72.2)	94 (66.2)	1.18 (0.85-1.63)	0.321
Age (years): mean (/-sd)	79.7 (6.8)	78.4 (6.5)	1.02 (1.00-1.04)	0.106
BMI (kg/cm2): mean (/-sd)	24.6 (5.5)	27.2 (4.5)	0.93 (0.90-0.96)	<0.001
MNA Score: mean (/-sd)	20.5 (2.6)	26.0 (1.5)		
Lives Alone: n (%)	68 (63.0)	66 (46.5)	1.47 (1.09-1.99)	0.012
Number of Medications: mean (/-sd)	5.8 (2.9)	4.3 (2.6)	1.08 (1.05-1.12)	<0.001
Formal Care (hours/month): median (IQ range)	1.0 (0.0-3.6)	0.0 (0.0-2.0)	1.01 (1.00-1.02)	0.093
Receive Meals on Wheels: n (%)	28 (25.9)	16 (11.3)	1.64 (1.24-2.17)	0.001
Hospital Admissions (days): median (IQ range)	10.0 (0.0-28.0)	5.0 (0.0-17.0)	1.00 (1.00-1.01)	0.116
Cardiovascular Disorders: n (%)	64 (59.3)	100 (70.4)	0.76 (0.58-1.01)	0.059
GI Disorders: n (%)	29 (26.9)	21 (14.8)	1.47 (1.10-1.97)	0.010
Cancer: n (%)	22 (20.4)	21 (14.8)	1.23 (0.88-1.72)	0.221
Diabetes: n (%)	24 (22.2)	20 (14.1)	1.34 (0.98-1.83)	0.071
Osteoporosis: n (%)	29 (26.9)	30 (21.1)	1.19 (0.87-1.62)	0.275
Respiratory Disorders: n (%)	35 (32.4)	24 (16.9)	1.55 (1.18-2.05)	0.002
Stroke: n (%)	20 (18.5)	29 (20.4)	0.93 (0.64-1.35)	0.712
Fractured Hip: n (%)	10 (9.3)	11 (7.7)	1.11 (0.69-1.79)	0.658
Parkinson's Disease: n (%)	7 (6.5)	5 (3.5)	1.37 (0.83-2.27)	0.213
Past Depression: n (%)	17 (15.7)	17 (12.0)	1.19 (0.82-1.72)	0.365
SF-36 Physical functioning (PF): mean (/-sd)	26.7 (9.1)	31.4 (10.1)	0.97 (0.95-0.98)	<0.001
SF-36 Role limitation due to physical problems (RP): mean (/-sd)	36.5 (9.5)	40.8 (10.6)	0.98 (0.96-0.99)	0.001
SF-36 Bodily pain (BP): mean (/-sd)	41.6 (13.4)	43.7 (13.2)	0.99 (0.98-1.00)	0.225
SF-36 Role limitation due to emotional problems (RE): mean (/-sd)	48.1 (8.3)	51.9 (7.0)	0.97 (0.96-0.99)	<0.001
SF-36 General mental health (MH) : mean (/-sd)	46.3 (12.8)	53.5 (8.1)	0.99 (0.99-1.00)	0.006
SF-36 Limitations in social functioning (SF): mean (/-sd)	39.9 (13.3)	47.0 (11.2)	0.97 (0.96-0.98)	<0.001
SF-36 Vitality (VT): mean (/-sd)	37.7 (10.1)	43.6 (9.6)	0.97 (0.96-0.98)	<0.001
SF-36 General health (GH): mean (/-sd)	37.8 (10.5)	43.1 (10.1)	0.98 (0.96-0.99)	<0.001
SF-36 Physical component scale (PCS): mean (/-sd)	32.2 (4.1)	32.9 (4.0)	0.97 (0.94-1.01)	0.118
SF-36 Mental Component Scale (MCS): mean (/-sd)	37.0 (5.1)	40.6 (3.7)	0.94 (0.92-0.95)	<0.001
SMMSE Score: median (IQ range)	28.0 (26.0-29.0)	28.0 (26.0-29.0)	0.98 (0.93-1.03)	0.434
GDS: mean (/-sd)	11.1 (6.0)	7.1 (4.8)	1.04 (1.03-1.05)	<0.001

Descriptive statistics of patients' clinical characteristics* Univariate analysis of subjects' clinical characteristics based on MNA score

BMI: Body mass index; MNA: Mini Nutritional Assessment (0-30); SF-36: 36-Item Short Form Health Survey; SMMSE: Standardized Mini Mental State Examination (0-30); GDS: Geriatric Depression Scale Score (0-30)

Table 6.2 12-Month Follow-up Data, log-binomial regression analysis of variables associated with clinical outcomes based on Mini-Nutritional Assessment (MNA) scores at baseline adjusted for age and living status as confounders

	Not-Well-Nourished (MNA<24) n (%)	Nourished (MNA≥24) n (%)	Unadjusted RR (95% CI)	Unadjusted P-value	Adjusted RR (95% CI)	Adjusted P-value
Deaths	9 (8.7)	11 (7.8)	1.11 (0.48-2.58)	0.8096	1.02 (0.44-2.38)	0.961
Move to more supportive accommodation	12 (12.9)	10 (7.9)	1.64 (0.74-3.63)	0.2236	1.32 (0.59-2.95)	0.493
Needing any form of admission	42 (45.2)	37 (29.1)	1.55 (1.09-2.20)	0.0146	1.51 (1.07-2.14)	0.021
Needing emergency admission	35 (37.6)	24 (18.9)	1.99 (1.28-3.11)	0.0024	1.94 (1.24-3.03)	0.004
Requiring ≥ 2 admissions	17 (18.3)	11 (8.7)	2.11 (1.04-4.29)	0.0391	2.17 (1.05-4.44)	0.035
Requiring≥2 emergency admissions	13 (14.0)	6 (4.7)	2.96 (1.17-7.50)	0.0222	2.96 (1.15-7.59)	0.024
Spending > 4 weeks in hospital	15 (16.1)	6 (4.7)	3.41 (1.38-8.47)	0.0081	3.22 (1.29-8.07)	0.012
Reported weight loss	41 (44.1)	21 (16.5)	2.67 (1.70-4.19)	0.0000	2.63 (1.67-4.15)	<0.001
Falls	39 (41.9)	33 (26.0)	1.61 (1.11-2.36)	0.0132	1.65 (1.13-2.41)	0.010

Chapter 7

Nutritional screening of older people in a sub-acute care facility in Australia and its relation to discharge outcomes

7.1 Summary

Many older people admitted to hospital are at nutritional risk. The aim of this study was 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 (SNA) and (2) discharge outcomes. A prospective study involving 65 (21 males) patients older than 65 years was performed in a sub-acute care facility in Adelaide, South Australia. The Mini Nutritional Assessment (MNA), SNA, 'rapid screen' and discharge outcome were recorded. The prevalence of under-nutrition was high, ranging from 35.4% to 43.1%, depending on the screening method used. Compared to the SNA the 'rapid screen' consisting of (1) Body Mass Index (BMI) < 22kg/m^2; and/or (2) reported unintentional weight loss of > 7.5% over the previous 3 months and the two–tiered MNA process (at-risk subjects [46% of total] further evaluated using SNA) had sensitivities of 78.6 and 89.5%, specificities of 97.3% and 87.5%, positive predictive values of 95.7% and 89.5% and negative predictive values of 85.7% and 87.5% respectively in diagnosing under-nutrition. Under-nourished [U] patients as identified by the SNA (50.0%[U] vs. 21.6%[N]; P=0.02), the two-tiered MNA process (50.0%[U] vs. 21.6%[N]; P=0.02) and the rapid screen (56.5%[U] vs. 21.4%[N]; P<0.01) were more likely to be discharged to an acute hospital or an accommodation with increased supports (poor discharge outcome) than nourished [N] patients. In conclusion, all screening methods identified patients who were more likely to experience a poor discharge outcome. The highly specific but less sensitive 'rapid screen' may be the best method in facilities with limited resources as it can be easily incorporated into nursing/medical admissions and avoids biochemical investigations in all patients. The more sensitive two-tiered MNA may be better if resources permit.

7.2 Introduction

Malnutrition is prevalent in the elderly and is associated with impaired muscle function, decreased bone mass, immune dysfunction, anaemia, reduced cognitive functioning, prolonged hospitalisation, delayed post-operative recovery, and increased falls, morbidity and mortality (MacIntosh *et al.*, 2000; Visvanathan *et al.*, 2003).

In two recent Australian studies (including the study described in Chapter 6), 20% of hospitalised patients and 4.8% of community dwelling functionally dependant elderly people (Chapter 6) were malnourished as assessed by the Mini Nutritional Assessment (MNA- Appendix 1) (Barone *et al.*, 2003; Visvanathan *et al.*, 2003). The prevalence of under-nutrition in sub-acute care facilities in Australia is not readily known. Nutritional status often deteriorates after acute hospitalisation, due to poor recognition and monitoring of nutritional status and inadequate intake of nutrients for days at a time (Kamath *et al.*, 1986; Riffer, 1986; Sullivan *et al.*, 1989; Sullivan *et al.*, 1999; Thomas *et al.*, 2002). In one study, 40% of patients admitted to an acute hospital in Scotland were under-nourished and 75% of these under-nourished patients when reassessed upon discharge had lost weight whilst in hospital (McWhirter & Pennington, 1994). It is therefore likely that more people are under-nourished at discharge from an acute hospital to a subacute care facility than in the acute hospital or in the community as a whole.

Impaired appetite, inadequate nutrient intake and weight loss may continue for long periods following discharge from acute hospitals (Williams *et al.*, 1990). Therefore, at admission to a subacute care facility, there may be a 'golden opportunity' for health care providers to screen for and correct under-nutrition. However, this is not done routinely in most facilities, because of the time and need for blood tests and nutritionally trained health professionals (eg dietitians) to complete more comprehensive nutritional assessments.

Any screening tool adopted in a high patient-load, sub-acute facility, would ideally be sensitive, specific, cheap, simple and rapid to administer. Several screening tools are available to detect under-nutrition in older people. The MNA, an easily administered, validated (in the elderly) and widely used clinical tool can be performed in 15 minutes without the need for biochemical testing or nutritional training (Guigoz *et al.*, 1994; Guigoz *et al.*, 1996). To the best of our knowledge, the results of MNA assessment have not been compared previously to those of comprehensive nutritional assessment in any Australian setting. A low body mass index (BMI) and unintentional weight loss are the two most important contributors to a low (impaired) MNA score and so a simple assessment incorporating these two variables ('rapid screen') could also possibly function as a quick measure of under-nutrition and predictor of subsequent worse outcome (Murphy *et al.*, 2000).

The aim of this study was to determine the prevalence and consequences of under-nutrition among older people in a sub-acute health care facility, using different screening methods (the single and two-tiered MNA processes and the 'rapid screen'), and compare the results to those of a more standard nutritional assessment (SNA).

7.3 Method

This study was conducted at the Hampstead Rehabilitation Centre in Adelaide, a sub-acute care facility admitting patients on discharge from surrounding acute hospitals. Consecutive patients admitted to the geriatric, medical and orthopaedic rehabilitation units were recruited and only the patient's first subacute-care admission during the study period was considered. Patients admitted to this facility are assessed for their rehabilitation potential and are selected for admission if 1) they have the potential to be eventually discharged directly to their own homes; 2) they are medically stable and 3) they would have been discharged home from the acute care facility if not for their physical disability and need to recover. A poor discharge outcome for this sub-acute care facility was therefore defined as a transfer to an acute hospital directly from the sub-acute care facility or discharge to accommodation with greater supports than they lived in before admission to the acute hospital (eg. home to nursing home/hostel). All participating patients were followed-up until they left the sub-acute care facility for home, hospital or other accommodation.

All patients (n=86) aged 65 years and over, admitted to the centre over a 3-month period, were invited to participate in this study. For logistical reasons, the following patients were excluded from the study: those who were unable to speak English (n=5), unable to provide informed consent (n= 4), with moderate to severe dysphasia (n=3), on nasogastric feeds (n=1) and amputees (n=8). All participating patients (n=65) provided informed consent and the study was approved by the Research Ethics Committee of the Royal Adelaide Hospital.

7.3.1 Nutritional assessment

All participating patients were assessed using the Mini Nutritional Assessment (MNA), standard nutritional assessment (SNA) (Table 7.1) and the rapid screen within 48 hours of admission by two investigators at separate times, in random order. One investigator always administered the SNA, the other the MNA. The patient and the investigators were initially

blinded to the results of the assessments. Once all 3 assessments were completed, a referral to the dietitian was made based on the results of the SNA (see below).

The standard nutritional assessment (SNA) (Table 7.1) was devised for this study based on the usual clinical practices of the trained dietitians at this facility and is similar to that used in previous studies (Azad *et al.*, 1999; Laporte *et al.*, 2001). The SNA was used as the 'gold standard' comparator in this study. Food records were not included due to time and personnel constraints. The parameters and cut-off values were selected based on literature evidence (see 3.3 and 3.4) and the clinical experience of the dietitians in this facility. In the Nutritional Screening Initiative, the normal BMI in the elderly was determined to be between 22 and 27 kg/m^2 and therefore a cut-off value of 22 kg/m^2 was chosen for this study to identify under-nourished patients [Table 7.1] (Omran & Morley, 2000a). The other cut-off values selected for the other parameters used in this study (Table 7.1) were based on a previous detailed nutritional assessment grid used by Azad et al. as the ' gold standard' comparator to assess three different nutritional screening tools (Azad *et al.*, 1999). In this study, patients were classified as moderately to severely under-nourished if they met the cut-off values for at least three criteria in the under-nourished column (U) as shown in Table 7.1. Patients with a combination of two values in the borderline (B) and one in the U columns or two in the U and one in the B columns were classified as mildly under-nourished. Patients classified by the SNA as having any degree of under-nutrition (mild, moderate-severe) were referred to the dietitian for further assessment and for treatment as deemed appropriate. Those with mild under-nutrition were monitored whilst those with moderate-severe under-nutrition received nutritional supplements whilst in this sub-acute care facility.

The MNA has been previously described in chapter 3 (Appendix 1). The single and two–tiered MNA results are derived from the MNA scores. In the single-tiered MNA process, subjects scoring less than 24 were classified as under-nourished. In accordance with a

previous validation study of the MNA (Guigoz *et al.*, 1994), in which the authors recommended a more in-depth assessment of the subjects at-risk of malnutrition (MNA= 17-23.5), in the two-tiered MNA process, patients scoring between 17 and 23.5 were investigated by the SNA–described earlier. This resulted in all 65 subjects being classified as under-nourished or nourished as opposed to three categories when the MNA is used alone (M, AR, N; see above).

Patients screened positive on the 'rapid screen' which was devised for use in this study, if they fulfilled one or both of the following 1) BMI < 22 kg/m^2; 2) reported unintentional weight loss of > 7.5% in the preceding 3 months. As previously stated, a low BMI and unintentional weight loss, are known to contribute greatly towards mortality and morbidity in older people. These cut-off values were chosen for the reasons previously described (see above- SNA).

7.3.2 Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the single and two-tiered MNA process and the 'rapid screen' when compared to the SNA were calculated. Sensitivity was defined as the proportion of patients classified as under-nourished by the SNA who were classified as under-nourished by the various screening tools. The specificity was defined as the proportion of patients identified as nourished by the SNA who were classified as nourished by the various screening tools. The PPV was defined as the proportion of patients screening positive (under-nourished) on the various tools that were classified as under-nourished by the SNA. The NPV was defined as the proportion of patients screening negative (nourished) on the various tools that were classified as nourished by the SNA. Chi-square analysis was used to evaluate the differences in the rate of occurrence of poor discharge outcomes between groups of subjects with different nutritional status. P values < 0.05 were considered to be statistically significant.

7.4 Results

The baseline characteristics of the study population are outlined in Table 7.2. Using the two-tiered Mini Nutritional Assessment (MNA) process, with further evaluation of the at-risk (AR) group using the Standard Nutritional Assessment (SNA), 28 (43.1%) patients were under-nourished and 37 (56.9%) were nourished [Table 7.3a]. The 'rapid screen' classified 23 (35.4%) patients as under-nourished and 42 (64.6%) as nourished [Table 7.3b]. Eight (34.8%) subjects screened positive as they had a BMI < 22kg/m^2, nine (39.1%) patients had weight loss (unintentional) > 7.5% of their body weight in the 3 months before evaluation and six (26.1%) fulfilled both criteria. The single–tiered MNA process classified 75.4% of patients as under-nourished and 24.6% as nourished [Table 7.3c]. The SNA classified 28 (43.1%) of the patients as under-nourished and 37 (56.9%) as nourished. 20 were mildly undernourished and eight were moderately-severely under-nourished.

When compared to the SNA (Table 7.3a and 7.3b), the two-tiered MNA process had a higher sensitivity (89.5% vs. 78.6%), a higher negative predictive value (NPV) (87.5% vs. 85.7%) but a lower specificity (87.5% vs. 97.3%) and lower positive predictive value (PPV) (89.5% vs. 95.6%) than the rapid screen. The single-tiered MNA process had a high sensitivity of 92.5%, NPV of 87.5%, but a low specificity of 37.8% and a low PPV of 53.1% (Table 7.3c).

Under-nourished [U] patients as identified by the SNA (50.0%[U] vs. 21.6%[N]; P=0.02), the two-tiered MNA process (50.0%[U] vs. 21.6%[N]; P=0.02) and the rapid screen (56.5%[U] vs. 21.4%[N]; P<0.01) were more likely to experience a poor discharge outcome than nourished [N] patients (Table 7.4).

7.5 Discussion

The prevalence of under-nutrition in the patients in this sub-acute care facility varied according to the nutritional screening method. The SNA and the two-tiered MNA process classified 43.1% of patients as having some degree of under-nutrition requiring review and/or intervention by the dietitian, whilst the rapid screen identified 35.4% of the patients as under-nourished. These results show that there is a high prevalence of under-nutrition in this sub-acute care facility, a much higher prevalence than that seen in the community as a whole [4.8% malnourished – chapter 6]. The results of this study are similar to previous studies in other countries, which have found that 29 to 33% of patients admitted to sub-acute care facilities are malnourished (score < 17) when assessed by the MNA (Salva *et al.*, 1999; Thomas *et al.*, 2002).

The BMI has been widely utilized as a surrogate marker of under-nutrition but controversy remains as to the best lower cut-off values, especially in older people. The 1990 United State guidelines for weight found that the healthy body-mass index was between 21 and 27 kg/m^2 for people aged 35 years and older but these values were biased by reverse causation and inadequate control for smoking (Department of Agriculture & Services., 1990; Willett *et al.*, 1999). In a recently published large prospective study of one million adults, the lowest rates of death from all causes were found at BMIs between 23.5 and 24.9 kg/m^2 in men and 22.0 and 23.4 kg/m^2 in women; relative risks were not significantly increased for the range of BMIs between 22.0 and 26.4 kg/m^2 in men and 20.5 and 24.9 kg/m^2 in women (Calle *et al.*, 1999). In this study, we arbitrarily selected a lower cut-off value of 22 kg/m^2 and this may need to be re-evaluated in the future when evidence based cut-off values are agreed upon.

In this study, under-nourished patients were more likely than well-nourished patients to transfer to an acute hospital directly from the sub-acute care facility or to require discharge to accommodation with increased supports. This too is consistent with the results of a larger

study which found that malnourished patients scoring less than 17 on the MNA in a tertiary geriatric hospital had a 3 fold increased risk of mortality and rate of discharge to a nursing home in comparison to those who were nourished [score ≥ 24] (Van Nes *et al.*, 2001).

We cannot be sure that under-nutrition per se is the cause of the worse discharge outcomes experienced by the 'under-nourished' patients in this study. There is likely to be some contribution, at least, from frailty and co-existing medical and other conditions that do not respond to nutritional intervention. Nevertheless, nutritional intervention has been shown to decrease mortality, hospitalisations and morbidity in under-nourished people in various clinical settings (Delmi *et al.*, 1990; Milne *et al.*, 2002; Schurch *et al.*, 1998; Tkatch *et al.*, 1992). We believe the results support the need for nutritional screening of patients in sub-acute facilities and nutritional intervention in those identified as under-nourished.

It is not possible to determine with certainty from this study the best screening tool for under-nutrition. As in previous studies, when the MNA was used with a cut-off value of 24 [single tiered MNA process; (Murphy *et al.*, 2000)], a high proportion of patients (75.4%) were designated as malnourished and, while this categorisation had a high sensitivity, it had a specificity of 37.8% and a positive predictive value of only 53.1% in relation to the results of the SNA (Table 7.3c). Such a low specificity and positive predictive value is unacceptable in our sub-acute facility, as it would result in many patients being unnecessarily referred to an over-worked part-time dietitian and maybe receiving unnecessary treatment. However, the use of the MNA in this way may be acceptable when screening for the use of interventions that are safe and cost-effective.

Both the two-tiered MNA process and rapid screen had a high rate of agreement with the results of the SNA (Table 7.3a and 7.3b). The two-tiered MNA process avoided the need to do the SNA (and hence blood sampling) in the 54% of patients who were initially classified as mal- (<17) or well-nourished (≥ 24) by the MNA. The rapid screen had a higher specificity and positive predictive value but a lower sensitivity than the 2-tiered method.

The use of the rapid screen avoided the need for biochemical investigations in all patients. It appears from the results of this study and the experience whilst conducting this study that it might be best to use the rapid screen (which can readily be included into nursing and/or medical admission procedures) if budgetary and staffing resources are limited and there is a need to minimise unnecessary referrals for detailed nutritional assessment and interventions as in this facility. If more resources are available, the 2-tiered approach with its higher sensitivity, would appear to be the better approach as the content of the MNA can prompt and guide clinical intervention (eg. medication review if taking more than three medications or screening for depression/cognitive impairment).

A major limitation of this study was that there was no one 'gold standard' diagnostic tool for the diagnosis of under-nutrition in older people against which these screening tools could be compared to. Two parameters in the SNA (BMI and unintentional weight loss) were also present in the MNA and the rapid screen and this would have influenced the sensitivity, specificity, PPV and NPV calculations somewhat. However, it is impossible to perform an in-depth nutritional assessment without the inclusion of these two very important parameters. Also, the SNA was devised based on the usual practices of the clinical dietitians in our facility and closely reflects the objective method that would normally be used by them to assess the older patient's nutritional status (minus clinical examination and food diaries). Therefore, it can be assumed that the rapid screen and the two-tiered MNA process would identify older people who would most benefit from further evaluation and management by the clinical dietitian. It is unlikely that older people who are nourished would be inappropriately referred to the clinical dietitian when these screening methods are used.

In conclusion, there is a need to systematically screen for under-nutrition in sub-acute care facilities and intervene, as the prevalence of under-nutrition is high. The choice of screening tool would be highly dependent on the staffing resources available at individual institutions.

Studies attempting to confirm the independent predictors of poor discharge outcomes (i.e. prolonged length of stay or mortality) are required, as addressing these risk factors very early on during an admission is likely to translate into improved health and functional outcomes. Studies demonstrating effective intervention strategies that result in beneficial health outcomes in facilities such as this should also be encouraged.

Table 7.1 The standardized nutritional assessment (SNA) devised based on the usual clinical practices of the dietitians at this facility was used in this study as comparator (see Table 7.3a-c).

	N	B	U
Total lymphocyte count ($\times 10^9$/l)	>1.5	1.2–1.5	<1.2
Serum albumin level (g/l)	>35	28–34	<28
Total cholesterol level (mmol/ l)	≥4.15	–	<4.15
No of risk factors:			
Nausea, vomiting, diarrhoea, constipation, difficulty			
Chewing or swallowing, history of gastrointestinal disease	0,1	2	≥3
% Unintentional weight loss over 3 months (subjective)	0	1.0–7.5	>7.5
BMI (kg/m^2)	≥22		<22

Under nourished (Mild) =1U +2B or 2U +1B

Undernourished (Moderate-Severe) = 3U and greater

Table 7.2 Baseline characteristics of the patients admitted to the Hampstead Rehabilitation Centre, South Australia between October 2002 and January 2003 who participated in this study.

Rehabilitation Units Surveyed	Medical	Orthopaedic	Geriatric
No of patients studied (n=65)	14 (21.5%)	25 (38.5%)	26 (40.0%)
Mean Age ± Standard Deviation [SD] (years)	76.5 ± 5.3	79.5 ± 5.6	79.8 ± 7.7
Total number male	6 (42.9%)	10 (40.0%)	5 (19.2%)
Body mass index (BMI) [kg/m^2] ± SD	26.3 ± 4.8	25.9 ± 5.7	25.0 ± 5.8
Main reason for rehabilitation	Cerebrovascular accident (CVA), critical care neuropathy	Fracture, joint replacement surgery	Pneumonia, post-abdominal surgery, minor CVA etc.

Table 7.3a Comparison of the 2-tired Mini Nutritional Assessment Process against the Standard Nutritional Assessment.

		Standard Nutritional Assessment	**Standard Nutritional Assessment**	
		Under-nourished	Nourished	
Mini Nutritional Assessment	Malnourished [Score <17]	17	2	19 (29.2%)
Mini Nutritional Assessment	Nourished [Score > 24]	2	14	16 (24.6%)
Mini Nutritional Assessment	At-risk [Score 17-23.5]	9	21	30 (46.2%)
	Total	**28 (43.1%)**	**37 (56.9%)**	**65**
This analysis excludes patient's classified as at-risk and they are further evaluated using the SNA		Sensitivity [%] (and 95% Confidence Interval [CI]) 89.5 (68.6-97.1) Positive Predictive Value [%] (and 95%CI) 89.5 (66.9-98.7)	Specificity [%] (and 95% CI) 87.5 (64.0-96.5) Negative Predictive Value [%] (and 95% CI) 87.5 (61.6-98.5)	

Table 7.3b Comparison of the Rapid Screen against the Standard Nutritional Assessment.

		Standard Nutritional Assessment	**Standard Nutritional Assessment**	
		Under-nourished	Nourished	
Rapid Screen	Under-nourished	22	1	23 (35.4%)
Rapid Screen	Nourished	6	36	42 (64.6%)
	Total	**28 (43.1%)**	**37 (56.9%)**	**65**
		Sensitivity [%] (and 95% Confidence Interval [CI]) 78.6 (60.5-89.8) Positive Predictive Value [%] (and 95%CI) 95.7(78.1-99.9)	Specificity [%] (and 95% CI) 97.3 (86.2-99.9) Negative Predictive Value [%] (and 95%CI) 85.7(71.5-94.6)	

Table 7.3c Comparison of the Single-tiered Mini Nutritional Assessment Process against the Standard Nutritional Assessment.

		Standard Nutritional Assessment	**Standard Nutritional Assessment**	
		Under-nourished	Nourished	
Single-tiered Mini Nutritional Assessment Process	Under-nourished	26	23	49 (75.4%)
Single-tiered Mini Nutritional Assessment Process	Nourished	2	14	16 (24.6%)
	Total	**28 (43.1%)**	**37 (56.9%)**	**65**
		Sensitivity [%] (and 95% Confidence Interval [CI]) 92.5 (77.4-98.0) Positive Predictive Value [%] (and 95%CI) 53.1 (38.3-67.5)	Specificity [%] (and 95% CI) 37.8 (24.1-53.9) Negative Predictive Value [%] (and 95%CI) 87.5 (61.7-98.5)	

Table 7.4 The ability of various screening tools to predict the occurrence of poor discharge outcomes.

	Total patients (n=65)	Re-admitted to acute care (AC)	Admitted to long term care facility (LTC)	Total with poor discharge outcome (AC+LTC)	P [chi-square analysis]
Rapid Screen					
Positive (under-nourished)	23 (35.4%)	8	5	13 (56.5%)	<0.01
Negative (nourished)	42 (64.6%)	6	3	9 (21.4%)	
Standard Nutritional Assessment					
Under-nourished	28 (43.1%)	9	5	14 (50.0%)	0.02
Nourished	37 (56.9%)	5	3	8 (21.6%)	
Two-tiered Mini Nutritional Assessment (MNA) process					
Under-nourished	28(43.1%)	9	5	14 (50.0%)	0.02
Nourished	37(56.9%)	5	3	8 (21.6%)	
MNA single-tiered process					
Under-nourished (<24)	49 (75.4%)	12	6	18 (66.7%)	*
Nourished (≥24)	16 (24.6%)	2	2	4 (10.5%)	

* chi square analysis not performed as event rate was too low amongst nourished patients

Chapter 8

Fasting plasma ghrelin levels are comparable in under-nourished and well-nourished older people

8.1 Summary

Ghrelin, an orexigenic hormone is thought to play an important role in meal initiation. The main aim of this study was to determine whether fasting plasma ghrelin levels were different between under-nourished and well-nourished older people. 25 under-nourished (10 male) and 12 well-nourished (6 male) community dwelling older people were investigated. Under-nourished subjects were required to have a score < 24 on the Mini Nutritional Assessment and a body mass index < 22 kg/m^2 and/or >7.5% unintentional weight loss in the preceding 3 months. Fasting plasma ghrelin levels (RIA) and food intake were determined. Body composition (free fat mass index [FFMI] and body fat mass index [BFMI]) was measured using dual-energy-x-ray absorptiometry. Under-nourished subjects were older (mean age 77.5 $\pm$ 1.4 [SEM] vs. 72.2 $\pm$ 1.6 years), leaner (FFMI 12.81 $\pm$ 0.41 vs. 15.45 $\pm$ 0.66 kg/m^2), had less body fat (BFMI 5.50 $\pm$ 0.29 vs. 8.69 $\pm$ 0.71 kg/m^2) and less oral intake (1465 $\pm$ 75 vs. 2097 $\pm$ 130 kcal/day) than well-nourished subjects (all significant). Fasting plasma ghrelin levels in malnourished and well-nourished older people were not significantly different (2598 $\pm$ 340 vs. 2314 $\pm$ 293 pg/ml). Fasting plasma ghrelin levels in under-nourished older people are comparable to those in well-nourished older people, not higher as may have been predicted from previous studies in under-nourished young adults. The lack of a significant rise in under-nourished older people may signify a defect in energy homeostasis, which may contribute to the development and/or progression of the anorexia of ageing.

8.2 Introduction

There is evidence that, ghrelin, a hormone produced primarily in the fundus of the stomach, which reaches brain centres via the bloodstream, has orexigenic activity and modulates energy balance (Arvat *et al.*, 2001; Muccioli *et al.*, 2002; Takaya *et al.*, 2000; Tschop *et al.*, 2000; Ukkola, 2003). Ghrelin is purported to play an important role in meal initiation and energy intake (Cummings *et al.*, 2004). Exogenous administration of ghrelin to healthy young volunteers and cachetic patients with cancer has been reported to increase appetite and energy intake (Neary *et al.*, 2004; Wren *et al.*, 2001).

In negative energy balance states (i.e. under-nutrition, acute weight loss) there may be a compensatory increase in plasma ghrelin levels. In a recent study by our group plasma ghrelin levels were shown to be higher (140%) in a small cohort of very under-nourished older women when compared to nourished older women, and it was postulated that this increase may reflect either ghrelin resistance, increased concentrations of bio-inactive ghrelin or a compensatory increase of plasma ghrelin levels (Sturm *et al.*, 2003). In another study in young subjects, weight loss, induced by a 3 month exercise program in combination with energy-deficit diet, was associated with a 70% increase in fasting plasma ghrelin levels in young volunteers (Leidy *et al.*, 2004). In the latter study, it was observed that weight loss preceded changes in plasma ghrelin levels; accordingly, it was suggested that the rise in plasma ghrelin levels represented a compensatory response to a state of negative energy balance (Leidy *et al.*, 2004). Similarly, in a study comparing young adults with anorexia nervosa (n=6), a state of negative energy balance, to healthy young controls (n=12), fasting plasma ghrelin levels were found to be approximately 160% higher (Rigamonti *et al.*, 2002).

The anorexia of ageing describes the physiological decrease in appetite and food intake that may accompany ageing (Chapman, 2004). Changes in hormonal responses to weight loss in older people may contribute to the anorexia of ageing. Ageing is said to be associated with

an impaired regulation of feeding. For example, in one study, following an underfeeding period that resulted in weight loss in both groups, older subjects continued to under-eat and did not regain lost weight whilst younger subjects ate more and regained the lost weight during the recovery period (Roberts *et al.*, 1994).

The main aim of this study was to determine whether plasma ghrelin was altered in malnourished older people. The potential effects of daily food intake, age, gender and body composition on fasting plasma ghrelin levels in community dwelling older people were also evaluated.

8.3 Method

The study involved 25 under-nourished and 12 well-nourished community-dwelling older people (age range 65-93 years). Informed consent was obtained from all participants and the protocol was approved by the Research Ethics Committee of the Royal Adelaide Hospital, South Australia.

8.3.1 Protocol

All subjects provided a venous blood sample (10ml) at approximately 09 00 h after an overnight fast (12 hours duration, with the exception of sips of water which was permitted until 06 00 h). Intake of water is known to not affect plasma ghrelin (Gottero *et al.*, 2003). Subjects also provided a record of their food intake (Crawford *et al.*, 1994; Gersovitz *et al.*, 1978; Jula *et al.*, 1999). Body composition was assessed using dual energy X-ray absorptiometry (DEXA). In all subjects blood sampling, DEXA and food intake estimation were performed within a 2-week period.

8.3.2 Subjects

Under-nourished

The under-nourished community dwelling older people were derived from a cohort who were to be enrolled in a randomized, controlled nutritional intervention study. Subjects were classified as under-nourished if they fulfilled the following criteria: i) a Mini Nutritional Assessment (MNA) score < 24 and/or ii) screened positive on the 'rapid screen' (Guigoz *et al.*, 2002; Visvanathan *et al.*, 2004b).

The MNA consists of 4 main components: a) anthropometric measurements (weight, height and weight loss); b) global assessment (six questions related to lifestyle, medication and mobility); c) dietary assessment (eight questions related to number of meals, food and fluid intake, and autonomy of feeding); and d) subjective assessment (self-perception of health

and nutrition)(Guigoz *et al.*, 1994). Patients are classified as well nourished [N] (MNA≥24), at risk of malnutrition [AR] (MNA= 17-23.5) or malnourished [M] (MNA<17) according to the MNA score (maximum=30).

Subjects screened positive on the 'rapid screen' if their body mass index (BMI) was < 22 kg/m^2; and/or their reported weight loss in the preceding 3 months was > 7.5% (Chapter 7). The 'rapid screen', which only evaluates BMI and weight loss, has been reported to have a sensitivity of 78.6% and specificity of 97.3% when compared to a more detailed nutritional assessment of patients of a sub-acute care facility (Chapter 7).

Nourished subjects

Nourished community dwelling older subjects were recruited by advertisement; all these subjects had a MNA ≥ 24.

8.3.3 Measurements

Plasma ghrelin

Venous blood was collected in ice-chilled EDTA tubes containing 1000 kallikrein inhibitory units aprotinin (Trasylol)/ml blood for measurement of fasting plasma ghrelin. Plasma was separated by centrifugation (3000 rpm for 15 min at 4^0C) within one hour of collection and stored at -70 C until assayed. Ghrelin was measured by radioimmunoassay (RIA), using an adaptation of a method developed by Prosearch International with a commercial antisera (RAST-4745, Bachem, Ca) which does not cross-react with secretin, orexin, motilin, galanin or vasoactive intestinal peptide (VIP). Human ghrelin was iodinated with an equimolar quantity of 125 iodine by the chloramines-T oxidisation method. Iodo-histidyl-ghrelin was separated from free 125 iodine and unlabelled ghrelin by reverse phase high performance liquid chromatography on a Phenomenex Jupiter C4 300A 5u column cat no. 00B-4167-EO 250 x 4.6 mm. The column was eluted isocratically with 27% acetonitrile in triethylamine phosphoric acid buffer pH 3.0. (Prosearch International, Victoria).

Standards were serially diluted from ghrelin peptide (Phoenix Pharmaceuticals, Ca) in a range from 4 to 256 pg/ml in buffer (50mM phosphate pH 7.4 containing 10 mM EDTA and 2g/L gelatin). Incubation was for 20-24 hours at 4°C and second antibody precipitation was used to separate the antibody bound peptide from free peptide. The second antibody was added at the time the assay was setup (100 µl of sheep antirabbit antibody (Prosearch International,Victoria) and 100 µl of 2% normal rabbit serum) and 1 ml 8% polyethylenglycol 6,000 added immediately prior to centrifugation. After centrifugation for 25 minutes at 4°C, tubes were decanted and counted on Crystal LKB gamma counter. The minimum detectable level was 40pg/ml, inter-assay coefficient of variation (CV) was 23% and intra-assay CV was 17%.

The performance of the ghrelin assay incorporating Bachem antisera (used in this study) was assessed by measuring ghrelin levels in 20 samples and comparing results to those obtained using a ghrelin kit (Phoenix Pharmaceuticals, Ca). There was an excellent correlation between the two assays ($r=0.932$; $P<0.001$). The absolute levels of ghrelin measured by the two assays varied markedly (slope$\pm$intercept: 8.5$\pm$-1686.7) as there is currently no standardized calibrator or reference method for the assay of human ghrelin.

Food intake

In the nourished subjects food intake was evaluated using a 3-day food diary. In contrast, in under-nourished subjects, food intake was assessed using the 24-hour recall method; this approach was selected because the under-nourished older subjects were about to participate in an intervention study, which required the administration of several other lengthy questionnaires. The nourished subjects were asked to complete a 3-day food diary as this method is reported to reflect food intake more accurately than the 24-hour recall method and is more likely to be completed than the longer 7-day food diary (Crawford *et al.*, 1994; Gersovitz *et al.*, 1978; Jula *et al.*, 1999).

Body composition

DEXA (Norland TM densitometer XR36, Norland Medical Systems, Fort Atkinson, Wisconsin, USA) was used to assess free fat mass (FFM) and body fat mass (BFM) and these measurements were then height adjusted to produce the free fat mass index (FFMI) and body fat mass index (BFMI). This investigation required each subject to lie supine on a scanning bed with minimal clothing whilst a low dose x-ray scans their body. Individuals were scanned at 130 mm/s using a scan resolution of 6.5 x 13 mm for approximately 20 minutes. When the DEXA-derived [Norland XR36] skeletal muscle mass values were compared to those calculated by a nuclear method from total body potassium and total body nitrogen in 75 older Australian, a good correlation was seen (men r=0.83, women r=0.87)(Hansen *et al.*, 1999; Wang *et al.*, 1996).

8.3.4 Statistical analysis

All values are expressed as mean $\pm$ standard error of mean [SEM]. Subject characteristics were compared using independent sample t-test analyses (equal variance not assumed). The relationships between fasting plasma ghrelin levels and other parameters were evaluated using the Spearman's non-parametric correlation analysis. Fixed effects 6-way ANOVA was used to determine if any of the subject factors (nutritional status, gender, age, food intake, FFMI, BFMI) had an independent effect on fasting plasma ghrelin levels. Adjusted mean ghrelin levels were derived from the fixed effects-6 way ANOVA model where raw mean values were adjusted for age, gender, food intake, FFMI and BFMI. SAS was the software program used (SAS Institute, inc, Cary, NC). P values < 0.05 were considered to be statistically significant.

8.4 Results

The characteristics of well-nourished and under-nourished subjects are summarized in table 8.1. Under-nourished subjects were older ($P<0.05$), leaner ($P<0.05$), had less body fat ($P<0.001$) and less energy intake ($P<0.001$) when compared to well-nourished subjects. Fasting plasma ghrelin levels in well-nourished older subjects were 11% lower than in under-nourished subjects, but this difference was not significant ($P=0.53$). Adjusted mean ghrelin levels derived by the 6-way ANOVA were also not significantly ($P=0.56$) different, although 33% lower in the under-nourished subjects compared to nourished subjects (i.e. reversal of trend). There was no independent effect of energy intake ($P=0.92$), FFMI ($P=0.26$), BFMI ($P=0.50$), age ($P=0.68$) or gender ($P=0.49$) on fasting plasma ghrelin levels. Consistent with this, the correlations between fasting plasma ghrelin levels and age ($r= -0.26$), body mass index [BMI] ($r= -0.37$) and FFMI ($r= -0.14$) were all weak and non-significant. There were also no significant correlations between fasting plasma ghrelin levels and either BFMI ($r=0.02$) or food intake ($r=0.06$).

8.5 Discussion

The novel observation in this study was that fasting plasma ghrelin levels in under-nourished and well-nourished community dwelling older people are comparable. We anticipated that ghrelin levels may be increased in the malnourished older people and the absence of a difference is consistent with the concept of a role for ghrelin in the impaired energy homeostasis seen in older people. States of negative energy balance have been associated with increased ghrelin levels and this would favor the maintenance of energy homeostasis by stimulating appetite and energy intake (Rigamonti *et al.*, 2002). Ghrelin is said to play an important role in meal initiation and therefore, given this relative ghrelin deficiency in under-nourished older people, the administration of exogenous ghrelin may prove effective in increasing appetite and energy intake (Cummings *et al.*, 2004; Neary *et al.*, 2004; Wren *et al.*, 2001).

The results of this study apparently conflict with observations in a smaller study by our group where fasting plasma ghrelin levels in older under-nourished subjects [n=8] were more than double those seen in well-nourished [n=8] older people (1320 + 348 [SEM] vs. 552 + 132 pg/ml)(Sturm *et al.*, 2003). There are, however, several differences which may well account for the discrepancies between these two studies. In the study by Sturm et al., the under-nourished subjects were more underweight and, almost certainly, more severely under-nourished than the under-nourished subjects in this study (i.e. mean BMI 16.9 vs. 19.0 kg/m^2; mean MNA score 18.7 vs. 20.4), although the under-nourished subjects in this study were demonstrably nutritionally impaired as evidenced by their lower scores on the MNA, reduced lean mass and reduced oral intake compared to nourished subjects. Four of the eight subjects in the study by Sturm et al. had a score of less than 17 [malnourished] on the Mini Nutritional Assessment (MNA) and two others (n=2) had a score between 17 and 23.5 [at-risk of malnutrition]. In contrast, in the current study, 24 subjects were at-risk of malnutrition (MNA score 17-23.5) and only one subject was malnourished (MNA score <

17). Perhaps, a compensatory increase in baseline plasma ghrelin levels does not occur in under-nourished older people until severe protein energy malnutrition has developed. The ghrelin assay used in the current study was different to that used by Sturm et al. (Phoenix Pharmaceuticals, Ca), but the results have been shown to correlate very closely (r=0.932), so this is unlikely to be an issue. No adjustment for age, gender, food intake and body composition measures were made in the study by Sturm et al. and some, but not all, studies have suggested that these measures may affect plasma ghrelin levels, especially in younger people (Cummings *et al.*, 2004; Fagerberg *et al.*, 2003; Greenman *et al.*, 2004; Itoh *et al.*, 2004; Purnell *et al.*, 2003; Rigamonti *et al.*, 2002; Sturm *et al.*, 2003).

The results of this study are inconsistent with observations in younger subjects with weight loss where acute weight loss, through the inducement of negative energy balance (e.g. exercise and an energy deficit diet), results in an increase in plasma ghrelin levels (Leidy *et al.*, 2004). Similarly, more chronic negative energy balance states in younger people such as anorexia nervosa, are associated with a substantial increase in plasma ghrelin levels than in healthy normal weight younger subjects (Rigamonti *et al.*, 2002). Accordingly, our observations support the hypothesis that with ageing, there may be an impairment in the regulation of ghrelin secretion, with failure of a compensatory rise in fasting ghrelin levels occurring in older people but not in younger people.

With increasing age, there is a decreased margin of homeostatic reserve and an increasing likelihood of experiencing numerous assaults to homeostasis (Bales & Ritchie, 2002). Frail older people are at high risk of homeostasis disruption and are also a heterogeneous group with varying pathology (Ferrucci *et al.*, 2002). In essence, the results of this study, unchanged ghrelin levels in response to what is presumably a state of chronic negative energy balance, lends support to the hypothesis that relative ghrelin deficiency may play a role in the development and/or progression of the anorexia of ageing in older people. The term ‘anorexia of ageing’ refers to the decline in energy intake and appetite that may

accompany ageing (MacIntosh *et al.*, 2000). In part, this decline in energy intake is in response to a decrease in energy expenditure, but in many cases the former exceeds the decline in energy expenditure leading to an overall loss of body weight (MacIntosh *et al.*, 2000). Based on this definition, the anorexia of ageing represents a state of negative energy balance and accompanying this, one may be expected to see a compensatory rise in plasma ghrelin levels. It remains to be determined whether exogenous administration of ghrelin to this population group may be beneficial in improving nutritional status by increasing food intake, as it has been found to do with short term administration to cachetic patients with metastatic cancer (Neary *et al.*, 2004).

Although in this study, only one fasting plasma ghrelin level was obtained for each subject, it has been shown that a single conveniently obtained plasma ghrelin level (i.e. fasting early morning levels) can sufficiently serve as a surrogate for an integrated 24-hour AUC ghrelin value in human subjects (Cummings *et al.*, 2001). A potential limitation of this study was small subject numbers. But based on these results, the likelihood of such under-nourished older people having significantly *higher* ghrelin levels than their healthy peers when we found adjusted mean values to be non-significantly lower is extremely low.

In summary, the main and novel finding of this study was that fasting plasma ghrelin levels in under-nourished and nourished older people were comparable. We hypothesize that these unchanged (if not lower) ghrelin levels in the setting of a negative energy balance state may contribute to the development and/or progression of the anorexia of ageing in older people.

Table 8.1 The baseline characteristics of the study population (mean ± SEM).

	Nourished (SEM)	Under-nourished (SEM)
n	12	25
Age [years]	72.17 (1.63)	77.52 (1.40) ±
Body Mass Index [kg/m^2]	24.58 (0.52)	19.02 (0.32) *
Food Intake [kcal/day]	2097.43 (130.07)	1465.28 (74.63) *
Mini Nutritional Assessment (max score 30)	28.92 (0.33)	20.44 (0.43) *
Free Fat Mass Index [kg/m^2]	15.45 (0.66)	12.81± (0.41)*
Body Fat Mass Index [kg/m^2]	8.69 (0.71)	5.50 (0.29) *
Fasting plasma ghrelin	2313.67 (293.16)	2597.56 (339.78)
Adjusted mean fasting plasma ghrelin (pg/ml) levels from fixed effects 6-way ANOVA analysis	3027.93 (891.74)	2287.53 (486.15)

[UN vs. N] * P≤ 0.001 ±P≤0.05]

SEM-standard error of mean

Chapter 9

Blood pressure responses in healthy older people to 50g carbohydrate drinks with differing glycaemic effects

9.1 Summary

The objective of this study was to determine the blood pressure response to 50g carbohydrate drinks with varying glycaemic effects. A randomized, cross-over study was performed. 10 healthy elderly subjects (age $\geq$ 65 years) participated in this study. Systolic (SBP), diastolic (DBP) and mean (MAP) blood pressure (BP), heart rate (HR), plasma glucose levels were determined following ingestion of equal volumes (379 ml) of water and 50g carbohydrate drinks with reported varying glycaemic indices [surrogate marker for glycaemic effect]: 1) low -'Apple & Cherry' juice, 2) intermediate -'Fanta Orange' and 3) high-glucose. Glucose (SBP and DBP- $P<0.001$, MAP- $P<0.01$) and Fanta (SBP- $P<0.01$, DBP and MAP- $P<0.001$) ingestion caused a significant decrease in BP whilst BP increased (SBP- $P<0.01$ and MAP– $P<0.01$) from baseline following Apple and Cherry juice ingestion. Water had no significant effect on post-ingestion BP. Fanta and Apple and Cherry juice ingestion had similar ($P=0.68$) glycaemic effects, which were significantly greater than water but lower than glucose ($P<0.001$). No significant correlation between the glycaemic effect of the carbohydrate drinks and BP changes from baseline were seen (SBP [$r = -0.12$, $P = 0.51$], DBP [$r = -0.05$, $P = 0.78$] and MAP [$r=-0.07$, $P=0.71$]). Apple and Cherry juice and Fanta orange had similar glycaemic effects but discrepant effects on BP. Therefore it is unlikely that the glycaemic effect of a drink can be used to predict the subsequent cardiovascular response.

9.2 Introduction

Blood pressure (BP) normally decreases after a meal and reaches a nadir between 30 to 60 minutes after eating (Jansen & Lipsitz, 1995; Smith *et al.*, 2003). When excessive, this decrease is termed post-prandial hypotension (PPH), defined as a decrease in systolic BP of 20 mmHg or more within two hours of the start of a meal. PPH is associated with an increased incidence of falls, syncope, angina and transient ischaemic attacks, particularly in older people and patients with autonomic neuropathy; the latter most frequently due to diabetes mellitus (Jansen & Lipsitz, 1995; Mathias *et al.*, 1989). PPH is a relatively common, yet under-recognized problem in older people. For example, in a study of 499 older, ambulatory or wheelchair-bound residents of a long-term health care facility, 24% were found to have PPH, with significantly greater post-prandial BP decreases occurring in those who had experienced falls or syncope in the preceding 6 months than in those who had not (Aronow & Ahn, 1994).

The pathophysiology of PPH is poorly understood, but likely to be multifactorial (Jansen & Lipsitz, 1995). The magnitude of the postprandial BP fall is dependant on meal composition. Ingestion of carbohydrates, particularly glucose and to a lesser degree starch but not fructose or xylose, lowers BP more than ingestion of protein, fat or water (Heseltine *et al.*, 1991a; Jansen & Lipsitz, 1995; Jansen *et al.*, 1990; Mathias *et al.*, 1989; Robinson TG, 1995). Guar, a naturally occurring, non-absorbed, gel-forming carbohydrate of vegetable origin has been shown to attenuate the fall in BP seen following the ingestion of a glucose drink (Jones *et al.*, 2001). Thus, modification of meal composition could provide a means of reducing excessive post-prandial BP falls in people with PPH.

A revised list of the relative glycaemic indices (GIs) of different foods was recently published (Foster-Powell *et al.*, 2002). Per gram of carbohydrate, foods with a high glycaemic index (GI) produce a higher peak in postprandial blood glucose and a greater overall blood glucose response during the first two hours after consumption, reflecting a

greater glycaemic effect than foods with a low GI. The GI is calculated by measuring the incremental area under the capillary blood glucose curve following ingestion of a test meal providing 50g carbohydrate, compared with the area under the capillary blood glucose curve following an equal carbohydrate intake from the reference meal (glucose drink or bread) multiplied by 100. Foods are classified as having a low (< 55), intermediate (55-69), or high (≥70) GI.

The addition of guar to a glucose drink reduces its glycaemic effect - adding 14.5 g of guar to a 50g glucose drink reduces its GI from 100 (arbitrarily designated) to 62 (Foster-Powell *et al.*, 2002). This reduction in glycaemic effect could be a mechanism by which it attenuates the fall in BP (Jones *et al* 2001). We therefore hypothesized that the lower the glycaemic effect of a food, the smaller the postprandial reduction in BP. If so, it may be possible to design diets for people with PPH based on the glycaemic effects of food using published GI values of foods as a surrogate marker.

The purpose of this study, therefore, was to determine the effects of drinks with equal volume and carbohydrate content but differing glycaemic effects, on post-ingestion BP.

9.3 Methods

9.3.1 Subjects

10 healthy, subjects (6 male), aged 65-77 years were recruited by advertisement. All subjects were non-smokers and had no history of gastrointestinal disease or surgery, diabetes mellitus, significant respiratory or cardiovascular disease, chronic alcohol abuse, epilepsy or symptoms of autonomic dysfunction. No subject was on any medications known to influence BP and all medications remained unchanged during the study.

9.3.2 Protocol

Each subject had blood pressure (BP), heart rate (HR) and plasma blood glucose measurements taken on four separate study days before and after ingestion of one of the study drinks (described below), in random order. The studies were not blinded and separated by at least 72 hours. All drinks were served at a temperature of 22^0C to avoid the potential effect of temperature on BP (Kuipers *et al.*, 1991). In one study, a warm glucose drink (50^0C) caused a fall in mean arterial BP whilst a cold drink (5^0C) caused an increase in mean arterial BP (Kuipers *et al.*, 1991). The carbonated drink (Fanta orange) was allowed to stand for 20 minutes to reduce carbonation. Subjects attended the Department of Medicine following an overnight fast (10 hours for solids and 6 hours for liquids), at the same time (08 30h) for all studies. The study room was air-conditioned with the temperature set at $22 \pm 3\ ^0$C. A cannula was placed in the left antecubital vein for blood sampling and subjects were seated comfortably in a chair to mimic normal physiological conditions during a meal. A BP cuff was attached to the right upper arm. Cardiovascular autonomic function was evaluated on one of the study days. Each subject gave written, informed consent and the study was approved by the Research Ethics Committee of the Royal Adelaide Hospital.

9.3.3 Study drinks

The study drinks were selected based on their predicted glycaemic effect using the GI as a surrogate marker (Foster-Powell *et al.*, 2002). The commercially available drinks (2 and 3) were manufactured in Australia and bought from the local supermarket.

- 50g glucose [GI= 100- arbitrarily designated] in 359 ml of water and 20ml of bottled lemon squeeze manufactured by Berri Ltd., Victoria, Australia (99.9% lemon juice with 2.5mg per 100ml carbohydrate content)**;**
- 368 ml 'Fanta Orange' [Fanta], a commercially available carbonated drink manufactured by Coca Cola Amatil, Australia [reported intermediate GI= 68 $\pm$ 6 (Foster-Powell *et al.*, 2002)] and 11ml of water;
- 379 ml 'Apple and Cherry' Juice [reported low GI= 43 $\pm$ 3 (Foster-Powell *et al.*, 2002)], a commercially available preservative free fruit juice manufactured by Wild About Fruit, Australia; and
- 379 ml of water (control drink).

9.3.4 Measurements

Blood pressure and heart rate

BP (systolic [SBP], diastolic [DBP], mean arterial pressure [MAP]) and heart rate (HR) were measured using an automated oscillometric BP monitor [DINAMAP ProCare, GE Medical Systems, NSW, Australia]. Following a 20-minute rest post cannula insertion, three measurements were obtained at 9, 6 and 3 minutes prior to drink ingestion at t = 0 min. The mean of these three readings formed the baseline value. Following ingestion of the drink, BP and HR measurements were measured three minutely for the first 60 minutes (to t=60).

Plasma glucose measurements

Venous blood was obtained from the intravenous cannula for glucose estimation at baseline and t=15, 30, 45 and 60 minutes and stored in tubes containing fluoride and potassium EDTA. These samples were than centrifuged for 15 minutes at 4000 rpm before being processed on an Olympus 5400 analyser using the hexokinase method at the Institute of Medical and Veterinary Science (IMVS), Frome Road, Adelaide, South Australia.

Cardiovascular autonomic function

Autonomic nerve function was evaluated using standardized cardiovascular reflex tests (Ewing & Clarke, 1982; Piha, 1991). Parasympathetic function was evaluated by the variation (R-R interval) of the heart rate during deep breathing and the response to standing from a lying position. The maximum and minimum R-R interval for each respiratory cycle (converted to beats/min) was determined. The ratio of the longest R-R interval (around the 30th beat) to the shortest R-R interval (around the 15th beat) upon standing was also determined ('30:15'). Sympathetic function was assessed by the fall in systolic BP in response to standing. Each of the test results was scored according to age-adjusted predefined criteria as 0=normal, 1=borderline, and 2=abnormal for a total maximum score of 6. A score $\geq$ 3 was considered to indicate autonomic dysfunction (Ewing & Clarke, 1982; Piha, 1991).

9.3.5 Analyses

Carbohydrate content analysis

An analysis of the carbohydrate content of the Apple and Cherry juice and Fanta was undertaken by Health Sciences and Nutrition Division of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Adelaide, South Australia. Sugars were extracted using aqueous ethanol (50% ethanol v/v), as described in 'Association of Official Analytical Chemists' Method 982.14, and quantified by high performance liquid

chromatography using a pump (GBC scientific equipment Pty Ltd., Melbourne, Victoria, Australia) and refractive index detector, and a polyamine-bonded polymeric gel column from Astec (Advanced Separation Technologies Inc., Whippany, NJ. USA). Acetonitrile:water (75:25, v/v) was used as the mobile phase.

Statistical analysis

All values are expressed as mean ± SEM. Two-way repeated measures analysis of variance (ANOVA) was used to examine the overall effects of time and drink type (treatment) and the treatment by time interaction on the change in cardiovascular and plasma glucose measurements from baseline. When a treatment effect was seen, post-hoc analysis using the Bonferroni/Dunn adjustment was performed. One-way repeated measures ANOVA were conducted to evaluate the effects of the drink type on BP, HR and plasma glucose measurements over the first 60 minutes. The correlation between BP response at time T [mean of measurements from t=30-60 as the nadir in blood pressure measurements is known to be reached in this time (Jansen & Lipsitz, 1995)] and the individual area under the plasma glucose curve (first 60 minutes) calculated by the trapezoidal method for each carbohydrate containing drink for each subject, was evaluated by the Spearman correlation analysis (i.e. combined analysis of 30 [10 subjects x 3 study days] values for each cardiovascular variable). All analyses were performed using Statview version 5.0 and SuperANOVA. P values < 0.05 were considered statistically significant.

9.4 Results

All subjects consumed the four drinks within the allocated time. The drinks were well tolerated. One person had sub-clinical autonomic dysfunction (score 3) without overt symptoms and so was not excluded from the study.

Carbohydrate content analysis

Approximately 50% of the total carbohydrate content of the Apple and Cherry juice was fructose, 29.3% glucose and 20.7% sucrose. 45% of the total carbohydrate content of Fanta was fructose, 45% glucose and 10% sucrose.

Plasma glucose

Plasma glucose concentrations are shown in Figure 9.1. There was no significant difference in the baseline plasma glucose values between the 4 study days (Table 9.1).

There were significant treatment ([drink type] $P<0.001$]) and time ($P<0.001$) effects and a treatment x time interaction ($P<0.001$) on plasma glucose values over the first 60 minutes. Glucose ($P<0.001$), Fanta ($P<0.001$) and Apple & Cherry juice ($P<0.001$) ingestion resulted in a significant increase in plasma glucose measurements over the first 60 minutes. Glucose concentrations were similar after Apple&Cherry juice and Fanta ($P=0.68$), with glucose concentrations after both significantly higher than after water, but significantly lower than after glucose ($P<0.001$).

Blood pressure

Figure 9.2a-9.2c show the changes in BP from baseline during the 60 minutes after drink ingestion. There was no significant difference in the baseline BP (SBP, DBP and MAP) values between the 4 study days (Table 9.1).

There were significant treatment (all BP measurements P<0.001) and time (all BP measurements P<0.001) effects and treatment x time (DBP and MAP - P<0.001) interaction on BP during the 60 minutes after drink ingestion. BP decreased significantly following glucose (SBP and DBP- P<0.001, MAP- P<0.01) and Fanta (SBP- P<0.01, DBP and MAP - P<0.001) ingestion, but did not change significantly following water ingestion (SBP - P=0.34, DBP - P=0.38, MAP - P=0.26). SBP (P<0.01) and MAP (P<0.01), but not DBP (P=0.10) increased significantly following Apple & Cherry juice ingestion. Glucose and Fanta had similar effects on post-ingestion SBP, DBP and MBP (all P>0.05). Similarly, water and Apple and Cherry juice ingestion also had similar effects on post-ingestion BP measurements (all P > 0.05). Fanta ingestion was associated with a greater fall in BP than Apple & Cherry juice ingestion (SBP and DBP P<0.001, MAP P=0.08) in the first 60 minutes.

Glycaemic effect and blood pressure change

There was no significant correlation between the glycaemic responses to the carbohydrate containing drinks and the change in SBP (r = -0.12, P = 0.51), DBP (r = -0.05, P = 0.78) and MAP (r=-0.07, P=0.71) from baseline to time T (mean 30-60 min).

Heart rate

The heart rate (HR) responses to the drinks are shown in Figure 9.2d. There was no significant difference in the baseline HR values between the 4 study days (Table 9.1). Significant treatment (P=0.03) and time (P <0.001) effects and treatment x time (P < 0.001) interaction were seen. The HR did not change significantly from baseline in the 60 minutes after glucose (P=0.07) and Fanta (P=0.12), increased following Apple and Cherry juice (P<0.001), and decreased following water ingestion (P < 0.001). Post-hoc analysis showed that glucose, Fanta and Apple and Cherry juice had similar effects on heart rate (P > 0.05) which were all significantly different than the bradycardic effect seen following water ingestion (P<0.001).

9.5 Discussion

The major finding of this study was the lack of a significant relationship between the glycaemic effects of the three 50g carbohydrate containing drinks, and the BP changes after their ingestion. No significant correlation between the fall in BP measurements and the glycaemic response after the ingestion of the carbohydrate drinks was found. It is not possible, therefore, to predict with any accuracy the BP response to a particular carbohydrate drink from its glycaemic effect. This was exemplified by the different BP responses to Apple and Cherry juice and Fanta. Their glycaemic effects were very similar, but their effects on BP were clearly different, with a slight rise after Apple and Cherry, fall after Fanta, and significant difference between these responses.

The fall in BP following the ingestion of carbohydrate drinks is related in part to the gastrointestinal response to their ingestion and not the ensuing hyperglycemia, as indicated by previous findings that intravenous glucose administration does not cause a fall in BP whilst oral glucose consumption resulting in a similar glycaemic response, does (Jansen *et al.*, 1987). A reduction of luminal glucose exposure is likely to attenuate the fall in BP, perhaps by preventing or delaying the release of vasoactive gut peptides as supported by a recent study by our group in which the addition of guar (naturally occurring, gel-forming carbohydrate of vegetable origin) to an intra-duodenal glucose infusion attenuated the fall in BP and rise in blood glucose, plasma insulin, glucagon-like peptide-1 and glucose-dependant insulinotropic polypeptide induced by intra-duodenal glucose (O'Donovan *et al.*, 2004).

Our results suggest that the change in BP following the ingestion of these carbohydrate drinks is determined by factors other than their glycaemic effects. Although the Fanta was allowed to de-carbonate in air for 20 minutes before consumption, it was still carbonated compared to the Apple and Cherry juice. Factors that decelerate gastric emptying of carbohydrate solutions act to decrease their glycaemic effect and attenuate the drop in BP (Jones *et al.*, 2001; Jones *et al.*, 1998). We did not measure the rate of gastric emptying in this study, but several studies have examined the effect of carbonation of drinks on the rate

of gastric emptying, and found either a delay (Ploutz-Snyder *et al.*, 1999) or no effect (Pouderoux *et al.*, 1997; Ryan *et al.*, 1991). The lower BP readings after Fanta than Apple and Cherry are therefore unlikely to be due to any effects of drink carbonation on gastric emptying. It remains possible that another, unknown effect of carbonation, may be involved.

We think a more likely cause is the differing types of saccharides contained in these drinks. The fall in BP from baseline following the ingestion of glucose in this study is consistent with the results of previous studies (Jones *et al.*, 2001; O'Donovan *et al.*, 2002). When the effects on BP of a fructose drink (75 g fructose in 300 ml) were compared to those of an equi-energetic glucose drink (75 g glucose in 300ml) in older people, there was no significant change in BP following fructose ingestion, while BP fell significantly following glucose (Jansen *et al.*, 1987). Analysis of the drinks in this study indicated that 50% of the Apple and Cherry drink was fructose and approximately 30% glucose (25 vs. 15 gm), with a fructose: glucose ratio of 1.7:1, whereas fructose and glucose both comprised 45% of the Fanta (22.5 gm each), for a ratio of 1:1. Even if allowance is made for complete post-ingestion breakdown of the sucrose in these drinks to equal parts fructose and glucose, the fructose: glucose ratio decreases only slightly to 1.5:1 (30 vs. 20 gm) for the Apple and Cherry drink and is unchanged at 1:1 for Fanta (25 gm each). As glucose lowers BP but fructose does not, the differing effects on BP of these drinks may be due to the greater amounts of fructose than glucose, both absolutely and relatively, in the Apple and Cherry drink.

In this study, we chose the drinks based on their published GIs as the GI is a surrogate marker for the glycaemic effects of food. However, we found that 'Fanta Orange' and Apple and Cherry juice had a similar glycaemic effects despite having differing published GIs. The direct comparison of the published GI values to our findings is not possible as we had not followed strict GI estimation methodology in that 1) we did not measure capillary blood glucose values; 2) each drink was not tested thrice to reduce intra-subject and day to

day variation; 3) most published GI studies have studied the glycaemic response of food in younger people as the GI may vary with age; and 4) the drinks were consumed in 3 minutes as opposed to 15 minutes used with GI testing (Foster-Powell *et al.*, 2002; Miller *et al.*, 1995; Wolever *et al.*, 1988; Wolever *et al.*, 2003).

In conclusion, the decrease in BP seen after the consumption of 50g carbohydrate containing drinks of equal volume is not closely related to, or predictable from, the glycaemic effects of the drink. It is more likely determined by the nature of the sugars in the drink. As equi-energetic drinks containing differing carbohydrates have varying effects on post-ingestion BP, manipulation of the carbohydrates in a meal may provide a means of reducing PPH. This requires more investigation and confirmation in a population with PPH.

Table 9.1 Subject characteristics and baseline blood pressure, heart rate and glucose measurements.

		Standard Error Of Mean
Mean Age (years)	71.30	1.38
Total subjects	10	
Female (%)	40	
Body Mass Index (kg/m^2)	26.69	0.82
Autonomic Nerve Function Score	0.90	0.31
Baseline systolic blood pressure [BP] (mmHg)		
Glucose drink	123.10	5.59
Fanta drink	123.75	5.82
Apple&Cherry drink	120.07	4.44
Water	121.80	3.87
Baseline diastolic BP (mmHg)		
Glucose drink	68.67	3.38
Fanta drink	68.77	3.91
Apple&Cherry drink	66.87	3.55
Water	67.87	3.26
Baseline mean arterial BP (mmHg)		
Glucose drink	89.83	3.96
Fanta drink	88.53	5.08
Apple&Cherry drink	85.97	3.63
Water	89.43	3.51
Baseline heart rate (bpm)		
Glucose drink	63.60	2.06
Fanta drink	63.67	3.09
Apple&Cherry drink	61.47	2.31
Water	65.23	1.76
Baseline plasma glucose (mmol/L)		
Glucose drink	4.61	0.23
Fanta drink	4.80	0.15
Apple&Cherry drink	4.72	0.15
Water	4.90	0.16

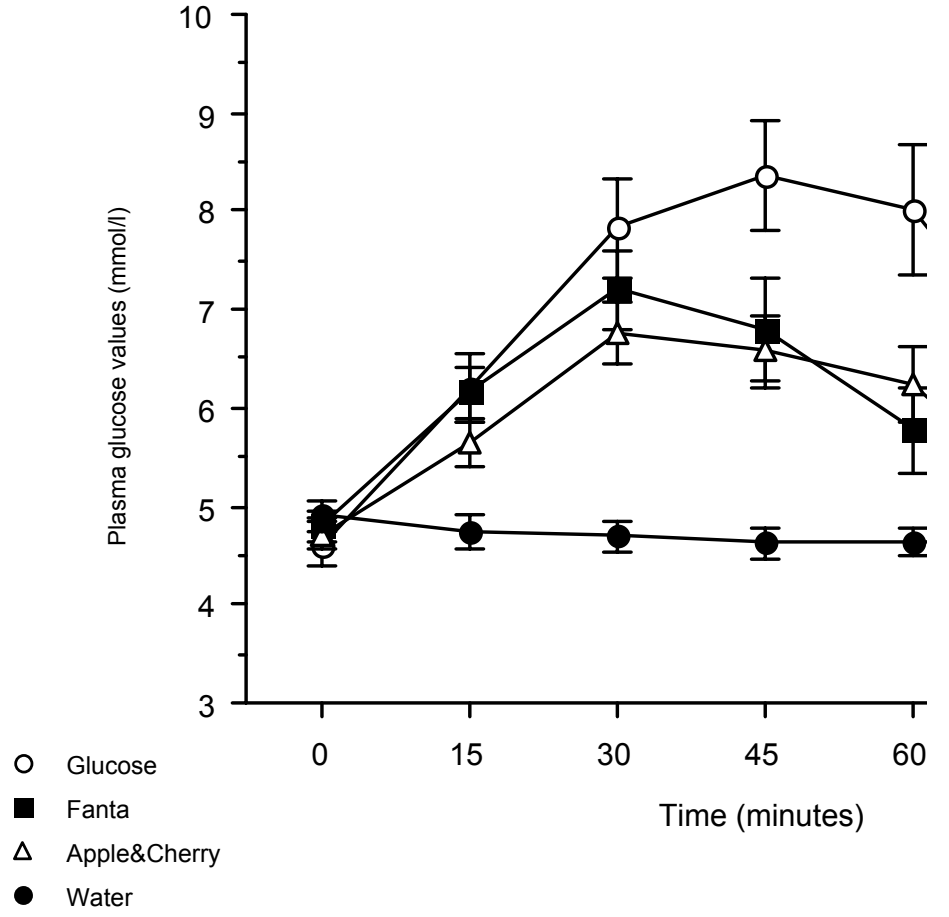
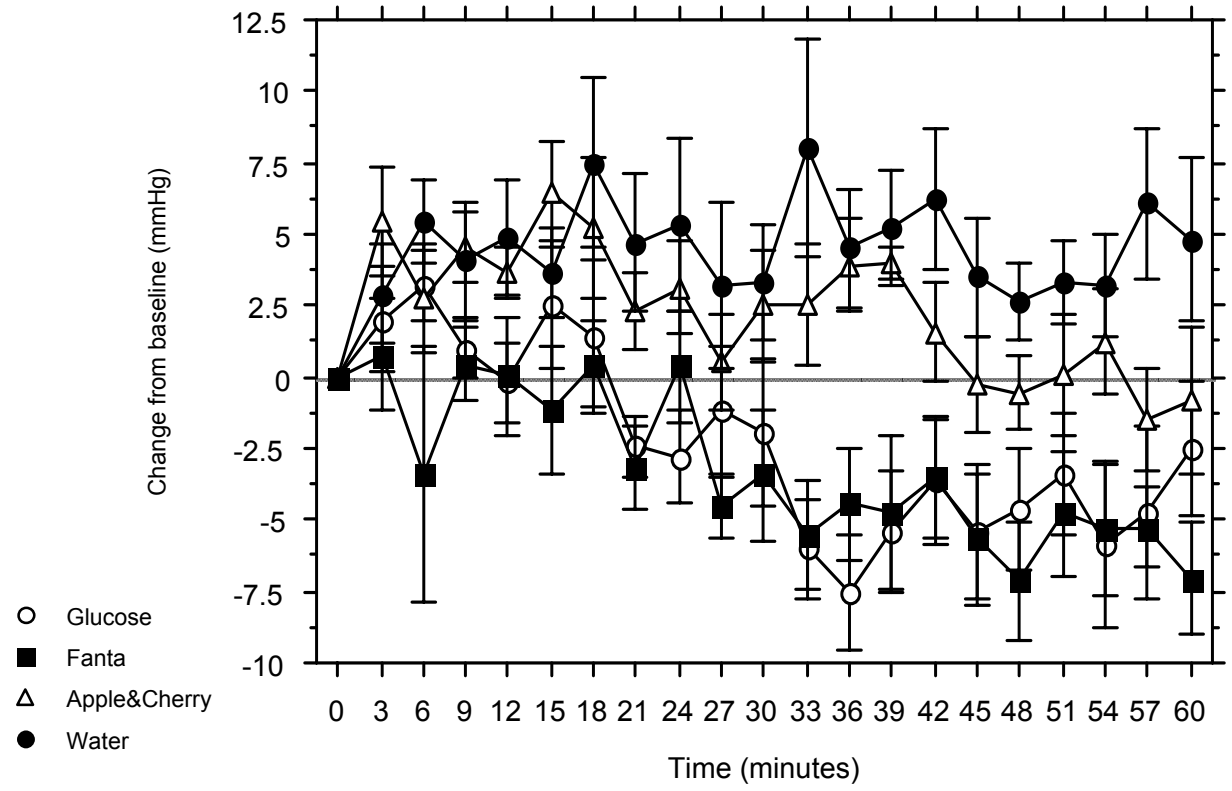
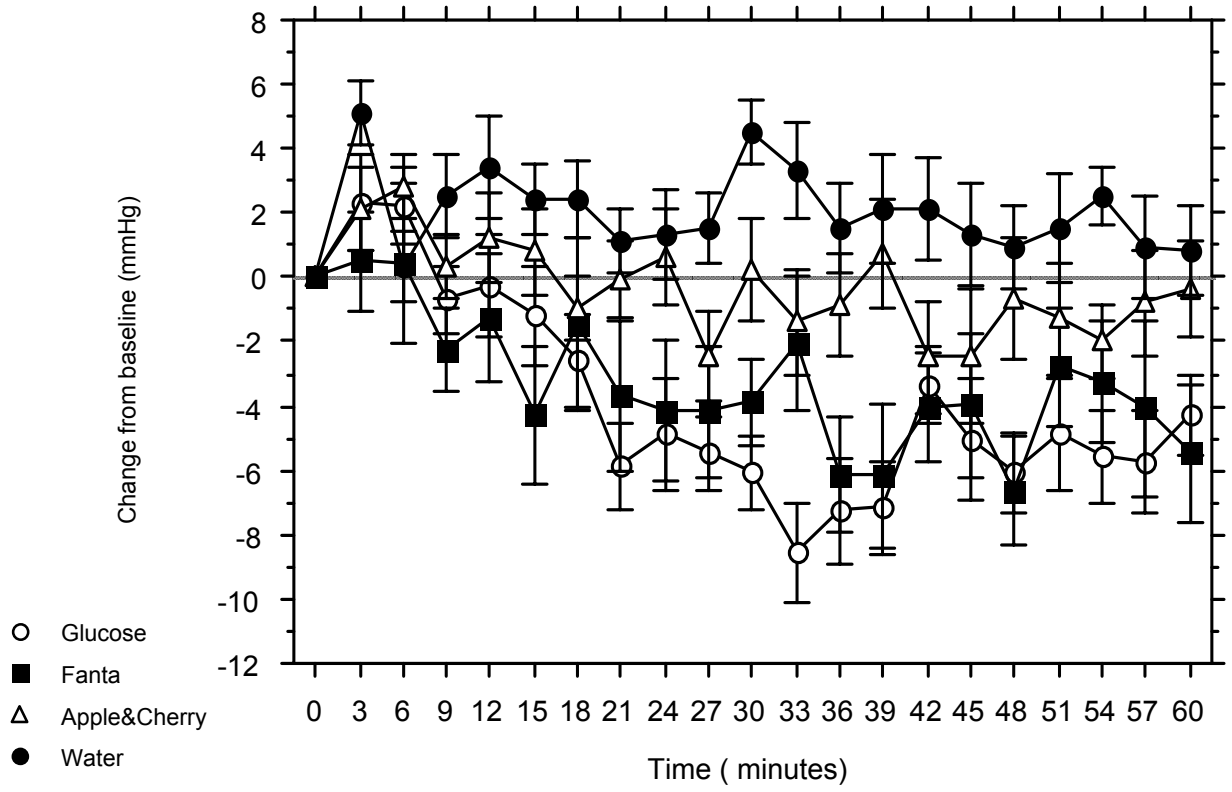


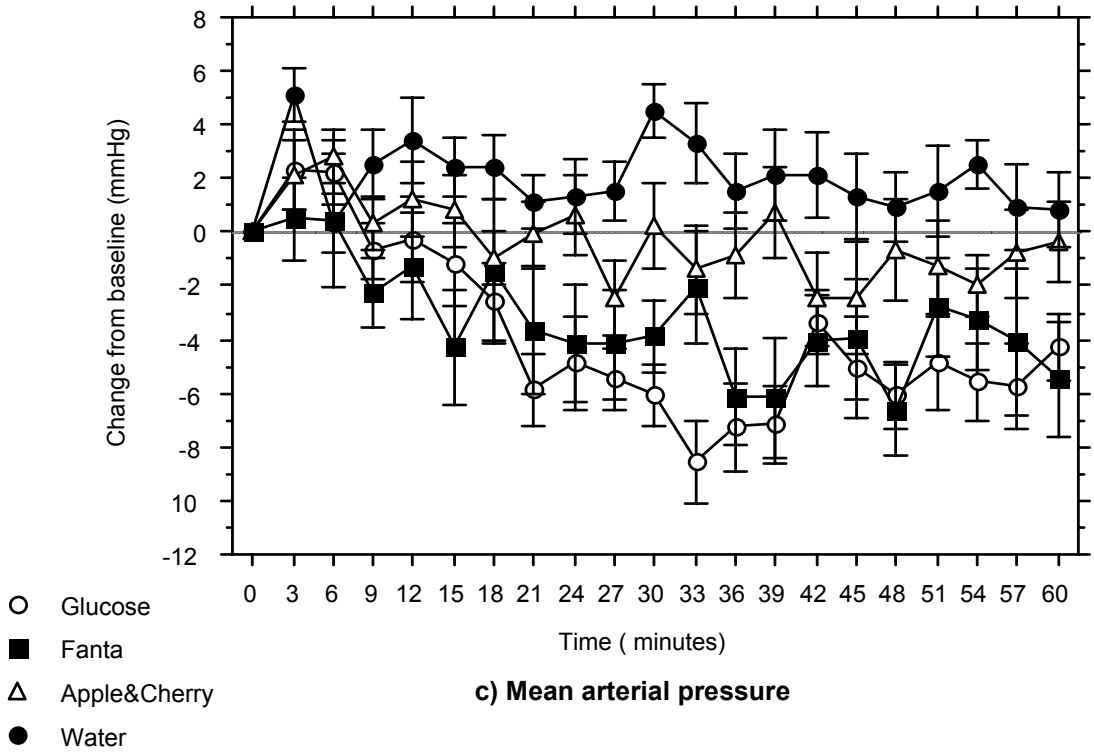
Figure 9.1 Mean (± SEM) plasma glucose values (mmol/L) over 60 minutes following the ingestion of 4 different test drinks in 10 healthy older people.



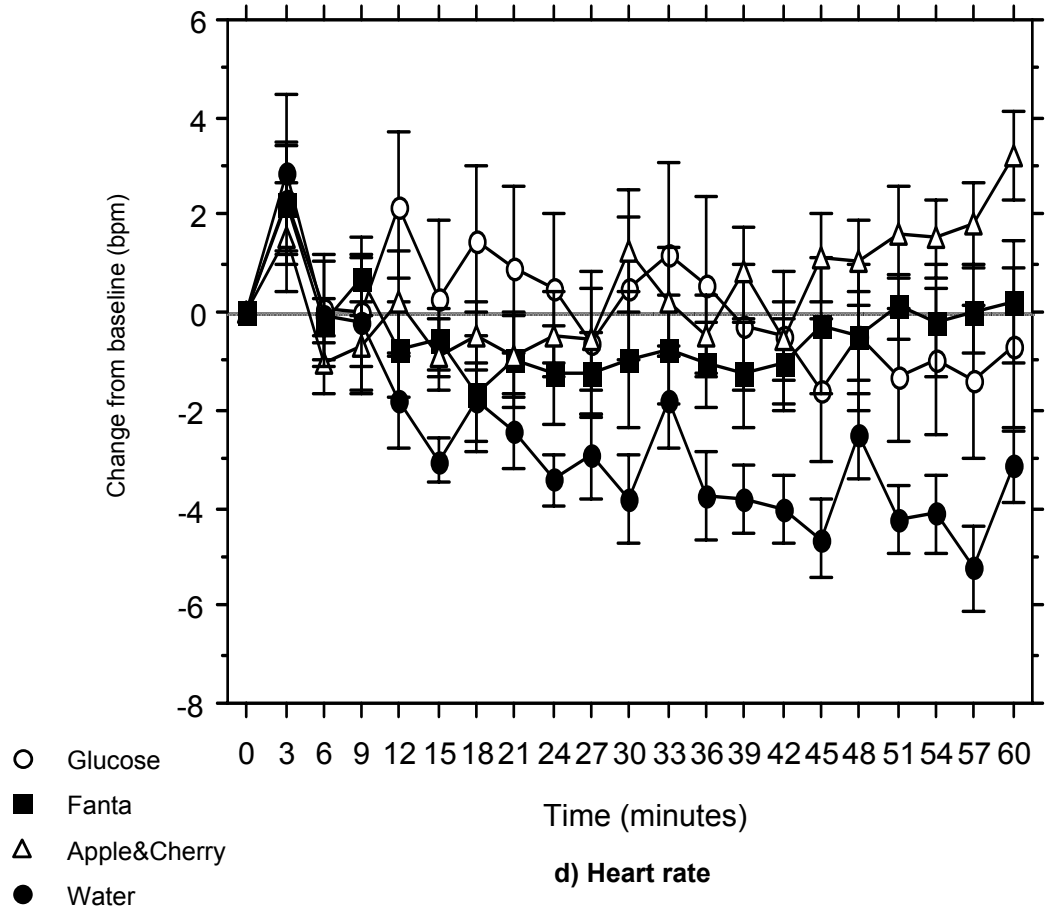
a) Systolic blood pressure



b) Diastolic blood pressure



c) Mean arterial pressure



d) Heart rate

Figure 9.2 (a-d) The change (mean ± SEM) in blood pressure (mmHg) and heart rate (bpm) from baseline over 60 minutes following the ingestion of 4 different test drinks in 10 healthy older people.

Chapter 10

The effects of drinks made from simple sugars on blood pressure in healthy older people

10.1 Summary

The objective of this study was to determine the blood pressure lowering effects of 50g carbohydrate drinks with varying carbohydrate content in healthy older people. A randomised, cross-over study was performed involving 10 (6 females) healthy older subjects (72.20 $\pm$ 1.50 years [mean age $\pm$ SEM]). Blood pressure (BP), heart rate (HR) and glucometer-derived blood glucose levels were determined at baseline and following the ingestion of equal volumes (300ml) of water and carbohydrate drinks with varying nutrient content (glucose, sucrose and fructose). A significant decline in BP over the first 60 minutes was seen following glucose (SBP P <0.01, DBP P< 0.01, MAP P=0.03) and sucrose (SBP P<0.01, DBP P<0.01, MAP P<0.01) ingestion, although the decrease occurred earlier after glucose than sucrose ingestion (SBP 7.33 $\pm$ 2.19 vs. 21.00 $\pm$ 4.30 minutes [P=0.03] and MAP 11.22 $\pm$ 3.10 vs. 17.00 + 3.78 minutes [P=0.03]). BP increased after water ingestion (SBP P=0.04, DBP P=0.18, MAP P=0.02) but did not change after fructose ingestion (SBP P=0.36, DBP P=0.81, MAP P=0.34). Post-hoc analyses revealed that the BP (SBP, DBP and MAP) decreases following glucose and sucrose ingestion were similar but significantly greater than following fructose or water ingestion. Sucrose, which is used widely (table sugar), reduces BP as much as glucose. In contrast no change in BP measurements were seen following fructose ingestion. Further studies are required to determine if the substitution of fructose for glucose or sucrose may be beneficial in the medical management of older people with severe symptomatic post-prandial hypotension.

10.2 Introduction

Blood pressure normally falls slightly after food ingestion in older people. When the fall is excessive it can produce post-prandial hypotension (PPH), which is defined as a decrease in systolic blood pressure of 20 mmHg or more within two hours from the start of a meal. The nadir is usually reached between 30 and 60 minutes after the start of eating (Jansen & Lipsitz, 1995; Smith *et al.*, 2003). PPH is associated with an increased incidence of falls, syncope, angina and transient ischaemic attacks, particularly in older people and patients with autonomic neuropathy; the latter most frequently due to diabetes mellitus (Jansen & Lipsitz, 1995). Despite a reported prevalence between 20 and 45%, PPH in older people is an under recognized problem (Aronow & Ahn, 1994; Grodzicki *et al.*, 1998; Le Couteur *et al.*, 2003; Puisieux *et al.*, 2002; Vaitkevicius *et al.*, 1991).

The pathophysiology of PPH is poorly understood, but is likely to be multifactorial (Jansen & Lipsitz, 1995). Meal composition is thought to be an important determinant of the degree of postprandial blood pressure decrease (Jansen & Lipsitz, 1995). Ingestion of carbohydrates, particularly glucose and to a lesser degree starch but not fructose or xylose, lowers blood pressure more than ingestion of protein, fat or water (Heseltine *et al.*, 1991a; Jansen *et al.*, 1990; Jansen *et al.*, 1987; Mathias *et al.*, 1989; Robinson TG, 1995). The addition of guar, a naturally occurring, non-absorbed, gel-forming carbohydrate of vegetable origin attenuates the fall in blood pressure seen following the ingestion of a glucose drink (Jones *et al.*, 2001). Reducing the total carbohydrate amounts in meals has also recently been shown to reduce the magnitude, duration and symptoms of PPH (Vloet *et al.*, 2001). Thus, modification of meal composition, particularly its carbohydrate content and type, could provide a means of reducing excessive post-prandial blood pressure falls in people with PPH.

Interestingly, the effects of sucrose the main constituent of table sugar, on post-prandial blood pressure have not been reported before. Therefore, the aim of this study was to determine the effects of drinks with equal volume and carbohydrate content (50g), but differing carbohydrate types (glucose vs. sucrose vs. fructose) on post-ingestion blood pressure in healthy older people.

10.3 Methods

10.3.1 Subjects

10 healthy, older subjects (6 female), aged 65-78 years were recruited by advertisement. All subjects were non-smokers and had no history of gastrointestinal disease or surgery, diabetes mellitus, significant respiratory or cardiovascular disease, autonomic dysfunction, chronic alcohol abuse or epilepsy. No subject was on any medications known to influence blood pressure (BP) and all medications remained unchanged during the study.

10.3.2 Protocol

This study protocol was similar to that previously described in the previous chapter (9.3.2).

10.3.3 Study drinks

The four study drinks were:

- 50g glucose in 270 ml of water and 30 ml of lemon juice
- 50g sucrose in 270 ml of water and 30 ml of lemon juice
- 50g of fructose in 270 ml of water and 30 ml lemon juice
- 270 ml of water and 30 ml of lemon juice (control)

10.3.4 Measurements

Blood pressure and heart rate

BP (systolic [SBP], diastolic [DBP], mean arterial pressure [MAP]) and HR were measured using an automated oscillometric BP monitor [DINAMAP ProCare, GE Medical Systems, NSW]. Following a 20-minute rest post cannula insertion, three measurements were obtained at 9, 6 and 3 minutes before drinks ingestion. The mean of these three readings formed the baseline value (t=0). The study drink was consumed within three minutes. BP and HR measurements were then measured three minutely for the first 60 minutes (to t=60) post drink ingestion.

Blood glucose measurements

Venous blood was obtained from the intravenous cannula for glucose estimation at baseline and t=15, 30, 45 and 60 minutes. Blood glucose levels from these venous samples were immediately determined at the bedside, using a glucometer [True Sense; Abbott Diagnostic Division, Australia].

Cardiovascular Autonomic Function

Autonomic nerve function was evaluated in the same way as previously described in 9.3.4.

10.3.5 Statistical analysis

All values are expressed as mean $\pm$ SEM. Two-way repeated measures analysis of variance (ANOVA) was used to examine the overall effects of time and drinks type (treatment) and the treatment by time interaction on BP and blood glucose changes from baseline. Post-hoc analysis using the Bonferroni/Dunn (all means) correction was performed when significant treatment effects were seen. One-way repeated measures ANOVA was conducted to evaluate the effects of each drink type on changes of BP and HR measurements from baseline over the first 60 minutes and a one-way ANOVA was conducted to compare the differences between the baseline BP, HR and whole blood glucose values between the study days. The time to BP decrease was the first time point after drink ingestion at which the BP was below the baseline value. The time values derived for glucose and sucrose were then compared using a paired t-test. All analyses were performed using Statview version 5.0 and SuperANOVA. P values < 0.05 were considered statistically significant.

10.4 Results

The drinks were well tolerated. One person had sub-clinical autonomic dysfunction (score 3) without overt symptoms and so was not excluded from the study.

Blood pressure (Figs.10.1a-c)

There was no significant difference in the baseline BP (SBP, DBP and MAP) values between any of the 4 study days (Table 10.1). One person had asymptomatic (≥ 20 mmHg) systolic BP decrease following both glucose and sucrose ingestion.

Significant treatment (P=0.04) and time (P=<0.01) effects on SBP [change from baseline values] over the first 60 minutes were seen. In the first 60 minutes, the SBP (Figure 10.1a) decreased significantly from baseline following glucose (P<0.01; -3.96 $\pm$ 1.38 mmHg [mean of 30-60 min post ingestion values when nadir reached (Jansen & Lipsitz, 1995)]) and sucrose (P=<0.01; -3.03 $\pm$ 1.37 mmHg) ingestion, increased non-significantly following fructose ingestion (P=0.36; 2.59 $\pm$ 1.62 mmHg) and increased significantly from baseline following water ingestion (P=0.04; 2.96 $\pm$ 2.39mmHg). The decrease in SBP occurred earlier after glucose than sucrose ingestion (7.33 $\pm$ 2.19 vs. 21.00 $\pm$ 4.30 minutes; P=0.03).

For DBP (change from baseline) there were significant treatment (P<0.01) and time (P<0.01) effects and treatment x time (P < 0.01) interaction. In the first 60 minutes, the DBP (Figure 10.1b) decreased significantly from baseline following glucose (P<0.01; -4.07 $\pm$ 1.09 mmHg) and sucrose (P<0.01; -4.491 $\pm$ 1.092 mmHg) ingestion, and increased slightly but not significantly following fructose (P=0.81; 0.97 $\pm$ 0.69 mmHg) and water (P=0.18; 2.46 $\pm$ 0.54 mmHg) ingestion. The decrease in DBP occurred at a similar time following glucose and sucrose ingestion (8.70 $\pm$ 2.12 vs. 8.70 $\pm$ 1.81 minutes; P=1.00).

For MAP [change from baseline] there were significant treatment (P<0.01) and time (P<0.01) effects and treatment x time (P=0.01) interaction. MAP (Figure 10.1c) decreased significantly from baseline following glucose (P=0.03; -3.22$\pm$ 1.35 mmHg) and sucrose (P<0.01; -3.46 $\pm$ 1.05 mmHg) ingestion, increased non-significantly following fructose

(P=0.34; 2.30 ± 0.92 mmHg) ingestion and increased significantly following water ingestion (P=0.02; 2.77 ± 0.78 mmHg). The decrease in MAP occurred sooner after glucose ingestion than sucrose ingestion (11.22 ± 3.10 vs. 17.00 ± 3.78 minutes; P=0.03).

Post-hoc analyses using the Bonferonni/Dunn correction found that glucose and sucrose ingestion had similar effects on post-ingestion BP (SBP, DBP and MAP) to each other (P > 0.05), water and fructose ingestion had similar effects on BP to each other (P > 0.05), and glucose and sucrose ingestion were each associated with a greater decline in BP than both fructose and water ingestion (P<0.01).

Heart rate (Figure 10.1d)

There was no significant difference in the baseline HR values between the 4 study days (Table 10.1). There was a significant treatment effect (P=0.04) and treatment x time interaction (P<0.01). The HR (Figure 1d) increased non-significantly from baseline following glucose (P=0.49; 1.43 ± 1.06 beats per minute [bpm]) and sucrose (P=0.33; 0.54 ± 0.72 bpm) ingestion, increased significantly following fructose ingestion (P=0.01; 2.49 ± 0.75 bpm) and decreased significantly following water ingestion (P<0.01; -1.68 ± 0.67 bpm).

Blood glucose (Figure 10.2)

There was no significant difference in the baseline blood glucose values between the 4 study days (Table 10.1). The blood glucose values increased significantly from baseline following the glucose (P<0.01), sucrose (P<0.01) and fructose drinks but did not change from baseline over time (60 minutes) following water (P=0.51) ingestion. The change in blood glucose value from baseline was greater following the glucose drink and lesser following the fructose drink in comparison to the changes seen following the sucrose drink (P<0.01).

10.5 Discussion

In agreement with the results of previous studies of healthy, young and older adult subjects, the BP of healthy, older subjects in this study decreased in the hour after glucose ingestion, increased after water ingestion and did not change after fructose ingestion (Jansen & Lipsitz, 1995; Lu *et al.*, 2003). Sucrose ingestion was followed by a significant BP decrease, similar in degree to that following glucose, but later in onset. During the 60 minutes after drink ingestion, SBP decreased on average between 3 – 4 mmHg following glucose and sucrose ingestion and one subject had a greater than 20 mmHg SBP decrease following both sucrose and glucose, fulfilling the criteria for PPH. To our knowledge, this is the first report of the effect of sucrose ingestion on BP in any age group.

Sucrose (molecular weight 342) is a disaccharide widely present in the diet as a component of food and also as table sugar. After ingestion it is hydrolysed by sucrase in the brush border of the small intestine to release an equimolar mixture of glucose and fructose, both with a molecular weight of 180. Sasaki *et. al.* have reported that the use of oral acarbose, a sucrase inhibitor, reduced the fall in post-prandial SBP in an elderly man with severe, symptomatic PPH from 45-50 mmHg to 18 mmHg, with resolution of symptoms (Sasaki *et al.*, 2001). This suggests that sucrose must be broken down to glucose and fructose to exert its full hypotensive effect, as does the delayed onset of the BP decrease after sucrose compared to glucose ingestion in the present study. It is unlikely that this difference is due to differences in gastric emptying rates as there is no evidence to suggest that gastric emptying is quicker following glucose ingestion than sucrose ingestion (Murray *et al.*, 1994). Although the presence of glucose in the small intestine is thought to be an important prerequisite for the development of post-prandial BP decreases, the changes in measured plasma glucose values are not predictive of subsequent post-prandial BP changes. A recent study by our group found that the BP response to carbohydrate drinks could not be reliably predicted from their glycaemic index (glycaemic effect)(Visvanathan *et al.*, 2004a).

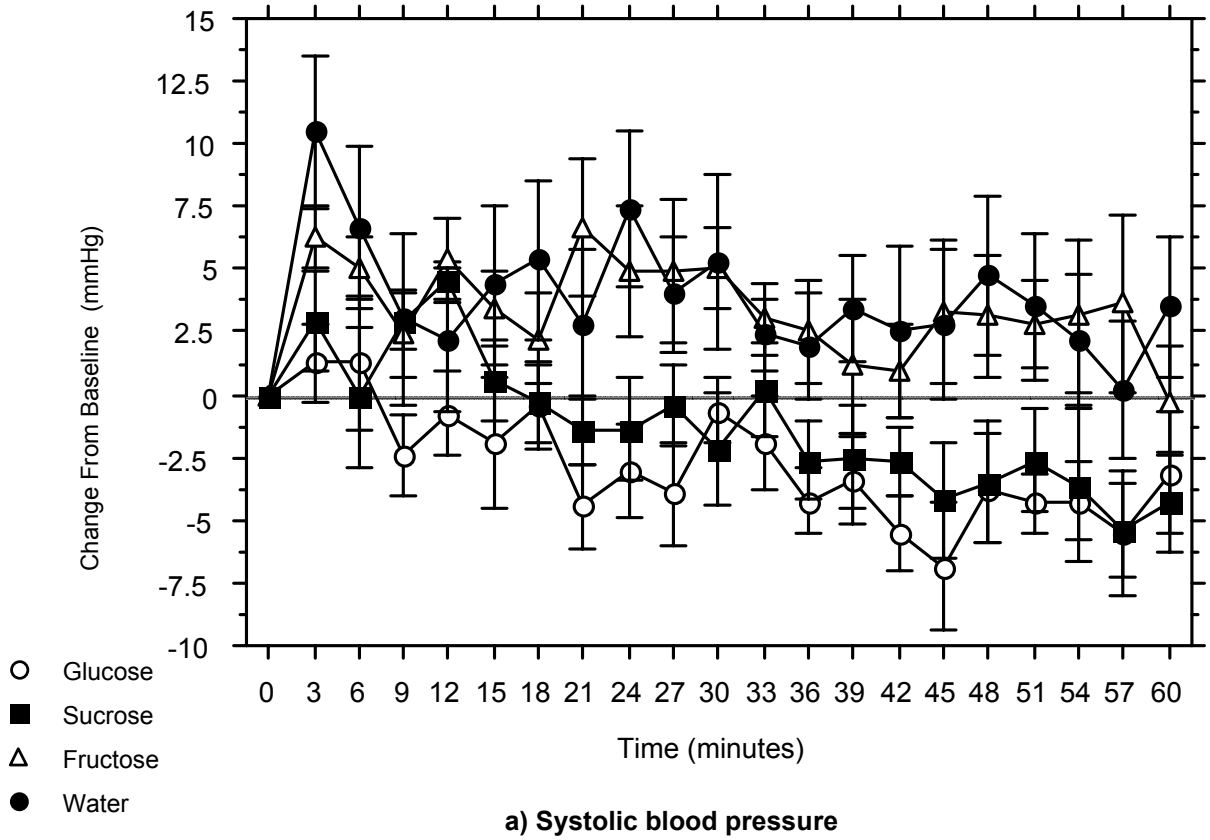
The BP decrease after 50g sucrose was not different to that after 50g glucose, despite the former only delivering 25g of glucose to the gut, together with 25g fructose which has no BP lowering effect. Sucrose may therefore exert a hypotensive effect additional to that of its glucose content. Alternately the hypotensive effect of glucose may be saturable at a dose of approximately 25g. The results of a recent study by Vloet et. al. supports this possibility (Vloet *et al.*, 2001). They found no increase in the BP lowering effect of a liquid meal when its carbohydrate content was increased from 65g (-39 $\pm$ 7 mmHg) to 100 g (-40 $\pm$ 5 mmHg). A glucose dose-response study would be required to distinguish between these possibilities.

This study was performed in healthy, older subjects, whose BP fell to be approximately 7.5 mmHg lower after sucrose and glucose than after fructose. There could be possible therapeutic implications for older people with PPH if they have similar (or greater) BP responses to these sugars. The substitution of fructose for sucrose (table sugar) is potentially an inexpensive and convenient treatment option in the management of symptomatic PPH. Further studies are required to assess the efficacy and safety of such a strategy, particularly in older people with symptomatic PPH.

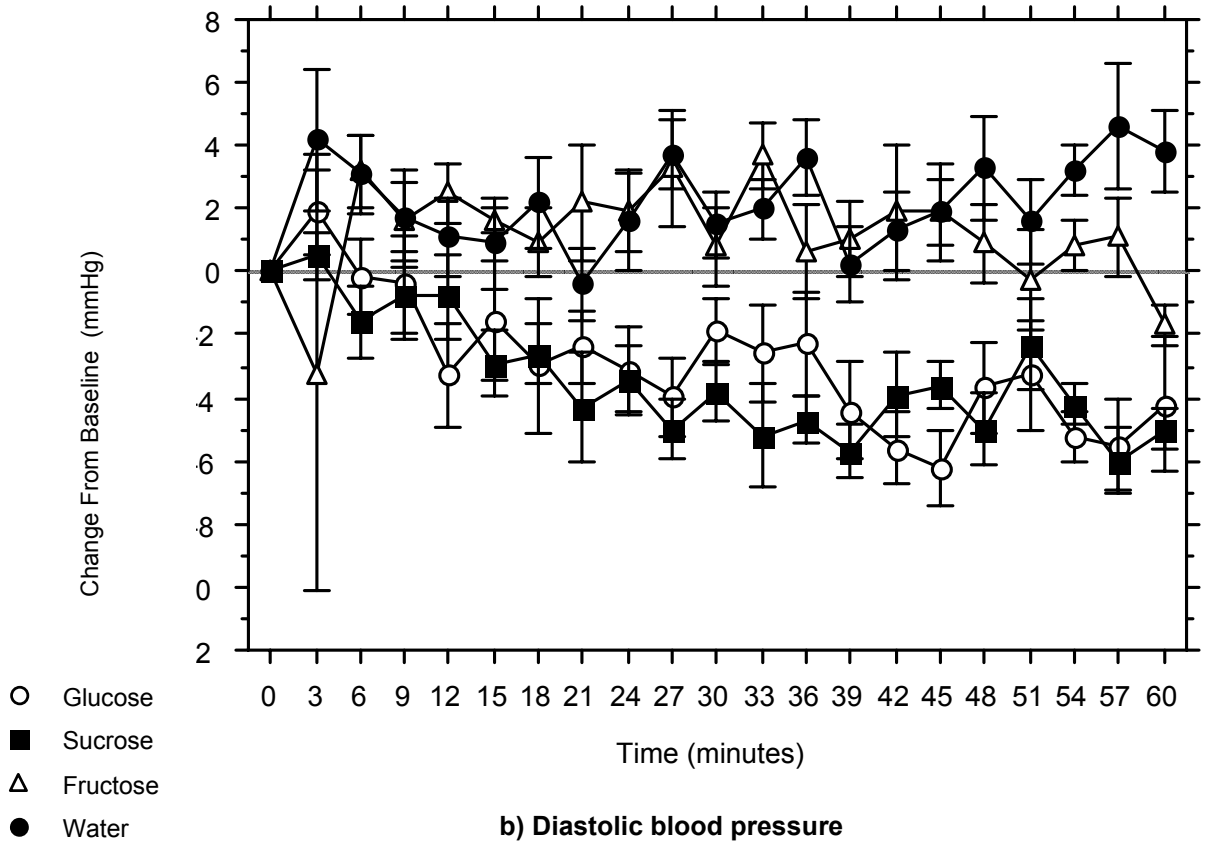
In conclusion, the decrease in BP in older people after the consumption of 50g carbohydrate containing drinks of equal volume was determined by the nature of the sugars in the drink, with glucose and sucrose, but not fructose, lowering BP. Manipulation of the carbohydrates in a meal to increase fructose and decrease glucose and sucrose content, may be a relatively simple and inexpensive management strategy for symptomatic PPH and this requires further evaluation.

Table 10.1 Subject characteristics and baseline blood pressure, heart rate and blood glucose measurements.

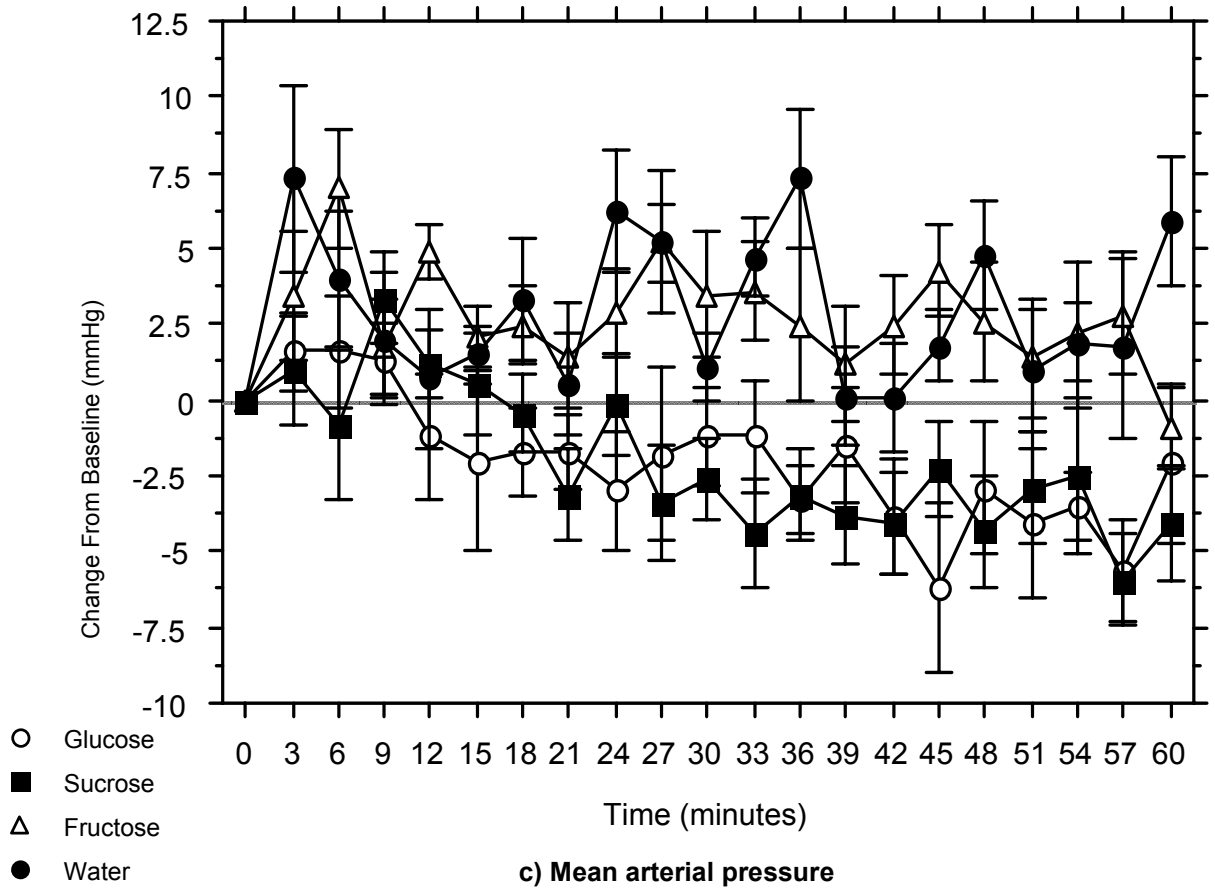
		Standard Error Of Mean
Mean Age (years)	72.20	1.50
Total subjects	10	
Female (%)	60	
Body Mass Index (kg/m^2)	26.14	0.95
Autonomic Nerve Function Score	0.8	0.2
Baseline systolic blood pressure [BP] (mmHg)		
Glucose drink	117.43	5.35
Sucrose drink	118.20	5.63
Fructose drink	116.37	5.24
Water	119.40	7.38
Baseline diastolic BP (mmHg)		
Glucose drink	65.19	3.25
Sucrose drink	65.80	3.27
Fructose drink	65.00	3.59
Water	63.90	4.23
Baseline mean arterial BP (mmHg)		
Glucose drink	83.60	3.98
Sucrose drink	84.93	3.79
Fructose drink	83.83	5.24
Water	84.40	5.80
Baseline heart rate (bpm)		
Glucose drink	65.47	1.78
Sucrose drink	65.13	1.72
Fructose drink	63.30	1.42
Water	62.57	2.01
Baseline blood glucose (mmol/L)		
Glucose drink	5.87	0.23
Sucrose drink	5.63	0.09
Fructose drink	5.89	0.16
Water	5.93	0.17



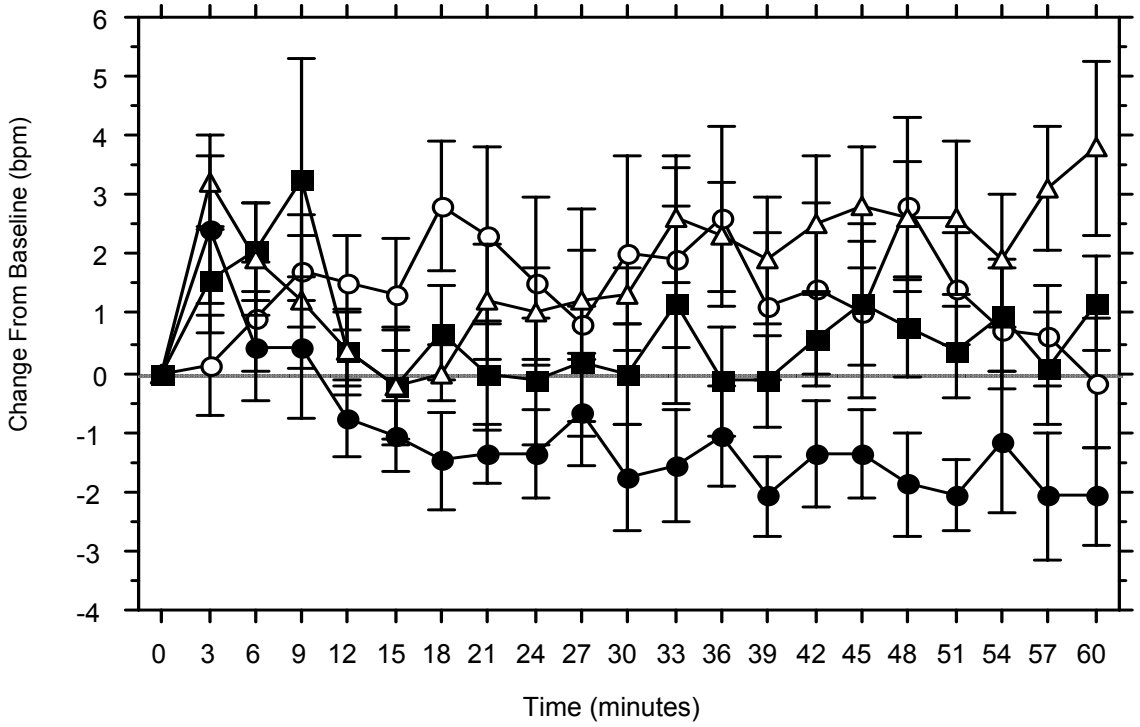
a) Systolic blood pressure



b) Diastolic blood pressure



c) Mean arterial pressure



d) Heart rate

Figure 10.1 (a-d) The mean blood pressure and heart rate changes from baseline following ingestion of the 4 different test drinks in ten healthy older people (SEM bars shown)

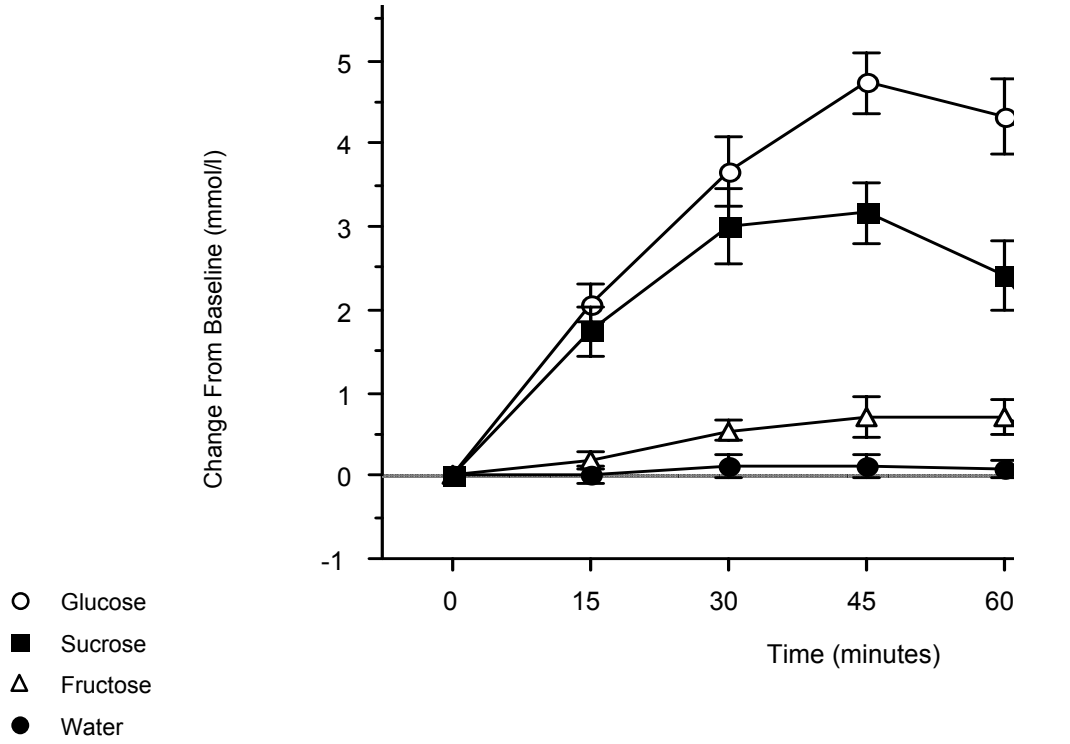


Figure 10.2 Changes in mean blood glucose values (mmol/l) from baseline over the first 60 minutes following ingestion of the four test drinks in 10 healthy older subjects.

Chapter 11

Nutritional frailty in older people – Discussion and future directions

The studies presented in Chapters 5-10 targeted two nutrition-related disorders, under-nutrition and post-prandial hypotension, which are commonly associated with ageing syndromes (i.e. frailty and falls). These studies confirmed that under-nutrition is indeed a common disorder in older people in both Australia and Malaysia, has many adverse health consequences and several simple screening measures were identified. Several non-physiological factors (i.e. medical illnesses, depression) were found to be independently associated with under-nutrition. It was also discovered that there may be a failure of energy homeostasis in under-nourished older people and this may possibly contribute to the physiological anorexia of ageing. Finally, dietary carbohydrate manipulation was found to be possibly beneficial in the management of post-prandial hypotension in older people. The impact of these studies on clinical practice is discussed in this final chapter.

Malaysia like Australia has an ageing population. Ageing research is relatively new to Malaysia. Unlike Australia, Malaysia currently has no national insurance or an aged pension scheme. Furthermore, there are no co-ordinated community services and so many elderly people with no financial or family support often become dependant on shelter home facilities. Like many other newly industrialized developing country, there is a high rate of rural to urban displacement of older people. This social disruption puts the older person at high risk of isolation, poverty and neglect. Therefore, there is urgent need for social policies to be developed to ensure that disadvantaged older people in Malaysia have adequate social and financial support in their twilight years. The author of this thesis had the fortunate opportunity to collaborate with a Malaysian community medicine specialist, Dr Zaiton Ahmad, and together they designed, conducted and analyzed the results of the pioneering study described in Chapter 5. It is now known that the prevalence of under-nutrition in these

facilities is indeed high and non-physiological factors, such as medical illnesses, depression, oral and dental health are important in determining nutritional health. Attention to the quality of meals served at these facilities is also important as it was shown that eating fruits, vegetables and diary products was protective against being underweight. Funding is presently being sought to evaluate the nutritional content of the meals served at this facility and perhaps with the help of dietitians, nutritious meal plans can be devised if shortcomings are identified. The author and her collaborator also hope to observe these residents over the next 5 years. Information with regards to institutionalization in high care facilities and mortality will be gathered. The results of this study have been presented to the Department of Social Welfare in Malaysia and it was well received. It is hoped that the results of this study will bring about beneficial changes for the elderly residents in these shelter care facilities and perhaps eventually guide new policy development within this Malaysian ministry. This study also evaluated for the first time the use of the 'DETERMINE Your Nutritional Health Checklist' in Malaysia. Similar to studies performed in Europe and North America, it confirmed that this questionnaire is best used as an awareness tool given its excellent negative predictive value. It is not a nutritional screening tool. Therefore, there is still a need to develop a nutritional screening tool for use in Malaysia.

The studies described in Chapters 6 and 7 determined for the first time the prevalence and consequences of under-nutrition in the community and in hospitals in South Australia. Approximately 5% of community dwelling recipients of domiciliary care services were found to be malnourished (MNA score < 17) as defined by the Mini Nutritional Assessment and this is comparable to community studies done overseas. The prevalence of malnutrition in the sub-acute hospital in South Australia was also high at 30% (MNA score < 17). These two studies confirmed that under-nourished older people were at risk of experiencing adverse health outcomes. The study described in Chapter 6 confirmed that frail older subjects in the community identified as being under-nourished by the Mini Nutritional Assessment (i.e. malnourished + at-risk groups [score <24]) were at increased risk of falls,

frequent and prolonged hospitalization. Similarly, the study described in Chapter 7 found that older under-nourished patients of a sub-acute care facility were more likely to be discharged to an accommodation with increased supports or re-admitted to an acute care facility than nourished subjects. Several nutritional screening measures (the rapid screen and the Mini Nutritional Assessment) were compared to more in-depth nutritional assessment in the study described in Chapter 7. It was concluded that the rapid screen, where an older person was classified as under-nourished if they fulfilled one or both of the following: 1) Body Mass Index < 22 kg/m^2; 2) > 7.5% weight loss in the preceding 3 months, was more suitable for resource limited (time, financial and staffing) settings given it's higher specificity. With the rapid screen, biochemical investigations are not needed. The Mini Nutritional Assessment may be better if resources permit given its better sensitivity in comparison to the rapid screen. However, older people scoring between 17 and 23.5 (at-risk of malnutrition) on the MNA would require further in-depth assessment and this is likely to require biochemical investigations. The responses to the questions in the questionnaire could guide the implementation of simple management strategies. For example, someone not eating three full meals a day could be encouraged to do so.

As a direct result of these two studies, the South Australian Department of Health has funded a large community project (healthy ageing-nutrition), which is currently ongoing. The aims of this project are to: 1) increase awareness and knowledge of the food and nutritional needs of older people among community, carers and professional groups; 2) increase knowledge and skills of these group in early identification of nutritional risk by the use of simple assessment and screening tools (i.e. MNA and rapid screen); 3) increase the use of appropriate early nutritional intervention strategies; and 4) increase inter-sectoral collaboration in addressing food and nutrition needs among organizations and groups who support healthy ageing. Our team has also secured funding to conduct a randomized placebo controlled nutritional intervention study evaluating the use of oral nutritional and testosterone supplementation in frail community dwelling older people. The power

calculations for this study and the selection criteria (the need to score < 24 on the MNA and to be under-nourished as per the rapid screen) were based on the results of the studies presented in Chapters 6 and 7. This intervention study is ongoing.

The study described in Chapter 8 found that a failure in energy homeostasis in older under-nourished people may be contributing to the development and/or progression of the anorexia of ageing. In this study, fasting plasma ghrelin levels in under-nourished and well-nourished older people were comparable and not higher as in previous studies in younger people. As ghrelin is said to be involved in meal initiation, it is expected that in a state of negative energy balance such as under-nutrition, ghrelin levels would increase to stimulate energy intake (compensatory increase). In this study, plasma ghrelin levels in under-nourished older people were non significantly lower (33%) than in well-nourished older people. Although this study was underpowered, the likelihood of fasting plasma ghrelin levels being higher in under-nourished older people is very unlikely. The results of this study provide some optimism that exogenous ghrelin administration may be beneficial in treating this homeostatic imbalance and increase food intake in under-nourished older people. This will require further evaluation.

The studies described in Chapters 9 and 10 investigated the effects of dietary carbohydrate manipulation on post-prandial blood pressure response. Post-prandial hypotension is a common blood pressure disorder occurring after meal ingestion, particularly in older people, that can contribute to frailty by increasing the risk of falls, cerebrovascular accidents, angina and syncope. These studies were performed with the intention of identifying simple non-pharmacological measures that could be used to manage symptomatic post-prandial hypotension in older people. The study described in Chapter 9 was performed to determine the effects of drinks with varying glycaemic effects (or glycaemic indices) on post-ingestion blood pressure. The results of this simple study were conclusive and it was determined that the glycaemic effect (or glycaemic index) of a drink

could not be used to predict the subsequent blood pressure response. Therefore, published glycaemic index tables cannot be reliably used to guide the choice of meals in patients with severe post-prandial hypotension. The study described in Chapter 10 evaluated the effect of carbohydrate drinks containing simple sugars (glucose, fructose and sucrose) on post-ingestion blood pressure. For the first time, it was shown that the fall in blood pressure following glucose and sucrose ingestion was of similar magnitude, although, the blood pressure fall occurred later following sucrose in comparison to glucose. The author postulated that the delay was possibly because sucrose exerted it hypotensive effect only once it had been hydrolyzed to its monosaccharide components (i.e. glucose and fructose). Perhaps, prevention of this hydrolysis might ameliorate this fall in blood pressure. Another PhD student in this department is currently investigating the effects of arcabose, a glucosidase inhibitor, on the post-prandial blood pressure fall normally seen following sucrose ingestion. This study also confirmed the results of a previous study performed a decade ago that unlike glucose or sucrose, fructose ingestion did not cause a significant fall in blood pressure in older people. Substituting sucrose (table sugar) with fructose may be a simple,cost-effective option in the management of symptomatic post-prandial hypotension in older people. The findings of this study need to be confirmed in a population of older people with post-prandial hypotension.

To summarize, nutritional frailty is a common disorder affecting older people with many adverse health consequences (for example falls). Frail older people are vulnerable to social and health insult that may overwhelm already strained homeostatic mechanisms. Failure of energy homeostasis, as evidenced by a lack of increase in plasma ghrelin levels in under-nourished older people in response to a negative energy balance state, may contribute to the development and/or progression of the anorexia of ageing. Perhaps, exogenous ghrelin administration may be beneficial and this requires further investigation in older people. Screening and awareness tools were identified and these should be used routinely in clinical practice to identify at-risk older people that may benefit from nutritional intervention. As

with many other geriatric syndromes (eg. Delirium), non-physiological factors (for example depression) should be sought and treated where possible. Frail older people are also at risk of post-prandial hypotension and it's many adverse consequences. As fructose ingestion was not associated with a significant fall in post-prandial blood pressure, substitution of sucrose with fructose (dietary carbohydrate manipulation) may be a useful non-pharmacological management option for older people with symptomatic post-prandial hypotension.

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Appendices

Appendix 1

NESTLÉ NUTRITION SERVICES

Nestlé

Mini Nutritional Assessment
MNA®

Last name: First name: Sex: Date:

Age: Weight, kg: Height, cm: I.D. Number:

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 loss of appetite
1 = moderate loss of appetite
2 = no loss of appetite ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (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 m)²
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 a nursing home or hospital)
0 = no 1 = yes ☐

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, yogurt) 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 fruits 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.: Guigoz Y, Vellas B and Garry PJ. 1994. Mini Nutritional Assessment: A practical assessment tool for grading the nutritional state of elderly patients. *Facts and Research in Gerontology.* Supplement #2:15-59.
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Appendix 2

The Warning Signs of poor nutritional health are often overlooked. Use this checklist to find out if you or someone you know is at nutritional risk.

Read the statements below. Circle the number in the yes column for those that apply to you or someone you know. For each yes answer, score the number in the box. Total your nutritional score.

DETERMINE YOUR NUTRITIONAL HEALTH

	YES
I have an illness or condition that made me change the kind and/or amount of food I eat.	2
I eat fewer than 2 meals per day.	3
I eat few fruits or vegetables, or milk products.	2
I have 3 or more drinks of beer, liquor, or wine almost every day.	2
I have tooth or mouth problems that make it hard for me to eat.	2
I don't always have enough money to buy the food I need.	4
I eat alone most of the time.	1
I take 3 or more different prescribed or over-the-counter drugs a day.	1
Without wanting to, I have lost or gained 10 pounds in the last 6 months.	2
I am not always physically able to shop, cook and/or feed myself.	2
TOTAL	

Total Your Nutritional Score. If it's –

0-2	**Good!** Recheck your nutritional score in 6 months.
3-5	**You are at moderate nutritional risk.** See what can be done to improve your eating habits and lifestyle. Your office on aging, senior nutrition program, senior citizens center or health department can help. Recheck your nutritional score in 3 months.
6 or more	**You are at high nutritional risk.** Bring this checklist the next time you see your doctor, dietitian or other qualified health or social service professional. Talk with them about any problems you may have. Ask for help to improve your nutritional health.

These materials developed and distributed by the Nutrition Screening Initiative
2626 Pennsylvania Avenue, NW Suite 301
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a project of:

American Academy of Family Physicians

The American Dietetic Association

National Council on the Aging, Inc.

Remember that the warning signs suggest risk, but do not represent diagnosis of any condition. Turn the page to learn more about the Warning Signs of poor nutritional health.

Appendix 3

GERIATRIC ASSESSMENT AMONG THE ELDERLY INMATES IN THE RUMAH SERI KENANGAN IN PENINSULAR MALAYSIA

JAB KEBAJIKAN MASYARAKAT MALAYSIA

1.	Cheras, Selangor	.....Penghuni	.....	**K/tangan**
2.	Seremban, Negeri Sembilan	..... Penghuni	.....	**K/tangan**
3.	Cheng, Melaka	..... Penghuni	.....	**K/tangan**
4.	Johor Bahru, Johor	..... Penghuni	.....	**K/tangan**
5.	Ipoh, Perak	..... Penghuni	.....	**K/tangan**
6.	Tanjung Rambutan, Perak	..... Penghuni	.....	**K/tangan**
7.	Pengkalan Chepa, Kelantan	..... Penghuni	.....	**K/tangan**
8.	Bedong, Kedah	..... Penghuni	.....	**K/tangan**
9.	Kangar, Perlis	..... Penghuni	.....	**K/tangan**

Fakulti Perubatan dan Sains Kesihatan

Universiti Putra Malaysia

A. BIODATA

1. Umur:..... tahun

2. Jantina:
   A. Perempuan B. Lelaki

3. Etnik:
   A. Melayu B. Cina
   C. India D. Lain-lain.....(sila nyatakan)

4. Agama:
   A. Islam B. Buddha
   C. Hindu C. Kristian
   D. Lain-lain.....(nyatakan)

5. Pendidikan:
   A. Sek. Rendah B. Sek. Menengah
   C. Lain-lain.....(sila nyatakan)

6. Kawasan Tempat Tinggal Asal Anda:
   A. Bandar B. Luar Bandar .....(sila nyatakan)

7. Ada mempunyai keluarga:
   A. Ya B. Tidak

8. Jika Ya:.....(nyatakan hubungan dan bilangan ahli keluarga)

9. Kekerapan Keluarga Melawat dalam sebulan...../setahun.....

B. SKALA KEMURUNGAN GERIATRIK

Sila jawab semua soalan

1.	Adakah anda pada asasnya berpuas hati dengan kehidupan anda?	Ya	Tidak
2.	Adakah anda telah meninggalkan banyak kegiatan dan minat anda?	Ya	Tidak
3.	Adakah anda berasa hidup anda kekosongan	Ya	Tidak
4.	Adakah anda sering berasa bosan?	Ya	Tidak
5.	Adakah anda bersemangat dalam kebanyakan masa?	Ya	Tidak
6.	Adakah anda bimbang sesuatu yang buruk akan terjadi pada anda?	Ya	Tidak
7.	Adakah anda berasa gembira dalam kebanyakan masa?	Ya	Tidak
8.	Adakah anda berasa tidak terdaya?	Ya	Tidak
9	Adakah anda lebih suka duduk di rumah daripada keluar dan melakukan sesuatu perkara/hal baru?	Ya	Tidak
10.	Adakah anda berasa bahawa anda mempunyai lebih banyak masalah ingatan daripada orang lain?	Ya	Tidak
11.	Adakah anda fikir alangkah baiknya untuk hidup sekarang?	Ya	Tidak
12.	Adakah anda merasa keadaan anda sekarang kurang berguna?	Ya	Tidak
	JUMLAH		

C. PENYELIAAN KESIHATAN NUTRISI ANDA

Berat:.....Kg Tinggi:.....M BMI:.....kg/m2

NO.	SOALAN	YA
1.	Saya mempunyai penyakit atau keadaan yang membuat saya menukar jenis makanan atau jumlah makanan yang saya makan?	2
2.	Saya makan kurang dari 2 sajian dalam sehari?	3
3.	Saya makan sedikit buah-buahan, sayur-sayuran atau jenis tenusu?	2
4.	Saya mengambil 3 atau lebih minuman bir, arak, dan samsu setiap hari.	2
5.	Saya mempunyai masalah gigi atau mulut yang membuatkan saya sukar untuk makan.	2
6.	Saya selalu tidak ada wang yang cukup untuk membeli makanan yang saya perlu.	4
7.	Saya makan seorang diri kebanyakan masa.	1
8.	Saya mengambil 3 atau lebih ubat-ubatan preskripsi atau ubat-ubatan dari kaunter setiap hari	1
9.	Tampa saya sedari saya telah hilang atau tambah 10 lb. dalam masa 6 bulan kebelakangan ini.	2
10.	Saya selalu tidak berupaya untuk membeli belah, masak atau menyuap diri sendiri	2
	JUMLAH	

0-2 normal
3-5 moderate risk for poor nutrition
≥6 high nutrition risk

0-4 very severe disability
5-9 severe disability
10-14 moderate disability
15-19 mild disability
20 independent

D. ACTIVITIES OF DAILY LIVING/AKTIVITI HARIAN (BASED ON THE BARTEL INDEX)

	Aktiviti	0	1	2	3
1.	*Feeding/* **Makan**	*Unable*/Tidak upaya ☐	*Need Help*/Perlu bantuan ☐	*Independent*/Tanpa bantuan ☐	
2.	*Bathing/* *Mandi*	*Dependent*/Tidak upaya ☐	*Independent*/Tanpa bantuan ☐		
3.	*Grooming/* **Mendandan**	*Dependent*/Tidak upaya ☐	*Independent*/Tanpa bantuan ☐		
4.	*Dressing/* **Berpakaian**	*Unable*/Tidak upaya ☐	*Need Help*/Perlu bantuan ☐	*Independent*/Tanpa bantuan ☐	
5.	*Bowel/* **Buang Air Besar**	*Incontient/Tidak* terkawal ☐	*Need Help*/Perlu bantuan ☐	*No accidents*/Boleh dikawal ☐	*Bil. Incontinent dlm seminggu* _____
6.	*Bladder/* *Buang Air Kecil*	*Incontient*/Tidak terkawal ☐	*Need Help*/Perlu bantuan ☐	*No accidents*/Boleh dikawal ☐	*Bil. Incontinent dlm seminggu* _____
7.	*Toilet/* **Ke tandas**	*Unable*/Tidak berupaya ☐	*Need Help*/Perlu bantuan ☐	*Independent*/Tanpa bantuan ☐	
8.	*Transfer/* **Beralih**	*Dependent*/Tidak upaya ☐	*Need major help*/Perlu banyak bantuan ☐	*Minimal Help*/Pertolongan Minimal ☐	*Independent*/Tanpa bantuan ☐
9.	*Ambulation/* **Pergerakan**	*Inmobile*/ Tidak boleh bergerak ☐	*Wheelchair but independent*/Kerusi roda tanpa bantuan ☐	*Need Help*/Perlu bantuan ☐	*Independent*/Tanpa bantuan ☐
10.	**Stairs/*Tangga***	*Unable*/Tidak upaya ☐	*Need Help*/Perlu Bantuan ☐	*Independent*/Tanpa bantuan ☐	

E. *FALLS*/KEJATUHAN

1. Pernahkah anda jatuh? Ya/Tidak

2. Jika ya, bila?
   A. Dalam masa 3 bulan kebelakangan ini
   B. Dalam masa 6 bulan kebelakangan ini
   C. Dalam masa setahun kebelakangan ini

3. Berapa kali anda telah mengalami kejatuhan dalam masa tempoh itu?

   1x 2x 3x lebih dari 3x

4. Di mana anda mengalami kejatuhan itu?
   A. Di bilik air B. Di katil
   C. Di ruang makan D. Di koridor
   E. Di ruang tamu F.Di bilik tidur
   G.Lain-lain……(sila nyatakan)

5. Adakah anda mengalami kecederaan akibat kejatuhan itu?
   A. Ya B. Tidak
   C. Tidak ingat

6. Jika Ya, apakah kecederaan yang anda alami?
   A. Kepatahan B. Luka
   C. Terlanggar D. Lain-lain…….(sila nyatakn)

7. Apa sebab anda jatuh?
   A. Merasa pening B. Silap langkah
   C. Terlanggar D. Kurang penglihatan
   E. Lain-lain …….(sila nyatakan)

8. Adakah anda mengalami apa-apa penyakit
   A. Ya B. Tidak
   C. Tidak tahu

9. Jika Ya, apakah penyakit yang anda alami?
   A. Kencing manis B. Darah tinggi
   C. Asma D. Sakit jantung
   E. Osteoarthritis F. Strok/Angin ahmar
   G. Lain-lain .....(sila nyatakan)

10. Adakah anda mengambil ubat-ubatan untuk penyakit anda?
   A. Ya B. Tidak

11. Jika Ya berapa jenis ubat?(termasuk ubat-ubatan tradisi, atau kaunter)
   A. 1 jenis B. 2 jenis
   C. 3 jenis D. Lebih dari 3 jenis

12. Adakah anda memakai cermin mata?
   A. Ya B. Tidak

13. Adakah anda mengunakan alat bantuan untuk berjalan?
   A. Ya B. Tidak
   C. Kadang-kadang

14. Semasa anda jatuh adakah anda berseorangan?
   A. Ya B. Tidak
   C. Tidak ingat

F. PENILAIAN KOGNITIF

INGATAN	**1 markah bagi setiap jawa yang betul**
1. Saya mahu anda mengingati nombor ini. Cuba anda ulangi(4517). Saya akan memguji anda dalam masa 10 minit	_____
2. Berapa umur anda?	_____tah
3. Bilakah tarikh lahir anda? Atau dalam tahun berapakah anda dilahirkan	_____

ORIENTASI MAKLUMAT

4. Hari ini hari apa? _____

5. Berapakah tarikh hari ini? Hari _____
6. Bulan _____
7. Tahun _____

8. Apakah nama tempat ini (rumah kenangan/hospital). Tidak semesti memberikan nama tempat _____

9. Apakah perkerjaannya(eg. Tukang sapu, penyelia) _____

MEMORI MENGINGAT

10. Bolehkah anda mengingat nombor itu kembali? _____

JUMLAH

Pencapaian

0-4: Berkemungkinan Dimensia
5-6: Tahap sempandan
>7 Normal

G. CORAK TIDUR

1. Adakah anda mempunyai masalah tidur?
   A. Ya B. Tidak
   Jika Ya, teruskan dengan soalan berikut.

2. Adakah anda susah hendak memulakan tidur (faling asleep).
   A. Ya B. Tidak

3. Adakah anda sukar hendak meneruskan tidur (maintaining sleep)
   A. Ya B. Tidak

4. Adakah anda tidur di siang hari (day time sleep)
   A. Ya B. Tidak

5. Adakah anda mengambil sebarang ubat tidur
   A. Ya B. Tidak

Kebiasaannya pukul berapakah anda tidur malam?.....

PENGHARGAAN

rima kasih yang tidak terhingga diucapkan di atas kerjasama dan keikhlasan an/Puan dalam menjawab soal-selidik ini. Kerjasama anda membantu tugas-gas kami dalam menghasilkan satu data penyelidikan yang terbaik.

TERIMA KASIH

JAMINAN

emua maklumat responden di dalam borang soal-selidik ini adalah sulit dan hanya ntuk tujuan penyelidikan sahaja. Kepercayaan anda kepada kami adalah sangat di rgai.

Appendix 4

Appendix 4: Elderly Cognitive Assessment Questionnaire

One mark is given for each correct answer.

Memory

1) I want you to remember these numbers: 4, 5, 1 and 7. Please repeat them. I will ask for them in 10 minutes.

2) How old are you (in years)?

3) What is your birth date? Which year were you born in?

Orientation

4) What day is it today?

5) What is the date today?

6) What is the month?

7) What is the year?

8) What is the name of this place (i.e. hospital, house, shelter home)?

9) What is your occupation?

Recall

10) Are you able to tell me the numbers I had asked you to remember earlier?

0-4 Probable cognitive impairment
5-6 Borderline
7-10 No cognitive impairment

Appendix 5

Appendix 5: Modified Barthel's Index

	0	1	2	3
Feeding	Dependent	Needs help	Independent	
Bathing	Dependent	Independent		
Grooming	Needs Help	Independent		
Dressing	Dependent	Can do half	Independent	
Bowels	Incontinent	Occasional accidents ≤ 1/week	Continent	
Bladder	Incontinent	Occasional accidents ≤ 1/week	Continent	
Toileting	Dependent	Needs some help	Independent	
Transfers	Unable	Major help (can sit)	Minor help	Independent
Mobility	Unable	Wheelchair independent	Walks with one person	Independent
Stairs	Unable	Needs help	Independent	
Total Score	/max 20			

0-4 Very severe disability
5-9 Severe disability
10-14 Moderate disability
15-19 Mild disability
20 Independent

Appendix 6

Appendix 6: The 12 Question Geriatric Depression Scale For People In Residential Care Facilities (GDS 12R)

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

1. Are you basically satisfied with your life? YES / NO
2. Have you dropped many of your activities and interests? YES / NO
3. Do you feel that your life is empty? YES / NO
4. Do you often get bored? YES / NO
5. Are you in good spirits most of the time? YES / NO
6. Are you afraid that something bad is going to happen to you? YES / NO
7. Do you feel happy most of the time? YES / NO
8. Do you often feel helpless? YES / NO
9. Do you think it is wonderful to be alive now? YES / NO
10. Do you feel pretty worthless the way you are now? YES / NO
11. Do you feel full of energy? YES / NO
12. Do you feel that your situation is hopeless? YES / NO

One point to underlined answers. Score ≥5 at-risk of depression.

Appendix 7

Royal Adelaide Hospital
MMSE

Subject Identification:

Subject number: __ __ __ __

Mini-Mental State Examination

Date of examination: __ __ / __ __ / __ __ __ __
d d m m y y y y

	Maximum Score	Score
ORIENTATION		
What is the <year> <season> <date> <day> <month>?	5	( )
Where are we: <state> <country> <town> <hospital> <floor>?	5	( )
REGISTRATION		
Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until the patient learns all 3. Count trials and record. Number of trials: _____	3	( )
ATTENTION AND CALCULATION		
Serial 7's. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.	5	( )
RECALL		
Ask for the 3 objects repeated above. Give 1 point for each correct.....	3	( )
LANGUAGE		
Name a pencil, and watch (2 points).....	2	( )
Repeat the following, "No ifs, ands or buts" (1 point)	1	( )
Follow a 3-stage command: "take a paper in your right hand, fold it in half, and put it on the floor." (3 points).....	3	( )
Read and obey the following: CLOSE YOUR EYES (1 point)	1	( )
Write a sentence (1 point)	1	( )
Copy design (1 point)	1	( )
ASSESS level of consciousness along a continuum:		
Alert Drowsy Stupor Coma		
Total	30	( )

Appendix 8

Royal Adelaide Hospital

Circle the best answer on the same line for how you felt this past week ...	Yes	No
1. Are you basically satisfied with your life?	0	1
2. Have you dropped many of your activities and interests?	1	0
3. Do you feel that your life is empty?	1	0
4. Do you often get bored?	1	0
5. Are you hopeful about the future?	0	1
6. Are you bothered by thoughts you cannot get out of your head?	1	0
7. Are you in good spirits most of the time?	0	1
8. Are you afraid that something bad will happen to you?	1	0
9. Do you feel happy most of the time?	0	1
10. Do you often feel helpless?	1	0
11. Do you often get restless and fidgety?	1	0
12. Do you prefer to stay at home, rather than going out and doing new things?	1	0
13. Do you frequently worry about the future?	1	0
14. Do you feel you have more problems with memory than most?	1	0
15. Do you think it's wonderful to be alive now?	0	1
16. Do you often feel downhearted and blue?	1	0
17. Do you feel pretty worthless the way you are now?	1	0
18. Do you worry a lot about the past?	1	0
19. Do you find life very exciting?	0	1
20. Is it hard for you to get started on things?	1	0
21. Do you feel full of energy?	0	1
22. Do you feel that your situation is hopeless?	1	0
23. Do you think that most people are better off than you are?	1	0
24. Do you frequently get upset over things?	1	0
25. Do you frequently feel like crying?	1	0
26. Do you have trouble concentrating?	1	0
27. Do you enjoy getting up in the morning?	0	1
28. Do you prefer to avoid social gatherings?	1	0
29. Is it easy for you to make decisions?	0	1
30. Is your mind as clear as it used to be?	0	1

Yesavage, J.A. "Geriatric Depression Scale". Reprinted with permission from the Psychopharmacology Bulletin 1988; 24(4):709-710.

Appendix 9

Royal Adelaide Hospital

SF–36© health survey

Instructions : This questionnaire asks for your views about your health, how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

In general, would you say your health is : excellent ☐ *(Check one box)*
very good ☐
good ☐
fair ☐
poor ☐

Compared to one year ago, how would you rate your health in general now?

much better now than one year ago ☐ *(Check one box)*
somewhat better now than one year ago ☐
about the same as one year ago ☐
somewhat worse now than one year ago ☐
much worse now than one year ago ☐

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(Check one box on each line)

Activities	yes, limited a lot	yes, limited a little	no, not limited at all
• Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
• Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
• Lifting or carrying groceries	☐	☐	☐
• Climbing several flights of stairs	☐	☐	☐
• Climbing one flight of stairs	☐	☐	☐
• Bending, kneeling, or stooping	☐	☐	☐
• Walking more than one kilometre	☐	☐	☐
• Walking half a kilometre	☐	☐	☐
• Walking 100 metres	☐	☐	☐
• Bathing or dressing yourself	☐	☐	☐

SF–36 health survey© (continued)

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down on the amount of time you spent on work or other activities	yes ☐ no ☐
Accomplished less than you would like	yes ☐ no ☐
Were limited in the kind of work or other activities	yes ☐ no ☐
Had difficulty performing the work or other activities (for example, it took extra effort)	yes ☐ no ☐

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down on the amount of time you spent on work or other activities	yes ☐ no ☐
Accomplished less than you would like	yes ☐ no ☐
Didn't do work or other activities as carefully as usual	yes ☐ no ☐

During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

not at all ☐ *(Check one box)*
slightly ☐
moderately ☐
quite a bit ☐
extremely ☐

SF–36 health survey© (continued)

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

How much bodily pain have you had during the past 4 weeks ?

no bodily pain ☐ *(Check one box)*
very mild ☐
mild ☐
moderate ☐
severe ☐
very severe ☐

During the past 4 weeks , how much did pain interfere with your normal work (including both work outside the home and housework)?

not at all ☐ *(Check one box)*
a little bit ☐
moderately ☐
quite a bit ☐
extremely ☐

These questions are about how you feel and how things have been with you during the past 4 weeks . For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks –

(Check one box on each line)

	all of the time	most of the time	a good bit of the time	some of the time	a little of the time	none of the time
• Did you feel full of life?	☐	☐	☐	☐	☐	☐
• Have you been a very nervous person?	☐	☐	☐	☐	☐	☐
• Have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐	☐
• Have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
• Did you have a lot of energy?	☐	☐	☐	☐	☐	☐
• Have you felt down?	☐	☐	☐	☐	☐	☐
• Did you feel worn out?	☐	☐	☐	☐	☐	☐
• Have you been a happy person?	☐	☐	☐	☐	☐	☐
• Did you feel tired?	☐	☐	☐	☐	☐	☐

SF–36 health survey© (continued)

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

all of the time ☐	*(Check one box)*
most of the time ☐	
some of the time ☐	
a little of the time ☐	
none of the time ☐	

How TRUE or FALSE is each of the following statements for you?
(Check one box on each line)

	definitely true	mostly true	don't know	mostly false	definitely false
• I seem to get sick a little easier than other people	☐	☐	☐	☐	☐
• I am as healthy as anybody I know	☐	☐	☐	☐	☐
• I expect my health to get worse	☐	☐	☐	☐	☐
• My health is excellent	☐	☐	☐	☐	☐