The nutritional status of long-term Home Enteral Nutrition (HEN) patients of Te Whatu Ora Counties Manukau: A focus on energy, macronutrients, vitamin D, and selenium

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Abstract

Background: Good nutritional status is important for well-being and reduced morbidity and mortality risk and pressure on healthcare systems. Despite being under the care of dietitians, home enteral nutrition (HEN) patients may be at risk of malnutrition and macro- and micronutrient deficiencies. It is important to understand the nutritional status of these patients to recommend appropriate feeding and nutrient monitoring practices.

Aim: To investigate the nutritional status (energy, macronutrients, vitamin D, selenium) of long-term home enteral nutrition (HEN) patients in Counties Manukau, New Zealand to determine the prevalence of malnutrition.

Methods: Data were collected from 42 long-term (≥4 weeks) HEN patients (18+ years) under the care of Te Whatu Ora Counties Manukau. Enteral and oral intake were collected through 5 x 24-hour recalls and compared against patients' prescriptions and estimated requirements (energy, macronutrients, vitamin D, selenium). Clinical signs of deficiency were assessed with a physical assessment (n=40), and nutritional biomarkers from a blood sample (n=22). Body composition was measured with bioelectrical impedance analysis (BIA) (n=29). Malnutrition prevalence was determined by the Global Initiative on Malnutrition (GLIM) criteria. Data were described by mean ± SD, geometric mean (95% confidence intervals), median (interquartile range), and frequencies. Independent t-tests, Mann-Whitney, and Chi-square tests were used to compare data by feeding route and prescription adherence.

Results: Malnutrition prevalence was 62.5% (n=25). Prevalence of low BMI and fat free mass index (FFMI) was 47.5% and 44.8% respectively. Mean body mass index (BMI) (21.1 ± 3.6 kg/m^2) was low but normal. Fat and/or muscle wasting occurred in at least 35%. Energy and/or protein intake was inadequate in 20% (n=8). Mean plasma vitamin D (143.55 ± 55.35 nmol/L) and selenium (1.37 ± 0.19 µmol/L) were within range with no evidence of deficiency, serum/plasma concentrations were high in 40% and 38.1% respectively. Mean vitamin D intake (13.2 ± 5.3 µg) was low in 26.2% (n=11) but met requirements for all age groups except ≥70 years. Mean selenium intake (95.0 ± 28.1 µg) was low in 7.1% (n=3) but met requirements for all. There were significant differences in nutritional status measures by feeding route and/or prescription adherence.

Conclusions: Many HEN patients had poor energy and protein status but maintained good vitamin D and selenium status. Adjustments to feeding practices regarding energy and protein, and more frequent monitoring of malnutrition may be beneficial for prevention of morbidity and mortality.

Key words: Malnutrition; oral; prescription; feeding route.

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Abbreviations

AMDR	Acceptable macronutrient distribution range
ASPEN	American Society for Parenteral and Enteral Nutrition
BCM	Body cell mass
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CRP	C-reactive protein
D_3	Cholecalciferol
DNA	Deoxyribonucleic acid
EAR	Estimated average requirement
ESPEN	European Society for Parenteral and Enteral Nutrition
FFMI	Fat free mass index
FFM	Fat free mass
FM	Fat mass
GLIM	Global Leadership Initiative on Malnutrition
HEN	Home enteral nutrition
MAMC	Mid arm muscle circumference
NG	Nasogastric
NJ	Nasojejunal
PEG	Percutaneous endoscopic gastrostomy
PEG-J	Percutaneous endoscopic gastrostomy with jejunal extension
PEJ	Percutaneous endoscopic jejunostomy
PG-SGA	Patient genterated subjective global assessment
RIG	Radiologically inserted gastrostomy
SGA	Subjective Global Assessment
SMM	Skeletal muscle mass
SOP	Standard operating procedure
UVB	Ultraviolet B
WC	Waist circumference
25(OH)D	25-hydroxyvitamin D

1. Chapter 1: Introduction

1.1 Background

Proper nutrition is essential for wellbeing and quality of life and contributes to prevention of morbidity and mortality risk and reduced burden on healthcare systems (Correia and Waitzberg, 2003). Ability to obtain adequate nutrition orally can be affected by dysphagia, increased nutritional requirements, and malabsorption or maldigestion due to the presence of malignant, neurological, or genetic conditions (Bischoff et al., 2020). These patients are at risk of malnutrition and can require home enteral nutrition (HEN) to meet requirements and maintain adequate nutritional status (Saunders and Smith, 2010, Bischoff et al., 2020). There are many patients requiring nutritional support as the prevalence of HEN in Australia and New Zealand is approximately 234 per million population (Flood et al., 2021).

Long-term HEN is the delivery of nutrients into the gastrointestinal tract via a gastrostomy or jejunostomy tube in an outpatient setting for patients who are medically stable and have a functioning gastrointestinal system (Martin and Gardner, 2017). This is used exclusively by some patients whereas some may have supplementary oral intake depending on their swallow function (Gramlich et al., 2018). Nutrition is typically delivered in the form of enteral formulas which are manufactured to be a complete nutrition source but can also be in the form of blended food (Bischoff et al., 2020). Dietitians prescribe HEN based on the patient's estimated energy and protein requirements which then determines the volume of feed, and therefore micronutrient provision.

Dietary energy is essential for all biological functions, and energy and protein both have important roles in body and muscle mass preservation. Protein has other essential roles in immunity, hormones, and blood production (Wu, 2016). Malnutrition is a consequence of poor energy and protein status which can negatively affect muscle, cardio-respiratory, gastrointestinal, and immune function and contributes to pressure on the healthcare system and rates of morbidity and mortality (Saunders and Smith, 2010). Measures of low body and muscle mass have previously been used to identify malnutrition prevalence of 42.1% (McWhirter et al., 1994) and 43.3% (Zeng et al., 2017) in HEN patients. These measures are components of the Global Leadership Initiative in Malnutrition (GLIM) criteria, which is a recent criterion for malnutrition identification (Cederholm et al., 2019). Measures of body composition, visceral protein concentration, and dietary intake have further identified poor energy and protein status in HEN patients (Okada et al., 2001, Kaw and Sekas, 1994, Klose et al., 2003, McWhirter et al., 1994). Nutrition focused physical assessment of muscle and fat stores are a useful indicator of energy and protein status that has seldom been used in previous literature reporting the nutritional status of HEN patients (Fischer et al., 2015, Detsky et al., 1987,

Bharadwaj et al., 2016). Poor energy and protein status is typically the result of inadequate intake but can also be disease related due to immobility or cachexia (Rommersbach et al., 2020, Gaafer and Zimmers, 2021). Contrastingly, these measures have also identified adequate energy and protein status in HEN patients (Gao et al., 2021, Obara et al., 2010).

Vitamin D is a micronutrient essential for musculoskeletal function and immunity. Osteomalacia and therefore, weakened muscles and increased falls and fracture risk, is a consequence of vitamin D deficiency due to improper bone mineralisation (Nowson et al., 2012). Home enteral nutrition patients are at risk of vitamin D deficiency due to limited sunlight exposure, suboptimal dietary intake, and diseases or medications influencing vitamin D metabolism (Pittas et al., 2010). Serum 25-hydroxy vitamin D (25[OH]D) concentration has identified deficiency in HEN patients in previous research (Osland et al., 2022). However, vitamin D content of formulas and sunlight exposure may differ to that in New Zealand.

Selenium is a trace element that has significant roles in antioxidant systems, the production of thyroid hormone T4, and immune function (Rayman, 2000). Cardiac dysfunction, poor wound healing, and altered immune function are potential consequences of deficiency (Rayman, 2000). Poor selenium status has been identified in HEN patients through the measure of plasma selenium concentration (Fischer et al., 1990, Kang et al., 2014, Saito et al., 1998). Suboptimal selenium intake put these patients at risk of deficiency, as enteral formulas with low or no selenium content were previously used. Risk of deficiency may differ in New Zealand because the formulas available have higher selenium content (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022).

Home enteral nutrition patients are at risk of compromised nutritional status for a variety of reasons. Nutrient deficiencies occur in long-term enterally fed patients despite being fed their estimated requirements (Baker et al., 2017). This suggests that the bioavailability, digestion, and absorption of nutrients from enteral formula may be different to that of whole foods or that their requirements are underestimated. The malignant and neurological conditions experienced by HEN patients may also cause their requirements to be higher than estimated due to a highly catabolic state or involuntary movements, leading to suboptimal prescriptions and intake (Henderson et al., 1992, McWhirter et al., 1994). Suboptimal intake may also be the result of poor prescription adherence. A systematic review by Gea Cabrera et al. (2019) reported that patient beliefs, administration ability, forgetfulness and carelessness, and gastrointestinal symptoms, may limit prescription adherence. It was also reported that good adherence occurs when patients are closely monitored and view their HEN as treatment rather than food. Patients who are nutritionally stable will be less closely monitored and may fluctuate their intake daily as does the general population, resulting in low prescription

adherence overall. Low volume of feed due to poor prescription adherence, concentrated formulas, or low energy requirements may result in inadequate micronutrient provision in these patients. It has also been suggested that HEN has limited ability to improve energy and protein status and evidence of poor nutritional status may be because it is preexisting (McWhirter et al., 1994).

Te Whatu Ora Counties Manukau is the organisation responsible for the public health service in South Auckland, New Zealand (Te Whatu Ora Counties Manukau, 2024). This organisation serves approximately 11% of New Zealand's population. The population of the Counties Manukau region is ethnically diverse; it has the largest Pacific population, and second largest Māori population in New Zealand. Socioeconomic deprivation is high in the Counties Manukau region which may negatively impact health outcomes of these patients (Lees et al., 2021).

1.2 Purpose of study

Compromised nutritional status has been identified as a potential issue in HEN patients. However, the nutritional status of HEN patients in New Zealand is not well understood because this topic has not been extensively studied, contradictory findings have been reported, and currently no New Zealand specific research exists. It is important to study the nutritional status of HEN patients in the New Zealand context due to differences in the enteral formulas available, cultural practices, and environmental influences.

It is not known if these patients' feeding regimes are adequate to supply their energy, protein, vitamin D, and selenium requirements and prevent malnutrition and micronutrient deficiencies. This thesis focuses on understanding the current nutritional status of HEN patients in the New Zealand context to inform appropriate feeding regimes and nutrient monitoring practices to ensure their wellbeing and quality of life, as well as reducing risk of morbidity and mortality and pressure on healthcare systems.

1.3 Aims and objectives

Aim:

To investigate the nutritional status (energy, macronutrients, vitamin D, selenium) of long-term home enteral nutrition (HEN) patients in Counties Manukau, New Zealand to determine the prevalence of malnutrition.

Objectives:

1. To investigate the adequacy of nutritional intake (energy, macronutrients, vitamin D, selenium).

2. To determine the impact of feeding practices on the nutritional status (energy, macronutrients, vitamin D, selenium) by comparing nutritional markers (body composition, physical assessment, and biomarkers) between groups:
    - Feeding regime (exclusive HEN vs supplementary oral),
    - Prescription adherence
3. To determine the prevalence of malnutrition and nutritional deficiency (energy, macronutrients, vitamin D, selenium) by investigating:
    - Body composition (BMI, FM, FFM, MAMC, WC)
    - Physical assessments (clinical signs)
    - Dietary intake, and
    - Nutritional biomarkers (visceral proteins, inflammatory markers, 25(OH)D, selenium)

1.4 Structure of thesis

This thesis is divided into four chapters. *Chapter one* introduces the study and outlines the purpose, scope, and justification of the research regarding the energy, protein, vitamin D, and selenium status of long-term HEN patients in New Zealand. The study aims and objectives, and researcher contributions are also outlined in this chapter. *Chapter two* provides a review of the current literature regarding HEN prevalence and indications, feeding practices, malnutrition, nutrient functions and requirements, nutritional assessment methods, and the nutritional status of HEN patients. *Chapter three* provides the research manuscript including a full description of the methods, results, and discussion. *Chapter four* presents the study conclusions, contributions to the literature, and strengths and limitations, as well as recommendations to the home enteral nutrition service and for future research. *Appendices* include supplementary methods relating to the participant information sheet and the standard operating procedures (SOP's) for the 24-hour recall, FoodWorks 10 analysis, bioelectrical impedance analysis, and the nutrition focused physical examination.

1.5 Researcher contributions

Table 1. Researcher contributions

Researcher	Contribution
Emma Soljan Master of Science Nutrition and Dietetics student	Review of literature; data collection of nutritional intake; statistical analysis and interpretation; preparation of the final manuscript; primary author of thesis.
Professor Rozanne Kruger Main academic supervisor	Research design; ethics application; funding application; thesis write up guidance and review.
Andrew Xia (NZRD) Academic co-supervisor	Research design; ethics application; funding application; thesis write up guidance and review.

Marilize Richter Statistician	Assisted with statistical analysis; provided guidance on interpretation.
Sally Pattison Research fellow	Participant recruitment; data collection of biomarkers, body composition, nutrition focused physical assessment, and nutritional intake.
Marcos Mantovani Research fellow	Participant recruitment; data collection and processing of biomarkers, body composition, nutrition focused physical assessment, and nutritional intake.
Sophie Turner Research assistant	Participant recruitment; data collection and processing of biomarkers, body composition, nutrition focused physical assessment, and nutritional intake; FoodWorks software nutrient analysis.
Dr Owen Mugridge Laboratory supervisor	Advised on biomarker processing.
Dr Thomas Russell **George King (NZRN)** **Liam Perrell (NZRN)** **Yongsijia Wei (Research assistant, Massey University)** Phlebotomists	Assisted with biomarker collection.

2. Chapter 2: Review of Literature

2.1 Introduction to Home Enteral Nutrition

Home enteral nutrition (HEN) is the provision of nutrients and fluid into the gastrointestinal tract through a feeding tube in the outpatient setting (Gramlich et al., 2018). Patients who cannot meet their nutrition requirements orally, have a functioning gastrointestinal tract, and are clinically stable use HEN as a long-term, life sustaining nutrition therapy (Martin and Gardner, 2017). Home enteral nutrition may be established when disease prognosis and quality of life is expected to deteriorate, and the patient is at risk of malnutrition without nutrition support (Bischoff et al., 2020).

2.2 Home Enteral Nutrition Prevalence

Many people require HEN across the world, but prevalence is greatest in the United States of America (USA), which is triple that of Canada and the whole of Europe which have similar prevalence, and 15 times that of the United Kingdom at similar time points (table 2). Home enteral nutrition prevalence across Australia and New Zealand is estimated to be similar to that of Europe in 1998 (table 2). The prevalence of HEN in the USA has increased in recent years, almost tripling between 1992 and 2013.

Table 2. Home enteral nutrition prevalence worldwide

Country (year)	Prevalence per million population
United States of America (1992)	463
Europe – Germany, Spain, Italy, France, United Kingdom (1998)	163
Canada (2005)	150
United Kingdom (2010)	92
United States of America (2013)	1385
Australia and New Zealand (2021)	234

(Howard et al., 1995, Mundi et al., 2017, Hébuterne et al., 2003, Cawsey et al., 2010, Smith et al., 2011, Flood et al., 2021)

2.3 Underlying conditions and indications for home enteral nutrition

There are many medical conditions that lead to the requirement of HEN, the most common being neurological disorders, malignancy, and gastrointestinal disorders (table 3). While the HEN population is heterogeneous by underlying condition, a homogenous sample is preferred and dominant in literature because nutritional requirements and challenges can be disease specific. Dysphagia is the main indication for HEN in previous research alongside maldigestion and/or

malabsorption (table 3). These are consequences of the patient's underlying conditions; dysphagia due to neurological conditions or radiation treatment for cancer, and maldigestion and/or malabsorption due to malignant related intestinal resection or gastrointestinal conditions (Logemann, 2007, Blaauw, 2011). The nutritional status of patients using HEN for up to 240 months has been studied but HEN duration reported in these studies is typically less than 15 months (table 3). The minimum HEN duration previously studied was 1.2 months which aligns with what is considered long-term HEN (>6 weeks) (Bischoff et al., 2020). Few studies assessing the nutritional status of HEN patients have had large sample sizes, with most studies comprising of 30-70 HEN patients (table 3).

Table 3. Underlying conditions, indications for, and duration of HEN

Author (country/year)	Underlying condition (%)	Indication	HEN duration (months)	Total sample size (number of EN fed)
(Schneider and Hébuterne, 2015)Hébuterne et al. (Europe/1998)	Neurological disorders (44.4) Head and neck cancer (30.3) GI conditions (10.6) Geriatric disease (7.2) AIDS (0.7) Other (6.8)	Dysphagia Oral failure Malabsorption or maldigestion	-	1397(1397)
Cawsey et al. (Canada/2005)	Neurological disorders (31.5) Cancer (46.4) GI conditions (15) Other (7.2)	-	4.1-6.2	727(727)
Folwarski et al. (Poland/2018)	Neurological disorders (54.5) Cancer (33.9) GI conditions (2.5) Inherited diseases (1.5) Other (7.5)	Dysphagia Mechanical GI obstruction	11.8	4586(4586)
Paccagnella et al. (Italy/2005)	Neurovascular disorders (26.7) Neurodegenerative disorders (40.9) Head and neck cancer (11.5) Abdominal cancer (9.8) Congenital abnormalities (2.6) Head injury (1.5) Other (7)	-	6.5	655(655)
McWhirter et al. (Scotland/1994)	Neurological disorders (52.6) GI conditions (36.8) Cancer (5.3) Anorexia nervosa (5.3)	-	7.6	19(19)
Gao et al. (China/2021)	Intestinal failure (100)	-	3	166(166)
Borges et al. (Spain/2011)	Short bowel syndrome (100)	-	6-84	10(10)
Donohoe et al. (Ireland/2017)	Oesophagectomy (100)	-	1.6	149(149)
Loeser et al. (Germany/2003)	Cancer (54.2) Neurological disorders (41.9)	-	4	56(56)

Author (country/year)	Underlying condition (%)	Indication	HEN duration (months)	Total sample size (number of EN fed)
	Other (3.9)			
Loeser et al. (Germany/1998)	Neurological disorders (47.1) Cancer (41.4) Other (11.5)	-	4.4	210(210)
Kaw et al. (America/1994)	Neurological disorders (91) Cancer (7) Other (2)	-	10.7	46(46)
Obara et al. (Japan/2010)	Stroke (100)	Dysphagia	2.5	68(68)
Klose et al. (Germany/2003)	Neurological disorders (67) Cancer (33)	Dysphagia	12	60(60)
Henderson et al. (America/1992)	Neurological disorders (90) Other (10)	Dysphagia Non-specific refusal to swallow	24.9	40(40)
McNamara et al. (Ireland/2000)	Stroke (46) Neurological disorders (26) Head and neck cancer (24) Other (4)	Swallowing defect	-	50(50)
Okada et al. (Japan/2001)	Stroke (100)	-	6	85(27)
Lee et al. (America/1998)	Head and neck cancer (100)	-	1.2-1.9	88(36)
Crotty et al. (Australia/1998)	HIV/AIDS (100)	-	5.4	71(71)
Baker et al. (UK/2017)	Oesophagectomy (78) Total gastrectomy (22)	-	2.5	41(24)
Bowrey et al. (UK/2015)	Oesophagectomy (78) Total gastrectomy (22)	-	1.8-2.4	41(20)
Obara et al. (Japan/2008)	Stroke (100)	Dysphagia	31.2	40(40)
Yagi et al. (Japan/1995)	Gastrointestinal resection (100)	-	84-240	4(4)
Kang et al. (South Korea/2014)	CNS disorder (70.5) Respiratory failure (13.6) CVD (6.8) Other (9.1)	-	-	44(44)
Fischer et al. (America/1990)	Congenital abnormalities (80) Trauma (20)	-	59	10(10)
Johtatsu et al. (Japan/2007)	Crohn's disease (100)	-	-	31(31)
Feller et al. (America/1987)	Neurological disorders CVD Diabetes	-	Group 1: 15 Group 2: 12	75(47)
Saito et al. (Japan/1998)	Cerebral Palsy (42.9) Cognitive disorders (57.1)	-	58	25(14)
Badireddi et al. (America/2014)	Neuromuscular diseases (100)	-	-	57(32)
Wong et al. (China/2006)	Neuromuscular diseases (100)	-	-	122(8)
Kim et al. (Korea/2017)	Stroke (100)	-	-	51(18)
Zeng et al.	Oesophagectomy (100)	-	6	60(30)

Author (country/year)	Underlying condition (%)	Indication	HEN duration (months)	Total sample size (number of EN fed)
(China/2017)				
Wu et al. (China/2018)	Oesophagectomy (100)	-	3	142(67)

Abbreviations: CNS, central nervous system; CVD, cardiovascular disease.

2.4 Feeding practices

Home enteral nutrition feeding regimes encompass the enteral route, the administration technique, the formula prescribed and how patients adhere to this, whether patients use HEN exclusively or have supplementary oral intake, and the use of nutritional supplements additional to HEN formula.

2.4.1 Enteral routes

The enteral route can either be gastric or jejunal and the tube type is selected based on the patient's underlying condition, gastrointestinal access, and duration of HEN (Bischoff et al., 2020). Gastric feeding is the preferred route and uses a nasogastric (NG) tube for short term feeding (<6 weeks), or gastrotomies, percutaneous endoscopic (PEG) or radiologically inserted (RIG), for long term feeding. The jejunal route is used to feed below the stomach in cases of altered gastrointestinal function or anatomy and gastroparesis; this requires a nasojejunal (NJ) tube for short term or jejunostomies, PEG with a jejunal extension (PEG-J) or percutaneous endoscopic (PEJ), for long term feeding (Bischoff et al., 2020). Gastrostomies and jejunostomies are the predominant routes of feeding in studies that have assessed the nutritional status of HEN patients (table 4). Despite being considered a short-term feeding route, the use of NG and NJ tubes have been reported in the HEN population (table 4). Nasal tubes have been used when the patient is very elderly, or if they do not consent to an ostomy tube but require nutritional support (Henderson et al., 1992, Obara et al., 2010, Okada et al., 2001).

2.4.2 Administration techniques

The administration technique is decided upon between the clinician and patient with consideration of their activity, environment, individual abilities, and tolerance, as well as the type of tube and feed (Bischoff et al., 2020). Continuous feeding is the accurate, slow infusion of enteral formula through a pump over a set time period, which is the preferred technique for high-calorie feeds and jejunostomies (Bischoff et al., 2020). Bolus feeding is the total daily feed volume divided across four to six administrations using a syringe and is beneficial for those who are physically active (Bischoff et al., 2020). Some patients may combine different feed administration methods, for example bolus feeding during the day and continuous feeding overnight (Bischoff et al., 2020).

2.4.3 Formulas

Formulas for HEN are chosen by dietitians based on the patients' energy, protein, and fluid requirements with consideration of their underlying condition (Escuro and Hummell, 2016). Standard polymeric formulas are recommended for HEN unless there is justification for another feed (Bischoff et al., 2020). Nutritional challenges associated with their underlying condition may justify a specialised feed; increased caloric density for increased energy requirements, fibre-containing feed to reduce transit time for diarrhoea and bind fluid in stool for constipation, modified carbohydrate for diabetes, and elemental or semi-elemental for abnormal digestive or absorptive function (Malone, 2005, Bischoff et al., 2020, Limketkai et al., 2019). Commercial feeds are usually recommended over blended feeds due to instability and risk of microbial contamination of the latter (Bischoff et al., 2020). However, patients may choose to have a blended feed to have similar food intake to their families, more control and flexibility with ingredients used, and better feed tolerance (Hurt et al., 2015).

A variety of enteral formulas have been used in studies assessing the nutritional status of HEN patients (table 4). The formulas used by different studies are similar as they have largely been polymeric, but energy, protein, and micronutrient content may differ between brands. The products used in the current literature that are relevant to patients in New Zealand are Ensure, Ensure Plus, and Nutrison Energy Multifibre which all contain selenium and vitamin D in varying amounts (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022).

2.4.4 Prescription adherence

Low adherence to the enteral prescription has been identified as an issue in HEN patients as it may result in suboptimal intake (Gea Cabrera et al., 2019). Lower rates of adherence are observed in the community compared to hospital settings which is likely due to the looser monitoring and autonomy over their feeding and viewing their HEN as food rather than essential medical treatment (Gea Cabrera et al., 2019). Patients who have low nutrition risk are not monitored as closely as those who are high risk; this may result in daily fluctuations in intake and low prescription adherence, but intake may be adequate over time. Adherence is also affected by forgetfulness and carelessness and gastrointestinal symptoms which are commonly disease related rather than a marker of feed tolerance as perceived by patients (Gea Cabrera et al., 2019).

2.4.5 Exclusive HEN and supplemental oral nutrition

Home enteral nutrition formula via tube or mouth can be used exclusively, or patients can have supplementary oral intake (Bischoff et al., 2020). Exclusive HEN is the feeding of full nutritional requirements with enteral formula via mouth or tube or blended food through the tube (Limketkai et

al., 2019). Supplementary oral intake is the intake of food orally alongside patients' HEN which is often used to meet energy and protein requirements and for quality of life (Baker et al., 2017). The extent of the oral intake is based on the patient's swallow function and if they are weaning off HEN (Cawsey et al., 2010). The contribution of supplementary oral intake may influence nutritional status, as the variations in foods chosen will affect their energy and nutrient intake, compared to the set nutritional composition of prescribed formula used in exclusive HEN. Exclusive and supplementary feeding practices have both been previously studied but few have compared them (table 4).

2.5 Energy and nutrient functions and requirements

2.5.1 Energy

Dietary energy intake is essential to maintain energy homeostasis in the human body, and therefore, health and survival. Adequate energy intake is required to support daily energy expenditure which is comprised of the resting metabolic rate (the energy required to support basic physiological functions); the thermic effect of food (the energy required for digestion, absorption, and storage of nutrients); physical activity (the energy required for exercise and activities of daily living) (Ohkawara et al., 2012). This may vary significantly between individuals. Energy intake inequal to energy expenditure causes negative energy balance, which over time can result in malnutrition due to the breakdown of body stores for energy (Hill et al., 2013). Negative energy balance may occur in HEN patients due to poor prescription adherence or underestimation of their energy requirements (Baker et al., 2017, Gea Cabrera et al., 2019, Borges et al., 2011, Klose et al., 2003, Henderson et al., 1992, Okada et al., 2001)

Energy requirements of HEN patients are calculated using either quick calculations or predictive equations because the gold standard indirect calorimetry is not accessible in community-dwelling patients (Reeves and Capra, 2003). The quick calculation commonly accepted for HEN patients, including those with cancer, is 25-30 kcal/kg/day (Gramlich et al., 2018, Muscaritoli et al., 2021) but 20-25 kcal/kg/day may be used for non-ambulatory patients who have suffered a stroke, due to inactivity (Gong et al., 2021) and those with malabsorption and inflammation, as with cystic fibrosis, may need energy of up to 150% that of other HEN patients (Turck et al., 2016). Predictive equations are suggested to be the most appropriate calculation of energy requirements for HEN patients as they are more individualised than quick calculations (Reeves and Capra, 2003). The practical and validated Oxford equation (Henry, 2005) calculates basal metabolic rate based on age, sex, and weight which is then adjusted with a nomogram for activity and disease stress (Elia, 1995), and weight loss or gain factors may be added as appropriate. The nomogram considers the variation

Table 4. Home enteral nutrition feeding practices

Author (year/country)	EN route (n)	Exclusive or supplementary (n)	Feed formula (n)	Supplements (n)
McWhirter et al. (1994/Scotland)	NG (10) PEG (9)	Exclusive (9) Supplementary (10)	-	-
Gao et al. (2021/China)	NG (70), NI (62) PEG-J (11), jejunostomy (7)	-	Standard (113) Fibre rich (5 Protein rich (6) Energy dense (2) Diabetic (6) Oligopeptide (25) Blenderized (9)	-
Borges et al. (2011/Spain)	NG (3) Gastrostomy (3) Oral (4)	Supplementary	Iso-osmolar polymeric (7) Iso-osmolar oligomeric (3)	Supplemental HPN
Donohoe et al. (2017/Ireland)	Jejunostomy	Supplementary	-	-
Loeser et al. (2003/Germany)	PEG	Exclusive (28) Supplementary (28)	-	-
Loeser et al. (1998/Germany)	PEG	Exclusive Supplementary	-	-
Kaw et al. (1994/America)	PEG	Exclusive Supplementary	Ensure Osmolite	-
Obara et al. (2010/Japan)	NG	Exclusive	-	-
Klose et al. (2003/Germany)	PEG	Exclusive (42) Supplementary (18)	Fresubin Plus Tube Supportan Energan Plus Tube	-
Henderson et al. (1992/America)	NG (4) PEG (35) Jejunostomy (1)	Exclusive	Ensure (10), Ensure Plus (3) Osmolite (10), Osmolite HN (12) Enrich (5)	Multivitamin (6)
McNamara et al. (2000/Ireland)	NG (1) Gastrostomy (46) Jejunostomy (3)	Exclusive (36) Supplementary (14)	Standard	-
Okada et al. (2001/Japan)	NG	Exclusive	Half-digested	-
Lee et al. (1998/America)	Gastrostomy	Assume supplementary	-	-

Author (year/country)	EN route (n)	Exclusive or supplementary (n)	Feed formula (n)	Supplements (n)
Crotty et al. (1998/Australia)	PEG	Supplementary overnight	Isotonic	-
Baker et al. (2017/UK)	Jejunostomy	Supplementary overnight	Nutrison Energy Multifibre	-
Bowrey et al. (2015/UK)	Jejunostomy	Supplementary overnight	-	-
Obara et al. (2008/Japan)	NG	Exclusive	-	-
Yagi et al. (1995/Japan)	NJ (1) Jejunostomy (3)	Supplementary	Elemental	100 µg selenium as IV selenious acid 60 mg selenium as sodium selenite
Kang et al. (2014/South Korea)	NG (33) PEG (11)	Exclusive	6 various, unspecified	25 µg selenium, 4 mg iron, 1 mg copper, 5 mg zinc (6)
Fischer et al. (1990/America)	Gastrostomy	Assume exclusive	Osmolite HN pretreatment Treatment product with added selenium, taurine, and carnitine	-
Johtatsu et al. (2007/Japan)		Assume exclusive	Elental	100 µg selenium and 10 mg zinc as V-Acccel (8)
Feller et al. (1987/America)	NG (10) Gastrostomy (33) Jejunostomy (4)	Exclusive	Isocal (36) Compleat B (11)	Multivitamin
Saito et al. (1998/Japan)		Exclusive	Ensure (12) Isocal (1) Harmonic-M (1)	5 µg/kg selenium as sodium selenate
Badireddi et al. (2014/America)	Gastrostomy	Exclusive (24) Supplementary (8)	-	Multivitamin
Wong et al. (2006/China)	NG	Exclusive	-	-
Zeng et al. (2017/China)	Jejunostomy	Supplementary	Supportan	-
Wu et al. (2018/China)	Jejunostomy	Supplementary	-	-

Abbreviations: HPN, home parenteral nutrition; IV, intravenous; NG, nasogastric tube; NI, nasointestinal tube; NJ, nasojejunal tube; PEG, percutaneous endoscopic gastrostomy; PEG-J, percutaneous endoscopic gastrostomy with jejunal extension. Half-digested formula contained dextrin and casein. Supplementary is defined as use of HEN with additional oral intake. Supplements is additional nutrition beyond the HEN prescription such as pills or formula fortification.

in energy requirements between underlying conditions due to their effects on body composition, inflammation, ambulation, and involuntary movement (Elia, 1995).

Energy is obtained from the three macronutrients carbohydrate, fat, and protein. Enteral nutrition formulas contain a combination of the macronutrients that align with the acceptable macronutrient distribution ranges (AMDR); 45-65% energy from carbohydrate, 20-35% energy from fat, and 15-25% energy from protein (Ministry of Health and Australian National Health and Medical Research Council, 2023). This AMDR is important to support intake of micronutrients and allow for dietary protein to be used for protein synthesis rather than energy production (Ministry of Health and Australian National Health and Medical Research Council, 2023, Munro, 1978). The energy density and range of macronutrients in food can vary greatly compared to the consistency of commercial formulas which may have an effect on the nutritional status of those with supplementary oral intake or blended feeds. Dietitians often encourage these patients to choose high energy foods.

2.5.2 Protein

Dietary protein provides the nine essential amino acids to support biological processes and prevent malnutrition (Wu, 2016). Amino acids are required for synthesis of muscle proteins, hormones, immunoglobulins, transport proteins, and neurotransmitters (Wu, 2016). Protein deficiency may cause impaired immunity, reduced muscle mass and function, and reduced functional capacity, and therefore increased risk of morbidity and mortality (Wu, 2016, Marzetti et al., 2017). Sarcopenia, the progressive and generalised loss of skeletal muscle mass (SMM), can lead to frailty; this typically occurs due to age or immobility but may be prevented with protein intake adequate to support muscle protein synthesis (Cederholm et al., 2017).

The protein requirements of HEN patients are typically between 0.8-1.2 g/kg/day (Gramlich et al., 2018) but 1-1.5 g/kg/day may be required for patients with highly catabolic conditions such as cancer (Muscaritoli et al., 2021). Previous research considered adequate intake to be 1.25g/kg/day in oesophagectomy or gastrectomy patients (Baker et al., 2017) which aligns with the recommendation, and even higher in patients with short bowel syndrome (1.5-2 g/kg/day) to account for malabsorption (Borges et al., 2011).

Enteral nutrition formulas are a complete source of protein as they provide all the essential amino acids. A range of products with varying protein content are available to meet the patients protein, energy, and fluid requirements. The protein content per 100 mL of products used in current literature available to New Zealand patients is 3.7g for Ensure, 6.25 g for Ensure Plus, and 6 g for Nutrison Energy Multifibre (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022). Patients who have supplementary oral intake or used blended feeds are encouraged to choose high protein foods

such as meats, eggs, and dairy products, which are complete proteins, and soy, beans, legumes, and nuts, which are incomplete proteins (Wu, 2016).

2.5.3 Vitamin D

Vitamin D is a fat-soluble vitamin and the common name for cholecalciferol (D_3). This is a molecule made when ultraviolet B radiation (UVB) acts upon 7-dehydrocholesterol in the skin which is then metabolised to the circulating form, 25-hydroxyvitamin D (25[OH]D), by the liver and hydroxylated to the biologically active form, calcitriol, by the kidneys (Wimalawansa, 2019). Vitamin D is important for musculoskeletal function due to the role of calcitriol in maintaining calcium and phosphate homeostasis by promoting absorption from the gut. This is important because if inadequate calcium is absorbed, parathyroid hormone will act to promote bone resorption to maintain the blood calcium concentration (Wimalawansa, 2019). Vitamin D deficiency can therefore negatively affect bone mineralisation, resulting in rickets or osteomalacia, and therefore, increased risk of falling and fracture. Other poor health outcomes associated with vitamin D deficiency are cardiovascular and metabolic diseases, cancer, and respiratory diseases (Nowson et al., 2012).

Home enteral nutrition patients are at risk of vitamin D deficiency due to low sunlight exposure and skin synthesis, malabsorption, and inadequate dietary intake (Pittas et al., 2010). Sunlight exposure may be limited in those with neurological conditions, living in care facilities, and/or using continuous HEN, as the result of immobility (Kim et al., 2017, Wong et al., 2006, Pittas et al., 2010). Skin synthesis may be lower in elderly and those with dark skin. Malabsorption of fat, and therefore fat-soluble vitamins, and calcium, for its role in maintaining 25(OH)D concentrations, puts HEN patients at risk of vitamin D deficiency (Davies et al., 1997, Margulies et al., 2015). These challenges indicate that enteral intake of vitamin D is important for HEN patients.

The New Zealand adequate intake for vitamin D varies by age; 5 µg/d for 18-50 year olds, 10 µg/day for 51-70 year olds, and 15 µg/d for people aged >70 years (Australian National Health and Medical Research Council and Ministry of Health, 2005). Although the New Zealand requirement is based on low sunlight exposure, some research recommends that intake should be 15 µg/day for adults <70 years and 20 µg/day for people ≥70 years when sunlight exposure is minimal (Nowson et al., 2012). There is no specific New Zealand guideline for safe UVB exposure, but it is recommended to have morning or late afternoon sun exposure from September to April and midday sun exposure from May to August (Nowson et al., 2012).

Enteral feed formulas available in New Zealand vary in vitamin D content. The vitamin D content per 100 mL of feed is 1.05 µg for Ensure, 2.0 µg for Ensure Plus, and 1.5 µg for Nutrison Energy Multifibre (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022). Requirements are likely to be met

with these formulas because the volume of feed and energy required to do so for a 70-year-old is relatively low; 1,430 mL or 1,430 kcal of Ensure, 750 mL or 1,125 kcal of Ensure Plus, and 1,000 mL or 1,530 kcal of Nutrison Energy Multifibre. Patients who have oral intake or blended feeds may get vitamin D from liver, eggs, and fortified margarine and milk, but these foods only contain small quantities (Nowson et al., 2012). Vitamin D supplementation does not appear to be common in the HEN population as only one study reported patients taking a vitamin D containing multivitamin (table 2.3).

2.5.4 Selenium

Selenium is an essential trace element that is involved in enzymatic and antioxidant processes. The nutritional functions of selenium are carried out by a range of selenoproteins which are formed from the selenium containing amino acid, selenocysteine (Rayman, 2000). Functions of selenium include hydrogen peroxide removal, DNA synthesis, active thyroid hormone production and regulation, reproduction, and muscle function (Rayman, 2000). Hydrogen peroxide removal prevents oxidative damage, associated with atherosclerosis and cancer risk, and inflammation, affecting inflammatory disease states such as Crohn's disease (Rayman, 2000, Johtatsu et al., 2007). Selenium deficiency can cause cardiomyopathy, skeletal myopathy, macrocytosis of red blood cells, and abnormal thyroid function (Li et al., 1985, Lockitch, 1989).

Malabsorption is a major cause of selenium deficiency in HEN patients but there is no dietary guideline for higher intake (Johtatsu et al., 2007). Absorption of selenium occurs in the duodenum and upper jejunum; this is negatively impacted by inflammatory bowel disease and intestinal resections (Johtatsu et al., 2007, Yagi et al., 1996). The Australia and New Zealand estimated average requirement (EAR) of selenium to prevent deficiency is 60 µg/d for adult men and 50 µg/d for adult women. These guidelines have been developed based on glutathione peroxidase activity at different selenium supplementation levels in healthy individuals (Australian National Health and Medical Research Council and Ministry of Health, 2005).

Enteral nutrition formulas available vary in selenium content. Previous research used enteral formulas with low or no selenium content prior to fortification and supplementation recommendations (table 2.3), whereas the formulas currently available in New Zealand are selenium containing; Ensure has 8.0 µg/100 mL, Ensure Plus has 8.7 µg/100 mL, and Nutrison Energy Multifibre has 8.6 µg/100 mL (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022). Selenium requirements are therefore likely to be met as the volume and calories required to meet the male EAR is relatively low; 875 mL or 875 kcal of Ensure, 804 mL or 1,206 kcal of Ensure Plus, and 814 mL or 1,245 kcal of Nutrison Energy Multifibre (Abbott Nutrition, 2023a, Abbott Nutrition,

2023b, Nutricia, 2022). Patients who have oral intake or blended feeds may obtain selenium from fish, organ meats, cereals, grains, nuts, and dairy products. Animal sources are preferred over plant sources because New Zealand soil is selenium poor which results in selenium poor plant foods (Thomson, 2003). There is no current literature describing selenium intake from food sources in HEN patients.

Selenium supplementation is effective at correcting selenium deficiency and should be considered for the HEN population if indicated (Yagi et al., 1996, Fischer et al., 1990, Saito et al., 1998). Only one study reported routine supplementation with a multivitamin containing 25 µg of selenium (Kang et al., 2014). Sodium selenite was used for supplementation by Yagi et al. (1996) and Fischer et al. (1990) due to its high bioavailability and being the most widely researched. Saito et al. (1998) used sodium selenate which has chemical stability and relatively high bioavailability but has not been as widely researched.

2.6 Concerns surrounding home enteral nutrition.

Patients are prescribed HEN to maintain their nutritional status and prevent malnutrition (Bischoff et al., 2020). However, HEN can be a predictor of malnutrition (Finestone et al., 1995). The European Society of Parenteral and Enteral Nutrition (ESPEN) guideline (2017) defines malnutrition as "a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease". This definition aligns with the recent diagnosis criteria proposed by the Global Leadership Initiative on Malnutrition (2018) (GLIM) which involves a combination of phenotypic and etiological components; either weight loss, low BMI (<20 kg/m^2 for adults <70 years old or <22 kg/m^2 for adults ≥70 years), or reduced muscle mass measured using validated body composition measures and either inflammation, reduced food intake, or a condition that affects food assimilation and absorption (Cederholm et al., 2019). Food assimilation and absorption may be affected in patients on HEN due to nutrition bypassing parts of the digestive tract. Bypassing the mouth, and stomach with jejunostomies, may affect food digestion because of reduced involvement of the enzymes that digest macronutrients (amylase, proteases, and lipases) at these sites (Boland, 2016). Jejunostomies may also reduce absorptive capacity because nutrition bypasses absorption sites at the duodenum and parts of the jejunum (Grant, 2005, Rosser Jr et al., 1999).

Malnutrition diagnosis generally focuses on energy and protein, but malnutrition also encompasses micronutrient deficiencies. There is a relationship between energy and protein intakes, and micronutrient intakes in HEN; higher energy and protein intakes generally also improve micronutrient intakes because the volume of feed, and therefore micronutrient provision, is dependent on the

amount of energy prescribed (Gramlich et al., 2018). The amount of energy from various formulas required to meet the American recommended daily allowances (RDA) is 2,000 kcal of Ensure or 2,130 kcal of Ensure Plus (Henderson et al., 1992). Therefore, lower energy intake may result in inadequate micronutrient intake and a higher risk of developing subsequent malnutrition and micronutrient deficiencies. However, the nutritional status (energy, protein, vitamin D, selenium) of HEN patients is not yet fully understood. The nutritional status of these patients must be understood to ensure adequate feeding practices and identify presence of malnutrition and micronutrient deficiencies among HEN patients earlier.

2.7 Assessment of nutritional status

The nutritional status of HEN patients has previously been reported through varying measures of dietary intake, nutritional biomarker concentrations, anthropometry, and/or physical signs and symptoms of nutrient deficiency (table 5).

2.7.1 Dietary intake

Adequacy of intake can be assessed to make conclusions about nutritional status and efficacy of HEN (Bischoff et al., 2020). Weighed and estimated diet records and 24-hour diet recalls are all valid assessments of dietary intake that have been used in previous research (table 5). Diet records produce high accuracy due to the prospective nature but may influence or change food choice whereas a retrospective 24-hour diet recall has no influence on food choice (Rutishauser, 2005). Three to five non-consecutive 24-hour diet recalls are required to be representative of habitual intake and describe prevalence in a population (Rutishauser, 2005, Ma et al., 2009, Castell et al., 2015). Both two random, non-consecutive 24-hour diet recalls and 5-day estimated diet records described similar energy, protein, and carbohydrate intakes (De Keyzer et al., 2011). Diet recalls are a favourable measure because they can be performed over the phone and have less burden on the patient. However, 24-hour recalls may not be suitable for patients with poor memory as this may result in an inaccurate or incomplete recall and therefore, under or overestimation of intake (Rutishauser, 2005). Dietary analysis software can be used for nutrient analysis of oral and enteral intake (The New Zealand Institute for Plant and Food Research Ltd and Ministry of Health, 2022).

2.7.2 Biochemical markers

Macronutrients

Visceral protein concentration was traditionally thought to reflect nutritional protein status but should not be used as the sole indicator due to the concentration lowering effect of poor liver function and inflammation (Keller, 2019, Evans et al., 2021, White et al., 2012). However, visceral

proteins may be used to support and understand findings from physical assessment of muscle and fat stores, anthropometrical measures, and dietary intake (Bharadwaj et al., 2016, Fischer et al., 2015).

Albumin is a visceral protein that is typically considered a poor nutritional indicator due to low sensitivity to protein intake (Fletcher et al., 1987). However, relationships between albumin and fat free mass (FFM) have been reported in elderly in non-acutely ill states regardless of chronic inflammation (Sergi et al., 2006, Zhang et al., 2017). Therefore, albumin may be used as a nutritional biomarker in the HEN population, as has been done in previous research (table 5), because they are not acutely unwell. It may be a beneficial measure of long term nutritional status because of the mobilisation from a large body pool, low daily synthesis by the liver, and long half-life of 20 days. A concentration of <35g/L is commonly used to indicate poor energy and protein status (Zhang et al., 2017). A higher cut point of up to 43 g/L may be required for albumin to be a sensitive and specific nutritional marker in patients ≥65 years as albumin is negatively correlated with age (Obara et al., 2010, Schalk et al., 2005, Kuzuya et al., 2007).

Prealbumin, otherwise known as transthyretin, is a visceral protein that transports thyroxine and retinol to the liver and is thought to be a sensitive nutritional biomarker (Ingenbleek and Young, 1994, Beck and Rosenthal, 2002, Fletcher et al., 1987). Significant relationships between prealbumin and malnutrition, low weight, and weight loss have been reported (Unal et al., 2013, Sergi et al., 2006). However, concentration can be affceted by dehydration, overhydration, renal failure, and corticosteroid therapy (Keller, 2019, Hodgens and Sharman, 2022). Prealbumin has successfully been used as nutritional biomarker in non-intensive care patients without inflammation, patients with chronic inflammation, elderly patients, head- and neck cancer patients undergoing radiotherapy, and patients receiving nutritional support (Keller, 2019, Zhang et al., 2017, Sergi et al., 2006, Fletcher et al., 1987, Unal et al., 2013, Bischoff et al., 2020). A short half-life of approximately two days and a small body pool means prealbumin is reflective of acute nutritional changes. Prealbumin concentration of < 20mg/dL is considered an indicator of poor protein and energy status in HEN patients (Fletcher et al., 1987).

Transferrin is a visceral protein that has been used as a protein biomarker (Keller, 2019). The half-life of 10 days and small body pool suggest that transferrin is sensitive to nutritional changes but effectiveness may be limited by its role as an iron transport protein (Fletcher et al., 1987, Roza et al., 1984). Transferrin concentration increases with renal dysfunction and iron deficiency, and decreases with iron overload and inflammation (Keller, 2019). There is conflicting research about the use of transferrin as a nutritional biomarker; it cannot differentiate poor and adequate nutritional status (Sergi et al., 2006), it is useful at a population level but not at an individual level (Roza et al., 1984),

and it is useful in patients receiving nutritional support (Fletcher et al., 1987). A transferrin concentration of <200mg/dL is considered indicative of poor nutrition status (Fletcher et al., 1987).

Haemoglobin is an oxygen transport protein that may be a useful nutritional biomarker of protein status and assist in the precision of malnutrition grading (Gavran et al., 2019, Keller, 2019, Schreiber et al., 2016). Subjective global assessment scores and haemoglobin have a significant, strong, inverse relationship, with haemoglobin significantly lower in malnourished patients than well-nourished patients with cancer (Enkobahry et al., 2023). This finding suggests that haemoglobin may be an appropriate protein biomarker in HEN patients as cancer is a common underlying condition. However, Pavlović et al. (2020) rated haemoglobin as a poor to fair indicator of protein status for primary care patients. Presence of iron, folic acid, and vitamin B_{12} deficiency, and haematological disease should be considered before using haemoglobin to draw conclusions of malnutrition status (Gavran et al., 2019). Haemoglobin values of < 135 g/L in men and 120 g/L in women may indicate poor protein status (Zhang et al., 2017).

Ferritin is a blood protein with the role of iron storage; it does not have a role as a nutritional biomarker for protein (Worwood, 1990, Pavlović et al., 2020, Schreiber et al., 2016). Mean ferritin concentrations were in the optimal range regardless of nutrition status and did not significantly differ between malnourished, at-risk, and well-nourished groups (Pavlović et al., 2020). Schreiber et al. (2016) also reported no relationship between ferritin and nutritional status, meaning it is not a useful biomarker of protein status in HEN patients.

Total protein is a biomarker that measures total albumin and globulins and may have a role as a nutritional biomarker for protein. The relationship between total protein and Subjective Global Assessment (SGA) scores was weak but statistically significant in malnourished cancer patients (Enkobahry et al., 2023). Cancer is a common underlying condition in HEN patients so this finding suggests that total protein may be able to be used as a nutritional indicator in HEN patients. Care should be taken with interpreting low total protein because the current borderline value of <6 g/dL may underdiagnose malnutrition (Zhang et al., 2017).

C-reactive protein (CRP) is a positive acute phase protein and is used as an inflammatory marker (Evans et al., 2021). Assessment of CRP is used to guide conclusions on whether changes in visceral negative acute phase proteins are due to inflammation or changes in nutrition status. Negative acute phase proteins decrease as CRP increases in response to inflammation, so poor protein status may be indicated when negative acute phase proteins decrease with no change in CRP (Bharadwaj et al., 2016). Despite CRP being called an acute-phase protein, chronic inflammation is evident in the HEN population (Obara et al., 2010). Normal CRP is < 5 mg/L and an inflammatory response is considered

Table 5. Methods of measuring nutritional status

Author (year/country)	Nutrients assessed	Intake measures	Anthropometry measures	Biochemistry measures	Physical signs and symptoms
McWhirter et al. (1994/Scotland)	Energy Protein Selenium	Calculated from prescription	Weight, height, BMI TSF, MAMC	Albumin Selenium, red cell glutathione peroxidase Magnesium, zinc, copper Vitamin A and E	-
Gao et al. (2021/China)	Energy Protein	-	Weight FFM, PhA (BIA)	Albumin, prealbumin, retinol-binding protein, fibronectin, insulin-like growth factor Transferrin, haemoglobin Liver enzymes, bilirubin Electrolytes Urea nitrogen, creatinine	-
Borges et al. (2011/Spain)	Energy Protein	3-day food record Calculated from volume of HPN and HEN	Weight, height, BMI, %UWL FFM, FM (BIA)	Albumin, total protein Total lymphocyte count	-
Donohoe et al. (2017/Ireland)	Energy Protein	Calculated from prescription	Weight, height, BMI, ideal weight FFM, FM	-	-
Loeser et al. (2003/Germany)	Energy	Intake controlled by the study	Weight, height, BMI, %UWL	-	-
Loeser et al. (1998/Germany)	-	-	Weight, height, BMI	-	-
Kaw et al. (1994/America)	Energy	Calculated from prescription	Weight	Albumin Total cholesterol	-
Obara et al. (2010/Japan)	Energy Protein	5-day food record Calculated from feed delivered	Weight, height, BMI TSF, AC, MAMC	Albumin, pre-albumin CRP Total cholesterol Haemoglobin	-
Klose et al. (2003/Germany)	Energy Protein Vitamin D	-	Weight, height, BMI TBW, LBM, BCM, ECM, FM (BIA)	Albumin, total protein Vitamin D	-
Henderson et al. (1992/America)	Energy Protein, fat	Calculated from feed delivered	Weight, knee height/height, BMI TSF, AC, MAMC	Albumin, total protein, retinol-binding protein BUN Haemoglobin, haematocrit Total cholesterol Calcium, phosphorous	-
McNamara et al.	Energy	24-hr recall	Weight, height, BMI	-	-

Author (year/country)	Nutrients assessed	Intake measures	Anthropometry measures	Biochemistry measures	Physical signs and symptoms
(2000/Ireland)		Calculated from prescription	TSF, AC, MAMC		
Okada et al. (2001/Japan)	Energy Protein, fat	Calculated from feed delivered	Weight, height, BMI TSF, SSF, AC, MAMC	Albumin, total protein Creatinine, BUN Haemoglobin	-
Crotty et al. (1998/Australia)	-	-	Weight	Albumin	-
Baker et al. (2017/UK)	Energy Protein Selenium	3-day food record Calculated from feed delivered	Weight, height, BMI, % weight change TSF, AC, MAMC	-	Hand grip dynamometry
Bowrey et al. (2015/UK)	Energy Protein	-	Weight, height, BMI, % weight change TSF, AC, MAMC	-	Hand grip dynamometry
Obara et al. (2008/Japan)	Energy Protein, fat, carbohydrate Iron, copper, zinc	Calculated from feed delivered	Weight, height, BMI	Albumin, prealbumin, total protein CRP Total cholesterol Transferrin, haemoglobin, iron Copper, zinc Lymphocyte, white blood cell, red blood cell counts	-
Yagi et al. (1995/Japan)	Selenium	-	-	Selenium	Echocardiograms Heart palpitation Muscular pain and weakness Gait disturbance Shortness of breath Hair lightening White nail beds
Kang et al. (2014/South Korea)	Energy Protein, carbohydrate Selenium, iron, copper, zinc	Calculated from feed delivered	Weight, height, BMI	Albumin CRP Total cholesterol, HDL cholesterol, LDL cholesterol Selenium, copper, zinc Iron Calcium, phosphorous	-
Fischer et al. (1990/America)	Selenium Carnitine, taurine	Controlled by the study	-	Selenium Plasma carnitine, taurine Glutamyl transpeptidase, glutamate-oxalacetate transaminase, lactic dehydrogenase	-

Author (year/country)	Nutrients assessed	Intake measures	Anthropometry measures	Biochemistry measures	Physical signs and symptoms
				Urinary carnitine, taurine	
Johtatsu et al. (2007/Japan)	Selenium, copper, zinc	Calculated from feed delivered	-	Albumin Selenium, selenoprotein P, glutathione peroxidase activity Copper, zinc	-
Feller et al. (1987/America)	Selenium Carnitine	Calculated from feed delivered	% of ideal weight	Albumin Selenium, glutathione peroxidase Manganese, chromium, molybdenum Free carnitine, total carnitine Free choline, phosphatidyl choline Creatine	-
Saito et al. (1998/Japan)	Selenium	Calculated from feed delivered	Weight	Selenium Total cholesterol, triglyceride Total and free carnitine, creatine kinase Haemoglobin, iron, ferritin, corpuscular volume Glutamic-oxaloaxetic transaminase Vitamin E, B1 Thyroid stimulating hormone, triiodothyronine, free T3, thyroxine, free T4	Cardiac function (chest X-ray, ECG, UCG) White fingernail beds
Badireddi et al. (2014/America)	Energy Protein Vitamin D	Calculated from feed delivered	Weight, height, BMI	Albumin, pre-albumin Transferrin Phosphorous, PTH, total calcium, Vitamin D	-
Wong et al. (2006/China)	Vitamin D	-	-	Vitamin D	-
Kim et al. (2017/Korea)	Vitamin D	Intake controlled by the study	Weight, height, BMI BMD (DXA)	Albumin, total protein BUN Vitamin D	-
Wu et al. (2018/China)	-	-	Weight, height, BMI	Albumin Haemoglobin	Nutrition impact symptoms, muscle and fat wasting, functional capacity (PG-SGA)

Abbreviations: AC, mid-arm circumference; BCM, body cell mass; BIA, bioelectrical impedance analysis; BMD, bone mass density; BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; DXA, dual-energy x-ray absorptiometry; ECG, electrocardiogram; ECM, extra cellular mass; FFM, fat free mass; FM, fat mass; HDL, high density lipoprotein; HEN, home enteral nutrition; HPN, home parenteral nutrition; LBM, lean body mass; LDL, low protein lipoprotein; MAMC, mid-arm muscle circumference; PG-SGA, patient generated subjective global assessment; PhA, phase angle; PTH, parathyroid hormone; SSF, subscapular skinfold thickness; TBW, total body water; TSF, tricep skinfold thickness;; UCG, ultrasound cardiogram; UWL, unintentional weight loss.

severe when CRP is >100 mg/L (Canterbury Health Laboratories, 2023a, Evans et al., 2021).

Micronutrients

Vitamin D status of HEN patients has been primarily assessed by serum 25(OH)D concentration (table 5). This is the most appropriate measure due to its abundance in circulation and association with clinical outcomes (Herrmann et al., 2017). Serum 25(OH)D is reflective of long term vitamin D status from both dermal production and dietary intake due to its long half-life of 2-3 weeks (Herrmann et al., 2017). Optimal serum 25(OH)D concentration is 50-150 nmol/L in New Zealand with 25-50 nmol/L considered insufficient and <25 nmol/L deficient (Canterbury Health Laboratories, 2023c). Reference ranges used in current literature varies; 50-300 nmol/L was used by (Klose et al., 2003), this low cut point is the same as the New Zealand range, and a higher cut point was used by Badireddi et al. (2014) (75-250 nmol/L).

Selenium status has been assessed in HEN patients previously using serum, plasma, and whole blood analysis via atomic absorption spectrometry (table 5). Plasma and serum selenium reflect short term changes in selenium status (Thomson, 2003), and are most commonly used among studies assessing selenium status of HEN patients. Kang et al. (2014) used whole blood selenium as reflective of long-term selenium status (Thomson, 2003). Variability of selenium status by geographical region means a global reference range has not been set (Thomson, 2004). The reference range for plasma selenium in New Zealand (0.45-1.40 µmol/L) (Canterbury Health Laboratories, 2023b) is lower than what has been used in previous research; 1.08-1.58 µmol/L (Fischer et al., 1990), 1.22-2.03 µmol/L (Yagi et al., 1996), 0.8-2.0 µmol/L (McWhirter et al., 1994). Analysis has varied between studies with some using carbon flame atomic absorption (McWhirter et al., 1994) and some using flameless atomic absorption (Yagi et al., 1996, Fischer et al., 1990). Flame atomic absorption is appropriate for concentrations >1 µg/mL, whereas concentrations of <100 ng/mL require the sensitivity of flameless atomic absorption spectrometry (Zam et al., 2019). However, inductively coupled plasma mass spectrometry is used for sample analysis in New Zealand due to its multi-element capability (Canterbury Health Laboratories, 2023b, Wilschefski and Baxter, 2019).

2.7.3 Anthropometry

Body mass index (BMI) has commonly been used as a measure of nutritional status in HEN patients (table 5) and is currently used as a component of malnutrition screening and diagnosis (Cederholm et al., 2019). The relationship between energy balance and body fat, which is indirectly represented by BMI, means that BMI can be used to assess nutritional status. However, fluid retention can falsely increase BMI, limiting its use as a nutritional marker (Campillo et al., 2004). Various BMI cut points have been used to reflect different nutritional states; previous research in HEN patients typically

considered <20 kg/m^2 as undernourishment and <18 kg/m^2 as severe undernourishment (Baker et al., 2017, Obara et al., 2010, McWhirter et al., 1994), aligning with the GLIM criteria (Cederholm et al., 2019). The Malnutrition Screening Tool considers 18.5 kg/m^2 as underweight which aligns with the World Health Organisation cut points of 18.5-24.9 kg/m^2 for normal weight, 25-29.9 kg/m^2 for overweight, and 30 kg/m^2 for obese (Boléo-Tomé et al., 2012); a higher cut point of 22 kg/m^2 is used for elderly (dos Santos et al., 2013). Body mass index does not reflect the body composition changes associated with poor nutritional status so measures of muscle mass and hydration (BIA and physical assessment) should be combined to make conclusions (dos Santos et al., 2013).

Bioelectrical impedence analysis (BIA) is a portable, inexpensive, non-invasive method of measuring body composition (Kyle et al., 2004b) which are appropriate measures for assessment of the efficacy of HEN (Bischoff et al., 2020). Home enteral nutrition patients who have a BMI of 16-34 kg/m^2, normal tissue hydration, and absence of neuromuscular diseases are considered appropriate for BIA (Kyle et al., 2004b). Involuntary movements and altered resisitivity in patients with neurological conditions can reduce the ability of BIA to produce accurate measures (Kyle et al., 2004a). Table 5 illustrates that BIA has successfully produced measures of body composition in HEN patients with maligancy, neurodegenerative disease, and gastrointestinal conditions in previous research.

Fat free mass (FFM), fat mass (FM), SMM, body cell mass (BCM), and mid arm muscle circumference (MAMC) are reliable body composition measures of nutritional status that have been used in previous research (table 5) (Bharadwaj et al., 2016). Absolute measures have been used by prospective and retrospective studies as they report change over time, whereas comparison of indexes and percentiles against reference standards may be more appropriate for assessing nutritional status in a cross-sectional design (Kyle et al., 2003). Fat free mass index (FFMI) considers the variation that occurs with height and sex; poor nutritional status is indicated by a measure of <17 kg/m^2 in men and <15 kg/m^2 in women (Cederholm et al., 2019). Mid arm muscle circumference percentiles considers the variation that occurs with sex and age (Frisancho, 1981, Burr and Phillips, 1984); measures of MAMC <15th percentile indicate mild malnourishment and <5th percentile indicate moderate malnourishement (McWhirter et al., 1994).

2.7.4 Physical signs and symptoms

Nutrition focussed physical findings are a physical assessment of the patient to determine clinical signs of nutrient deficiency in an efficient, cost-effective way (Fischer et al., 2015, Hummell and Cummings, 2022).

Macronutrients

Physical assessment of body fat and muscle mass stores is indicative of adequacy of energy and protein intake and are used as part of malnutrition diagnostic tools (Detsky et al., 1987, White et al., 2012). Body mass stores should be assessed in the upper body as this area is easily accessible, less affected by oedema, and reflective of whole-body stores (Fischer et al., 2015). Fat stores are assessed at the triceps, mid-axillary line at the lower ribs, and under the eye, and muscle stores are assessed at the deltoids, temple, clavicle, scapula, interosseous, knee, calf, and quadricep muscles (Detsky et al., 1987, Prasad and Sinha, 2018). Assessment of oedema informs clinical judgement when assessing body fat and muscle mass stores because excess fluid can cause fluctuations that are unrelated to body mass (Fischer et al., 2015). The physical assessment should check for symmetry to rule out non-nutrition causes when making conclusions about nutritional status (Fischer et al., 2015). Loss of fat and muscle mass in each examination region are categorised as either normal, mild-moderate, or severe as per the SGA and ASPEN malnutrition tools (Prasad and Sinha, 2018, White et al., 2012). Categorisation requires clinical judgement, this may explain why the study by Wu et al. (2018) is the only study that used this method to draw conclusions about HEN patients' energy and protein status. However, good interrater agreement and reproducibility when assigning SGA scores, and a significant association between the SGA physical assessment and malnutrition suggests that this is a useful measure of nutritional status (Detsky et al., 1987, Bharadwaj et al., 2016). Physical assessment of muscle stores should be used in conjunction with measures of biochemical markers, dietary intake, and weight to draw conclusions (Fischer et al., 2015).

Micronutrients

Vitamin D status can be indicated by the assessment of the range of motion, swelling, and fluid accumulation in the arm, shoulder, wrist, fingers, leg, and ankle due to its functions in the musculoskeletal system. Swollen and painful joints, rickets, knock knees, and bowlegs are abnormal findings that may be indicative of vitamin D deficiency (Esper, 2015). These nutrition focussed physical findings have not been employed in the current literature on HEN patients (table 5), this may be because they are non-specific to vitamin D (Esper, 2015).

Selenium status can be indicated by assessment of nail bed whitening. Nail bed whitening is indicative of long-term selenium deficiency (DiBaise and Tarleton, 2019). This measure has seldom been used to report the nutritional status of HEN patients in current literature (table 5).

2.7.5 Nutritional status of home enteral nutrition patients

Mixed findings on the energy, protein, vitamin D, and selenium status of HEN patients have been reported in current literature on the nutritional status of HEN patients (table 6).

Macronutrient status of HEN patients

Current literature demonstrates mixed findings about the macronutrient status of patients using HEN. Some studies have found that these patients are at risk of macronutrient depletion and becoming malnourished (table 6). Retrospective and prospective studies have reported evidence of weight loss and reduction of BMI, fat mass, and fat free mass (Borges et al., 2011, Donohoe et al., 2017, Henderson et al., 1992, Kaw and Sekas, 1994). Furthermore, Henderson et al. (1992) and Kaw and Sekas (1994) agreed that the incidence and degree of weight loss were associated with longer duration of HEN. Observational studies concluded that malnutrition occurred in patients despite using HEN through evidence of low BMI and muscle mass (McWhirter et al., 1994, Okada et al., 2001, Obara et al., 2008). These studies demonstrated that HEN might not maintain body mass and prevent malnutrition. However, the findings of another prospective study by Klose et al. (2003) suggested that nutritional status is maintained by HEN, but not improved (table 6).

Biochemical measures were used alongside anthropometric measures to support conclusions that poor energy and protein status were evident in HEN patients (table 6). High incidence of hypoalbuminemia has been reported in HEN patients (Kaw and Sekas, 1994, Obara et al., 2008). However, high incidence of hypoalbuminemia as reported by Obara et al. (2008) may be explained by the similar incidence of increased CRP. No improvement in albumin was observed over 18 months by Kaw and Sekas (1994) whereas Klose et al. (2003) reported albumin entering normal ranges after nine months. Contrarily, serum proteins were reported to stay within normal range by Borges et al. (2011) and Henderson et al. (1992).

Energy and protein intake can be used to both provide evidence for and explain poor nutrition status but not all studies reported energy and protein intakes. Some patients using HEN reported inadequate energy and protein intake (Borges et al., 2011, Klose et al., 2003, Obara et al., 2008), which can explain the decreasing and low anthropometrical measures reported in these patients. Although energy and protein intakes were reported by Kaw and Sekas (1994), no comparison was made to requirements to draw conclusions about adequacy of intake. However, it can be assumed that their intake was inadequate due to decreased BMI and muscle mass (Kaw and Sekas, 1994). Interestingly, energy and protein intakes were considered adequate in two studies concluding that HEN patients had poor nutritional status(Henderson et al., 1992, Okada et al., 2001). Patients who had poor nutritional status despite being fed adequately had neurological conditions and were often bed-ridden so markers of poor nutritional status may be due to immobility and disease processes. However, Loser et al. (1998) concluded that HEN can improve nutritional status despite disease progression.

Table 6. Study design and outcomes of current literature on the nutritional status of HEN patients.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
McWhirter et al. (1994/Scotland) Observational	Assess the nutritional status of patients receiving HEN. Determine whether these patients are at risk of developing micronutrient deficiency.	N/A	19 (19)	- 10/19 adequately nourished. - BMI <20 and TSF >15th percentile in 8/19 o 2 participants with muscle wasting diseases classified as malnourished rather than disease related. - Plasma selenium <0.8umol/L and red cell glutathione peroxidase <13 units/gHb in 6/19. - Albumin <36g/L in 3/19. - Patients receiving HEN may be at risk of developing nutrient depletion regardless of diagnosis, duration, or method of feeding.	No dietary data.
Gao et al. (2021/China) Prospective observational	Determine the effect of HEN on nutritional status, body composition, phase angle, quality of life, and physiological function in malnourished patients with intestinal failure.	6 months	166 (166)	- BW, FM, FFM, and PhA significantly increased during HEN, especially within 3/12 post hospital discharge. - Albumin, prealbumin, retinol binding protein, transferrin, fibronectin, and IGF-1 were significantly higher at 1, 3, and 6 months on HEN vs prehospital. - HEN can improve and maintain the nutritional status of patients with intestinal failure.	Limited sample size Relative heterogeneity of disease types.
Borges et al. (2011/Spain) Longitudinal retrospective	Verify whether EN+OI in severe short bowel syndrome patients can maintain adequate nutritional status long term.	84 months	10 (10)	- %UWL significant and progressive, 20% BW loss by the end of the observation period. - FFM and FM decreased significantly (*P*<0.05). o FFM 54.81kg at 6/12 to 50.21kg at 24/12 o FM 15.51kg at 6/12 to 9.88kg at 24/24 - FFM and FM remained <50th percentile but did not reach 5% (serious alteration). - Albumin, total protein, and total lymphocyte count were within normal range; no significant changes. - Maximum energy intake:1007.7 ± 229.9kcal/d - Maximum protein intake: 43.33 ± 11.72g/d. - Sufficient energy uptake achieved at only 60- and 84-months post operation. - Sufficient protein uptake by 12/12 post-op.	Restrospective study design.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
				- Long term EN achieved minimally adequate energy recommendations at only two periods of the study. - HEN+OI was inadequate to maintain body composition and long-term nutritional wellbeing when being weaned of HPN.	
Donohoe et al. (2017/Ireland) Prospective cohort study	Analyse impact of supplemental HEN post-oesophageal cancer surgery on nutrition parameters.	6 months	149 (149)	- 58/149 lost >10% BW by 6/12. Median (IQR) 6.8 (4-9) kg. - 62/149 lost >10% BMI by 6/12. - 54/149 weight stable post operation. - BMI change (%) was 4.4 ± 3.9% in the first month and 1.2 ± 3.4% in the 3–6-month period. - 25/149 weight stable from diagnosis to 6/12 post operation. - 29/149 lost weight preoperatively but not postoperatively. - At 6/12, 23/149 were >5kg under IBW. - Relative LBM preservation (loss 6.1±7.04%) at 3-6 months but continued decline of FM (loss 14.76±30.3%). - FM loss significantly greater in those who lost >10% BMI. Mean change in FM was 30.6±16.24%. - Weight and BMI loss may be substantial despite HEN.	Short period of supplementation. No detailed dietary data.

Loeser et al. (2003/Germany)
 	
Prospective longitudinal
	Assess nutrition status in competent and non-competent HEN patients.	4 months	56 (56)	- 4/12 on HEN increased or stabilised BMI.
				- At 4/12, BMI was 20.9±3 kg/m^2 for competent and 21.2±3 kg/m^2 for non-competent.
				- Weight loss in 8 from each group.
				  o 1.5 kg/m^2 for competent patients,
				  o 1.1 kg/m^2 for non-competent patients.
				- Weight gain in 14 competent (1.5 kg/m^2) and 3 non-competent (0.4 kg/m^2).
				- Remaining weight stable.
				- HEN is beneficial at preventing further weight loss.
					-

Loeser et al. (1998/Germany) Prospective	Evaluate the individual outcome after PEG insertion.	24 months	210 (210)	- Weight loss 3/12 before HEN was 11.4±1.5 kg. - Weight gain at 12/12 was 3.5±1.7 kg. - BW between malignant or benign diseases not significant.	-

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
				- HEN is beneficial at stopping the catabolic process of ongoing weight loss and can increase BW despite disease progression and improve nutritional status.	
Kaw et al. (1994/America) Retrospective	Assess the nutritional and functional benefits of PEG tube placement.	18 months	46 (46)	- Incidence of weight loss increased with time spent on HEN. o At 1-6 months, 19% had decrease, 50% had increase31% stable. o At 13-18 months, 36% had decrease, 36% had increase, and 28% stable. - Hypoalbuminemia common with no significant improvement. - 1520-2290 kcal energy provided daily. - 53.6-80.4 g protein provided daily. - No significant improvements in nutritional status in nursing home patients after PEG placement.	-
Obara et al. (2010/Japan) Prospective	Clarify the improvement in nutritional status of very elderly patients who receive long-term complete tube feeding after stroke.	12 months	68 (68)	- BMI, AC, and TSF were significantly higher at 12/12 vs baseline. - BMI improved to normal range. o 17.6 kg/m^2 to 20.4 kg/m^2 in elderly o 17.0 kg/m^2 to 20.2 kg/m^2 in very elderly. - Albumin, prealbumin, total cholesterol, and haemoglobin were significantly higher at 12/12 vs baseline. o Raise significantly greater in elderly. o Did not improve to normal. o Albumin negatively correlated with age. - Mild inflammatory response in both groups. - Energy and protein intake at baseline and 12/12 not significantly different. o Intake at 12/12 was 1273±205 kcal and 63.6±10.3 g (elderly) and 1235±260 kcal and 61.8±13.0 g (very elderly). - Full HEN is effective for improving the nutritional status of elderly and very elderly stroke patients.	-
Klose et al. (2003/Germany)	Measure serum and plasma parameters and record nutritional status using BIA.	12 months	60 (60)	- BMI stabilised at low normal values. o 19.7 ± 1.0 kg/m^2 (baseline), 20.3 ± 1.1 kg/m^2 (12/12)	Inadequate dietary intake data from patients.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
Prospective				- ECM/BCM remained >1.0, indicating no improvement in BCM with HEN. o Favourable in patients with neurological diseases vs malignancy. - Albumin, protein, and vitamin D deficiency at the initial examination. - Biochemical markers returned to normal range within 1-9 months. o Protein 1/12, vitamin D 2/12, albumin 9/12. - 80% received <2000 kcal/d, (inadequate). o 1500 kcal (500-3200 kcal) was provided enterally. - HEN via the PEG can ensure adequate supply of vitamins and minerals. However, nutritional status concerning the BIA did not change and BMI partially improved.	
Henderson et al. (1992/America) Prospective	Prospectively follow the nutritional status of a subset of medically stable patients entirely dependent on EN. Investigate relationship between nutritional status indicators and adverse clinical outcomes.	3 months	40 (40)	- 31/33 were ≤50th age-appropriate BMI percentile, 13 were ≤5th percentile. - 35/38 were ≤50th percentile for LBM estimated from MAMC, 12 were ≤5th percentile. - 12/33 gained FM as they lost LBM. - 22.5% lost ≥5% of their baseline BW. o Continued weight loss was associated with longer dependence on HEN. - Serum proteins were within range and did not change. - Energy 1.6x the calculated BEE was provided. o 3/40 were prescribed <20kcal/kg. - Protein intake (1.4g/kgBW) was higher than RDA. - Average of 104% of the micronutrient RDA was provided. o 3/40 received <75% RDA. o 23/40 received ≥100% RDA. - Attempts at HEN may be undermined by effects of chronic disease, immobility, and neurological deficits.	Low generalizability due to the chronic disease hospital setting. Short period of observation.
McNamara et al. (2000/Ireland) Retrospective	Investigate patients and their caregivers' experiences of community EN.	N/A	50 (50)	- Low BMI in those >65 years. o 23.09kg/m^2 (men), 21.04kg/m^2 (women) - BMI <20.0kg/m^2 in 3 patients <65 years. - No patients with BMI <16.0kg/m^2.	Retrospective design (Underrepresentation of people with short survival time, reliance

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations

				- 10/13 gained weight.
				  o 4.4kg over 78/365 (cancer patients).
				  o 5kg over 119/365 (remainder).
				- 3/13 lost weight
				  o 6.8kg over 168/365 (cancer patients).
				  o 3.1kg over 71/365 (remainder).
				- 34/50 met energy EAR, 7/50 had <EAR.
				- 7/36 with exclusive HEN were on ≤1500mL of feed for over 12/12.
					on memory, problems associated with retrospectively reviewing medical records)
					Small sample of anthropometry collected due to difficulty measuring.
					Heterogeneity of the sample.

Okada et al. (2001/Japan)
 	
Cross-sectional
	Assess the nutritional status of elderly patients who received long-term EN.	N/A	27 (85)	- AC <80% of normal in 5/10 male and 6/17 female HEN. Significantly higher than free eating.
				- Albumin <35g/L in 7/10 male. Significantly higher than free eating.
				- Weight and BMI significantly higher in free eating.
				  o Weight 61.1±8.6 kg and BMI 24±4 kg/m^2 male free eating.
				  o Weight 48.8±9.0 kg and BMI 19±2 kg/m^2 male HEN.
				  o Weight 48.5±6.7 kg and BMI 23±3 kg/m^2 female free eating
				  o Weight 43.6±5.0 kg and BMI 20±3 kg/m^2 female HEN.
				- Total protein, albumin, RBC, haemoglobin, and creatinine not significantly different between groups.
				- Energy intake 1,171±286 kcal, protein intake 44.9±13.1g (optimal).
				- No significant differences in nutritional status between HEN patients receiving normal and excess requirements.
				- Bed-ridden patients can become malnourished despite being fed energy and protein calculated to be adequate with predicted values.
					-

Lee et al. (1998/America)
 	
Retrospective
	Evaluate effect of prophylactic gastrostomy tubes on the rates of weight loss, unplanned interruption, and hospitalization during high intensity head and neck radiotherapy.	N/A	36 (88)	- Patients with PGT lost significantly less weight.
				  o 3.1kg with PGT, 48% lost ≥5% pretreatment BW.
				  o 7.0kg without PGT, 71% lost ≥5% pretreatment BW.
				- Weight loss is significantly reduced by use of PGTs in head and neck cancer patients.
					Selection bias to place gastrostomy in patients with less favourable performance status.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
Crotty et al. (1998/Australia) Retrospective	Describe experience of prolonged EN via PEG in malnourished adults with HIV/AIDS.	N/A	71 (71)	- 51/71 gained weight (5.8 ± 4.4kg). o 17/71 gained <5% of their pre-gastrostomy BW. - Median time to maximum weight was 74/365. - 19 had increased albumin alongside increased weight. o 31.1g/L to 37.9g/L. - Weight gain is not attributed to ani-retroviral therapy. - HEN can reverse weight loss and maintain nutrition status in patients with HIV/AIDS.	-
Baker et al. (2017/UK) Prospective	Determine nutrient intake in first 6m following surgery, the contribution of dietary and supplementary jejunostomy feeding to meeting requirements, and the effect of supplementary jejunostomy feeding on nutritional status.	6 months	24 (41)	- Weight gain or maintenance in 12/16 HEN and 1/17 non-HEN. - Weight and grip strength preservation was significantly better in planned HEN patients. o At 6/12, loss of >10% BW occurred in 43% HEN and 76% non-HEN. - 13/25 who lost weight had energy intake > requirements. - Oral intake between HEN and non-HEN not significantly different. o Both failed to meet requirements orally. - Energy and protein intake significantly higher in HEN. o 100% HEN met requirements due to enteral contribution. - Selenium intake 33.5 µg /d at 3/12 and 48 µg/d 6/12 (inadequate). - EN post-operation significantly contributes to meeting nutritional requirements and reducing deterioration of body weight.	Use of estimation calculations for energy and protein. Didn't report NFPF
Bowrey et al. (2015/UK) Randomised control pilot and feasibility trial	Pilot an investigation of the impact of six weeks of home jejunostomy feeding in patients undergoing oesophagectomy or total gastrectomy for cancer. Assess the feasibility of conducting a subsequent appropriately powered multi-centre trial	6 months	26 (54)	- Weight loss was greater in the non-HEN group at 6/52. o 1.2% BW loss in non-HEN o 0.8% BW loss in HEN. - Weight differences remained at 3 and 6 months. - BMI difference between groups was 1.3kg/m^2 at 6/52. - HEN patients had greater AC, MAMC, TSF, and hand grip dynamometry. - Tube feeding resulted in better weight, muscle, and fat store preservation post oesophagectomy or gastrectomy.	-
Obara et al. (2008/Japan)	Determine nutritional indices that are predictors of serum trace elements in patients with	N/A	40 (40)	- 55% had low BMI, mean BMI was 19 kg/m^2. - 58% had low albumin, mean albumin 3.3 g/dL. - 53% had moderate or severe inflammation, mean CRP 1.9 mg/dL.	-

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
Cross-sectional	neurological dysphagia on long-term tube feeding.			- Mean energy intake was < requirements by 138kcal/d. - Elderly bedridden patients with neurological conditions on long term enteral nutrition develop malnutrition.	
Yagi et al. (1995/Japan) Case report	Describe 4 patients with postoperative malabsorption who developed selenium deficiency in the setting of long term EN.		4 (4)	- 100% had low plasma selenium (0.9-8.0 µg /d). - 100% had bilateral muscular pain and leg weakness/gait disturbance. - 1 complained of palpitations and shortness of breath. - Selenium supplementation (10-20d) improved selenium to normal range and symptoms resolved in 100%. - Long term EN with formula low in selenium increases risk of deficiency.	-
Kang et al. (2014/South Korea) Cross-sectional	Find the feature of trace element deficiencies such as iron, copper, zinc, and selenium in long-term tube fed patients.	N/A	44 (44)	- Those on HEN for 2-6 months had significantly lower albumin than on HEN for >6/12. - 9.1% were selenium deficient. o Most common >6/12 group (15.8%). - 2-6 month and >6/12 groups had significantly lower selenium than the 1–2-month group. - OR for selenium significantly decreased by increasing tube feeding period. - Energy intake (1,287±286 kcal) was < requirement (1,460±227 kcal). - Protein intake (52.5±11.9 g) was < requirement (58.4±9.1 g) - Selenium intake was 3.3±8.6 µg. - Selenium deficiency was observed in long term HEN patients and risk of deficiency may increase with time on HEN.	No baseline comparison due to study design. Small sample size.
Fischer et al. (1990/America) Prospective	Describe selenium status in an enterally fed population and investigate efficacy of selenium supplementation.	6 months	10 (10)	- Plasma selenium after 59/12 on HEN 0.26±0.08 µmol/L (low). - At 9/52 of selenium rich formula, mean plasma selenium increased significantly into normal range (1.08±0.39 µmol/L). o 40% were low. - At 24/52, selenium improved to 1.13±0.12 µmol/L. o 100% in range. - No related NFPF were observed. - Selenium fortified enteral formula is capable at improving blood selenium concentration in handicapped, gastrostomy fed patients.	-

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations

Johtatsu et al. (2007/Japan)
 	
Prospective
	Investigate the trace element status in Crohn's disease patients and evaluate the effects of trace element rich supplementation.	2 months	31 (31)	- Mean albumin 4.1±0.4 g/dL.
				  o Low in 9/31.
				- Mean selenium 11.2±2.8 µg /dL.
				  o Low in 12/31.
				- Selenium supplementation for 2/12 significantly improved selenium status.
				- No NFPF were observed.
				- Long term HEN may result in low selenium status.
					-

Feller et al. (1987/America)
 	
Cross-sectional
	Report data on circulating levels of trace elements and carnitine in chronically tube-fed patients.	N/A	47 (75)	- Serum selenium was significantly lower in HEN groups than free eating.
				  o Compleat B group (HEN) 60.82 ng/mL (low).
				  o Isocal group (HEN) 33.72 ng/mL (low).
				  o Free eating 110.70 ng/mL (normal).
				- Compleat B group energy intake (2014 kcal) was > Isocal group (1861 kcal).
				- Enteral formula should contain >100 µg selenium per 1600 kcal.
					-

Saito et al. (1998/Japan)
 	
Prospective
	Determine whether selenium deficiency is present in patients undergoing long-term tube feeding.
	
	Examine if selenium supplementation has beneficial effects on their cardiac function.
		3 months	14 (25)	- No significant difference in haemoglobin, cholesterol, and triglyceride between HEN and orally fed participants.
				- Serum selenium significantly lower in HEN.
				  o HEN 3.0±1.8 nmol/L
				  o Oral 13.7±2.2 nmol/L
				- Supplementation increased serum selenium in HEN (10.0±1.8 nmol/L).
				- 2 oral and 7 HEN had ECG abnormalities.
				  o Improved in 4 HEN post selenium supplementation.
				- 8 HEN had white fingernail beds.
				- No skeletal myopathy, RBC macrocytosis, or thyroid function abnormalities.
				- Mean selenium intake was 0.33 µg/kg/d in HEN.
				- Low selenium content in enteral formulas may result in clinical manifestations of selenium deficiency.
				- It is reasonable to supplement selenium in tube fed patients.
					Short follow-up period.
					Small sample size.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
Badireddi et al. (2014/America) Retrospective	Evaluate the vitamin D and nutrition status of patients seen for the first time in an outpatient clinic.	36 months	32 (57)	- 25(OH)D was significantly lower in mixed EN/oral and oral fed groups than exclusive HEN. o 14.7±3.9 ng/mL in mixed. o 22.6±13 ng/mL in oral o 32.4±18.8 ng/mL in exclusive (only in normal range) - Albumin, transferrin, and PTH were within range and did not differ significantly by feeding route. - Vitamin D intake (n=29) was 351±172 IU/d, higher in HEN, likely due to more precise quantification. - Vitamin D status is related to route of nutrition (exclusive HEN best). - Vitamin D supplementation and maintenance should be routine care of patients with neuromuscular diseases and chronic respiratory failure.	Oral intake not recorded. Heterogenous in age and condition. Absence of bone mass markers e.g., DEXA, due to retrospective study design.
Wong et al. (2006/China) Cross-sectional	Survey serum 25(OH)D of patients with learning disabilities residing in a hospital unit.	12 months	8 (122)	- 91.8% of had vitamin D deficiency. - Plasma vitamin D of HEN patients was >25 nmol/L (31.50 ± 12.31 nmol/L), significantly higher than participants with normal and soft diets.	-
Kim et al. (2017/Korea) Retrospective case-control	Investigate serum vitamin D level and its determinant factors in stroke patients.	N/A	14 (51)	- 25(OH)D not significantly different between oral and HEN. o 12.3±5.6 ng/mL oral (low). o 13.5±2.7 ng/mL HEN (low). - 25(OH)D was significantly lower in patients with history of TPN compared to HEN, indicating that nutritional content is a determining factor of vitamin D status. - Vitamin D supplementation should be considered for stroke patients.	Retrospective case control study design. Small sample size.
Zeng et al. (2017/China) Prospective	Characterise the effect of HEN on the nutritional status and QOL of patients who underwent oesophagectomy for cancer.	6 months	30 (60)	- 26.7% HEN, and 20% control patients were malnourished pre-operation. - At 12/52, 50% HEN, and 83.3% control patients were malnourished (significant). - At 24/52 the nutrition status of both groups improved. - At 24/52, incidence of malnutrition was lower in the HEN group (43.3%) than the control group (63.3%), not statistically significant.	Did not have strict randomisation and unable to be blinded. Short follow up period. Small sample size.

Author (year/country) Study design	Study aim	Duration of follow up	Number of HEN participants (total number of participants)	Main outcome	Limitations
				- HEN can reduce incidence of malnutrition in the early period post oesophagectomy.	
Wu et al. (2018/China) Prospective	Investigate the effect of 3 months HEN on nutritional status of oesophageal patients who were preoperatively malnourished.	N/A	67 (142)	- At 3/12, the PG-SGA score was < at baseline, demonstrating improved nutritional status. - At 3/12, the PG-SGA score was significantly lower in HEN. o 5.7 HEN. o 7.9 non-HEN - BMI significantly higher in HEN. o 22.1 kg/m^2 HEN (normal) o 20.1 kg/m^2 non-HEN (normal). - At 3/12, albumin, and haemoglobin were significantly higher in HEN. - PG-SGA, BMI, albumin, and haemoglobin were not significantly different between groups at the pre and post operative phases. - 3 months HEN supplementation can reduce the risk of malnutrition.	-

Abbreviations: AC, mid-arm circumference; BCM, body cell mass; BEE, basal energy expenditure; BIA, bioelectrical impedance analysis; BMI, body mass index; BW, body weight; EAR, estimated average requirement; ECM, extracellular mass; EN, enteral nutrition; FFM, fat free mass; FM, fat mass; Hb, haemoglobin; HEN, home enteral nutrition; HPN, home parenteral nutrition; IBW, ideal body weight; IGF-1, insulin like growth factor; LBM, lean body mass; MAMC, mid-arm muscle circumference; NFPF, nutrition focussed physical findings; OI, oral intake; OR, odds ratio; PEG, percutaneous endoscopic gastrostomy; PG-SGA, patient generated subjective global assessment; PGT, prophylactic gastrostomy tube; PhA, phase angle; PTH, parathyroid hormone; QoL, quality of life; ; RBC, red blood cells; RDA, recommended daily allowance; TPN, total parenteral nutrition; TSF, tricep skinfold thickness; UWL, unintentional weight loss; 25(OH)D, 25-hydroxycholecalciferol.

Previous research has reported HEN to be beneficial for preventing weight loss and improving nutritional status despite evidence of these patients having poor energy and protein status (table 6). Few studies that reported improved nutritional status used body composition markers of muscle mass (table 6). Muscle mass significantly improved with use of HEN but the time period for this to occur differed; three months (Gao et al., 2021), or 12 months (Obara et al., 2010). Similarly, Baker et al. (2017) reported the benefits of HEN on muscle mass; higher in oesophageal patients who used HEN compared to those with exclusive oral intake. Lower incidence of weight loss was also reported in HEN patients compared to those with oral feeding (Baker et al., 2017, Bowrey et al., 2015). Despite HEN appearing to prevent weight loss, Baker et al. (2017) still reported extreme weight in almost half of the HEN patients. These findings indicate that while nutrition status is better in HEN patients than patients with oral intake, it can still be poor. Body mass index was significantly higher in patients using HEN compared to those with exclusive oral intake but was within normal range for both groups (Wu et al., 2018), these findings align with those of Baker et al. (2017). Similar results of increased or stabilised weight and BMI have been reported in HEN patients (Crotty et al., 1998, Obara et al., 2010, Loeser et al., 2003, Loser et al., 1998).

Biochemical measures were seldomly used to support conclusions about HEN being beneficial for energy and protein status (table 6). Significant improvements in albumin were observed after only one month of HEN by Gao et al. (2021) and after 12 months by Obara et al. (2010). Increased albumin was also reported by Crotty et al. (1998) who found it to be associated with increased weight in some patients. Albumin and haemoglobin were significantly higher in HEN patients than those with exclusive oral intake, supporting conclusions about HEN being beneficial for nutritional status (table 6).

Clinical signs and symptoms of energy and protein status were generally not considered in the assessment of HEN patients (table 6). Hand grip dynamometry was reported to be better in HEN patients compared to those with exclusive oral intake (Bowrey et al., 2015, Baker et al., 2017), thus indicating preservation of muscle strength. Patient generated subjective global assessments (PG-SGA), one of the few diagnostic tools for malnutrition available, were only carried out by one study assessing nutritional status of HEN patients (Wu et al., 2018). At three months, PG-SGA scores had decreased in HEN patients and were lower in HEN patients than patients with exclusive oral intake (Wu et al., 2018), suggesting that HEN can reduce the risk of malnutrition..

Dietary intake information was only available for two studies demonstrating improved nutritional status with HEN use. One study reported that HEN patients received 100% of their energy and protein requirements due to the contribution of the feed (Baker et al., 2017). These patients had

higher energy and protein intakes than the patients feeding orally (Baker et al., 2017). Obara et al. (2010) reported energy and protein intakes which were relatively low but were not compared to requirements, so conclusions about adequacy of intake could not be made. However, the nutritional status of these patients improved, so intake was likely adequate. Interestingly, Obara et al. (2010) reported that energy and protein intake did not differ significantly over the 12 month period despite changes in nutritional status.

Micronutrient status of HEN patients

Few studies have assessed the vitamin D status of HEN patients. Two studies found vitamin D status to be related to the route of nutrition, with enteral feeding being beneficial over oral feeding for maintaining vitamin D status (Badireddi et al., 2014, Wong et al., 2006). Contrarily, Kim et al. (2017) found no significant difference in vitamin D status between enterally and orally fed participants and reported poor nutritional status for both. However, Kim et al. (2017) reported significantly higher vitamin D status in patients who had exclusive enteral nutrition compared to those who had history of total parenteral nutrition, concluding that nutritional content is a determining factor of vitamin D status rather than feeding route. Only one study reported mean enteral vitamin D intake, this met the New Zealand adequate intake for adults under the age of 50 years, and no studies reported oral vitamin D intake (table 6). These studies have been completed in the United States of America, China, and Korea where the vitamin D content of enteral formulas and sunlight exposure may differ to that in New Zealand. The sample for all studies was small and homogenous, focusing only on patients with neurological conditions so the findings may not be applicable to the heterogenous HEN population in New Zealand.

Current literature concludes that use of long-term enteral nutrition increases risk for poor selenium status, but supplementation is beneficial. Mean baseline selenium concentrations were below reference ranges in HEN patients (Yagi et al., 1996, Fischer et al., 1990, Feller et al., 1987, Saito et al., 1998). Deficiency may be evident despite mean selenium concentrations being in range, as occurred in a study by Johtatsu et al. (2007) who reported low selenium in 38.7% (n=12) of HEN patients with Crohn's disease. Of these studies, only Saito et al. (1998) reported mean habitual selenium intake, this was lower than the New Zealand recommended daily intake. However, all studies reported use of enteral formulas low in selenium. Although enteral formulas have changed over the years, more recent studies continued to report inadequate selenium intakes in HEN patients (Kang et al., 2014, Baker et al., 2017). The findings of Kang et al. (2014) support older findings, reporting selenium deficiency in patients using long-term enteral nutrition and that risk of deficiency may increase with duration of HEN. An extended period is required for selenium deficiency to manifest clinically, this combined with muscle weakness not being an appropriate measure in patients with neuromuscular

conditions, may explain why clinical signs have been seldom assessed and noted in the HEN population (Fischer et al., 1990, Saito et al., 1998). No clinical signs of deficiency were observed by Fischer et al. (1990) despite having poor selenium status after 59 months on HEN. Clinical signs of selenium deficiency were reported by two studies which resolved after adequate supplementation (Yagi et al., 1996, Saito et al., 1998). Selenium supplementation and enrichment of selenium poor enteral formulas improved selenium status (Yagi et al., 1996, Fischer et al., 1990, Johtatsu et al., 2007, Saito et al., 1998). Enteral formulas must contain adequate selenium content to maintain the selenium status of HEN patients. Based on average energy intakes, Feller et al. (1987) suggested that enteral formulas should contain 100 µg of selenium per 1600 kcal of feed to be adequate. Free eating adults had better selenium status than enterally fed patients, however, these studies were carried out in the United States of America and Japan where the selenium content of food and enteral formulas differs to that in New Zealand (Feller et al., 1987, Saito et al., 1998).

The nutritional status of HEN patients is not yet fully understood and there is currently a lack of New Zealand specific literature. Micronutrient requirements, enteral formulas available, and environmental factors differ in New Zealand compared to the countries that have conducted research in this population; their findings may not be applicable to New Zealand HEN patients. Research is yet to assess patients' enteral and oral intake, nutritional biomarker concentration, body composition, and nutrition focused physical findings to make conclusions about the nutritional status of HEN patients.

3. Chapter 3: Research Study Manuscript

3.1 Abstract

Background: Home enteral nutrition (HEN) patients may be at risk of malnutrition and nutrient deficiencies. Adequate energy, protein, vitamin D, and selenium status are important for prevention of morbidity and mortality risk. This study aimed to investigate the nutritional status (energy, macronutrients, vitamin D, and selenium) of long-term home enteral nutrition patients in Counties Manukau, New Zealand to determine the prevalence of malnutrition.

Methods: Home Enteral Nutrition patients (n = 42, 18+ years) under the care of Te Whatu Ora Counties Manukau were recruited. They completed 5x 24-hr recalls including both enteral and oral nutrition intakes. Energy, macro- and micronutrient intakes were compared against their prescription and estimated requirements. Only 22 participants were able to provide blood samples, and 29 participants completed bioelectrical impedance analysis (BIA) to assess body composition. A nutrition-focused physical assessment was conducted on 40 participants to assess muscle and fat wasting and clinical signs of micronutrient deficiency.

Results: Twenty-five (62.5%) participants were malnourished according to the Global Leadership Initiative on Malnutrition (GLIM) criteria. Mean body mass index (BMI) (21.1 ± 3.6 kg/m^2) was low within the normal range. Low BMI and fat free mass index (FFMI) were identified in 19 (47.5%) and 13 (44.8%) participants respectively. At least 35% of participants had fat and/or muscle wasting. Energy and/or protein intakes were lower than requirements in 20% (n=8). Plasma vitamin D concentration (143.55 ± 55.35 nmol/L) was adequate in all, and high in 40% (n=8). Mean vitamin D intake (13.2 ± 5.3 µg) met the requirement for all age groups except > 70 years, and 11 (26.2%) participants had low intakes. Plasma selenium concentration (1.37 ± 0.19 µmol/L) was adequate in all, and high in 38.1% (n=8). Mean selenium intake (95.0 ± 28.1 µg) met requirements for all and intake was low in only 3 (7.1%) participants. There were significant differences between exclusive HEN and supplementary oral intake and prescription adherence for nutritional markers.

Conclusion: There is evidence of poor energy and protein status in HEN patients, however they mostly have adequate vitamin D and selenium status. Nutritional status may be influenced by feeding route and prescription adherence. The use of personalised energy calculations and more frequent monitoring may be required to prevent malnutrition.

3.2 Introduction

Home enteral nutrition (HEN) is utilised to prevent malnutrition and maintain the nutritional status of patients who are unable to meet their nutritional requirements orally (Bischoff et al., 2020).

However, Zeng et al. (2017) and McWhirter et al. (1994) reported malnutrition in 43.3% and 42.1% of HEN patients respectively. These studies used varying malnutrition criteria which largely focused on measures of BMI and muscle mass, with little focus on dietary intake. Malnutrition is reflective of patients' energy and protein status (Saunders and Smith, 2010). Dietary intake, nutritional biomarkers, body composition, and nutrition focussed physical findings can be used as measures of this. While malnutrition has been identified in the HEN population, other literature has reported benefits of HEN in BMI and muscle mass, indicating good energy and protein status in these patients (Obara et al., 2010, Wu et al., 2018, Gao et al., 2021). Baker et al. (2017) reported poor energy and protein status in almost half of the participants despite HEN still being beneficial over oral feeding.

Few studies have reported on the vitamin D status of HEN patients with mixed findings. Some HEN patients in Germany and America were reported to have adequate serum 25-hydroxy vitamin D (25[OH]D) concentration, albeit at the lower end of normal range (Klose et al., 2003, Badireddi et al., 2014). However, Korean and Chinese studies reported low serum 25(OH)D concentration in HEN patients (Kim et al., 2017, Wong et al., 2006). While Badireddi et al. (2014) and Wong et al. (2006) report that vitamin D status is significantly higher in HEN patients, Kim et al. (2017) reports no significant difference by feeding route. Vitamin D intake is not well reported in current literature, with Badireddi et al. (2014) being the only known to the author to do so. Vitamin D contributes to musculoskeletal health which is important for maintenance of functionality and independence (Nowson et al., 2012).

Poor selenium status has previously been identified in HEN patients. Home enteral nutrition patients in Japan, America, and South Korea had inadequate selenium intake due to use of enteral formulas with low or no selenium content which has resulted in continuous reporting of low plasma selenium concentration (Yagi et al., 1996, Kang et al., 2014, Johtatsu et al., 2007, Fischer et al., 1990, Feller et al., 1987, Saito et al., 1998). Selenium is important for prevention of oxidative damage and deficiency can cause abnormal thyroid function and cardiomyopathy (Rayman, 2000).

The literature available on the nutritional status of HEN patients is limited and sometimes contradictory. The nutritional status of New Zealand HEN patients has not yet been reported. Previous overseas findings may not be applicable to the New Zealand HEN population due to differences in the manufacturing of enteral formulas, dietetic practices, environmental factors (sunlight and soil), and nutrient requirements. No current literature known to the author has reported the nutritional status of HEN patients using the measures of dietary intake, biochemistry, body composition, and nutrition focussed physical findings in a single study or reported malnutrition prevalence in HEN patients using the GLIM criteria. The GLIM criteria focuses on standardising

malnutrition diagnosis in clinical settings (Cederholm et al., 2019), but has not yet been used to determine prevalence in HEN patients. Understanding the nutritional status of New Zealand HEN patients is important to inform feeding and nutrient monitoring practices to prevent malnutrition and micronutrient deficiencies and reduce risk of morbidity and mortality, and burden on the healthcare system.

The aim of this study was to investigate the nutritional status (energy, macronutrients, vitamin D, selenium) of long-term home enteral nutrition (HEN) patients in Te Whatu Ora Counties Manukau, New Zealand to determine the prevalence of malnutrition. In particular, this study aimed to investigate the (1) adequacy of dietary intakes, (2) impact of feeding practices on nutritional status, (3) prevalence of malnutrition and micronutrient deficiency.

3.3 Materials and Methods

3.3.1 Study design and recruitment

This study was carried out as a cross-sectional study observing dietary intake, biomarker concentrations, body composition measures, and nutrition focused physical findings to determine the nutritional status of HEN patients. One to two in person study visits with each participant were required to collect the demographic information, blood sampling, body composition measures, nutrition focused physical findings, and the first 24-hour diet recall. The remaining 24-hour diet recalls were conducted via phone, or email as required. Data were collected by student dietitians and a research assistant under the supervision of a senior researcher and senior clinician from August 2022 to October 2022.

Sample size was calculated based on the iron deficiency prevalence of 22.7% reported by Kang et al. (2014) as data were collected as part of a wider study. Based on this prevalence, a sample size of 66 participants was required to estimate a deficiency prevalence of 22.7% with a 10% level of precision and 95% confidence interval.

Potential participants were identified with inclusion and exclusion criteria. Inclusion criteria were men and women aged ≥18 years, and must have used HEN for ≥4 weeks, and used either a gastrostomy or jejunostomy tube. Exclusion criteria were use of parenteral nutrition and having terminal illness. This eligibility criteria identified 79 potential participants out of the 101 HEN patients under the care of Te Whatu Ora Counties Manukau, 65 of which were contacted by either phone or email for recruitment into the study. Forty-two patients provided consent and participated in partial or complete data collection. Partial data collection occurred for the blood sample, BIA, and physical

assessment due to lack of consent, patient complexity making the measure inappropriate or difficult to collect, and/or haemolysed or lipaemic blood samples.

3.3.2 Demographics

Participants answered an online questionnaire to obtain information regarding sex, age, ethnicity, underlying condition, and HEN practices (tube type, exclusive or supplementary oral, duration).

3.3.3 Anthropometry

Body weight (kg) was measured using standing or wheelchair scales, or the participants home scales. Height (cm) was estimated from ulna length (cm). Ulna length was measured from the olecranon process to the midpoint of the styloid process using a metal tape measure and converted to height using the BAPEN "Estimating Height from Ulna Length" conversion chart (Silva and Figueira, 2017). Body mass index was calculated with the Quetelet index (weight/height^2). The InBody S10 (InBody Co., Ltd, Korea) was used to conduct an unfasted BIA to measure body composition; waist circumference (WC) (cm), arm circumference (AC) (cm), mid arm muscle circumference (MAMC) (cm), fat mass (FM) (kg), fat free mass (FFM) (kg), skeletal muscle mass (SMM) (kg), body fat (%), body cell mass (BCM) (kg), and bone mineral content (BMC) (kg). Fat free mass index (FFMI) was calculated using FFM/height^2 and MAMC was categorised into percentiles (Frisancho, 1981). Bioelectrical impedance analysis was conducted with participants in the supine position either in bed or on a chair with limbs separated from each other and the body and electrodes placed on both hands and ankles.

3.3.4 Nutrition focussed physical assessment

Nutrition focused physical assessments of muscle and fat stores, and signs of micronutrient deficiency were conducted by a trained researcher. The researcher was guided by the standard operating procedure (SOP) which contained instructions and reference photos to ensure consistent categorisation. Energy status was assessed using physical assessment of the fat stores at the orbital, thoracic lumbar, and triceps regions. Protein and energy status were assessed using physical assessment of the muscle stores at the temple eye pad, clavicle, deltoid, trapezius, interosseous, quadricep, and gastrocnemius. Stores were recorded as either "well-nourished", "mild/moderate depletion", or "severe depletion". Excess fluid was assessed through the presence of oedema, and dehydration through a skin pinch test. Selenium status was assessed using physical assessment of the nails.

3.3.5 Dietary analysis

Participants completed five non-consecutive 24-hour diet recalls over a 3-week period with at least one weekend day recorded. The first 24-hour diet recall was conducted face-to-face at the initial

study visit by a trained researcher. The four following 24-hour diet recalls were conducted via phone or email. All oral and enteral intake was recorded in a 3-pass interview. The first pass involved participants listing their intake over a 24-hour period (midnight to midnight the previous day). The second and third passes involved the researcher asking detailed questions about the type, amount, route, processing, and timing of food and fluid delivered. Participants portion size judgement was aided by household measures (cups and spoons), food models, and photos. Recipes and photos of food products were obtained when possible. The participants enteral prescription was recorded the from Te Whatu Ora Counties Manukau database. The nutrient content of the 24-hour diet recalls (enteral and oral intake) was analysed using the FoodWorks10 (Xyris Software (Australia) Pty Ltd, 2019) using the New Zealand database (The New Zealand Institute for Plant and Food Research Ltd and Ministry of Health, 2022) and enteral nutrition product websites as required. Energy, protein, vitamin D, and selenium intakes were compared to participants' estimated requirements (Henry, 2005) and the Australia and New Zealand nutrient reference values (Australian National Health and Medical Research Council and Ministry of Health, 2005).

3.3.6 Nutritional biomarker analysis

Non-fasting plasma selenium, vitamin D (25[OH]D), and protein (albumin, prealbumin, transferrin, haemoglobin, and CRP) biomarkers were collected. Blood samples were collected by a phlebotomist, medical doctor, and/or a registered nurse into EDTA and heparin coated tubes which were kept at 4°C for transport to the laboratory. The blood samples were allowed to clot for 30 minutes prior to being centrifuged for 15 minutes at 3500 rpm. The plasma or serum sample was then pipetted into separate serology tubes and snap frozen and stored at -80°C until analysis, this was completed within 2 hours of blood collection. Biomarker analysis was conducted by Canterbury Health Laboratories, a fully internationally accredited medical diagnostic laboratory in Christchurch, New Zealand. Biomarker concentrations were compared against the laboratory reference values.

3.3.7 Data processing and statistical analysis

Data were analysed using the IBM SPSS statistics package version 28 (SPSS Inc., Chicago, IL, USA). Kolmogorov-Smimov (K-S) and Shapiro-Wilk (S-W) tests were used to test normality, a *p*-value of >0.05 indicated normally distributed data. Non-normal data were transformed using log 10 and tested for normality again, normal data were transferred back using the antilog and non-normal data were left in the original form. The mean ± SD was used to describe normal data (dietary intake, biochemical markers, anthropometry). The geometric mean (95% confidence intervals) was used to describe data that was normal after log transformation (dietary intake, biochemical markers). The median (interquartile range) was used to describe non-normal data (demographics, dietary intake, biochemical markers, anthropometry). Frequencies were used to describe categorical data

(demographics, prescription adherence, adequacy of dietary intake, biochemical markers and anthropometry, nutrition focused physical findings, and malnutrition prevalence). Malnutrition prevalence was determined using the GLIM criteria (Cederholm et al., 2019). Prescription adherence was determined by comparing energy intake from enteral formula against the energy content of formula prescribed.

Groupings used for analysis were feeding route (exclusive HEN or HEN with supplementary oral intake) and prescription adherence (meets prescription or not). These groups were chosen for statistical analysis because they had similar proportions in each condition. Independent t-tests compared groups for independent, normal data (dietary intake, biochemical markers, anthropometry) and Mann-Whitney tests compared groups for independent, non-normal data (dietary intake, biochemical markers, anthropometry). Chi-square tests were used to compare groups for nominal data (nutrition focused physical findings, malnutrition prevalence, prescription adherence, and adequacy of dietary intake, biochemical markers, and anthropometry). A level of $p < 0.05$ was accepted as statistically significant. Correlations were reported using Pearson's correlation co-efficient for normal data and Spearman's correlation coefficient for non-normal data.

3.3.8 Ethics approval

All participants were given a participant information sheet outlining the reason for the research and what was involved. Written, informed consent was gained from all participants for inclusion into the study. Participants were then assigned an ID number to maintain confidentiality. Data were kept securely on a Massey University SharePoint.

Ethics approval for the "The health, wellbeing and nutritional outcomes of long-term enterally fed patients – Home Enteral nutrition Performance (HELP)" study was sought and granted by the Massey University Human Ethics Committee on 26th June 2022 (HEC: Southern A Application SOA 22/20). Approval was also granted by the Australia New Zealand Clinical Trial Registry in July 2022 (registration number: ACTRN12622001044718) and by Te Whatu Ora – Health New Zealand Counties Manukau (research registry 1631). Funding was provided by the Counties Manukau Tupu fund (Mātātupu grant) and the Massey University Research Fund.

3.4 Results

3.4.1 Demographics

The study population comprised 42 participants with a median (IQR) age of 51.5 (38) years. Enteral nutrition was used exclusively by 54.8% (n=23) of participants and 45.2% (n=19) had supplementary

oral intake, this grouping was used for statistical analysis. The median (IQR) duration of HEN was 53.5 (134) months. See table 7 for further demographic characteristics.

Table 7. Demographic characteristics of study population.

	n	Median (IQR)	HEN patients n (%)
Age (years)	42	51.5 (38)	-
Sex (n)	42	-	-
Male	-	-	23 (54.8)
Female	-	-	19 (45.2)
Ethnicity (n)	42	-	-
Māori and Pacific Peoples	-	-	11 (26.2)
Asian	-	-	5 (11.9)
European	-	-	26 (61.9)
HEN route (n)	42	-	-
PEG/RIG	-	-	19 (45.2)
MIC-KEY	-	-	19 (45.2)
NG	-	-	3 (7.2)
NGJ	-	-	1 (2.4)
Exclusive HEN	-	-	23 (54.8)
Supplementary oral	-	-	19 (45.2)
HEN duration (months)	42	53.5 (134)	-
Diagnosed with a LTC	42	-	39 (92.9)
Reason for HEN	40#	-	-
Neurological	-	-	14 (35)
Malignant	-	-	15 (37.5)
Genetic	-	-	4 (10)
Other	-	-	7 (17.5)
Diagnosis timeframe	39#	-	-
From birth	-	-	10 (23.8)
1990-2000	-	-	5 (11.9)
2000-2010	-	-	9 (21.4)
2010-2023	-	-	15 (35.7)

Values are given as median (IQR) for scale data and n (%) for categorical data. # = smaller sample due to participant not providing information. Abbreviations: HEN, home enteral nutrition; LTC, long term condition; MIC-KEY, low profile gastrostomy; NG, nasogastric tube; NGJ, nasogastric tube with a jejunal extension; PEG, percutaneous endoscopic gastrostomy; RIG, radiologically inserted gastrostomy.

3.4.2 Nutritional intake and prescription

Information about the HEN prescription was obtained from 40 participants (table 8). The mean ± SD daily energy and protein prescribed to HEN patients was 1,576 ± 520 kcal and 63.6 ± 21.3 g, respectively. Energy and protein intakes from prescribed formula were significantly higher in those using exclusive HEN (1,784 ± 450 kcal and 72.4 ± 18.2 g) compared to those with supplementary oral intake (1,295 ± 484 kcal and 51.7 ± 19.7 g). The actual daily energy and protein intake from prescribed nutrition (formula taken orally and enterally) was lower than what was prescribed, with intakes of 1,488 ± 560 kcal and 59.9 ± 23.5 g respectively. Sixty percent (n=24) of participants did not adhere to their prescription, having less energy from formula than what was prescribed by median (IQR) of 287(458) kcal. The HEN prescription did not fulfil requirements for energy for 47.4% (n=18) or for protein for 44.7% (n=17). The prescription was 328.5 (231.3) kcal and 5 (11.5) g of protein less than requirements for these participants.

Dietary intake data was available for 42 participants (table 9). The mean daily intake of vitamin D was 13.2 ± 5.3 µg. Vitamin D intake was significantly higher in participants on exclusive HEN and in those who adhered to their prescribed energy from formula. On average, vitamin D intake was adequate for participants ≤70 years (table 9). Participants >70 years had inadequate vitamin D intake of 13.1 ± 2.5 µg. Of all participants, 26.2% (n=11) had inadequate vitamin D intake. The mean vitamin D intake of those who did not meet requirements (9.1 ± 3.3 µg) was not significantly different to those who met requirements (14.7 ± 5.1 µg), this result may be skewed because requirements are age specific. The mean daily selenium intake of 95.0 ± 28.1 µg was adequate for both men and women. Selenium intake was significantly higher in participants who adhered to their prescribed energy, as well as those on exclusive HEN, however this was not statistically significant (table9). Inadequate selenium intake was observed in three (7.1%) participants. The mean selenium intake of participants not meeting requirements (41.4 ± 13.2 µg) was not significantly different to those meeting requirements (99.2 ± 24.5 µg), however, this result may be skewed because requirements are sex specific.

Mean daily energy and protein intakes were 2050 ± 607 kcal and 82.8 ± 26.6 g respectively. Energy, protein, carbohydrate, and total fat intakes were significantly higher in participants with supplementary oral intake (table 9). Intake of energy, protein, carbohydrate, and total fat was also higher in participants who adhered to their prescribed energy from formula, but this was not statistically significant (table 9). Energy and/or protein intake did not meet individually calculated requirements for 20% (n=8) of participants. The mean energy and protein intakes of those not meeting individual requirements (1,242 ± 183 kcal and 57.5 ± 13.5 g) was not significantly lower than those meeting requirements (2262.5 ± 502.1 kcal and 86.9 ± 24.4 g). For participants not meeting requirements, energy and protein intakes are lower than requirements by 31.53 ± 176.0 kcal and 8.3

± 7.7 g, respectively. Adequate carbohydrate intake based on the acceptable macronutrient distribution range (AMDR) was not met by 35.7% (n=15) of participants, with an intake of 216.2 ± 75.1 g (40.3 ± 4.2% of AMDR), this was significantly lower than the intake of those meeting requirements (243.8 ± 73.3 g, 48.4 ± 2.8% of AMDR). No participants consumed inadequate total fat. Not meeting nutrient requirements was independent of feeding route and prescription adherence.

Prescribed formula provided significantly more nutrition for all nutrients than food for HEN patients (table 10). Twenty-three (54.8%) participants consumed food products, this included one participant who had a fully blenderised diet and three participants who had some oils and milk products enterally. The supplemental oral intake of HEN patients was largely from food, although four participants had oral nutrition support which contributed significantly to vitamin D (3.9 ± 2.6 µg) and selenium (26.2 ± 14.6 µg) intake.

Table 8. Adequacy of HEN prescription and compliance.

Nutrient (unit)	HEN prescription n=40#	Overall intake from prescribed nutrition	The number of participants whose HEN prescription does not fulfill requirements n=38	How much lower is their prescription than requirements?	The number of participants whose intake from prescribed nutrition does not fulfill HEN prescription n=40	How much lower is their actual nutritional intake from prescribed nutrition than what was prescribed?
Energy (kcal)	1575.7 ± 519.6[b]	1488.3 ± 589.9	18 (47.4)[b]	328.5 (231.3)	24 (60)	287.3 (458.4)
Protein (g)	63.6 ± 21.3[b]	59.6 ± 23.5	17 (44.7)[b]	5 (11.5)	23 (57.5)[a]	14.9 ± 11.9

Values are given as mean ± SD or median (IQR) for scale data and n (%) for categorical data. # = calculated from the enteral product feeding regime, unable to do this for one participant who had a blenderised feed and one participant who reported type of feed but not the prescribed volume and rate. Prescribed nutrition is the manufactured formula prescribed to them. Abbreviations: HEN, home enteral nutrition. [a] Significantly different between people who fulfill their energy prescription and those who do not. [b] Significantly different between people with supplementary oral and exclusive HEN. *P*-value <0.05 represents a significant result.

Table 9. Nutrient intake and adequacy in HEN patients.

Nutrient (unit)	Requirement	Overall intake	The number of participants not meeting individual requirements n (%)	Intake of those meeting requirements	Intake of those not meeting requirements	Intake of those on exclusive HEN n=23	Intake of those with oral intake n=19	Intake of those meeting their prescription n=16	Intake those not meeting their prescription n=24
Vitamin D (µg) n=42 (overall) n=20 (19-50 years) n=15 (51-70 years) n=7 (>70 years)	5 (19-50 years) 10 (51-70 years) 15 (>70 years)	13.2 ± 5.3 (overall) 13.7 ± 5.7 (19-50) 12.7 ± 5.8 (51-70) 13.1 ± 2.5 (>70)	11 (26.2)	14.7 ± 5.1	9.1 ± 3.3	14.9 ± 5.0	11.2 ± 5.1[b]	15.7 ± 5.3	11.4 ± 4.6[c]
Selenium (µg) n=42 (overall) n=23 (male) n=19 (female)	60 (male) 50 (female)	95.0 ± 28.1 (overall) 107.6 ± 24.1 (male) 79.8 ± 25.3 (female)	3 (7.1)	99.2 ± 24.5	41.4 ± 13.2	98.8 ± 22.3	90.5 ± 33.9	108.8 ± 26.3	86.7 ± 26.6[c]
Energy (kcal) n=40	1594.4 ± 226.2	2050.0 ± 606.7	8 (20)	2262.5 ± 502.1	1242 ± 183.3	1826.6 ± 490.6	2320.3 ± 635.1[b]	2195.7 ± 643.7	1873.2 ± 506.8
Protein (g) n=40	58.2 ± 13	82.8 ± 26.6	8 (20)	86.9 ± 24.4	57.5 ± 13.5	74.9 ± 22.9	92.5 ± 28.2[b]	87.4 ± 26.2	73.0 (64.6-82.5)
Carbohydrate (g) n=42	179.4 ± 25.5 – 259.1 ± 36.8	233.9 ± 74.2	15 (35.7)	243.8 ± 73.3	216.2 ± 75.1[a]	209.6 ± 58.8	263.4 ± 81.6[b]	255.6 ± 75.1	213.6 ± 69.9
Total fat (g) n=42	35.4 ± 5.0 – 62.0 ± 8.8	81.2 ± 26.8	0 (0)	81.2 ± 26.8	N/A	71.5 ± 22.8	92.8 ± 27.3[b]	85.8 ± 26.9	73.6 ± 22.2

Values are given as mean ± SD or geometric mean (95%CI) for scale data and n (%) for categorical data. Vitamin D adequate intake and selenium estimated average requirement values are from the Australia and New Zealand Nutrient Reference Values (Australian National Health and Medical Research Council and Ministry of Health, 2005). Energy requirement calculated using the Henry Oxford equation (Henry, 2005) multiplied by a 1.2 disease factor. Protein requirement based on 1g/kg/d. Carbohydrate and total fat requirements based on AMDR of 45-65% and 20-35% respectively (Australian National Health and Medical Research Council and Ministry of Health, 2005). Abbreviations: AMDR, acceptable macronutrient distribution range. [a] Significantly different to those meeting requirements. [b] Significantly different to those on exclusive HEN. [c] Significantly different to those meeting their prescribed energy from formula. *p*-value <0.05 represents significant result.

Table 10. Contribution to nutrition from different routes and sources.

Nutrient (unit)	Formula n=41	Food n=23	Oral food n=19	Oral nutrition support n=4
Vitamin D (µg)	12.4 ± 5.6	0.97 (2.60)	0.97 (2.42)	3.9 ± 2.6
Selenium (µg)	81.7 ± 31.7	13.9 (7.6-25.4)	15.6 (31.6)	26.2 ± 14.6
Energy (kcal)	1488.3 ± 589.9	1090.1 ± 796.5	1065.2 ± 723.2	506.6 ± 306.8
Protein (g)	59.6 ± 23.5	45.0 ± 37.5	42.8 ± 31.4	20.5 ± 12.8
Carbohydrate (g)	176.0 ± 68.5	113.5 ± 93.4	115.0 ± 89.8	57.5 ± 32.9
Total fat (g)	57.0 ± 24.3	46.6 ± 34.8	44.3 ± 30.6	20.5 ± 13.5

Values are given as mean ± SD, median (IQR), or geometric mean (95%CI). Formula is manufactured nutrition support products taken both enterally or orally. Food is whole foods taken both enterally (blenderised feed) or orally. Oral food is whole food taken orally. Oral nutrition support is manufactured nutrition support products taken orally.

3.4.3 Nutritional biochemical markers

A successful blood sample was only able to be taken for 22 participants (table 11). Mean biomarker concentrations were within normal ranges for all measures. Mean plasma 25(OH)D and selenium were 143.55 ± 55.35 nmol/L and 1.37 ± 0.19 µmol/L, respectively. These results were at the higher end of the reference ranges and were not significantly different between groups. No participant had low plasma 25(OH)D or selenium concentrations. Vitamin D was however high in 40% (n=8) of the participants (204.0 ± 25.3 nmol/L). This result was not statistically significant by feeding route or prescription adherence. Eight (38.1%) participants had high plasma selenium (1.5 (1.4-1.7) µmol/L). Significantly more participants who did not adhere to their prescribed energy from formula had high plasma selenium than those who did adhere.

The visceral proteins albumin and prealbumin were both low in six (28.6%) and two (10.5%) participants, respectively, while a further two (10.5%) had high prealbumin and six (28.6%) had high CRP (15.4 (5.5-43.6) mg/L). These results were not statistically significant between groups. Total protein was significantly higher in participants who adhered to their prescription (82.3 ± 3.8 g/L) compared to those who did not (74.4 ± 3.3 g/L).

Table 11. Nutritional biochemical biomarkers and adequacy in HEN patients.

Biochemical marker(unit)	Reference range	Measure	Low n(%)	Normal n(%)	High n(%)	Measure of those with high concentration
Vitamin D (nmol/L) n=20	50-150	143.55 ± 55.35	0 (0)	12 (60)	8 (40)	204.0 ± 25.3
Selenium (µmol/L) n=21	0.45-1.40	1.37 ± 0.19	0 (0)	13 (61.9)	8 (38.1)[a]	1.5 (1.4-1.7)
Albumin (g/L) n=21	35-48	37 (5)	6 (28.6)	15 (71.4)	0 (0)	-
Prealbumin (g/L) n=19	0.2-0.3	0.25 ± 0.05	2 (10.5)	15 (79.0)	2 (10.5)	-
Transferrin (g/L) n=20	1.7-3.4	2.4 (0.5)	0 (0)	20 (100)	0 (0)	-
Haemoglobin (g/L) n=22 (overall) n=14 (male) n=8 (female)	130-170(male) 120-150(female)	149.7 ± 22.5 (overall) 153.8 ± 27 (male) 142.5 ± 8 (female)	3 (13.6)	15 (68.2)	4 (18.2)	-
Total protein (g/L) n=9	64-83	77.1 ± 4.9[a]	0 (0)	7 (77.7)	2 (22.3)	-
CRP (mg/L) n=21	<5	3 (3)	N/A	15 (71.4)	6 (28.6)	15.4 (5.5-43.6)

Values are given as mean ± SD, median (IQR), or geometric mean (95%CI) for scale data and n (%) for categorical data. [a] Significantly different between people who fulfill their energy prescription and those who do not. P-value <0.05 represents significant result.

3.4.4 Anthropometry and body composition

Body mass index was able to be calculated for 40 participants, and BIA was carried out on 29 participants (table 12). Mean BMI was 21.1 ± 3.6 kg/m^2 was not significantly different by feeding route or prescription adherence but was significantly higher in those not meeting their energy requirement (22.0 ± 2.6 kg/m^2). Overall, five (12.5%) participants were classified as overweight and 19 (47.5%) as underweight. The mean BMI of underweight participants was 18.1 ± 2.1 kg/m^2. Fat mass and waist circumference were significantly higher in participants using exclusive HEN (19.4 ± 8.3 kg and 85.4 ± 15.1 cm) compared to those with supplementary oral intake (10.2 ± 6.5 kg and 74.1 ± 8.3 cm). Mean FFM was 44.2 ± 11.4 kg and was significantly higher in those meeting energy requirements (45.3 ± 11.6 kg) but not significantly different by feeding route or prescription adherence. Mean FFMI was 15.9 ± 3.2 kg/m^2, being low in 44.8% (n=13) of participants (13.0 ± 1.8 kg/m^2). However, this statistic may be skewed because FFMI is sex specific. Skeletal muscle mass, AC and MAMC were significantly higher in those meeting energy requirements than those who did not. Mid arm muscle circumference was below the 25th percentile for 57.2% of participants and 17.9% of participants were below the 5th percentile.

3.4.5 Nutrition focussed physical findings

A nutrition focussed physical assessment of muscle and fat stores and clinical signs of micronutrient deficiency was performed on 40 participants. Each examination area of muscle and fat stores demonstrated wasting for some patients (table 13). Evidence of depletion was more commonly mild to moderate than severe for all areas. Out of all the areas that severe depletion was evident, the clavicle (17.5%, n=7), deltoid (15%, n=6), and patella (15%, n=6) were the most common (table 13). More than 50% of participants were well nourished at the interosseous, orbital eye, thoracic lumbar, and triceps. Mild to moderate or severe muscle loss was evident in >50% of participants at the temple, deltoid, calf gastrocnemius, and patella and quadricep. Depletion at the patella and quadricep was observed in 70% of participants. The clavicle and trapezius were well nourished in 50% and depleted to some degree in 50% of participants. Oedema was present in 27.5% (n=11) of participants. Significantly more people who adhered to their prescribed energy from formula had muscle wasting at the trapezius than those who did not adhere.

Table 12. Anthropometry and body composition.

Measure (unit)	n	Overall	Measure of those who are low	Measure of those on exclusive HEN (n=17)	Measure of those with supplemental oral intake (n=12)	Measure of those meeting energy requirements	Measure of those not meeting energy requirements
Weight (kg)	40	58.2 ± 13.27	-	-	-	-	-
Height (m)	40	1.67 (0.12)	-	-	-	-	-
BMI (kg/m^2)	40	21.1 ± 3.6[a]	18.1 ± 2.1	-	-	20.9 ± 3.7	22.0 ± 2.6
BMI categories	40		-	-	-	-	-
Underweight		19 (47.5)	-	-	-	-	-
Normal weight		16 (40)	-	-	-	-	-
Overweight		5 (12.5)	-	-	-	-	-
FM (kg)	29	15.6 ± 8.8[b]	-	19.4 ± 8.3	10.2 ± 6.5	-	-
FFM (kg)	29	44.2 ± 11.4[a]	-	-	-	45.3 ± 11.6	38.7 ± 9.7
FFMI (kg/m^2)	29	15.9 ± 3.2	13.0 ± 1.8	-	-	-	-
% Low FFMI		13 (44.8)	-	-	-	-	-
SMM (kg)	29	23.8 ± 6.8[a]	-	-	-	24.5 ± 6.8	20.1 ± 6.2
Body fat percentage (%)	29	25.4 ± 13.4	-	-	-	-	-
WC (cm)	28	77.3 (18.1)[b]	-	85.4 ± 15.1	74.1 ± 8.3	-	-
AC (cm)	28	27.4 ± 3.6[a]	-	-	-	27.4 ± 3.7	27.2 ± 3.9
MAMC (cm)	28	22.5 ± 2.7[a]	-	-	-	22.6 ± 2.5	22.0 ± 3.8
MAMC percentiles	28		-	-	-	-	-
<5th		5 (17.9)	-	-	-	-	-
5th-10th		4 (14.3)	-	-	-	-	-
10th-25th		7 (25.0)	-	-	-	-	-
25th-50th		6 (21.4)	-	-	-	-	-
>50th		6 (21.4)	-	-	-	-	-
BCM (kg)	28	27.9 ± 7.3	-	-	-	-	-
BMC (g)	28	2.7 ± 0.7	-	-	-	-	-

Abbreviations: AC, arm circumference; BCM, body cell mass; BMC, bone mineral content; BMI, body mass index; FFM, fat free mass; FFMI, fat free mass index; FM, fat mass; MAMC, mid arm muscle circumference; SMM, skeletal muscle mass; WC, waist circumference. Values given as mean ± SD or median (IQR) for scale data and n (%) for categorical data. Underweight is considered <20 kg/m^2 for people under 70 years old and <22 kg/m^2 for people 70 years and older. Normal weight is considered 20-24.9 kg/m^2 for people <70 years old and 22-30 kg/m^2 for people 70 years and older. Overweight is considered 25-29.9 kg/m^2 for people <70 years old and >30 kg/m^2 for people 70 years and older. FFMI low when <17 kg/m^2 for men and <15 kg/m^2 for women. [a] Significantly different between people who do and do not meet their energy requirement. [b] Significantly different between people with supplementary oral and exclusive HEN, independent t-test and Mann-Whitney U test. P-value <0.05 represents significant result.

Table 13. Macronutrient nutrition focused physical findings results (n=40).

Parameter	Area	Well-nourished	Mild/moderate	Severe	Mild/moderate AND severe
Muscle	Temple	18 (45)	20 (50)	2 (5)	22 (55)
Muscle	Clavicle	20 (50)	13 (32.5)	7 (17.5)	20 (50)
Muscle	Deltoid	16 (40)	18 (45)	6 (15)	24 (60)
Muscle	Trapezius	20 (50)	18 (45)	2 (5)	20 (50)[a]
Muscle	Interosseous	23 (57.5)	14 (35)	3 (7.5)	17 (42.5)
Muscle	Patella and quadricep	12 (30)	22 (55)	6 (15)	28 (70)
Muscle	Calf gastrocnemius	13 (32.5)	24 (60)	3 (7.5)	27 (67.5)
Fat	Orbital eye	22 (55)	16 (40)	2 (5)	18 (45)
Fat	Thoracic lumbar	22 (55)	17 (42.5)	1 (2.5)	18 (45)
Fat	Triceps	26 (65)	12 (30)	2 (5)	14 (35)
Water	Oedema	29 (72.5)	10 (25)	1 (2.5)	11 (27.5)

Values are given as n (%). [a] Significantly different between people who fulfill their energy prescription and those who do not. [b] Significantly different between people with supplementary oral and exclusive HEN. P-value <0.05 represents significant result.

Micronutrient nutrition focused physical findings were not commonly present (table 14). Slow wound healing was the most common finding present in 17.5% (n=7) of participants. Transverse ridges and/or central vertical ridges were present in 15% (n=6), and patchy, thin, sparse hair was observed in 7.5% (n=3) of participants. Results for wound healing, nails, and sparse hair were not statistically significant. Easily plucked hair was present in five (12.5%) participants.

Table 14. Micronutrient nutrition focused physical findings (n=40).

Symptom	Present	Not present
Hair loss, easily plucked	5 (12.5)	35 (87.5)
Hair loss, thin, sparse, patchy	3 (7.5)	37 (92.5)
Nails, transverse ridges	6 (15)	34 (85)
Nails, central vertical ridges	6 (15)	34 (85)
Slow wound healing	7 (17.5)	33 (82.5)

Values are given as n (%).

3.4.6 Malnutrition prevalence

According to the GLIM criteria, 25 (62.5%) participants were identified as malnourished (figure 1). The remaining 15 (37.5%) participants had both a healthy BMI and adequate FFMI. There was no significant difference in prevalence between exclusive HEN and supplementary orally fed participants or between participants who did and did not adhere to their prescribed energy from formula.

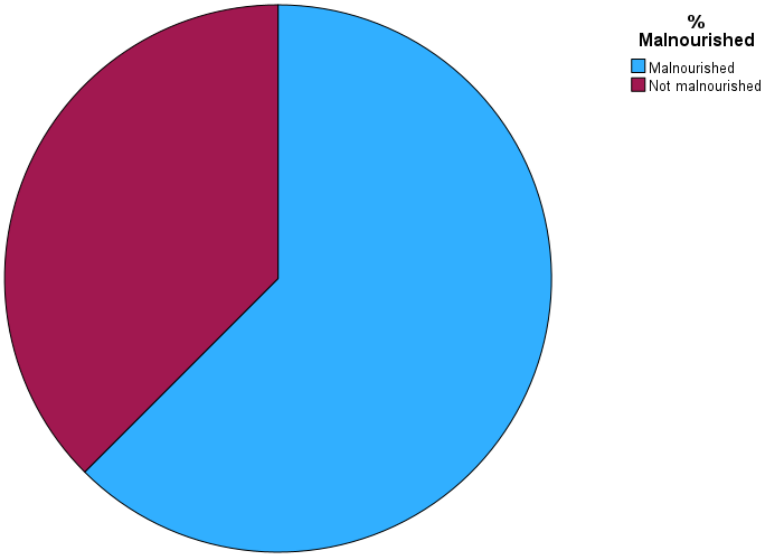

Figure 1. Malnourished participants according to the Global Leadership Initiative on Malnutrition criteria (n=40).

3.4.7 Correlations investigating the relationship between nutrient intake, duration of HEN and evidence of depletion, and macro and micronutrient intake.

Energy intake positively correlated with FFM, SMM, and triceps muscle stores and negatively correlated with body fat mass. Protein intake was similarly correlated with body fat mass and triceps stores. Energy and protein intake were strongly positively correlated. Energy and vitamin D and selenium intakes were also positively correlated. Energy from the enteral route and total vitamin D intake were more strongly correlated than total energy and vitamin D intake (table 15). Duration of feeding and triceps stores were negatively weakly correlated.

Table 15. Correlations with intake

Measures	Correlation	P-value
Energy intake and fat free mass	.410[a]	<0.05
Energy intake and body fat mass	-.538[a]	<0.05
Energy intake and skeletal muscle mass	.409[a]	<0.05
Energy intake and tricep stores	.322[b]	<0.05
Protein intake and tricep stores	.363[b]	<0.05
Protein intake and body fat mass	-.441[a]	<0.05
Energy and protein intake	.887[a]	<0.05
Energy and vitamin D intake	.362[a]	<0.05
EN energy intake and total vitamin D intake	.762[a]	<0.05
Energy and selenium intake	.537[a]	<0.05
HEN duration and tricep stores	-.377[b]	<0.05
HEN duration and oedema	.323[b]	<0.05

[a] Peasron's correlation coefficient. [b] Spearman's correlation coefficient. Abbreviations: HEN, home enteral nutrition.

3.5 Discussion

Poor nutritional status can cause reduced functional capacity and impaired immune response, increasing the risk of morbidity and mortality (Saunders and Smith, 2010). While HEN is implemented with the goal of maintaining or improving nutritional status long term, these patients are still at risk of developing malnutrition and nutrient deficiencies due to any of the following: catabolic disease conditions, inadequate feeding regimes due to underestimated nutrient requirements, inadequate micronutrient content of formula, and/or poor prescription adherence (McWhirter et al., 1994, Baker et al., 2017). The energy, protein, vitamin D, and selenium status, and prevalence of malnutrition is yet to be determined in New Zealand's HEN patients. Understanding the extent and potential reasons for the development of poor or compromised nutritional status among HEN patients will help to inform development of appropriate feeding and nutrient monitoring practices.

3.5.1 Prescription adherence

The energy and protein prescription set by dietitians was not adhered to by 24 (60%) participants. These participants were consuming 287.3 (458.4) kcal energy and 14.9 ± 11.9 g protein less than what was prescribed. Low prescription adherence may be due to feeding interruptions, presence of gastrointestinal symptoms, forgetfulness, or patients treating HEN as food rather than medical treatment (Gea Cabrera et al., 2019). Patients who are nutritionally stable require less frequent monitoring and have more autonomy over their feeding. Feeding autonomy and less monitoring may be associated with lower prescription adherence (Gea Cabrera et al., 2019). Reported intake being lower than the prescription may have been due to the method used for analysis of dietary intake; 24-hour diet recalls could produce inaccuracies due to reliance on memory, however, five recalls were taken to increase reliability. Motivation and social supports are important factors that could have impacted the participants' ability to pick up their prescription and administer the feed, and therefore may have impacted prescription adherence. The energy and protein prescription did not meet nutritional requirements for 47.4% and 44.7% of participants, respectively, as these participants were prescribed 328.5 (231.3) kcal and 5 (11.5) g of protein less than their requirements. However, a similar proportion of the study population had supplementary oral intake (45.2%) so this finding regarding prescription adequacy may be due to dietitians accounting for their patient's oral nutrition which is assumed to fill the gap.

3.5.2 Energy and protein

The GLIM malnutrition criteria (Cederholm et al., 2019) were used to identify the prevalence of malnutrition in this group of HEN patients. Low BMI or low muscle mass were assessed alongside a state of reduced food assimilation due to the enteral feeding method. Over half (62.5%) of the

participants were identified as being malnourished, of which, 18 were European, three were Asian, and four were Māori or Pacific peoples. Prevalence of malnutrition in HEN patients did not differ by feeding route or prescription adherence. While still relatively high, previous studies reported lower malnutrition prevalence in HEN patients; 42.1% (McWhirter et al., 1994) and 43.3% at 24 weeks post-oesophagectomy (Zeng et al., 2017). Smaller HEN sample sizes were used by McWhirter et al. (1994) (n=19) and Zeng et al. (2017) (n=30) than our study (n=40). The sample size of Asian (n=5) and Māori and Pacific (n=11) participants were particularly low in our study. The small sample sizes may explain the differing findings and mean that the reported malnutrition prevalence is not representative of the HEN population and ethnic groups. Furthermore, varying malnutrition criteria were employed to report prevalence. Low BMI and muscle mass were used to identify malnutrition by McWhirter et al. (1994) while Zeng et al. (2017) used the Mini Nutritional Assessment tool. These measures share some similarities with the GLIM criteria used in our study. However, our study used a BMI cut point of 22 kg/m^2 for older adults, whereas previous research used a cut point of 20 kg/m^2 for all participants, which may underdiagnose malnutrition in older adults (Burman et al., 2015), thus explaining the differing findings. Different low muscle mass measures were also used; our study used the FFMI from BIA whereas McWhirter et al. (1994) and Zeng et al. (2017) measured MAMC. Based on this data, it can be proposed that malnutrition is a nutritional issue in HEN patients that requires attention.

Malnutrition prevalence was similar in participants who had used HEN in the short or long term in our study. Twelve participants (30%) who used HEN for less than the median duration of 53.5 months and 13 participants (32.5%) who used HEN for longer than 53.5 months were malnourished. The malnutrition prevalence in patients using HEN for shorter duration may be because it is preexisting and being treated, whereas malnutrition in longer term HEN patients may be the result of inadequate feeding due to underestimated requirements or poor prescription adherence. McWhirter et al. (1994) previously concluded that HEN patients are at risk of malnutrition regardless of nutrition treatment duration, which aligns with the present study findings. However, Zeng et al. (2017) and Wu et al. (2018) both reported that early HEN treatment can reduce the risk of malnutrition. These contrasting findings may be due to the patient group studied as previous studies demonstrating the benefit of HEN focused on post-oesophagectomy patients whereas the present study population had heterogeneous disease conditions.

Plasma albumin, prealbumin, transferrin, haemoglobin, total protein, and CRP were measured and compared to reference standards to assess protein status. The means or medians for all measures were within normal ranges. Previous studies reported similar results of normal ranges for plasma albumin (Gao et al., 2021, Borges et al., 2011, Klose et al., 2003, Henderson et al., 1992, Johtatsu et

al., 2007, Badireddi et al., 2014, Wu et al., 2018), as well as plasma transferrin, total protein, and CRP (Gao et al., 2021, Borges et al., 2011, Obara et al., 2010, Okada et al., 2001, Badireddi et al., 2014) in HEN patients. Two earlier studies reported normal plasma haemoglobin in this population (Henderson et al., 1992, Wu et al., 2018), and one study reported plasma prealbumin as normal at 12 months in younger elders on HEN (Obara et al., 2010). These reports suggest that HEN patients have adequate protein status. However, six (28.6%) participants who were able to provide a blood sample had low plasma albumin. This may be explained by the albumin lowering effect of inflammation (Evans et al., 2021) which is evidenced by high CRP in six (28.6%) participants (15.4 (5.5-43.6) mg/L). Similar prevalence of hypoalbuminemia was reported by McWhirter et al. (1994) (15.8%), Johtatsu et al. (2007) (29%), and Okada et al. (2001) (37%). Prevalence reported by Johtatsu et al. (2007) may be falsely similar due to their use of a higher plasma albumin cut point (40 mg/L). Some studies have reported contrasting findings regarding mean visceral protein concentration and low albumin prevalence; borderline normal or low mean plasma albumin and/or haemoglobin (Obara et al., 2010, Okada et al., 2001, Obara et al., 2008), low mean plasma prealbumin (Gao et al. (2021) and Obara et al. (2010), and hypoalbuminemia prevalence of 54.5% (Kaw and Sekas, 1994) and 84.6% (Obara et al., 2008) in HEN patients. It is well known that albumin concentration decreases with age (Salive et al., 1992), which may have contributed to the hypoalbuminemia prevalence in our study, and explain the contrasting findings as the populations previously studied were elderly whereas the median (IQR) age of our population was 51.5 (38) years (Obara et al., 2010, Obara et al., 2008, Okada et al., 2001, Kaw and Sekas, 1994).

There were no significant differences in plasma albumin, prealbumin, transferrin, haemoglobin, or CRP according to feeding route or prescription adherence. Previous research has reported that albumin, transferrin, and haemoglobin did not differ significantly by feeding route (Saito et al., 1998, Badireddi et al., 2014, Okada et al., 2001). Exclusive HEN, supplementary oral, and exclusive oral feeding routes were compared in these previous studies. These reports coincide with the present finding that feeding route may not influence protein status. Contrasting findings have previously been reported; significantly higher plasma albumin and haemoglobin in HEN with supplementary oral intake than exclusive oral intake (Wu et al., 2018), and lower plasma albumin and haemoglobin in HEN patients than free eating, healthy adults (Okada et al., 2001). However, the studies with contrasting results compared different feeding routes to the present study. The sample size was over six times larger in the study of Wu et al. (2018) than the present study, making their results stronger and more representative.

The mean BMI of 21.1 ± 3.6 kg/m^2 is at the low end of the normal range for adults aged 18 to 70 years and is considered underweight for older adults. Similarly, previous studies reported the BMI of

HEN patients to be between 20 kg/m^2 and 22.1 kg/m^2 (Loeser et al., 2003, Obara et al., 2010, Klose et al., 2003, Mcnamara et al., 2000, Okada et al., 2001, Wu et al., 2018). This data initially suggests that the energy status of HEN patients is adequate. However, considering the higher cut point that should be considered for older adults (22 kg/m^2) and the standard deviation of 3.6 kg/m^2, it can be proposed that their energy status is compromised. Nineteen (47.5%) participants had low BMI (18.1 ± 2.1 kg/m^2) according to their age group and interestingly, five (12.5%) participants were classified as overweight. Similar prevalence of low BMI was reported by McWhirter et al. (1994) (47.4%), Henderson et al. (1992) (39.4%), and Obara et al. (2008) (55%), confirming that approximately half of HEN patients were underweight. In contrast, Mcnamara et al. (2000) reported low BMI in only 8.8% of participants. Mcnamara et al. (2000) did not consider the prevalence of older adults having a BMI under 22 kg/m^2 as we did because they used a cut point of 20 kg/m^2 for all participants, including older adults. A lower cut point of 18.5 kg/m^2 was used by Obara et al. (2008) which may mean prevalence of being underweight between the studies was falsely similar.

Low muscle mass was identified in HEN patients able to complete the BIA; 13 (44.8%) participants with FFMI below 17 kg/m^2 for men and 15 kg/m^2 for women, and in 22 (78.6%) participants with MAMC below the 50th percentile. Higher prevalence of MAMC below the 50th percentile was reported by (Henderson et al., 1992) (92.1%). These results indicate that HEN patients have poor protein and energy status but may also be influenced by cachexia and immobility due to their underlying disease conditions.

There were no significant differences in BMI, FFM, or MAMC based on feeding route or prescription adherence, but FM and WC were significantly higher in those who used exclusive HEN in our study. These findings indicate that feeding route and/or nutrition source may influence body composition but not body mass. This is an interesting finding considering those with supplementary oral intake had higher energy (2320.3 ± 635.1 kcal) and protein (92.5 ± 28.2 g) intakes which is likely due to patients with oral intake choosing comfort foods or the encouragement of high energy and high protein foods by their dietitians. However, the consistency of energy and protein obtained with exclusive HEN compared to the daily variance that likely occurs from supplementary oral intake may explain this finding. This finding may also be explained by the bioavailability of nutrients, the protein in enteral formulas may have been more easily utilised than that in food. Two studies reported higher BMI in patients using HEN with supplementary oral intake than those with exclusive oral intake (Bowrey et al., 2015, Wu et al., 2018) and one reported greater MAMC in enterally fed participants than orally fed (Bowrey et al., 2015). These findings are non-comparable to our study as we did not have patients with exclusive oral intake but offer insight to the importance of the HEN contribution for maintenance of nutritional status.

Skeletal muscle mass, FFM, AC, and MAMC were significantly higher in those who met their energy requirements than those who did not. This is an expected result as markers of muscle mass and energy intake are positively correlated. However, BMI was significantly higher in participants who did not meet their energy requirements (22.0 ± 2.6 kg/m^2) than those who did (20.9 ± 3.7 kg/m^2). This unexpected result may be due to recent changes in dietary intake which are not captured by an observational study design, or due to uneven sample sizes as eight (20%) participants had inadequate energy intake whereas 32 (80%) participants had adequate intake.

The nutrition focused physical assessment revealed high prevalence of muscle wasting at all examination sites. This measure has been seldom used in previous studies assessing the nutritional status of HEN patients. However, Wu et al. (2018) reported a Patient Generated Subjective Global Assessment (PG-SGA) score of 5.7 after three months of HEN use. It can be assumed that the report of Wu et al. (2018) aligns with the current finding that muscle and fat wasting is evident as a physical assessment is a component of the PG-SGA score. Prevalence of muscle wasting at the trapezius was significantly higher in participants who adhered to their prescribed energy from formula. This interesting and unexpected result may be explained by the close monitoring and encouragement of prescription adherence by dietitians in response to identifying malnutrition. Whereas well-nourished and nutritionally stable patients do not require such close monitoring and may fluctuate their intake daily as does the general population due to treating their HEN as food not treatment, resulting in low prescription adherence (Gea Cabrera et al., 2019).

The findings regarding malnutrition and fat and muscle wasting prevalence, and BMI reported in our study indicate that HEN patients have poor energy and protein status. However, only eight (20%) participants did not meet their energy and/or protein requirements, with intakes of 1242 ± 183.3 kcal and 57.5 ± 13.5 g, respectively. Surprisingly, these intakes were not significantly lower than those meeting their energy (2262.5 ± 502.1 kcal) and/or protein requirements (86.9 ± 24.4 g). The large standard deviation of the group meeting requirements may explain the lack of significance. Prevalence of inadequate intake aligns with the finding of Mcnamara et al. (2000) that 14% of HEN patients had energy intake below their estimated average requirement. However some studies have reported contrasting findings; inadequate energy intake in 80% (Klose et al., 2003), and adequate energy and protein intake in 100% (Baker et al., 2017). Our study considered individual requirements whereas Klose et al. (2003) considered energy intake below 2000 kcal inadequate, this may explain the contrasting results. Baker et al. (2017) attributed high prevalence of adequate intake to contribution of the enteral feed. Muscle wasting can occur despite meeting predicted energy and protein requirements due to immobility (Okada et al., 2001), this may explain why prevalence of muscle wasting, malnutrition, and low BMI is higher than that of inadequate energy and/or protein

intake in our study. The dietitian's calculations for energy and protein requirements were unavailable, so the same energy and protein requirement calculations were applied to the entire study population. Therefore, energy and protein requirements may have been underestimated by the study, thus explaining the differing prevalence of adequate intake and evidence of poor nutritional status. The quick calculations used by dietitians may underestimate the requirements of patients who are highly catabolic due to malignant diseases or have involuntary movements as with neurological conditions. Underestimation results in inadequate feeding regimes and poor nutritional status, indicating for use of individualised calculations. While muscle wasting and low BMI can occur from inadequate feeding, previous research has suggested that the effects of HEN patients' underlying conditions, such as cachexia with malignancy, may limit the ability of HEN to maintain nutritional status (Henderson et al., 1992, McWhirter et al., 1994). However, Loser et al. (1998) concluded that HEN can improve nutritional status despite disease progression.

3.5.3 Vitamin D

Serum 25(OH)D concentration was assessed against reference standards to determine the vitamin D status of HEN patients. The mean serum 25(OH)D concentration of 143.55 nmol/L was at the higher end of the normal range of 50-150 nmol/L. Badireddi et al. (2014) and Klose et al. (2003) reported serum 25(OH)D concentrations of 64 nmol/L and 62.7 nmol/L, respectively. Despite being at the low end of the normal range, these reports align with the present finding that HEN patients had adequate Vitamin D status. Low serum 25(OH)D concentrations were reported by Kim et al. (2017) (47 nmol/L) and Wong et al. (2006) (31.5 nmol/L). These reports were more than three times lower than the current report and contradicted the finding that none of the participants able to provide a blood sample in this study had a low serum 25(OH)D concentration. At their 12 month follow-up, Klose et al. (2003) reported serum 25(OH)D concentrations of 165.3 nmol/L. This was considered normal by the study but was high according to the New Zealand reference range. This report aligns with the finding that some HEN patients have high vitamin D status, as 40% (n=8) of participants able to provide a blood sample had serum 25(OH)D concentrations of 204.0 ± 25.3 nmol/L which was well above the reference range.

Serum 25(OH)D was not significantly higher in participants who used exclusive HEN and/or adhered to their prescribed energy from formula. No significant differences in serum 25(OH)D concentration between enterally fed and free eating adults were reported by Kim et al. (2017). This report coincides with the present finding that feeding route does not affect serum 25(OH)D concentration. However, some studies have reported contrasting findings; concentrations were significantly higher in HEN than free eating (Wong et al., 2006), and significantly higher in exclusive HEN than supplementary oral and free eating participants (Badireddi et al., 2014). These reports indicate that nutrient source

influences vitamin D status, with enteral nutrition offering a more consistent and appropriate supply of vitamin D than oral nutrition.

Mean vitamin D dietary intake (13.2 ± 5.3 μg) met the adequate intake requirements for adults aged 18-70 years. The intake of those aged >70 years (13.1 ± 2.5 μg) did not meet their adequate intake of 15 μg/d. Daily intakes of adults aged 18-50 years (13.7 ± 5.7 μg) were much higher than their adequate intake of 5 μg/d and the intake of those aged 51-70 years (12.7 ± 5.8 μg) was also higher than their adequate intake of 10 μg/d. This is likely due to the use of vitamin D enriched enteral formulas. These results suggest that older adults are an at risk group and may make up a large proportion of the 26.2% of participants who had inadequate intake (9.1 ± 3.3 μg). Energy requirements may be lower in older adults due to reduced basal metabolic rate and thus, energy and formula intake and may be inadequate to supply the higher vitamin D requirement. This may explain why Badireddi et al. (2014) reported lower vitamin D intake (8.8 ± 4.3 μg) than the present study (13.2 ± 5.3 μg) as their participants had lower energy requirements due to muscular dystrophy. This differing result may also be explained by differences in the vitamin D content of the formula but this information was not available.

Dietary vitamin D intake was significantly higher in participants who used exclusive HEN (14.9 ± 5.0 μg) and/or adhered to their prescribed energy from formula (15.7 ± 5.3 μg). While there were significant differences, the intake of those with supplementary oral intake (11.2 ± 5.1 μg) and/or not adhering to their prescribed energy from formula (11.4 ± 4.6 μg) was still adequate for majority of the population. Intake was previously reported to be higher in patients with HEN than exclusive oral intake (Badireddi et al., 2014). This report aligns with the present finding that enteral feeding is associated with higher vitamin D intake. These differences may occur because the contribution from food (0.97 (2.6) μg) is less than from enteral formulas (12.4 ± 5.6 μg). The correlation between energy from enteral nutrition and vitamin D intake (0.762) was also stronger than total energy and vitamin D intake (0.362), indicating the importance of the HEN contribution.

Contrasting results may be explained by differences in sample size, sunlight exposure, or feeding regimes. The HEN sample sizes of Kim et al. (2017) (n=14) and Wong et al. (2006) (n=8) were smaller than our study and are not representative of the HEN population. Sunlight exposure influences serum 25(OH)D concentration (Herrmann et al., 2017), this is different between New Zealand and Korea and Hong Kong, where previous research was conducted (Kim et al., 2017, Wong et al., 2006). Participants in previous research potentially had low sunlight exposure due to immobility or living in a hospital setting and relied on dietary contribution to maintain vitamin D status (Kim et al., 2017, Wong et al., 2006, Badireddi et al., 2014). However, sunlight exposure was not recorded in our study

and is assumed. Amount and type of formula administered may differ between studies, but intake data was not previously reported.

3.5.4 Selenium

Plasma selenium was assessed against reference standards to determine the selenium status of HEN patients. Mean plasma selenium of 1.37 µmol/L was at the higher end of the normal range (0.45-1.40 µmol/L). Previous reports of selenium concentrations ranged from 1.08 µmol/L to 1.42 µmol/L (Fischer et al., 1990, Johtatsu et al., 2007), which aligned with the present finding that HEN patients have good selenium status when using a selenium-rich formula. Selenium concentrations were considered low by Yagi et al. (1996) (0.56 µmol/L) and McWhirter et al. (1994) (0.76 µmol/L) but adequate by our study due to their use of higher reference ranges of 1.22-2.03 µmol/L and 0.8-2.0 µmol/L respectively. Other studies have reported low concentrations of 0.43-0.77 µmol/L (Feller et al., 1987) and 0.26 µmol/L prior to formula changes (Fischer et al., 2015). Previous studies have also reported the prevalence of selenium deficiency; 100% by Yagi et al. (1996), Fischer et al. (1990), and Feller et al. (1987), 31.5% by McWhirter et al. (1994), and 38.7% by Johtatsu et al. (2007). These reports contrasted the present finding that HEN patients have normal (61.9%), and sometimes high (38.1%, n=8), selenium concentrations on normal feeding regimes without supplementation other than enteral formulas. Participants in studies reporting low selenium status were using formulas with no or low selenium content, whereas formulas used in the present study had higher selenium content. This is illustrated by a concentration rise from 0.26 µmol/L to 1.08 µmol/L (Fischer et al., 1990) and concentration coming into range for 100% of participants (Fischer et al., 1990, Yagi et al., 1996) with a change in formula and/or selenium supplementation. Jejunostomy feeding may also result in lower absorption of selenium because it bypasses the duodenum which is a selenium absorption site (Thomson, 2003). This may explain the lower concentration reported by Yagi et al. (1996) as their population was largely jejunostomies, whereas this study and other previous research were largely gastrostomies.

Significantly more participants who did not adhere to their prescribed energy from formula had high plasma selenium concentrations. This is an interesting and unexpected result considering this group had significantly lower, but still adequate, intake (86.7 ± 26.6 µg) than those adhering to their prescription (108.8 ± 26.3 µg). Unaccounted selenium intake due to underreporting of dietary intake, selenium containing medications, and/or supplements and/or differences in feeding regimes and monitoring between malnourished and well-nourished participants may explain this result. Patients with malnutrition, which may reduce selenium concentration, have their energy intake, and therefore selenium intake increased, and adherence closely monitored by a dietitian. However, well-nourished patients may fluctuate their intake and not strictly adhere to their prescription due to

viewing HEN as food not treatment and not being as closely monitored. The potentially long-term, adequate selenium intake of well-nourished patients compared to a recent increase in selenium intake in response to malnutrition may explain the unexpected result.

Plasma selenium concentration did not significantly differ by feeding route. This is likely because both groups had consistent enteral contributions. In contrast, previous studies reported significantly lower selenium concentrations in participants with exclusive HEN than exclusive oral feeding (Saito et al., 1998, Feller et al., 1987). However, previous research compared participants with no HEN contribution whereas our study compared HEN patients with exclusive and supplementary oral intake.

Mean selenium intakes (95.0 ± 28.1 µg) met the estimated average requirements of all HEN patients in this study, and mean intakes of female (79.8 ± 25.3 µg) and male (107.6 ± 24.1 µg) participants met sex specific requirements. Previous studies reported selenium intakes of 3.3 ± 8.6 µg (Kang et al., 2014), 33.5 µg and 48 µg at three and six months respectively (Baker et al., 2017), and 0.33 µg/kg which equates to 23.1 µg in a 70 kg adult (Saito et al., 1998). These reports were lower than the New Zealand EAR of 60 µg/day (male) and 50 µg/day (female) and contrasted the present finding that HEN patients had sufficient selenium intakes. While previous studies did not report prevalence of adequate intake, it can be assumed to be low due to these low intakes and use of selenium poor formulas prior to selenium fortification (Saito et al., 1998, Johtatsu et al., 2007, Fischer et al., 1990, Yagi et al., 1996). This contrasts our finding of high prevalence of adequate intake, with only three (7.1%) participants having inadequate selenium intake (41.4 ± 13.2 µg). Low selenium intake in our study may be the result of low formula intake due to use of a concentrated feed, low energy prescription, or low prescription adherence. These ideas are supported by the finding that selenium intake was significantly higher in patients who adhered to their prescribed energy from formula (108.8 ± 26.3 µg), and higher in those who used exclusive HEN (98.8 ± 22.3 µg), although this was not significant. These findings highlight the importance of HEN for maintenance of selenium status. Feller et al. (1987) suggested that enteral formula should contain >100 µg selenium per 1600 kcal. New Zealand formulas align with this; selenium content per 1600 kcal is 128 µg for Ensure, 115 µg for Ensure Plus, and 110 µg for Nutrison Energy Multifibre (Abbott Nutrition, 2023a, Abbott Nutrition, 2023b, Nutricia, 2022).

3.6 Conclusion

In conclusion, patients using HEN in New Zealand may have compromised energy and protein status but maintain adequate vitamin D and selenium status. Poor energy and protein status was identified by anthropometric measures, high prevalence of malnutrition (62.5%), and muscle and fat wasting

despite intake being seemingly adequate. Therefore, changes to feeding practices regarding energy and protein calculations and closer monitoring is required. Plasma selenium status was adequate, and sometimes high, and dietary intake met requirements in HEN patients. Vitamin D status of HEN patients is adequate as serum 25(OH)D concentration was within range in all, and sometimes high, and intake met requirements for patients <70 years old. Despite no evidence of vitamin D insufficiency, care should be taken with older adults whose intake did not meet requirements. Higher vitamin D and selenium intakes being associated with exclusive HEN and prescription adherence demonstrate the importance of enteral nutrition for maintenance of micronutrient status in these patients. For other measures, prescription adherence may not influence nutritional status, but rather be in response to recognition of compromised nutritional status by their dietitians. This study is the first of its kind in New Zealand and one of few studies globally to report an association between prescription adherence and/or feeding regimens (exclusive HEN or supplementary oral) and nutritional status (vitamin D, selenium, energy, and protein). It is also one of a handful of studies to report prevalence of vitamin D biomarker adequacy and quantify vitamin D and selenium intake from food and enteral nutrition in HEN patients.

4. Chapter 4: Conclusions and Recommendations

This study aimed to investigate the nutritional status (energy, macronutrients, vitamin D, selenium) of long-term home enteral nutrition (HEN) patients in Counties Manukau, New Zealand to determine the prevalence of malnutrition. The objectives were to investigate the adequacy of nutritional intake (energy, macronutrients, vitamin D and selenium), determine the impact of feeding practices on nutritional status, and determine the prevalence of malnutrition and nutritional deficiency (energy, macronutrients, vitamin D, selenium.

The main findings in relation to each objective are presented below:

Objective one: To investigate the adequacy of nutritional intake (energy, macronutrients, vitamin D, selenium).

Eight (20%) participants did not meet estimated energy and/or protein requirements by 31.53 ± 176.0 kcal and 8.3 ± 7.7 g respectively. Energy and protein intake from prescribed formula did not fulfil the enteral prescription for 24 (60%) participants, the energy intake from formula in these participants was 287 (458) kcal less than what was prescribed. Overall, mean vitamin D intake (13.2 ± 5.3 µg) and intake by age group (13.7 ± 5.7 µg for 18-50 years, 12.7 ± 5.8 µg for 51-70 years) met the adequate intake for all participants except those aged ≥70 years (13.1 ± 2.5 µg). Eleven (26.2%) participants had inadequate vitamin D intake (9.1 ± 3.3 µg). Selenium intake was inadequate in only 3 (7.1%) participants (41.4 ± 13.2 µg). The mean selenium intake (95.0 ± 28.1 µg) met the estimated average requirement for men and women.

Objective two: To determine the impact of feeding practices on the nutritional status (energy, macronutrients, vitamin D, selenium) by comparing nutritional markers (body composition, physical assessment, and biomarkers) between groups:

- Feeding regime (exclusive HEN vs supplementary oral),
- Prescription adherence

Participants using exclusive HEN had significantly higher waist circumference (85.4 ± 15.1 cm) and fat mass (19.4 ± 8.3 kg), this indicated that the enteral feed contribution may influence body composition. Vitamin D intake was significantly higher in those using exclusive HEN (14.9 ± 5.0 µg), whereas those using HEN with supplementary oral intake had significantly higher energy (2320.3 ± 635.1 kcal), protein (92.5 ± 28.2 g), carbohydrate (263.4 ± 81.6 g), and fat intakes (92.8 ± 27.3 g).

Significantly more people who adhered to their prescription had muscle wasting at the trapezius and high plasma selenium. We hypothesise that this is likely due to changes in feeding practices and

monitoring in response to dietitians recognising malnutrition when monitoring patients. Participants who adhered to their prescription had significantly higher vitamin D (15.7 ± 5.3 µg) and selenium (108.8 ± 26.3 µg) intakes.

Objective three: To determine the prevalence of malnutrition and nutritional deficiency (energy, macronutrients, vitamin D, selenium) by investigating:

- Body composition (BMI, FM, FFM, MAMC, WC)
- Physical assessments (clinical signs)
- Dietary intake, and
- Nutritional biomarkers (visceral proteins, inflammatory markers, 25(OH)D, selenium)

Twenty-five (62.5%) participants were malnourished according to the Global Leadership Initiative on Malnutrition (GLIM) criteria. Low BMI, FFM, and MAMC were identified in 47.5% (n=19), 44.8% (n=13), and 32.2% (n=9) respectively. Fat and/or muscle wasting was evident in at least 35% and up to 70%. These findings indicate that HEN patients have poor energy and protein status despite dietary intake being seemingly adequate, it was only low in 20% (n=8). This indicates that energy and protein requirements may have been underestimated. Albumin was low in 28.6% but this might not have reflected nutritional status as CRP was high in the same proportion. There was no evidence of vitamin D or selenium deficiency through biochemical markers, but interestingly, concentrations were high in 40% and 38.1% respectively. Home enteral nutrition patients may be at nutritional risk with regard to vitamin D despite adequate biomarker concentrations, as 26.2% did not meet requirements and mean intake for older adults (13.1 ± 2.5 µg) was lower than the adequate intake (15 µg). Selenium intake was low in only 3 (7.1%) participants.

4.1 Strengths

1. The implementation of a cross sectional study design allowed for data collection that had relatively low demand on participants which contributed to consenting to participation. This study design was also affordable, time efficient, and easily repeated.
2. The use of a variety of measures of nutritional status including dietary intake, nutritional biomarkers, body composition measures, and a nutrition focussed physical assessment allowed for a well-rounded analysis of nutritional status, unlike previous research which used less variety.
3. The inclusion of serum 25(OH)D makes this study valuable as few studies have previously assessed the vitamin D status of HEN patients due to the associated cost.

4. The exclusion of terminally ill patients as the goal of feeding for these patients is not to maintain nutritional status.
5. The use of the GLIM criteria makes this study relevant to current dietetics as it is one of the more recent diagnostic tools.
6. This study was the first to report the energy, protein, vitamin D, and selenium status of long-term enterally fed patients in New Zealand. It provides evidence that malnutrition is a nutritional issue in this population.
7. The collection of data about the enteral prescription allowed for analysis of prescription adherence in HEN patients. This study was the first known to the author to do so in New Zealand.

4.2 Limitations

1. The small sample size of 42 participants may have underpowered the study and increased the occurrence of type 2 errors. This may explain why significant differences by feeding route and/or prescription adherence were seldom noted.
2. The complexity of the patient group made some data collection difficult and/or inappropriate. Involuntary movement, inaccessible veins, and being wheelchair bound contributed to reduced sample sizes for nutritional biochemical markers, body composition assessment despite using equipment suitable for in-bed assessment, and nutrition focused physical assessment which meant the findings may not have been representative.
3. The study had low ethnic diversity, largely consisting of European participants. This may have been due to the recruitment technique required by the ethics committee – cold calling rather than recruiting through the trusted dietitian. This participant group rely on their medical team for guidance on these decisions and thus refused to participate. When we indicated that they could discuss the study with their dietitian, some were willing to do so and participate.
4. Participant's energy and protein requirements as calculated by their dietitian were not recorded which meant that the Oxford equation (Henry, 2005) with a disease factor of 1.2 and a protein requirement of 1 g/kg/d were applied to all participants to allow for assessment. This may have resulted in over or underestimation of requirements because of the variance in energy requirements that occurs with different conditions and therefore, inaccurate prevalence of inadequate intake.
5. The heterogeneity of the population limited the ability to make inferences about nutritional status for specific conditions as they had varying nutritional requirements and challenges.

6. The cross-sectional study design only captures one point in time so data may be influenced by recent changes and not be representative of what occurred in the population long term.

4.3 Final recommendations

4.3.1 Impact

The study's findings will make an important contribution to understanding the nutritional status (energy, protein, vitamin D, and selenium) of long-term HEN patients both in New Zealand, as it is the first study to do so, and globally. The nutritional status of these patients must be understood for clinicians to know where and how to focus their nutritional care. The findings of this study may promote changes to feeding and nutrient monitoring practices. Changes to HEN care due to the findings of this research have potential to improve and prevent the development of compromised nutritional status in HEN patients. Prevention of malnutrition and maintenance of selenium and vitamin D status may reduce the risk of morbidity and mortality in HEN patients, contributing to their quality of life and reduced burden on already overworked healthcare systems.

4.3.2 Recommendations

The following recommendations should be considered for the development of the home enteral nutrition service in New Zealand:

1. Increase the use of nutrition focussed physical assessment and the GLIM criteria as part of routine dietetic assessment to monitor energy and protein status of HEN patients.
2. Consider higher energy prescriptions and use individualised predictive equations to increase accuracy of calculations for different conditions and prevent underestimation of energy requirements and malnutrition.
3. Document energy and protein requirements calculated at each consult so they can be adjusted in future appointments according to disease progression, weight change, or physical evidence of fat and muscle wasting.
4. At this time, is not recommended to provide vitamin D supplementation to all patients aged ≥70 years old. However, their vitamin D status should be monitored through either intake or serum 25(OH)D concentration and supplemented as appropriate. Encouragement of sunlight exposure as practical for elderly patients is also recommended.

The following recommendations should be considered for future research investigating the energy, protein, vitamin D, and selenium status of long-term enterally fed patients in New Zealand:

1. Replicate this study in other selected Te Whatu Ora regions including the South Island to add to the current data and increase the sample size before re-analysing the data. This would strengthen the results and increase the representativeness of New Zealand HEN patients.
2. Future research should consider recruitment of a more ethnically diverse population as feeding practices may differ for cultural reasons.
3. With a larger sample size, it is recommended to segment the data into homogenous disease conditions prior to analysing nutritional status.
4. With a larger sample size, it is recommended to run sensitivity and specificity statistics to determine markers that identify risk of malnutrition in HEN patients and are practical for use by dietitians.
5. Mid arm muscle circumference should be measured with a tape measure rather than estimated from bioelectrical impedance analysis to increase accuracy of the measure.
6. The energy and protein requirements as calculated by the participants dietitian should be obtained to increase understanding of adequacy of intake.
7. Include other diagnostic tools such as the patient generated subjective global assessment to identify prevalence of malnutrition in comparison to the GLIM criteria.

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Appendix A: Participant information sheet

Participant Information Sheet

HELP (Home EnteraL nutrition Performance) Study

Kia ora,

As a patient receiving home enteral nutrition (HEN), you are invited to take part in a research study titled "**The health, wellbeing and nutritional outcomes of long-term enterally fed patients"**. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve.

WHAT IS THIS RESEARCH ABOUT?

The number of patients receiving home enteral feeding has increased considerably in recent years. It is now estimated that the number of patients receiving enteral feeding at home is increasingly higher than in hospitals.

Patients receiving home enteral nutrition may receive adequate nutrients from the feed. However, it has been shown that the nutrients in these feeds may be digested and absorbed differently than those found in whole foods. Therefore, nutrient deficiency may develop over time, leading to physical signs and symptoms associated with not having enough of a particular nutrient or a combination of them e.g., anaemia and poor wound healing due to not enough iron and zinc. It is in our best interest to know when such deficiencies may develop, and when to test for insufficiency. Therefore, we want to investigate the timeframe of developing deficiencies.

The aim of this study is to investigate the nutrition status, quality of life, care, health, and wellbeing of long-term enterally fed patients older than 18 years in CM Health.

Thus, the findings of this study can assist in determining guidelines for timely micronutrient monitoring, and potential micronutrient replacement could be established depending on the results.

Who are we looking for?

We are looking for men and women to participate in this study. To take part in this study, you need to be:

- adults ≥18 years old,
- using percutaneous endoscopic gastrostomy (PEG), percutaneous endoscopic jejunostomy (PEJ); nasojejunal tube (NJT), or jejunostomy tube (JJ),
- on this feeding regime for longer than four weeks,
- able to give a blood sample.

What is involved in the study?

If you meet the above eligibility criteria, you will be invited to participate in the study. The study will be explained to you, and the Participant Information Sheet will be provided to you to review. When you decide to participate, a visit from the researcher at your location of choice (which will take about an hour and 30 minutes) will be organised.

At the initial (first) appointment, you can first ask any questions you may have about the study. Next, you will be asked to sign a consent form for participating in the study and complete a demographic questionnaire.

During this initial visit, we will ask you to:

- Participate in a 24-hour diet recall interview.
- Complete a physical sign and symptoms examination.
- Complete electronic questionnaires about Quality of Life, HEN satisfaction, Comorbidities, and Patient experiences with assistance from the researcher including some questions on your HEN experience.
- A blood sample will be taken from a vein in your arm by a trained person (a phlebotomist) – this may happen on the same day or we will organise a suitable time for you. We will use the blood sample to measure trace element nutrients (iron studies, zinc, copper, selenium), vitamins (vitamin B12, folate, vitamin D), markers of inflammation (C-reactive protein, albumin), and a Full Blood Count. There will be no requirements for fasting before the event.

After the initial appointment, we will ask you to:

- Participate in another four 24-hour diet recalls with the researcher, but this time over the phone, which we will organise at a time that suits you. It will include some week and weekend days. It will take about 15-30 minutes per phone interview. The last 24-h recall interview will also include a few short questions on the presence of other long-term conditions.

What are the benefits of taking part in this study?

There will be no charges made for any of the tests that you undertake. Taking part in this study will help to find out if you have any micronutrient deficiencies. This is also an opportunity for you to tell us about your journey in receiving HEN. Your insights will hopefully lead to further studies and may influence the optimal care of HEN patients. In recognition of your participation, you will receive a $50 supermarket or petrol voucher at the end of the study.

You will also receive a brief report summarising the main findings of the project via mail or e-mail after analysis of the data has been completed. If any of your blood results are outside normal parameters you will be advised to talk to your medical practitioner or at your request, we can send your results directly to them to ensure that you receive the required treatment.

What are the risks of taking part in this study?

There are no risks involved in taking part. Some people may fear having a blood sample taken or experience discomfort when the blood sample is taken. Occasionally, a slight bruise may result. We will take every measure to ensure you are comfortable and respected. You may also be accompanied by a support person if required.

Sample Handling and Storage

Samples will be stored in a secure laboratory freezer at the Human Nutrition Research Unit until completion of the study for a maximum of 10 years. Samples will be analysed by fully accredited laboratories in NZ. The data will be used only for the purposes of this project, and no individual will be identified. Only the investigators and administrators of the study will have access to personal information, and this will be kept secure and strictly confidential. Participants will be identified only by a study identification number to ensure anonymity and confidentiality of these samples. After analysis, any additional blood will be destroyed following usual procedures. However, if you prefer to rather have your blood samples, it can be returned to you if you request it.

Additionally, there may be participants who identify as Māori and if specific concerns develop, the support of Dr Bevan Erueti (Taranaki, Te Ati Haunui-ā-Papārangi, Ngāti Tūwharetoa), Associate Dean Māori, will be afforded. Dr Erueti has expressed that he is happy to act in the capacity of advisor and if required will assist and facilitate the project's

Māori agenda and ensure that relational aspects of trust and appreciation are upheld with Māori participants. We are also cognisant that a diversity of beliefs and cultural concerns regarding the removal, storage and transport of tissue samples exists, and because of this, it would be more appropriate to discuss this with your whānau (family) and/or seek take advisement from hapū and iwi leaders. Nonetheless, the right to decline or withdraw from the study can be done at any stage of the project.

Data Handling

The results of the study may be published in journals, presented at conferences or at other professional forums. No individual will be able to be identified. At the end of this study, the list of participants and their study identification numbers will be disposed. Any raw data on which the results of the project depend will be retained in secure storage for 10 years, after which it will be destroyed. Results of the study will be provided to you if you wish.

Who is funding the research?

The research is funded by the Massey University Research Fund, and the CM Health TUPU Research Fund - "MAATAATUPU" Fund for new or emerging researchers.

Participant's rights

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- Withdraw from the study at any time,
- Decline to answer any particular questions,
- Ask any questions about the study at any time during participation,
- Provide information on the understanding that your name will not be used unless you give permission to the researcher,
- Be given access to a summary of the project findings when it is concluded.

Withdrawing from the study, should you choose to do so, will not result in any disadvantage to you.

Project contacts

If you have any further questions or concerns about the project, either now or in the future, please contact the research team.

The researchers for this study include:

Marcos Mantovani, MSc candidate; Phone: [redacted]; Email: m.mantovani@massey.ac.nz

and

Sally Pattison, MSc candidate; Email: S.Pattison@Massey.ac.nz

The lead researchers for this study are Professor Rozanne Kruger and Mr Andrew Xia.

If you have any concerns, please contact Rozanne at r.kruger@massey.ac.nz; phone +649 213 6661 or Andrew at Andrew.xia@middlemore.co.nz; +64 21 510 941.

Committee approval statement

This project has been reviewed and approved by the Massey University Human Ethics Committee: Southern A, application 22/20. If you have any concerns about the conduct of this research, please contact Dr Negar Partow, Chair, Massey University Human Ethics Committee: Southern A, telephone: 04 801 5799 x 63363, email: humanethicssoutha@massey.ac.nz*.*

The Counties Manukau Health Research Committee has also reviewed and approved this project: Application _/_.

Appendix B: Supplementary results

Table 16. Nutrition composition of feeds used by participants.

Feed	Energy (kcal) per 100 mL	Protein (g) per 100 mL	Selenium () per 100 mL	Vitamin D () per 100 mL
Abbott Nutrition Ensure TwoCal HN	200	8.4	9	1.7
Nutricia Nutrison Energy Multifibre	154	6	8.6	1.5
Nutricia Fortisip Chocolate	150	6	8.6	1.1
Nutricia Fortisip Vanilla	150	6	8.6	1.1
Nutricia Fortisip Multi Fibre Vanilla	150	6	8.6	1.1
Nutricia Fortisip Multi Fibre Strawberry	150	6	8.6	1.1
Nutricia Fortisip Multi Fibre Chocolate	150	6	8.6	1.1
Abbott Nutrition Ensure Plus HN RTH	150	6.3	7	1
Nutricia Nutrison 800 Complete Multi Fibre	83	5.5	8.5	2
Abbott Nutrition Jevity RTH	106	4	5.3	0.75
Abbott Nutrition Jevity HiCal	153	6.4	7.6	1
Nutricia Nutrison Multi Fibre	103	4	5.7	1
Abbott Nutrition Ensure Plus Can	150	5.5	7.6	1.05
Nutricia Nutrison Advanced Diason	104	4.3	7.5	0.67
Nutricia Nutrison Energy	150	6	8.6	1.5

Appendix C: Nutrition focused physical examination form.

Standard Operating procedure: Nutrition Focused Physical Examination

No.	Main Operating Steps	Rationale
1	Ensure you and the patient is wearing an appropriate mask covering and that hands are clean and well sanitized.	To protect yourself and the patient from contagious viruses and diseases.
2	Greet the patient and introduce yourself i.e., NZRD, student, nurse, etc.	Helps to build a good rapport with the patient and ease the assessment.
3	Confirm patient name, date of birth and study number.	Prevents examining the incorrect patient.
4	Explain what the examination is and why it's being conducted.	To inform the patients on the procedures i.e., I'm examining you to check for signs of deficiency or malnutrition.
5	Consent from the patient: • Ask for the patient's consent before initiating any type of examination and touching the patient. For example, ask: Is it okay if I touch you to feel your muscle resistance?	The patient has the right to make an informed choice about their care and, in most instances, and must give permission to proceed with the examination.
6	Offer a chaperone or ask for a family member to be present during the whole physical examination.	For safety of the interviewer and patient: to help protect and enhance the patient's comfort, safety, privacy, security, and/or dignity during sensitive examinations or procedures.
7	Ask patient if they have any questions or concerns.	Allow the interviewer to qualify any questions and concerns.
8	Initiate examination: 1. Begin examination from the head and move down the body towards the lower body. 2. Only examine the next part of the body after you have completed the part that you are at. 3. Ensure you use the Score Rating "well nourished", "mild/moderate", "severe". 4. Read each the NFPE finding's description carefully, and utilise the IMAGES provided to assist the examination. 5. Stop physical examination if patient says "NO" or "STOP" (before or during examination). 6. Complete the examination and thank the patient for their time. Additional comments: • Make necessary notes. • Respect patient's decision change. • Show gratitude for the patients' time.	

Nutrition focused physical examination: Macronutrients.

Name of interviewer: _____ Date:_____ Time:_____

Qualification (Student, NZRD, Nurse etc.):_____

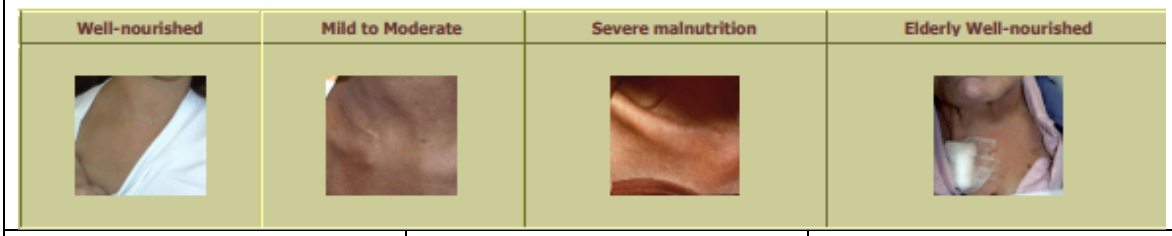
Patient study number:_____

Region	Muscle/fat	Rating (well-nourished, mild/moderate, or severe)
Temple	Muscle	

Temple - Look for the muscle at the temple. Look full at the patient and look for scooping at the temple. You can feel the muscle if you put your finger on the muscle and have the patient open and shut their teeth or clench.

Clavicle	Muscle	

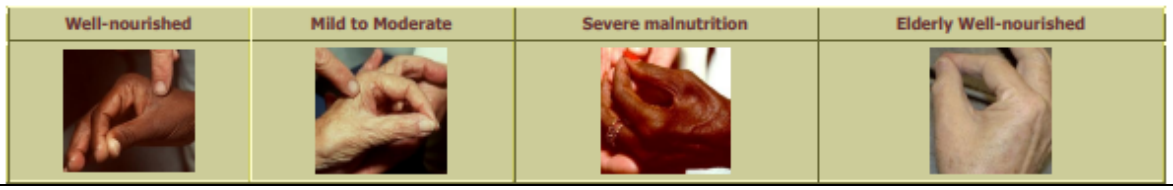
Clavicle - Clavicle in nourished women should show slightly, in men it should not be visible. More prominence = more wasting.



Deltoid/shoulder	Muscle	

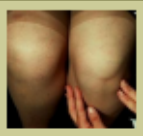
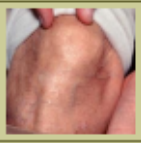
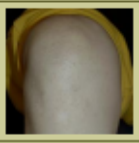
Interosseous	Muscle	

Interosseous Muscle - Interosseous muscle should be flat or bulged when thumb/forefinger are put together. Scooping indicates loss of muscle tissues



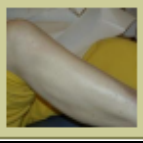
Patella/quadricep	Muscle	

Knee/Thigh - The knee should be covered with muscle and rounded without the appearance of prominent bone. Check with the patient about what is "normal" for him/her. Support the leg so that the thigh is not resting on the chair seat. Look for smooth, rounded appearance. When the thigh muscle is wasted, there is often a distinct line between muscle and fat/skin from the knee to the groin.

Well-nourished	Mild to Moderate	Severe malnutrition	Elderly Well-nourished
			

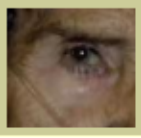
Calf	Muscle	

Thigh/Calf - Lower body changes develop more slowly. If wasting has taken place, may see a distinct line between knee and groin where muscle and fat seem to separate. Knee, calf should be well covered with muscle, not prominent bone.

Well-nourished	Mild to Moderate	Severe malnutrition	Elderly Well-nourished
			

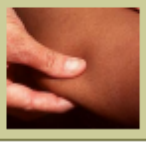
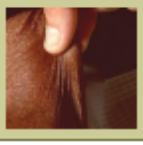
Orbital eye pad	Fat	

Eye - Look at the fat pad under the eye. Look for dark circles that indicate fat loss. Beware of the patient who carries excess fluid under the eye. If questionable, move to triceps and biceps to check fat stores.

Well-nourished	Mild to Moderate	Severe malnutrition	Elderly Well-nourished
			

Triceps	Fat	

Triceps - Triceps, again, should have fat layer between pinch. Continually ask the patient what changes they have seen and evaluate based on reported weight change.

Well-nourished	Mild to Moderate	Severe malnutrition	Elderly Well-nourished
			

Appendix D: Bioelectrical impedance analysis SOP

1. Ask the patient for consent to proceed with the BIA.
2. Ask the patient if they have a pacemaker. Do not perform the BIA if they answer yes.
3. Connect the electrode cables to the InBody S10. Connect electrodes of RA (Right Arm), LA (Left Arm), RL (Right Leg), LL (Left Leg) to each corresponding part of the InBody S10. Red to red, black to black.
4. For seated posture, maintain a straight position with their back not touching the chair. Arms should be lowered in a natural position, not touching their trunk. Thighs should be separated with knees shoulder width apart and legs spread to the front and do not maintain a 90-degree angle.
5. For lying posture, ensure the patient's arms are not touching their trunk and legs are separated so thighs are not touching.
6. Connect electrodes to the patient: LA connects to left arm and RA connects to right arm, electrode marked THUMB for the thumb and MIDDLE for the middle finger. LL connects to left leg and RL connects to right leg, positioned between anklebone and heel, part marked in red should be positioned on the inner ankle.
7. Connect the adapter cable to the power input port.
8. Turn BIA on.
9. Select "touch type" on the BIA.
10. Select "lying posture" for patients who are lying down or "seated posture" for patients who are sitting down.
11. Enter personal information as appropriate (ID, weight, height, age, gender).
12. Press "enter" to start the test.
13. Results will automatically save.

Appendix E: 24-hour recall form and SOP

Standard Operating Procedure

Operation: 24-hour Diet Recall Interview

The 24h diet recall interview is expected to take 20 to 30 minutes to complete, depending on the different amount of food consumed each day.

Follow the steps below for the in-person and phone interview. The SOP will help maintain the same standard method of collecting the 24-h diet recall for each patient.

Prior to the interview ensure the operational steps are followed:

1. Interviewer and patient must wear a face mask at all the time during interview, and have hands clean and sanitized with alcohol gel.
2. Greet the patient and Introduce yourself i.e., NZRD, student, nurse, etc.
3. Confirm patient name, date of birth and study number.
4. Explain what the interview is and why it's being conducted.
5. Ask for consent to begin interview.
6. Stop interview if patient says "NO" or ask to "STOP" (before or during interview).
7. Complete the examination and thank the patient for their time.

The 24-hour diet and enteral feeding recall will be collected in three phases:

1. A quick list of foods eaten, drunk and enteral feeding.

- Begin asking the subjects to recall and describe all the foods, drinks consumed and enteral feeding (including flushes) in the previous 24 hours, from waking to sleeping or from midnight to midnight. At the end of the recall, ask patient to report additional item not initially recalled.

2. Collection of detailed information concerning the items in the quick list.

❖ For each item of food, drink and enteral feeding ask participants to provide additional details.

1. The time at which the food and drink was consumed, including all meals, snacks, drinks, "nibbles", sweets etc.
2. A full description of the food or drink, including brand name where available.
3. Any foods likely to be eaten in combination e.g. milk in coffee
4. Recipes and other combinations of foods e.g. sandwiches
5. The quantity consumed, portion sizes of foods based on participants measure e.g., 6 tablespoons, 1cup, 1slice, etc.
6. Any leftovers or second helpings

3. Participants are given an opportunity to provide additional information and for the interviewer to prompt for information about foods or drink not mentioned.

- Interviewer reviews all the food eaten and drunk in chronological order, clarifies any uncertainty regarding type of food eaten or portion size.
- Asks the participant to name the place where each food or drink item was consumed.
- Record all of the information gathered on the 24-h diet recall sheet provided.

Detailed information concerning Enteral Feeding Prescription:

❖ Recall the following information about the patient's daily enteral feeding routine (complete in *ENTERAL FEEDING PRESCTION* section).

1. Enteral formula e.g., Nutrison 1.5kcal
2. Enteral access/delivery site e.g., Gastrostomy (PEG)
3. Method of administration e.g., Pump-assisted, gravity-assisted, bolus (syringe)
4. Administration rate e.g., 800mL (mL feeding), 12h (feeding over), 1 time/day (times daily)
5. Flushes e.g., 50mL water, before and after each feeding, and other times as instructed.

24-HOUR DIET RECALL (oral and enteral feeding routine)

Name of interviewer: _____Date:_____ Time:_____

Qualification (Student, NZRD, Nurse etc.):_____

Patient study #number: _____

DAY OF THE WEEK/WEEKEND: _____

Time	Food, beverage consumed, Supplements and Enteral Nutrition	Quantity/Amount consumed	Method of preparation, Brand name, Delivery site	Comments

Time	Food, beverage consumed, Supplements and Enteral Nutrition	Quantity/Amount consumed	Method of preparation, Brand name, Delivery site	Comments

ENTERAL FEEDING PRESCRIPTION
ENTERAL NUTRITION FORMULA:
DELIVERY SITE (ROUTE AND ACCESS):
METHOD OF ADMINISTRATION (METHOD AND RATE): mL feeding_____over_____min_____times daily_____
Amount of Water Taken/Flush feeding tube: mL of water_____times daily_____
Other/Comments:

Appendix F: FoodWorks10 analysis SOP

General process:

- Enter as a 5-day food record*
- General tab:
    - Make name participant ID.
    - Complete age/gender/weight/height
    - In description, write “entered by…”
    - In description, enter any other relevant notes from the file.
- Foods tab:
    - Enter date food was consumed (DAY column)
    - Enter time food was consumed in 24-hour time (MEAL column)
    - Enter food or drink (FOOD column).
    - Enter quantity (QUANTITY column). Where possible use ml/g.
    - Record route of intake in NOTES column.
    - Record any other information in NOTES column.
- Record anything that is not immediately obvious or clear in a shared file to go through later.
- If the time is not clear/ cannot be assumed, put 0000.
- For continuous feeds, enter total day volume at feed start time. Enter the flushes at times specified.
- If no flavour of ONS specified, check photos to see if you can identify flavour. If none specified or is via tube only – pick vanilla.
- For water flushes, enter these as consumed (before/after or both)
- In Foodworks spreadsheet note the date, person and completion status.