A Longitudinal Study of Factors that Impact on the Quality of Life of Intestinal Failure Patients treated with Home Parenteral Nutrition

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A thesis submitted to Newcastle University in fulfilment of the requirements for the degree of Doctor of Philosophy
Date of Submission: June 2025

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Abstract

Background: Home parenteral nutrition (HPN) is a lifesaving therapy for patients with intestinal failure, aiming to improve survival and quality of life (QoL). However, patients often experience burdensome symptoms including fatigue, pain, gastrointestinal discomfort, and social isolation. Complications such as intestinal failure-associated liver disease and multi-morbidity further compromise QoL. This project investigated the impact of HPN on QoL and explored the role of nutritional status and liver function.

Methods: A multi-phase study was conducted, including a systematic review, national survey of healthcare professionals (HCPs), and a prospective longitudinal cohort study of adults on HPN across three centres. The primary outcome was change in QoL scores over 12 months. Secondary outcomes included the influence of liver function, nutrition, parenteral nutrition (PN) composition, and muscle function on QoL.

Results: The systematic review identified limited high-quality evidence to guide nutrient provision in adult HPN. The HCP survey revealed inconsistent use of QoL tools and limited integration of Patient Reported Outcome Measures (PROMs). In the longitudinal study (n = 199 at baseline; n = 145 at follow-up), QoL remained significantly impaired, particularly in physical and functional domains. Sociodemographic factors such as employment and higher education were consistently associated with better outcomes across EQ-5D, SF-36, and HPN-QoL scores. Employment was associated with improved general health and EQ-5D VAS (β = 10.8, p = 0.001; β = 12.5, p = 0.005). Handgrip strength was linked to reduced fatigue (β = –1.2, p = 0.004), while skeletal muscle mass predicted improved physical functioning (β = 1.66, p = 0.014). Phase angle was associated with lower immobility scores and higher emotional functioning (β = –9.2, p = 0.100; β = 7.5, p = 0.024).

Conclusion: QoL in HPN is shaped by a complex interplay of nutritional, clinical, and psychosocial factors. PROMs should be integrated into routine care to support multidisciplinary, patient-centred service development.

Declaration

I declare that this thesis is an original report of my research, has been written by me and has not been submitted for any other degree or professional qualification. The contribution of me and my co-authors to the parts of the thesis that have been published, have been acknowledged, and indicated clearly.

Acknowledgements

Firstly, I would like to acknowledge the generous support of the National Institute for Health and Care Research (NIHR) and NIHR Newcastle Biomedical Research Centre (BRC), who funded this research (grant number 301258).

To my supervisors, Professors Dave Jones, John Mathers, Mark Pearce and Dr Nick Thompson – I am truly grateful. I have learned so much from working alongside you and have greatly valued your encouragement, insight, and expertise throughout the past five years. This PhD would not have been possible without your guidance and support.
I would also like to extend my sincere thanks to my collaborators—Dr Martyn Dibb, Dr Peter Mooney, Professor Julian Griffin, Professor Chris Lamb, and Dr Chris Stewart—for your invaluable input. I really appreciate your patience, especially when answering my many (often confused) questions.

To my fantastic colleagues at the Freeman Hospital, including the nutrition team, phlebotomy and clinic staff, dietitians, and secretaries, thank you for your kindness, enthusiasm, and practical support. I'm especially grateful for your flexibility with sample collection, postal logistics, patient queries, and for being so supportive of my academic journey.

To each and every patient who took part in my studies - thank you for your time, openness, and contribution to this research.

To my family and friends, thank you for your constant encouragement and belief in me. A special thanks to my husband Jonny, my partner in life and unofficial IT support! Your unwavering support over the past five years has meant everything. Thank you for taking over childcare so I could spend all hours writing, and for flying solo across the Atlantic with a three-year-old so I could work in Chicago! I couldn't have done this without you.

Co-author contributions

Chater 2: The Effects of Different Parenteral Nutrition Lipid Formulations on Clinical and Laboratory Endpoints in Patients Receiving Home Parenteral Nutrition: A systematic review.

Study conception and design	Colette Kirk (CK), Professor John Mathers (JCM), Professor Mark Pearce (MP), Professor Dave E Jones (DEJ), Dr Nick Thompson (NT). Fiona Beyer and Hannah O'Keefe helped to formulate the protocol and search strategy.
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Analysis and interpretation of data	CK synthesised narratively.
Drafting of chapter	CK.
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Chapter 3: Quality of Life and Home Parenteral Nutrition: A Survey of UK Healthcare Professionals' Knowledge, Practice and Opinions

Study conception and design	Colette Kirk (CK) with the assistance of JCM, MP, DEJ, and NT.
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Chapter 4: Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition: Protocol for a multicentre, longitudinal observational study

Study conception and design	CK, JCM, MP, DEJ, and NT.
Acquisition of data	Not applicable.
Analysis and interpretation of data	Not applicable.
Drafting of chapter	CK.
Critical revision	JCM, MP, DEJ, NT.

Chapter 5: Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition: Results

Study conception and design	CK, JCM, MP, DEJ, and NT.
Acquisition of data	CK.
Analysis and interpretation of data	CK with the assistance of JCM, MP, DEJ, NT and Aidan Mullins who supported the Linear Principal Component Analysis.
Drafting of chapter	CK.
Critical revision	JCM, MP, DEJ, NT.

Publications and presentations arising from this thesis

Peer reviewed journal articles:

1. **Kirk C,** Mathers J, Pearce M*, et al.* Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition: protocol for a multicentre, longitudinal observational study. *BMJ Open* 2024;14:e082163. doi: 10.1136/bmjopen-2023-082163
2. **Kirk C,** Pearce MS, Mathers JC, Thompson NP, Gemmell L, and Jones DE. Quality of Life and Home Parenteral Nutrition: A Survey of UK Healthcare Professionals' Knowledge, Practice and Opinions. 2022. *J Hum Nutr Diet.*
3. **Kirk C,** Haigh L, Thompson NP, Pearce M, Jones DE, and Mathers JC. The effects of different parenteral nutrition lipid formulations on clinical and laboratory endpoints in patients receiving home parenteral nutrition: A systematic review. 2022. *Clinical Nutrition;* 41(1):80-90.
4. Haigh L, **Kirk C,** Gallacher J, Errington L, Mathers J and Anstee Q. The effectiveness of Mediterranean diet versus calorie restriction in non-alcoholic fatty liver disease (NAFLD): a systematic review with clinical implications. 2020. *Journal of Hepatology.* 73:S450. DOI: 10.1016/S0168-8278(20)31382-9

Conference abstracts (posters presentations):

1. **Kirk C,** Mathers J, Pearce M, *et al.* Body composition in adults with chronic intestinal failure. Poster presentation, Congress of Intestinal Rehabilitation and Transplantation, 2025, Gothenburg, Sweden.
2. **Kirk C,** Mathers J, Pearce M, *et al.* Hand grip strength is associated with impaired quality of life in patients on home parenteral nutrition. Poster presentation, BAPEN annual conference 2024, Newcastle upon Tyne.
3. **Kirk C,** Pearce M, Mathers J, *et al*. Assessment of health-related quality of life and health utility in patients on home parenteral nutrition. Poster presentation, BAPEN annual conference 2023, Edinburgh.
4. **Kirk C,** Pearce M, Mathers J, *et al.* A cross-sectional study of quality of life of adult patients treated with home parenteral nutrition in North-East England and Cumbria. Poster presentation, BAPEN annual conference 2023, Edinburgh.

5. **Kirk C,** Pearce M, Mathers J, *et al.* Quality of Life and Home Parenteral Nutrition: A Survey of Healthcare Professionals' Knowledge, Practice and Opinions. Poster presentation, BAPEN annual conference 2022, Brighton.
6. **Kirk C,** Pearce M, Mathers J, *et al.* Quality of Life and Home Parenteral Nutrition: A Survey of Healthcare Professionals' Knowledge, Practice and Opinions. Poster presentation, ESPEN Congress 2022, Vienna.
7. **Kirk C,** Haigh L, Thompson NP, Pearce M, Jones DE, and Mathers JC. The effects of different parenteral nutrition lipid formulations on clinical and laboratory endpoints in patients receiving home parenteral nutrition: A systematic review. 2022. *Clinical Nutrition ESPEN;* 48:486.
8. Gemmell L, Hankins C, Leeds J, **Kirk C,** Thompson N, Leyland H, and Mountford C. Longitudinal analysis of quality of life of patients on home parenteral nutrition at a regional centre. 2022. *Clinical Nutrition ESPEN*; 48:501.
5. Gemmell L, Hankins C, Leeds J, **Kirk C,** Thompson N, Leyland H, and Mountford C. Quality of life of patients on home parenteral nutrition at a regional centre. 2022. *Clinical Nutrition ESPEN;* 48:505-506.

Oral presentations (invited speaker):

1. BAPEN annual conference, November 2024:
    a. Symposium: Insights from our future leaders.
    b. Title: Research reflections: Growing through the challenges
2. Annual tripartite meeting between Newcastle Hospitals, Southampton General Hospital and Cambridge University Hospitals, November 2023:
    a. Title: Health related quality of life in patients on home parenteral nutrition
3. HNERC annual research day, October 2023:
    a. Title: Health utility & health related quality of life in patients on home parenteral nutrition.
4. HNERC seminar series, August 2022:
    a. Title: Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition

Awards/ prizes:

1. Student recognition of achievement: BAPEN annual conference, November 2024.
2. Runner up: Ella Forster Memorial Award for excellence in nutrition, liver and gastroenterology research. The Freeman Hospital, July 2024.
3. Winner for highly commended poster: Assessment of health-related quality of life and health utility in patients on home parenteral nutrition. BAPEN annual conference, November 2023.
4. Winner for highly commended poster: A cross-sectional study of quality of life of adult patients treated with home parenteral nutrition in North-East England and Cumbria. BAPEN annual conference, November 2023.

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Abbreviations

AA	Amino acid
AAR	Alanine aminotransferase ratio
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ARA	Arachidonic acid
AST	Aspartate aminotransferase
Adj.	Adjusted
BANS	British Artificial Nutrition Survey
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BP	Bodily pain
CI	Confidence interval
CIPO	Chronic intestinal pseudo-obstruction
COPD	Chronic obstructive pulmonary disease
CRBSI	Catheter-related blood stream infections
CRP	C-reactive protein
CV	Cardiovascular
DAG	Directed acyclic graph
DGLA	Di-homo-γ-linolenic acid
DHA	Docosahexaenoic acid
DNL	De novo lipogenesis
DPA	Docosapentaenoic acid
EASL	European Association for the study of liver
ED	Enteric Dysmotility
EDS	Ehlers-Danlos syndrome
EFA	Essential fatty acid
EN	Enteral nutrition
EORTC-QLQ,C30	The EORTC Core Quality of Life questionnaire
EPA	Eicosapentaenoic acid
EQ-5D	Euroqol 5-dimension
ESPEN	European Society of Parenteral and Enteral Nutrition
EWB	Emotional wellbeing
FBC	Full blood count
FFM	Fat free mass
FFMI	Fat free mass index
FIB-4	Fibrosis-4 index
FO	Fish oil
GGT	Gamma-glutamyltransferase
GH	General health
GI	Gastrointestinal
GLA	Gamma-linoleic acid
HADS	Hospital anxiety and depression questionnaire
HCP	Healthcare professional
HDL	High-density lipoprotein
HGS	Handgrip strength

HPN	Home parenteral nutrition
HPN-PROQ	Home parenteral nutrition impact questionnaire
HPS	Home parenteral support
HRQoL	Health-related quality of life
IBD	Inflammatory Bowel Disease
IF	Intestinal failure
IFALD	Intestinal failure associated liver disease
IQR	Inter-quartile range
IVLE	Intravenous lipid emulsions
Itx	Intestinal transplant
LA	Linoleic acid
LCT	Long chain triglycerides
LDL	Low-density lipoprotein
LE	Lipid emulsions
LFT	Liver function test
LRT	Likelihood ratio test
LSM	Liver stiffness measure
LeedsTH	Leeds Teaching Hospitals
MAC	Mid-arm circumference
MAMC	Mid-arm muscle circumference
MCS	Mental component score
MCT	Medium chain triglyceride
MRC	Medical research council
MUFA	Monounsaturated fatty acid
N/A	Not applicable
NHS	National Health Service
NI	No information
NUH	Nottingham University Hospital
NuTH	The Newcastle upon Tyne Hospitals NHS Foundation Trust
OA	Oleic acid
OO	Olive oil
OO-SO	Olive oil soybean oil
OR	Odds ratio
PA	Phase angle
PC	Principal component
PCA	Principal component analysis
PCF	Physical component score
PEMT	Phosphatidylethanolamine N-methytransferase
PF	Physical functioning
PN	Parenteral nutrition
PNIQ	Parenteral nutrition impact questionnaire
PO	Phospholipids
POTS	Postural tachycardia syndrome
PPIE	Patient and public involvement and engagement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	Prospective Register of Systematic Reviews
PUFA	Polyunsaturated fatty acid

QoL	Quality of life
RCT	Randomised controlled trial
REC	Research Ethics Service
RLEH	Role limitations due to emotional health
RLPH	Role limitations due to physical health
ROBINS-I	Risk of bias in non-randomised studies of interventions
RoB 2.0	Risk of bias for RCTs 2.0
SAE	Serious adverse events
SB	Small bowel
SBO	Small bowel obstruction
SBS	Short bowel syndrome
SBS-QoL	Short bowel syndrome quality of life questionnaire
SD	Standard deviation
SE	Standard errors
SF	Social functioning
SF-36	Short-form 36
SFA	Saturated fatty acid
SMM	Skeletal muscle mass
SMOF	Soybean, medium chain triglycerides, olive oil and fish oil
SO	Soybean oil
TE	Trace elements
TG	Triglyceride
TSF	Tricep skinfold
UK	United Kingdom
USA	United States of America
VAS	Visual analogue scale
VIF	Variance inflation factor
WCC	White cell count
n-3	Omega-3
n-6	Omega-6
y-LA	y-linoleic acid

Chapter 1: General introduction

1.1 Intestinal failure

Intestinal failure (IF) is defined as a reduction in gut function below the minimal necessary for the absorption of macronutrients and/or water and electrolytes, requiring intravenous supplementation (1). There are three subclassifications in relation to time scale, metabolic changes, and outcome. Patients with Type I IF (acute) typically receive parenteral nutrition (PN) short term in hospital (<28 days) for a self-limiting condition; type II IF (prolonged acute) is used when patients are metabolically unstable and receive PN in hospital, or at home, for a period of weeks to months; patients with type III IF (chronic) typically receive PN at home for months to years (2). The focus of this thesis is on Type III IF. Patients experience Type III IF because of four pathophysiological mechanisms:

1. Short bowel syndrome
2. Gastrointestinal fistulae
3. Gastrointestinal dysmotility
4. Gastrointestinal mechanical obstruction

1.1.1 Short bowel syndrome

Short bowel syndrome refers to the physical loss, or loss of function, of a section of small and/or large intestine (3). This may be due to surgical resection of the bowel to treat conditions such as inflammatory bowel disease or ischaemia, or to treat injury or trauma. The resultant altered anatomy means that there is a reduced ability to absorb nutrients and fluids from the gut (malabsorption) (Figure 1.1). Specificity and severity of symptoms vary between individuals but typically include diarrhoea, dehydration, malnutrition, vitamin and mineral deficiency.

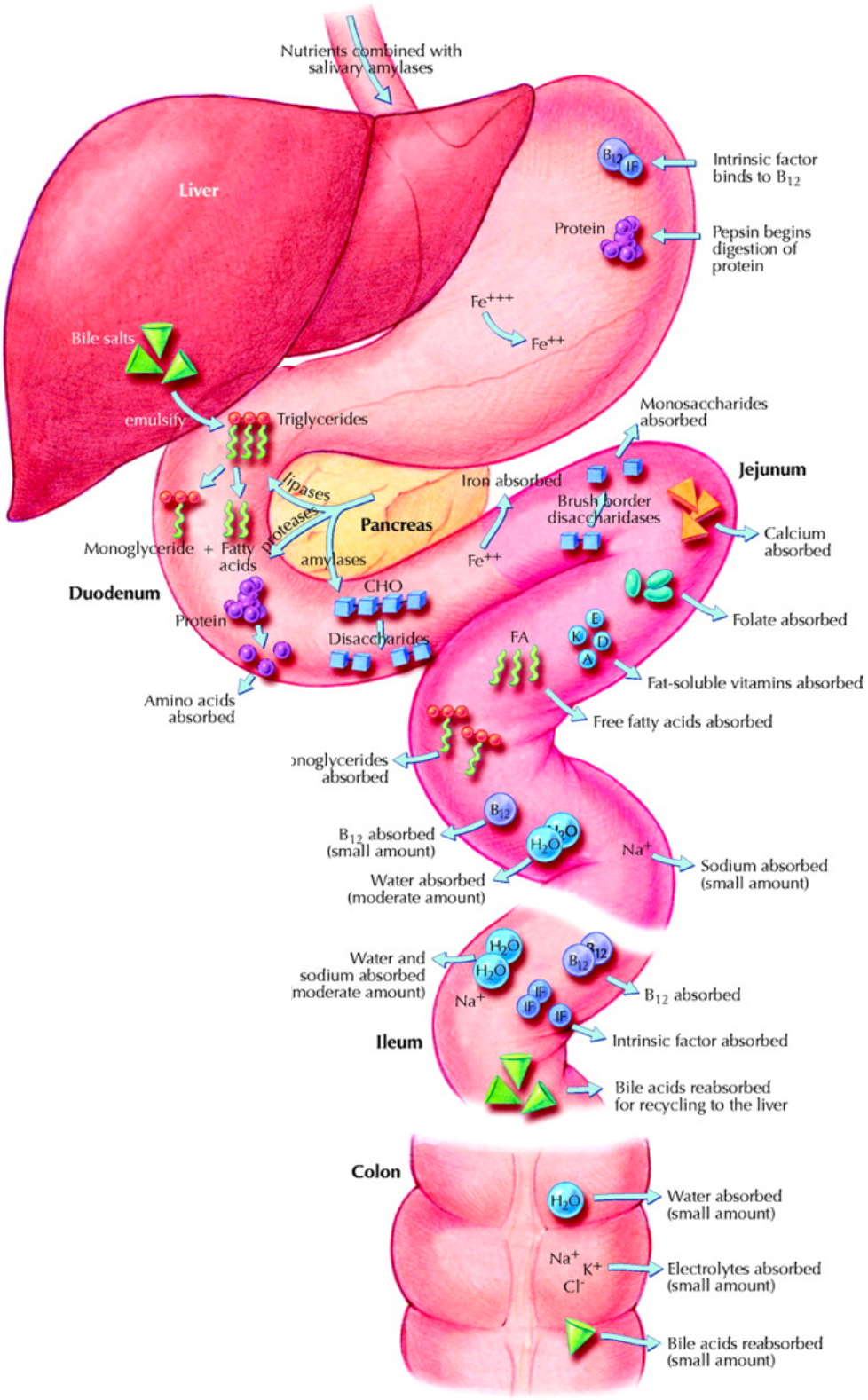


Figure 1.1: The relative locations of digestion and absorption of nutrients in the healthy gastrointestinal tract. Adapted from reference (3).

1.1.2 Gastrointestinal fistulae

A gastrointestinal (GI) fistula is an abnormal connection between the intestine to an adjacent organ or surface, often the skin (enterocutaneous fistula), bladder (enterovesicular fistula), or vagina (recto-vaginal fistula) (3-5). Fistulae are typically complications arising from surgical procedures, diverticular disease, Crohn's disease, malignancy, radiation, or trauma (6).

In the UK, the number of patients referred for HPN due to GI fistula is increasing (7, 8). This trend coincides with an ageing HPN population and a rise in comorbid conditions. Since surgical complications are more prevalent in older adults and represent a major cause of GI fistulae, the demographic shift towards older, more comorbid patients likely contributes to the observed rise in HPN referrals (9).

1.1.3 Gastrointestinal dysmotility

Gastrointestinal (GI) dysmotility occurs when there is a failure of coordinated intestinal peristalsis. Patients experience symptoms of bowel obstruction such as abdominal pain, nausea and vomiting in the absence of a mechanical cause (10). There are three aetiologies of GI dysmotility disorders with many contributing factors (Figure 1.2):

1) Myopathic or chronic intestinal pseudo-obstruction (CIPO) (11). Radiological investigations show features of a dilated bowel without any lumen-occluding lesions. Patients struggle with chronic or recurrent obstructive type symptoms. This may be because of a primary intestinal disease (e.g. hollow visceral myopathy), or a secondary disease (e.g. systemic sclerosis, radiation, muscular dystrophy or dermatomyositis).

2) Neuropathic or enteric dysmotility (ED) (11) is when there is objective evidence of impaired GI peristalsis in the absence of a dilated bowel. This may be secondary to an underlying neurological process (e.g. Parkinson's disease, multiple sclerosis, or Guillain-Barre syndrome), or be a consequence of autonomic failure (e.g. diabetes mellitus).

3) Idiopathic dysmotility (10) is used where the pathological process is unknown. Hypermobile Ehlers-Danlos syndrome (EDS), a genetic disorder of the connective tissue, falls within this category. Many patients with EDS experience visceral hypersensitivity with symptoms mimicking dysmotility, rather than having a true dysmotility. That being said, EDS itself can contribute to dysmotility, particularly in the presence of opiates and postural tachycardia syndrome (PoTS).

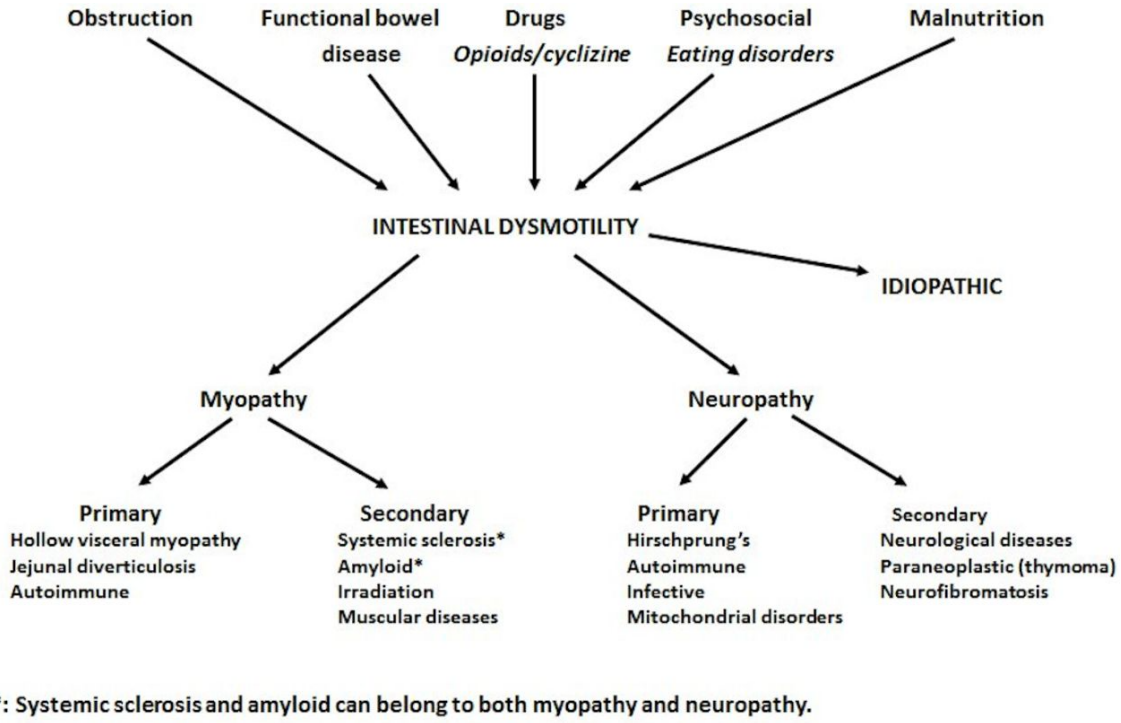


Figure 1.2: Factors contributing to, and sub-classifications of, chronic GI dysmotility. Taken from reference (10)

1.1.4 Gastrointestinal mechanical obstruction

Bowel obstructions occur when the lumen of the intestine becomes partially or completely blocked. This causes the patient to experience abdominal pain, nausea, vomiting, constipation, and abdominal distension. Obstructions of the small intestine are more common than those of the large and are a frequent indication for surgery on the small bowel. GI obstructions can be classified as partial, complete, or closed loop which is when there is complete obstruction distally and proximally in the given segment of bowel. Post-operative adhesions are the most common cause of small bowel obstructions (SBO). Other causes are tumours that compress the bowel, untreated hernias, and intrinsic disease

that cause thickening of the bowel wall, for example Crohn's disease. The bowel wall gradually becomes compromised, and a stricture forms.

1.2 Home parenteral nutrition

The primary life-sustaining treatment for type III IF is home parenteral nutrition (HPN). This refers to the intravenous infusion of macronutrients, micronutrients, fluids and electrolytes (12). It is costly in terms of NHS resources (£55,000 per patient / year) (9) and quality of life (QoL) for patients and poses a considerable challenge for 21st century healthcare.

1.2.1 Prevalence of HPN

Data from the British Artificial Nutrition Survey (BANS) demonstrate that between January 1, 2005 and December 31, 2015, there was a significant increase in the number of new registrations for home parenteral support (HPS) in the UK (7). There are no published data beyond 2015. The majority of new HPN registrations occurred in England (89%), followed by Wales (5%), Scotland (4%), and Northern Ireland (2%) (Figure 1.3) (Figure 1.3).

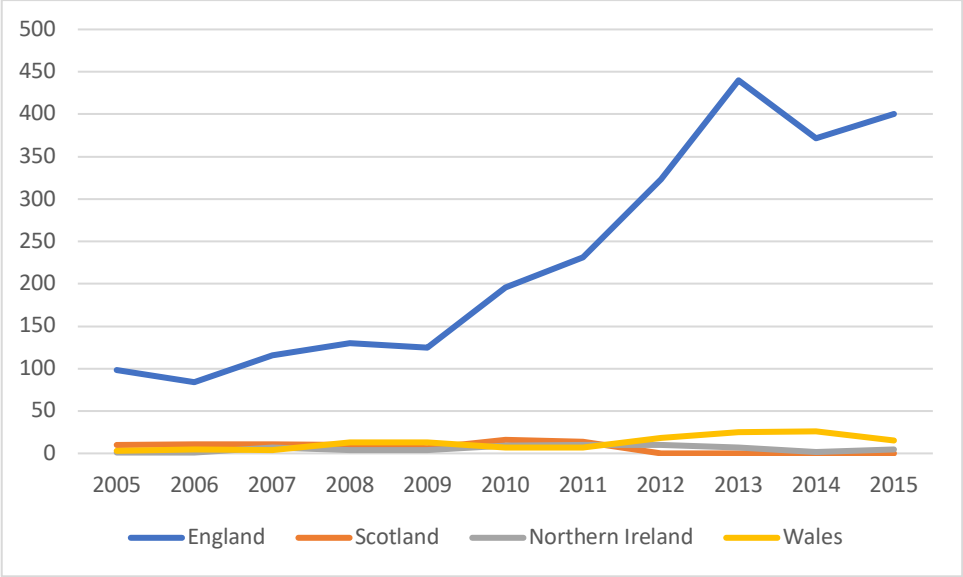


Figure 1.3: New UK HPN registrations by country (7)

The rise in home parenteral support (HPS) prevalence is not unique to the UK, it has also been demonstrated across Europe (Table 1.1). This upward trend may reflect not only increasing clinical need, but also the expansion of HPS services and improved access to specialist care.

Table 1.1: Prevalence (per million of population) of adult HPS, taken from reference (7)

Country	1992	1993	2008	2010	2012	2013	2015	2018	2020	Trend
UK	-	0.8	15.0	-	-	-	36.1	-	-	?
Poland	-	0.2	-	18.0	-	-	-	-	53.0	?
Spain	-	0.3	-	-	-	-	-	5.4	-	?
Italy	-	2.2	-	-	45.0	-	-	-	-	?
France	-	2.2	-	6.0	-	-	-	-	-	?
Belgium	-	2.4	-	11.0	-	-	-	-	-	?
Denmark	-	4.6	-	66.0	-	-	-	-	-	?
New Zealand	-	-	-	7.2	-	-	-	-	-	?
Australia	-	-	-	6.7	-	-	-	-	-	?
Canada	-	-	-	-	12.0	-	-	-	-	-
USA	120.0	-	-	-	-	79.0	-	-	-	?

Abbreviations: UK, United Kingdom; USA, United States of America.

1.2.2 Aims of HPN therapy

Patients are discharged on HPN with the aims of increasing survival, minimising HPN related complications and maximising QoL (13). Whilst there is good evidence that HPN increases survival and that survival is good (88% at year 1 and 64% at year 5 (14)), the remaining aims are more difficult to achieve. Complications are discussed in detail below with potential mechanisms for their development. Studies of QoL in people on HPN are much more challenging. HPN radically changes a person's life not least because it is time-consuming and invasive. Patients struggle with ongoing symptoms of their underlying condition (pain, fatigue, dehydration, gastrointestinal discomfort), live with multiple health problems, and are consequently required to manage a range of drug and lifestyle management regimes. Furthermore, HPN patients have higher rates of depression and anxiety compared with the general population and are unlikely to return to meaningful employment (15). QoL is discussed further in sub-section 1.3.

1.2.3 Complications of HPN

1.2.3.1 Intestinal failure associated liver disease

Intestinal failure associated liver disease (IFALD) remains one of the most serious complications of HPN. It manifests in several ways from steatohepatitis and cholestasis to portal hypertension, cirrhosis and end-stage liver failure. In most cases it is preventable and,

if diagnosed early, reversible. In contrast, rapid progression leads to hepatic failure, followed by the need for a multi-visceral transplant (the simultaneous transplantation of liver, intestine and pancreas) with high morbidity and mortality (16).

1.2.3.1.1 Risk factors for IFALD

The pathogenesis of IFALD is not yet fully understood. There are potentially five primary factors underpinning the molecular pathways responsible for liver injury, and each of these factors is an independent complication of HPN and include: nutrient deficiency (choline, taurine, carnitine, and essential fatty acids), nutrient toxicity (total energy, lipid, glucose, phytosterols, copper, manganese and aluminium), altered intestinal microbiome, altered bile acid metabolism, and catheter-related blood stream infections (CRBSI) (17).

All patients being treated with HPN are at risk of developing IFALD, however, those with ultrashort bowel (<20cm residual length), co-existing liver disease and recurrent CRBSI, are at an increased risk (17). Known risk factors for IFALD are summarised in Table 2 and multiple studies have shown that intestinal anatomy plays a key role. It is not clear, however, whether the length of bowel relates to the dependency on PN, or to physiological factors relating to bowel function. Similarly, the presence of a colon is considered protective and, although not fully understood, it may be the additional absorptive capacity, or the increased microbial products in the portal circulation which are beneficial (17). The link between IFALD and sepsis is possibly mediated by pro-inflammatory cytokines causing systemic inflammation in the liver. The release of these cytokines can cause altered membrane function of the bile canaliculi and reduced bile flow (17). Changes in intrahepatic bile acid synthesis and feedback regulation have also been observed, although this is in the critically ill population rather than the IF population (18). The nutritional composition of the PN solution itself also plays a role. The balance of macronutrients seems key with high glucose infusions leading to steatosis (19), soybean oil based lipid emulsions being associated with IFALD (20-22), and mixed lipid emulsions (soybean, medium chain triglycerides, olive oil and fish oil; SMOF) seeming protective (22, 23). Lastly, there are multiple studies suggesting that choline deficiency is linked with reduced triglyceride transportation from the liver, promoting steatosis (24, 25). Nutrient imbalances are discussed further in section 1.2.3.4.

Table 1.2: Summary of evidence for risk factors in IFALD

Risk factor	Hypothesised link to IFALD	Study type/ patient details	Details/ mechanism
Sepsis (26)	General link between sepsis and cholestasis	100 adult and paediatric in-patients with positive blood cultures	54% had elevated serum total bilirubin levels
Lipid in PN (20, 27)	Absolute amount of parenteral lipid given (soybean) in relation to IFALD development	Prospective cohort study of 90 patients (adults and children)	Multivariable analysis: Parenteral lipid >1g/kg/day associated with a RR of 3.4 for developing complicated liver disease
Lipid in PN (22)	Type of lipid – mixed lipid emulsions lower risk than soybean oil	Short term randomised, double blind study 34 adult patients receiving SMOF lipid vs 39 receiving intralipid	Significantly lower ALT, AST and bilirubin in SMOF group, significantly higher □- tocopherol in SMOF group
Lipid in PN (23)	Fish oil as a component of mixed lipid emulsion may be protective	5 year randomised open label trial of three intravenous lipid emulsions	Significantly lower bilirubin level in SMOF lipid group compared to formulations not containing fish oil
Parenteral energy (27)	Proportion of calories delivered parenterally relates to IFALD risk	113 adults on HPN, of which 24% had biochemical chronic cholestasis (CC)	Higher parenteral calories intake associated with CC (OR 1.2 on multivariable analysis)
Parenteral energy (28)	Influence of enterally vs parenterally delivered calories	29 patients with IBD randomised to isocaloric/isonitrogenous PN or EN	Incidence of deranged LFTs 61.5% in PN group vs 6.2% in EN group
Glucose energy (19)	Fast glucose infusion exceeding glucose oxidation rate leads to steatosis	Patients with burns injuries	>5mg/kg/minute glucose infusion leads to steatosis
Intestinal anatomy (29)	Residual small bowel length relates to IFALD risk	107 adults on HPN	SB length <100cm significantly associated with deranged LFTs on multivariable analysis
Intestinal anatomy (20)	Residual SB length relates to IFALD risk	Prospective cohort study of 90 patients (adults and children)	Multivariable analysis: SB length <50cm associated with Relative risk of 2.1
Intestinal anatomy (27)	Presence of colon protects against IFALD development	113 adults on HPN, of which 24% had biochemical chronic cholestasis (	Colon in continuity protective (OR: 0.2 on multivariable analysis)

Nutrient Deficiencies (24)	Choline deficiency impairs hepatic triglyceride exportation, promoting steatosis	41 adults and children receiving PN	Plasma free choline levels low in >90% of patients receiving HPN and levels correlate with LFT abnormalities
Nutrient Deficiencies (25)	Supplementation of choline improved liver disease	15 adult patients receiving supplemental choline	Radiological improvement in steatosis after treatment, also improved ALT, AST
Nutrient Deficiencies (30)	Lack of taurine reduces bile flow	32 adults receiving taurine-free HPN with 10 subsequently receiving taurine enriched HPN	Reduction in AST following supplementation
Cycling PN (31)	Cyclical vs continuous PN associated with better liver outcomes	Prospective study of 65 patients with varying degrees of cholestasis, half switched from continuous to cyclical PN	Significant improvement in biochemical cholestasis after switching

Abbreviations: IFALD, intestinal failure associated liver disease; SMOF, soybean, medium chain triglycerides, olive oil and fish oil; ALT, alanine transaminase; AST, aspartate aminotransferase; IBD, inflammatory bowel disease; LFTs, liver function tests; PN, parenteral nutrition; EN, enteral nutrition; HPN, home parenteral nutrition; SB, small bowel

The challenge with interpreting the limited evidence highlighted in Table 1.2, is that many of the studies date back to the 1990s, with one study being published in 1979. PN has evolved considerably in the past 30 years with solutions now being safer and more accessible (32). Although there have been advances in enteral feeding techniques and venous access, IFALD remains an issue. This highlights the need to strengthen the evidence base through well-designed, prospective cohort studies and randomised controlled trials with sufficiently large sample sizes to test specific hypotheses.

1.2.3.1.2 How is IFALD defined and diagnosed

There is currently no standardised definition of IFALD. It was formerly called 'parenteral nutrition associated liver disease' before it was recognised that factors beyond the PN solution itself play a role in the pathogenesis of the disease (33). A current European Society of Parenteral and Enteral Nutrition (ESPEN) position paper states that: '*the term IFALD refers to liver injury as a result of one or more factors relating to intestinal failure including, but not limited to, parenteral nutrition and occurring in the absence of another primary parenchymal liver pathology (e.g. viral or autoimmune hepatitis), other hepatotoxic factors (e.g. alcohol/*

medication) or biliary obstruction' (34). Similarly, there are no established consensus criteria to diagnose and classify IFALD. The gold standard method is to perform a liver biopsy (35). However, due to the invasive nature of this procedure, biopsies are not performed routinely and very few data assessing the prevalence of IFALD via this method are available. Consequently, numerous different criteria are used in clinical practice and in the medical literature (Table 1.3).

Table 1.3: Assessment of IFALD according to different diagnostic criteria

Reference	Year of publication	
		IFALD-cholestasis
Cavicchi et al (20)	2000	A value of >1.5 ULN on two of y-GT, ALP and serum conjugated bilirubin >0.3 mg/dL for > 6 months
ConBil criterion (36)	2018	Conjugated bilirubin >0.3 mg/dL for > 6 months
TotBil criterion (36)	2018	Total bilirubin >1 mg/dL and conjugated bilirubin >0.3 mg/dL for >6 months
		IFALD-steatosis
AAR index according to Sorbi et al (37)	1999	AST/ALT ratio <1 when AST and ALT > ULN
US criterion, according to EASL guidelines (38)	2016	Liver ultrasound echogenic appearance of steatosis
		IFALD-fibrosis
APRI index (39)	2016	AST to platelet (PTL) ratio index = [(AST/ULN AST) x 100]/PLT (10^9/L] >0.88
FIB-4 index (40)	2006	Fibrosis-4 index = age (years) x AST)/[PLT (10^9/L) x $ALT^{1/2}$]; advanced fibrosis: >2.67
		IFALD-unclassified
Luman et al (29)	2002	Any deranged LFT >1.5 the ULN after >6 months of HPN starting
Beath et al (41)	2016	ALP and y-GT >1.5 the ULN and US signs of liver steatosis

Abbreviations: IFALD, intestinal failure associated liver disease; ULN, upper limit of normal; y-GT, gamma-glutamyl transferase; ALP, alkaline phosphatase; AAR, alanine aminotransferase ratio; AST, aspartate aminotransferase; ALT, alanine transaminase; EASL, European Association for the Study of Liver; APRI, AST to platelet ratio index; HPN, home parenteral nutrition

Unsurprisingly, the prevalence of IFALD varies greatly depending on which criteria are used. This was elegantly demonstrated by Sasdelli et al (2018) who categorised 113 IF patients according to the 9 different criteria for IFALD outlined in Table 1.3 (42). At study inclusion,

the prevalence of cholestasis ranged from 5-15%; steatosis 17-43%; fibrosis 10-20% and unclassified 7-38% (Table 1.4). Interestingly, upon starting PN, the prevalence of IFALD was higher for cholestasis (13-40%), steatosis (28-90%), and IFALD-unclassified (8-75%), but not for fibrosis (2-5%), demonstrating that in some patients, a positive IFALD diagnosis using the above criteria became negative between starting HPN and study inclusion, suggesting other factors beyond HPN are at play. When comparing the above criteria, steatosis was more prevalent when diagnosed by US criterion, cholestasis by the ConBil criteria, and fibrosis using the FIB-4 index.

Table 1.4: Prevalence of intestinal failure associated liver disease (IFALD) at study inclusion. Taken from reference (42)

IFALD diagnostic criteria	Sample size (n)	Prevalence of IFALD (n (%))
IFALD-cholestasis		
Cavicchi et al (20)	103	8 (8)
ConBil criterion (36)	100	15 (15)
TotBil criterion (36)	100	5 (5)
IFALD-steatosis		
AAR index according to Sorbi et al (37)	111	19 (17)
US criterion, according to EASL guidelines (38)	99	43 (43)
IFALD-fibrosis		
APRI index (39)	112	11 (10)
FIB-4 index (40)	110	22 (20)
IFALD-unclassified		
Luman et al (29)	104	40 (38)
Beath et al (41)	99	7 (7)

This variation in reported IFALD mirrors the wider literature. Cross-sectional studies have reported impaired liver function in 5-85% of patients with the incidence of advanced liver disease ranging from 0-50% (20, 29, 43, 44). Evidently, there is a need for an international consensus definition and classification of IFALD to enable objective comparison between IF centres, nationally and internationally for both clinical and research purposes.

An additional concern with much of the current literature is that clinical and biochemical signs of liver dysfunction do not always correlate with the histologic severity of liver disease and therefore findings should always be interpreted with caution. Kalish et al investigated

this further by performing lipidomics on animal models (45). Lipidomic profiling provides a comprehensive picture of lipid metabolism, offering the opportunity to predict and monitor responsiveness to HPN treatment, and therefore study how the components of the HPN solution contribute to liver disease. As expected, the authors found that PN solutions high in carbohydrate with no lipid induced de novo fatty acid synthesis resulting in profound hepatic steatosis. Carbohydrate solutions with soybean oil-based lipid were associated with macro and micro-vesicular hepatic steatosis and carbohydrate solutions containing fish oil-based lipid prevented the development of steatosis (45). The challenge is to understand these same metabolic pathways in HPN patients, and how the resultant liver disease impacts QoL.

1.2.3.2 Sepsis

Catheter-related blood stream infections (CRBSI) are the most common complication of HPN and often lead to further complications such as thrombosis, endocarditis, septic emboli, and even death (45-48). Patients typically present with fever, rigors and general malaise. The reported incidence in the UK varies between 0.21 and 0.51 episodes per 1000 catheter days (49, 50). Education relating to the aseptic management of the catheter device is crucial to protect the patients from bacteraemia. Compared with training for two weeks in hospital, training the patient at home has been reported to reduce the risk of CRBSI ($P=0.001$) (51). Similarly, the primary underlying disease of the patient seems to play a role. Crohn's disease is associated with increased infections ($p<0.05$), which may be related to the treatment with corticosteroids increasing susceptibility (52). Malignancy is associated with fewer infections and those patients with a background of dysmotility have significantly more infections than patients with inflammatory bowel disease, vascular disease and radiation enteritis ($p<0.0001$) (52). Drug dependency (opiates and sedatives), and smoking are also associated with increased infections ($p=.0007$ and $p<0.05$, respectively) (53, 54). Patients who are independent in managing their catheter device have a lower incidence of CRBSI, as do those who have access to an experienced HPN centre ($p=0.001$ and $p<0.05$, respectively) (52). Lastly, although there are no data relating to adults, each individual septic episode in infants has been found to increase the risk of IFALD by 3.2-fold (55).

1.2.3.3 Microbiota

The gut microbiome refers to the microbes including bacteria, fungi, viruses and archaea that are present in the gastrointestinal tract. It is important for many metabolic functions such as fermentation of undigested carbohydrates and protein yielding short-chain fatty acids that are absorbed and used as an energy source (56). The microbiome also influences the production and absorption of other nutrients in the colon, intestinal mucosal growth and integrity, and development of the immune system (57). Certain groups of bacteria such as Clostridia are essential for normal intestinal function and protection against intestinal diseases. Conversely, certain species belonging to Enterobacteriacaea are proinflammatory and therefore harmful.

Although there is a paucity of research on IF and gut microbiota dysbiosis, the findings from the few studies that are available are remarkably consistent. Data show a reduction in the diversity of bacteria within the gut, with an increase of Lactobacillus, Proteobacteria, particularly Enterobacteriaceae, and a decrease of Bacteroidetes and Firmicutes. A recent literature review by Neelis et al (2019) (57) included ten studies about the gut microbiome in IF, five each from children and adults. Table 1.5 summarises the findings from adults only. The changes found in children are in accordance with those in adults.

Table 1.5: Summary of findings of studies on the gut microbiome in adults with IF (adapted from reference (57))

Reference	**Finding**
Joly et al 2010 (58) & Huang et al 2017 (59)	Reduced diversity of bacteria
Huang et al 2017 (59)	Reduction in bacterial richness
Boccia et al 2016 (60)	Reduction in total bacterial count
Huang et al 2017 (59)	Increase in Proteobacteria (Enterobacteriaceae)
Joly et al 2010 (58), Gillard et al 2017 (61)& Huang et al 2017 (59) Joly et al 2010 (58) & Mayeur et al 2013 (62) Huang et al 2017 (59)	Changes in Firmicutes: Increased Bacilli/ Lactobaillaceae/ *Lactobacillus* Detection of *Lactobacillus mucosae* Increase Enterococcaceae Decrease Lachnospiraceae, Ruminococcaceae, Peptostreptococcaceae & Erysipelotrichaceae
Joly et al 2010 (58), Boccia et al 2016 (60) & Huang et al 2017 (59)	Decrease in Bacteroidetes
Boccia et al 2016 (60)	Decrease in Actinobacteria and Bifidobacterium

The alterations observed in the composition of the microbiome likely contribute to liver injury. More specifically, the increased abundance of *Lactobacillus* and Proteobacteria, have been associated with the development of IFALD (Figure 1.4). A 2017 study in children compared the gut microbiota of 23 patients with IF with 58 healthy controls (63). An increase in Proteobacteria (10-fold average increase compared with healthy adults) was strongly associated with liver steatosis, portal and intestinal inflammation, and liver fibrosis. The changes in the gut microbiota were more predictive of IFALD than the length of remaining bowel, or the duration of the HPN therapy. The Lactobacillus family are a second group of bacteria that may promote liver injury through deconjugation. The Lactobacillus family represents another group of bacteria that may contribute to liver injury through the deconjugation of bile acids. When deconjugation is excessive, particularly in the context of impaired reabsorption in the terminal ileum, free bile acids can accumulate in the gut. This may lead to bile acid malabsorption and dysregulation of hepatic bile acid metabolism, ultimately promoting hepatic steatosis (63).

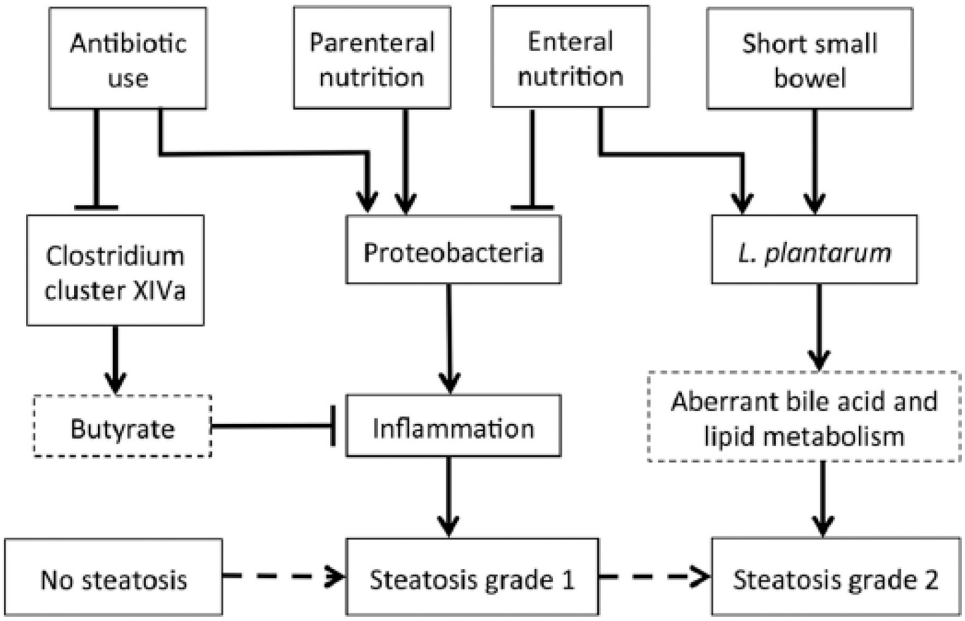


Figure 1.4: Proposed mechanisms for the development of steatosis in IF. Taken from reference (63). *Lactobacillus plantarum* refers to the genus-level group related to that species. Hypothetical links are indicated by the dashed lines.

Unfortunately, there are no data currently available that demonstrate the link between gut microbiota dysbiosis and liver injury in adults with IF. To understand the role of the gut microbiome as a modifiable therapeutic target to improve clinical outcomes of patients on HPN, studies involving the prospective collection of faecal samples are required.

1.2.3.4 Nutrient imbalances

1.2.3.4.1 Deficiencies

Choline

Choline is a quaternary amine that is essential for the synthesis of very low-density lipoproteins which are necessary for the export of triglycerides from the liver. Although it is synthesised through the phosphatidylethanolamine N-methytransferase (PEMT) pathway, this provides insufficient amounts, and therefore, humans rely on dietary sources of choline (64).

Choline's use as a methyl donor is a major determinant of how quickly a choline-deficient diet leads to a pathological condition. However, both choline and methionine provide methyl groups, and pathways of their catabolism and endogenous remethylation intersect (65). When choline is unavailable, it is synthesised *de novo* from methionine but this endogenous

process is complicated in the case of intestinal failure. When methionine is infused parenterally, it is metabolised through extrahepatic transamination rather than intrahepatic transsulfuration, thereby making the methyl group of methionine unavailable for choline synthesis (66) (Figure 1.5).

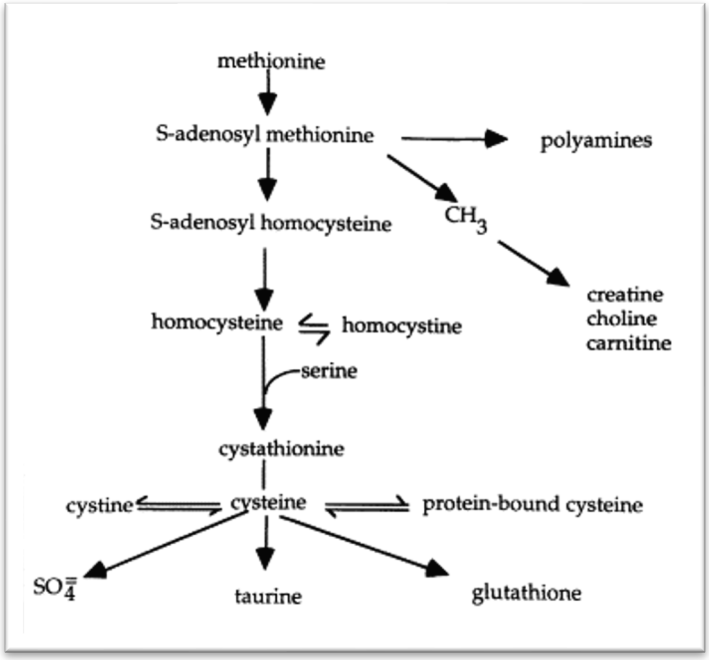


Figure 1.5: Intrahepatic transsulfuration pathway. Taken from reference (67)

Because dietary intakes are low and endogenous production of choline from parenteral methionine is inadequate, accumulating evidence demonstrates that choline deficiency in patients on HPN is associated with progressive liver disease due to the reduced transport of triglycerides from the liver, ultimately leading to steatosis, and eventually, cirrhosis. In one study by Buchman et al (24), it was reported that more than 80% of the participants were deficient in plasma-free choline, despite the provision of methionine. In a second study by the same author, parenteral choline supplementation was shown to reverse hepatic steatosis and return the concentrations of liver enzymes to normal (25).

Vitamin E

Alpha-tocopherol (a form of vitamin E) is an antioxidant that helps to reduce lipid and free radical peroxidation. Deficiency of vitamin E has been implicated in the development of liver steatosis (68). Twenty percent of patients treated with HPN are reported to have vitamin E deficiency, and this figure increases to 33% in patients receiving lipid free HPN (69). Whilst there are data to support vitamin E supplementation in patients with NAFLD patients, similar

data are not currently available for patients with IFALD. In animal models, supplementing lipid emulsions with vitamin E prevented increases in lipidemic markers of IFALD (70).

Essential fatty acids

Essential fatty acids are discussed in detail in the systematic review included in Chapter 2.

1.2.3.4.2 Toxicities

Lipids

Lipids are discussed in detail in the systematic review reported in Chapter 2.

Glucose

Excess or continuous glucose administration results in a lipogenic state, triggered by high plasma glucose concentration and subsequent elevated serum insulin concentration. The consequences are excess lipogenesis and triglyceride deposition within the liver (71). Moreover, insulin suppresses fatty acid oxidation, glycogenolysis and gluconeogenesis, whilst stimulating glycolysis, fatty acid synthesis, glycogen synthesis, and fatty acid esterification (72). This process is worsened further when lipid-free PN is used as there is an absence of omega 3 and omega 6 polyunsaturated fatty acids, which inhibit de novo lipogenesis (73).

Manganese

Manganese is trace element (TE) that acts as a cofactor for metalloenzymes, some of which are involved in processes such as immune and reproductive function, detoxification of free radicals, and neuronal health (74). In HPN, manganese is typically provided as part of commercially available pre-mixed TE preparations and is also present through contamination, likely at a level to meet requirements (75). However, HPN patients often have potentially toxic concentrations of Mn in their blood, questioning why Mn continues to be added to TE preparations. Excess Mn accumulates in the brain and can lead to neurotoxicity or manganism (a parkinsonian-like neurodegenerative disorder). Excretion is primarily via bile and accumulation can result if liver disease/cholestasis is present (74).

1.2.3.5 Sarcopenia and metabolic bone disease

The hallmark characteristic of sarcopenia is the progressive loss of skeletal muscle mass and function. This contributes to falls, fractures, physical disability, reduced quality of life and even death (76). The prevalence of sarcopenia in patients with IF is reported to be as high as 72.7% and it is likely that the pathophysiology involves an interplay between different factors. For example, IF is a condition that is characterised by malabsorption, inflammatory diseases, and patients often present following a prolonged period of under- or malnutrition. Many patients have multiple hospital admissions, sedentary lifestyles, and low activity levels; all of which are known to be frequent underlying causes of sarcopenia (76).

1.3 Quality of life

QoL is a multidimensional construct, typically encompassing physical, psychological, social, and functional well-being. It can be measured using validated questionnaires that capture patient-reported outcomes. These instruments vary in scope: some are generic, designed to assess QoL across different diseases and populations, while others are disease-specific, tailored to capture issues most relevant to a particular patient group.

Generic questionnaires provide a broad assessment of HRQoL and allow for comparisons across diseases and with the general population. Two widely used examples are:

- Short Form-36 (SF-36): Assesses eight health domains (e.g., physical functioning, role limitations, mental health) and provides summary physical and mental health scores(77).
- EuroQol EQ-5D-5L: Measures QoL across five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with an additional visual analogue scale for overall health (78).

However, generic measures may miss aspects of QoL unique to patients requiring HPN. For this reason, disease-specific instruments have been developed, including:

- HPN-QoL: A validated 48-item questionnaire specifically designed for HPN patients, covering functional domains (e.g., physical, emotional), symptom burden (e.g., fatigue, sleep, gastrointestinal issues), and global health/QoL (79).

- Parenteral Nutrition Impact Questionnaire (PNIQ): A more recently developed patient-centred tool, created with direct patient involvement, to better reflect the lived experience of HPN (80).

In clinical and research settings, the choice of QoL instrument depends on the aim of assessment. Generic tools are useful for comparisons across conditions and populations, while HPN-specific tools capture the nuanced impact of long-term parenteral nutrition on daily life and well-being.

Building on this, two systematic reviews have been published evaluating the impact of home parenteral support (HPS) on the QoL of patients and their family members. Included in the two reviews were a total of 38 studies conducted between 1965 and 2020. A further six studies have been published since the last systematic review. All relevant studies published since 2000 are summarised in Table 1.6 (n=23).

Table 1.6: Summary of QoL studies in people undergoing HPN, published since 2000

Author, year, country	Sample size	Method/ study design	QoL tool used	Main findings
Malone, 2002 (81) US	13 HPN, 4 nutrition therapy	Longitudinal cohort study	SF-36	Health status was lower in all categories of the SF-36 compared with US population norms (p<.05).* No significant difference in SF-36 scores between the 2 time periods (1993 & 1996).
Smith et al, 2002 (82) US	95	Case-controlled study with telephone interviews	Dossier analysis QoL Index Center of Epidemiologic Studies-Depression Scale	Patients supported by an organisation experienced higher QoL (19.8 +/- 4.7 vs 17.6 +/- 5.6; p.05), less reactive depression (10.9 +/- 10.4 vs 20.4 +/- 13.6; p.01), and a lower incidence of catheter-related sepsis (0.10 +/- 0.3 vs 0.60 +/- 0.55; p.01).
Carlsson et al, 2003 (83) Europe	8 HPN, 20 nutritional therapy	Cross sectional	SF-36	Low QoL (48/100) and low perceived health in HPN group (29/100). The most intense concerns were being a burden, energy level, surgery, feeling alone, and loss of sexual drive
Pironi et al, 2003 (84) Europe	17	Retrospective review of routinely collected data	SF-36	QoL was lower than healthy population in 6/8 domains; PF: 64.7 +/- 26.5 vs 84.5 +/- 23.2; p<.005, RP: 38.2 +/- 46.0 vs 78.2 +/- 35.9; p <.001, BP: 46.7 +/- 23.5 vs 73.7 +/- 27.6; p<.001, GH: 40.9 +/- 23.3 vs 65.2 +/- 22.2; p<.001, SF: 61.0 +/- 22.9 vs 77.4 +/- 23.3; p.003 and RE: 49.0 +/- 44.3 vs 76.2 +/- 37.2; p.011).

Author, year, country	Sample size	Method/ study design	QoL instrument used	Main findings
Pironi et al, 2004 (85) Italy	31 – baseline 20 – 2nd timepoint	Longitudinal cohort study	SF-36	Baseline Z scores were reduced in 5/8 domains (PF (-2.48 +/1 2.10), RP (1.60 +/- 1.70), BP -1.07 +/- 1.19), GH (-1.52 +/- 1.39) and SF (-1.23 +/- 1.25)). Follow up - QoL worsened in 8 patients and improved in 10. Worsened subgroup had a decrease in BMI, an increase in no. of HPN infusions/ week, a greater incidence of dysmotility disorders, of liquid oral diet and of nycturia.
Silver et al, 2004 (86) US	9	Qualitative, non-interventional interview study	N/A	Participants described persistent hunger and difficulty resisting restricted foods, with inconsistent adherence and repeated attempts to consume contraindicated items.
Persoon et al, 2005 (87) The Netherlands	48	Cross sectional	Cantril's ladder	Low QoL related to fatigue, sleep disorders, anxiety, depression, and social impairment (p<.02)
Pironi et al, 2006 (88) Italy	18 HPS 12 Itx	Cross sectional	SF-36	Only BP differed between groups (HPS: –1.01 ± 0.94 vs Itx: –0.00 ± 1.14;p=.012). HPS patients scored lower than the general population in 4 of 8 domains (PF, RF, BP, GH).
Chambers et al, 2006 (89) UK	30	RCT – telemedicine vs standard follow up HPS vs general population Baseline & 6 months	SF-36 Euroqol (EQ5D)	No significant differences between follow-up methods. PCS and MCS improved over 6 months (30.5 and 45.79; p = .13 and .01), with no EQ5D domain changes.

Author, year, country	Sample size	Method/ study design	QoL instrument used	Main findings
Pironi et al, 2012 (90) Italy	33 HPS 18 Itx	Cross sectional	HPN-QOL HPN-QoL modified for ITx	ITx recipients had a statically significant better score in ability to travel (48.6 +/- 23.4 vs 25.7 +/- 16.2; p<.0001), gastrointestinal symptoms (12.3 +/- 13.6 vs 36.8 +/- 17.0; p<.0001), stoma management or bowel movements (10.7 +/- 9.3 vs 35.0 +/- 27.2; p.001) and fatigue (20.3 +/- 21.8 vs 37.3 +/- 26.0; p.022).
Schliefert & Carey, 2014 (91) Australia	8	Cross sectional	SF-36 HPN-QoL	QoL did not correlate with BMI, weight, TSF, MAMC. HPN-QoL correlated with grip strength (p<.05). SF36 scores were significantly lower than the general Australia populations norms for all dimensions except MH
Aeberhard et al, 2015 (92) Switzerland	33	Cohort Baseline & 3 months	SF-36	Mean PCS and MCS improved after 3 months (34 to 39.4/ 100 and 41.9 to 46.4/ 100, respectively)
Burden et al, 2019 (93) UK	466	Observational cohort study	PNIQ	Poorer QoL with increased number of infusions per week (11.78 for 6-7 nights vs 9.20 for 1-3 nights). Similar QoL for patients with cancer (mean 10.82, SD 6.00) vs IBD (mean 11.04, SD 5.91). Patients with severe GI dysmotility had a better QoL (effect size -3.03, CI -5.593 to -0.468) compared other disease states . Patients with surgical complications had poorest QoL of all disease states (-3.03, CI -5.593 to -0.468).

Author, year, country	Sample size	Method/ study design	QoL instrument used	Main findings
Sowerbutts et al, 2020 (94) UK	15 HPN 5 family members	Qualitative, non-interventional interview study		Lives were dominated by IF. Physical restrictions comprised of restrictions on daily life, actives of daily living and physical functioning. There were negative feelings and social impacts e.g. difficulties socialising and maintaining relationships. Patients coped through support and attitudes of gratitude and acceptance. Family members were affected and appreciated the respite of a night off from infusions.
Kot et al, 2020 (95) Poland and Israel	203	Cross sectional	Adapted HPN-QoL	Higher mean QoL score in males compared to females (86 ± 11.5 vs 81 ± 12.9, respectively; p<.001).
Beurskens-Meijerink et al, 2020 (96) The Netherlands	147 IF patients with SBS or intestinal dysmotility	Cross sectional	HPN-QoL	Overall QoL was moderate (60/100) No significant difference in QoL between the two groups. However, dysmotility experienced more symptoms with regard to their ability to E&D (mean 31 (SD 21.4) vs 58 (21.7); p<.0001), fatigue (62 (37.6) vs 43 (32.2); p.0012), GI symptoms (42 (24.5) vs 18 (20.1); p<.0001), and immobility 54 (27.4 vs 38 (28.5); p.007)

Author, year, country	Sample size	Method/ study design	QoL instrument used	Main findings
Bluthner et al, 2020 (97) Germany	90	Cross sectional	SF-36	QoL lower than population norms across all categories (p<.001). GH was inversely correlated with number of weekly infusions (p.015) and body composition positively correlated with PF (p.014) QoL was strongly impacted by citrulline levels, presence of stoma/fistula and oral intake.
Nordsten et al, 2021 (98) Denmark	60	Cross sectional	SBS-QoL	High HPS volume was associated with a significant impairment in QoL scores (β = 7.91; SE = 3.90; P = .048).
Geisler et al, 2021 (99) Denmark	44	Mixed methods study with semi-structured interviews (13) and questionnaires (31)	HPN-QoL EORTC-QLQ-C30	Low QoL was found by EORTC-QLQ-C30, for general health (51.26/100). QoL was slightly better measured by the HPN-QoL (69.85/100). The worst scores were for employment (44.7/100), sexual function 40.48/100), ability to holiday (33.46/100), fatigue (63.13/100) and sleep 62.67/100).
Jeppesen et al, 2022 (100) Europe and US	181	Cross sectional	Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI:SHP) HPN-QoL	75% experienced fatigue and 50% anaemia. 37% had difficulty spending time with family and 30% with friends. Mena HPN-QoL scores were higher for patients who were satisfied with treatment (17.1) than for patients who were dissatisfied/neither (1.7).

Author, year, country	Sample size	Method/ study design	QoL instrument used	Main findings
French et al, 2022 (101) UK	678 IF patients 339 family members	Cross sectional	PNIQ Burden scale for family caregivers (BSFC)	PNIQ scores represented moderate impact of HPN on patients' QoL. 23% of family members reported a moderate to very severe subjective burden indicating an increased risk of psychosomatic symptoms. Employment status, disease type, number of nights on HPN and length of time on HPN were not associated with BSFC.
Schonenberger et al, 2023 (102) Switzerland	70	Cross sectional	Self-designed questionnaire for the purpose of the study Optum SF-36v2	HPN affected feelings of dependency (70%), traveling/leaving home (53%), attending events (36%), and sleep (31%). Most frequently reported symptoms were diarrhoea (43%), polyuria (40%), nausea (39%) and cramps (29%).
Jones et al, 2023 (103) UK	572: baseline 202: 2nd follow up 145: 3rd follow up	Longitudinal cohort study	PNIQ	Mean PNIQ score was 11.25/20 indicating poor QoL. Any reduction in HPS infusions per week was associated with an improved PNIQ score of -1.10. Per day change to the number of infusions per week was associated with a change in the PNIQ score of 0.32.

*Abbreviations: HPN, home parenteral nutrition; SF-36, short-form 36; QoL, quality of life; PF, physical functioning; RP, role limitations due to physical health; BP, bodily pain; GH, general health; SF, social functioning; RE, role limitations due to emotional problems; HPN, home parenteral support; Itx, intestinal transplant; BMI, body mass index; TSF, tricep skinfold thickness; MH, mental health; MAMC, mid-arm muscle circumference; PCS, physical component score; MCS, mental component score; IF, intestinal failure; SBS, short bowel syndrome; EORTC-QLQ,C30, The EORTC Core Quality of Life questionnaire; PNIQ, parenteral nutrition impact questionnaire. *Data only provided for the study population.*

It is clear that, despite heterogeneity across studies, patients treated with HPN report poor QoL and have significantly worse QoL scores when compared with population norms. However, the studies summarised in Table 5 have focussed primarily on the impact of HPN programs and intestinal anatomy on the QoL of patients. Since QoL is a rich multidimensional concept encompassing mental and physical health and is likely affected by disease status and treatment, such studies fall short. Patients are affected not only by their intestinal disease, but also by decreased physical health due to multi-morbidity and the threat of potentially life-threatening complications, such as IFALD. No studies were found that investigated the association between QoL and the complications of HPN treatment such as IFALD, sepsis, reduced microbiota diversity, sarcopenia and metabolic bone disease.

The remainder of this thesis will focus on understanding the association between QoL and the complications of treatment. Chapter 2 includes a systematic review that evaluates the evidence for the differential effects of PN regimens. Chapter 3 includes a survey of healthcare professionals to understand current practice, attitudes, and knowledge around QoL and Chapter 4 includes the methods. Results of a multi-centre longitudinal study investigating the QoL of HPN patients are presented in Chapter 5 and discussed in Chapter 6.

1.3: Aims, hypotheses and objectives

Aims

In line with Medical Research Council (MRC) guidance on developing and evaluating complex interventions (104), the main aim of this PhD thesis is to understand how home parenteral nutrition (HPN) impacts on the quality of life (QoL) of patients, and the contribution played by liver disease. My first aim is to systematically review and evaluate the evidence for the differential effects of PN solutions (Chapter 2). A second aim is to carry out a survey of current practice, attitudes and knowledge amongst healthcare professionals involved in the care of patients on HPN (Chapter 3). My third aim is to complete a longitudinal investigation of the QoL of patients treated with HPN (Chapter 4 onwards).

Hypotheses

My hypotheses for this project are that:

1. There will be significant variability between clinicians in the assessment and management of QoL. Covered in Chapter 3.
2. QoL scores will improve during the first year of HPN therapy and plateau thereafter. Covered in Chapters 4-6.
3. QoL scores will be influenced by the underlying disease and reason for HPN, gastrointestinal anatomy and HPN regime. Covered in Chapters 4-6.
4. QoL scores will be influenced adversely by co-morbidities, for example, the presence of intestinal failure associated liver disease (IFALD). Covered in Chapters 4-6.
5. Parenteral nutrition causes an upregulation of *de novo* lipogenesis (DNL).
6. Parenteral nutrition causes alterations in phospholipid metabolism with reductions in plasma free choline.

Hypotheses 5 and 6 were not directly tested within this PhD, but they were developed to extend the mechanistic insights gained in Chapter 2. Both hypotheses will be addressed using the biological samples collected prospectively as part of the study protocol outlined in Chapter 4. This will allow investigation of whether PN induces upregulation of de novo lipogenesis and whether it alters phospholipid metabolism with reductions in plasma free choline.

Objectives

The aims of the project were addressed through the following objectives:

1. To investigate the relationship between the composition of parenteral nutrition (PN) solutions and (a) QoL; (b) markers of health status including liver enzymes, nutritional status, inflammatory and antioxidant markers; and (c) clinical safety and tolerance.
2. To design a survey for healthcare professionals to identify (a) the importance of QoL assessment from a clinical perspective; (b) frequency and method of QoL assessment; (c) management of QoL issues.
3. To explore (a) clinician views on IFALD as a contributor to poor QoL; and (b) management of IFALD.
4. Recruitment of participants on HPN from Newcastle hospitals (NuTH), Leeds Teaching Hospitals (LeedsTH) and Nottingham University Hospital (NUH) to the longitudinal study.
5. Collection of data and biological samples.
6. To quantify baseline QoL score in HPN patients, those new to treatment (<6 months), and those with longer exposure to HPN (>6 months).
7. To investigate longitudinal changes in QoL scores for patients on HPN.
8. To investigate what factors contribute to the QoL deficit and to establish whether there are any links between them.

Chapter 2: Systematic review

The Effects of Different Parenteral Nutrition Lipid Formulations on Clinical and Laboratory Endpoints in Patients Receiving Home Parenteral Nutrition

The research reported in this chapter, prior to the searches being updated in February 2025, has been published in *Clinical Nutrition* and the full manuscript can be found using reference: **Kirk C**, Haigh L, Thompson NP, Pearce M, Jones DE, and Mathers JC. The effects of different parenteral nutrition lipid formulations on clinical and laboratory endpoints in patients receiving home parenteral nutrition: A systematic review. 2022. *Clinical Nutrition*; 41(1):80-90.

2.1: Background

Home parenteral nutrition (HPN) refers to the intravenous infusion of macronutrients, micronutrients, fluids and electrolytes (12). It is a life-sustaining therapy for individuals with intestinal failure (IF), defined as a reduction in gut function below the minimal necessary for the absorption of macronutrients and/or water and electrolytes, requiring intravenous supplementation (1). There are three subclassifications of IF in relation to time scale, metabolic changes and outcome. Patients with Type I IF (acute) typically receive parenteral nutrition (PN) short term in hospital (<28 days) for a self-limiting condition; type II IF (prolonged acute) is used when patients are metabolically unstable and receive PN in hospital, or at home, for a period of weeks to months; patients with type III IF (chronic) typically receive PN at home for months to years (2).

The essential components of HPN are carbohydrate in the form of glucose, lipid, amino acids (AA), vitamins, trace elements (TE), electrolytes and water. Lipid emulsions (LEs) are an integral component of PN that prevent essential fatty acid (EFA, linoleic acid and α-linolenic acid) deficiency and enable patients to meet their energy requirements without the need to infuse large amounts of glucose. Early forms of HPN consisted of glucose solutions only but these proved unsatisfactory for prolonged use because high glucose loads can contribute to hyperglycaemia, hepatic steatosis and impaired respiratory function (105). Since the discovery of the importance of EFA in the 1970s and 80s, four generations of LEs have been developed. The oldest LE was based on 100% soybean oil (SO) (Intralipid). However, the high content of phytosterols and ω-6 polyunsaturated fatty acids (PUFA) (linoleic acid (52-54%) and α-linolenic acids (7-9%)) in SO raised concerns related to central line infections, inflammation and the development of intestinal failure associated liver disease (IFALD) (106, 107). Second generation LEs combined SO (long-chain triglycerides) with saturated medium-chain triglycerides (MCTs). The proposed advantages of MCTs include lower immunosuppressive effects and less impact on the liver (108), but much of the research to date has been performed in intensive care settings and it is not known whether these putative advantages extend to long-term HPN use in the community. Third generation LEs replaced a proportion of SO with olive oil which has high oleic acid content. Oleic acid is less susceptible to lipid peroxidation than are ω-6 and ω-3 PUFAs and the high concentration of α-tocopherol in these 3rd generation HPN solutions may provide anti-oxidant benefits. Fish

oils, theoretically with enhanced anti-inflammatory and anti-oxidant properties, were combined with one or more of the vegetable oils to form 4th generation LEs (Table 2.1).

Table 2.1: The composition of commercially available intravenous LEs

Generation of LE	**First**	**Second**		**Third**	**Fourth**		
Type of LE	Soybean oil	MCT/LCT	Structured TG	Olive oil	Pure fish oil	MCT/SO/FO	SO/MCT/OO/FO
Oil source (% by wt)	100% SO	50% SO, 50% CO	64% SO, 36% CO	20% SO, 80% OO	100% FO	50% OO, 40% SO, 10% FO	30% SO, 30% CO, 25% OO, 15% FO
Trade name	Intralipid 20%	Lipofundin MCT/LCT 20%	Structolipid 20%	ClinOleic 20%	Omegaven 10%	Lipidem/ Lipoplus 20%	SMOFlipid 20%
Ratio of n-6:n-3	7:1	7:1	7:1	9:1	1:8	2.7:1	2.5:1
Fat content (g/L)	200	200	200	200	100	200	200
pH	8	6.5-8.5	8	7-8	7.5-8.7	6.5-8.5	8
Osmolarity (mOsmol/L)	350	380	350	270	273	410	380
A-Tocopherol (mg/L)	38	85±20	6.9	32	150-296	190±30	200
Phytosterols (ug/ml)	342.89±5.87	278.14±5.09	345.85±1.64	274.38±2.6	3.66±0.59	NA	297
FAC (% by weight of total FAs)							
SFA	15	59.4	46.3	14.5	21.2	58.3	81.1
OA	24	11	14	62.3	15.1	7.9	55.3
LA	53	29.1	35	18.7	4.4	24.4	37.2
α-LA	8	4.5	5	2.3	1.8	3.3	4.7
ARA	0.1	0.2	N/A	0.5	2.1	NR	1.0
EPA	NA	NA	NA	NA	19.2	3.1	4.7
DHA	NA	NA	NA	0.5	12.1	2.3	4.4 [12]

Data are taken from reference (109)

The amounts of non-lipid components also differ between HPN formulations. The inclusion of AA aims to preserve a positive nitrogen balance and to promote muscle protein synthesis. Personalised HPN solutions aim to meet the specific needs of individual patients, but commercially available AA preparations are often used. Even with the same total AA content, each commercial preparation has a different ratio of essential to non-essential amino acids (110). Similarly, vitamins and TE are often supplied in the form of pre-mixed multi-TE or vitamin combinations which may not suit individual patient requirements. Many of these contain TE doses in excess of current recommendations (13, 111). The potential and variable components of HPN are shown in (Figure 2.1).

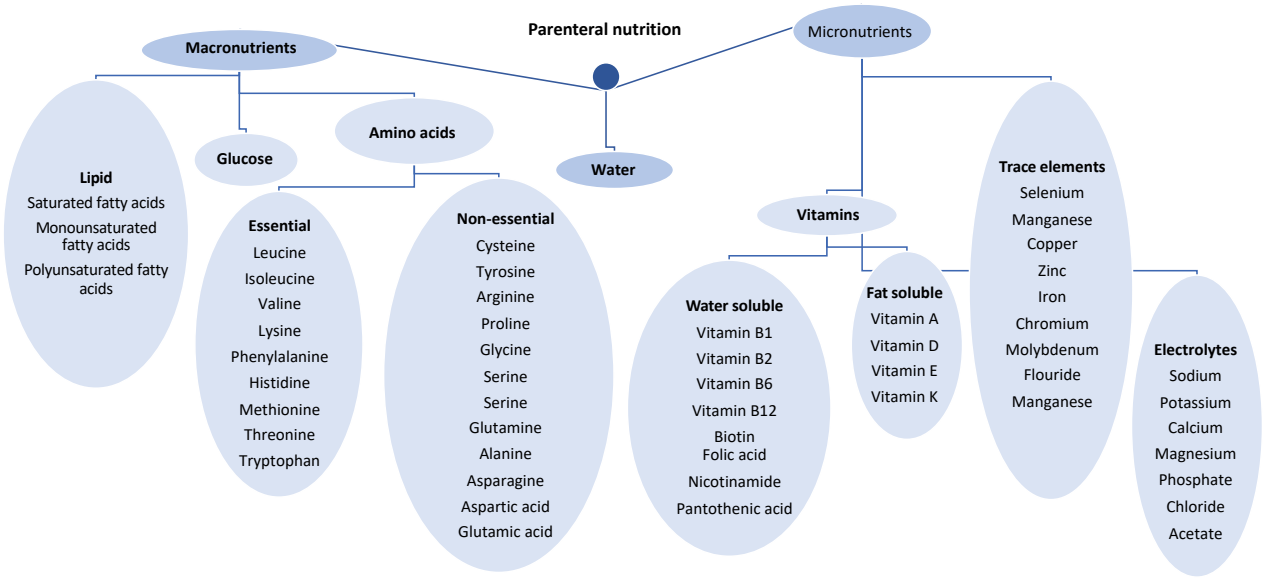


Figure 2.1: *Example of the large number of nutrients added to parenteral nutrition solutions. Each of these nutrients may be added in different quantities/ concentrations in particular preparations.*

It is clear that HPN solutions vary considerably in terms of fatty acid, macronutrient and micronutrient composition. As such, each solution may impact metabolism, inflammation and oxidative stress differently and have different effects on risk of adverse health sequelae such as the development of metabolic bone disease, IFALD, central venous catheter infections and poor quality of life (112). The effect of different intravenous LE used in adult HPN has been reviewed systemtically and included six randomised controlled studies (113). However, that review focussed on the lipid component of HPN only and excluded all other

study designs, potentially discounting a significant proportion of the literature. Thus, the aim of this chapter is to systematically review and evaluate the effects of HPN solutions on clinical and laboratory endpoints using evidence from RCTs, prospective cohort studies and cross-sectional studies.

2.2: Methods

In accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA 2020 guidelines) (114), this systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 20th January 2021 (registration number CRD42021230074).

2.2.1: Information sources

Literature search strategies were developed using Free Text and Mesh terms related to home parenteral nutrition (HPN). MEDLINE (Ovid) without revisions 1946 – December week 1 2020, EMBASE 1946 – December week 1 2020, Scopus, and Web of Science were searched for articles that were published in the English Language. Initial searches were conducted between September and December 2020, and updated in July 2021 and February 2025. Only studies published between 2020 and 2025 were included in the updated searches. The search strategies were verified by two members of the evidence synthesis team at Newcastle University using the Peer Review of Electronic Search Strategies (PRESS) checklist. To ensure data saturation, hand searching of reference lists from relevant articles was performed. The search strategies for all databases can be found in Additional files 1-4.

2.2.2: Eligibility criteria

Studies were selected according to the following criteria (a) adult participants (>18 years old) dependent on HPN; (b) randomised controlled trials, prospective cohort and cross-sectional study designs; (c) primary research comparing two or more HPN solutions and (d) published in English language. Case series, case reports, conference abstracts, animal and in vitro studies were excluded.

2.2.3: Selection of studies

Relevance of studies was determined through an initial screen of titles and abstracts. Full papers of publications that seemed to meet the inclusion criteria were retrieved and final papers for inclusion in the review identified. Screening was completed by me and verified by a second reviewer.

2.2.4: Data extraction and analysis

A second reviewer and I extracted the following data independently from each publication: first author, publication year, study location, study design, participants, intervention and comparator feeds, inclusion and exclusion criteria, intervention length, outcomes, adverse events and statistical methods. These data were first extracted onto an adapted version of the Cochrane Collaboration data extraction form and then integrated into Microsoft Excel 2019 and used to compile a narrative synthesis of results using descriptive statistics and summary tables.

2.2.5: Assessment of quality

A second reviewer and I assessed study quality independently for all publications using the Cochrane Collaborations tools: Risk of Bias for Randomised Controlled Trials (RCTs) (RoB) (115), Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I tool) (116), and the Newcastle Ottawa Scale for cross-sectional studies (117). The data were then integrated into Microsoft Excel 2019 and any discrepancies were discussed with a PhD supervisor. An overall risk of bias judgement that summarised findings across domains was formulated using the criteria for each of the tools.

2.2.6: Data synthesis

The characteristics of the studies were not sufficiently homogenous to justify performing statistical analysis. Hence, in line with the guidance from the Centre for Reviews and Dissemination, a narrative synthesis was performed to explore findings within and between the included studies. The order of the synthesis was based on the importance of clinical outcomes as decided by the review team. All evidence related to outcome one, safety, is presented first, followed by outcome two, liver function, followed by quality of life, anthropometry, micronutrients, inflammation, and fatty acids.

2.3: Results

2.3.1: Study selection

6442 publications were returned from the electronic literature search and one additional publication was identified through manual searching of reference lists. The updated search performed in February 2025 found five additional publications. After de-duplication, 4005 articles remained. A further 3955 were excluded through a title and abstract screen. A total of 50 full-text articles were assessed for eligibility from which 12 articles were excluded as there was no indication of participants being treated with home parenteral nutrition (HPN); a further 10 were excluded as they were case studies; seven did not compare two or more HPN solutions; six were conference abstracts and one was a study protocol only. No studies were excluded due to not being in English language. Data from 15 publications were included in the review (Figure 2.2).

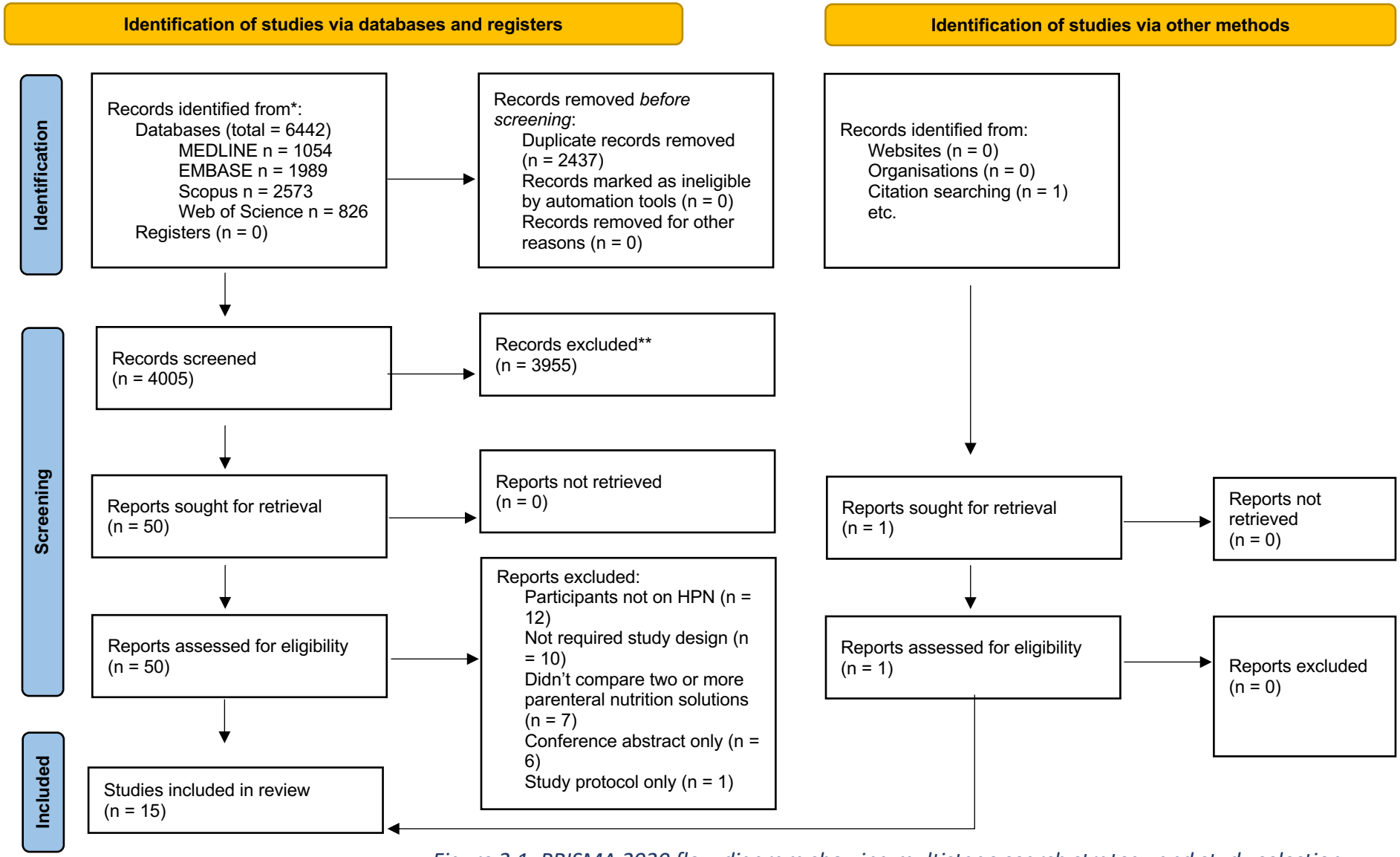


Figure 2.1: PRISMA 2020 flow diagram showing multistage search strategy and study selection

2.3.2: Study characteristics

The study characteristics are presented in Table 2.2. Eight randomised controlled trials (RCTs) (22, 23, 118-123), six prospective cohort (124-129) and one cross-sectional study (130) were identified with a total of 519 (237 male) participants, mean age 51.2 years. All articles were published between 1992 and 2024. There were 11 single-centre studies, two were conducted in each of France, Germany and Canada. There was one conducted in each of Poland, Belgium, Israel, Italy and Czech Republic. There were three multi-centre studies, one conducted in 11 centres in seven countries (22), one conducted in two Polish centres (125) and one conducted in nine centres in five countries (123). Of the 15 papers selected, a variety of intravenous lipid emulsions (IVLEs) were compared; SO and MCT/LCT or structured MCT/LCT (118, 119); SO and SMOF (22, 128, 129); MCT/LCT/FO and MCT/LCT (121, 123); SO, MCT/LCT, OO/SO and SMOF (122); MCT/LCT, OO-SO and SMOF (23); SO and OO-SO (124); SMOF and OO-SO (125); SO/MCT and SO/MCT/FO (126); and SO/MCT/FO, OO/SO and SMOF (127). There were no studies that compared the amino acid, vitamin, trace element or electrolyte component of HPN solutions and only one cross-sectional study included patients prescribed lipid-free HPN. The authors compared OO-SO, SMOF and No-intravenous lipid emulsion (No-IVLE) (130). All IVLE compared across studies were similar for energy and glucose content. Five authors reported that AA, TE, vitamins and electrolytes were given as part of an AIO solution (22, 23, 119, 122, 123); six authors provided vitamins and TE according to individual needs or to maintain normal concentrations (118, 120, 121, 124, 126, 127), and four authors made no reference to vitamins, TE or electrolytes (125, 128-130). The main indications for HPN were short bowel syndrome, Crohn's disease, ischaemia, surgical and dysmotility. Sample sizes were small between five and 120 participants per study. The mean length of HPN prior to study commencement or cross-sectional analysis was reported in eight studies and ranged from one month to five years. In terms of study duration, one study published initial results after 12 months and further outcomes after 5 years (23, 122). These were treated as two separate studies. The length of follow up in the remaining studies was variable between 1-24 months (22, 118-121, 124-129). Baseline characteristics of the participants within the included studies were comparable between treatment group.

Table 2.1: Characteristics of included studies

Reference	Study design	IVLEs compared	Sample size (randomised/ completed)	Age (yrs) Mean (SD)/ Median (range)	BMI (kg/m2)	Duration of HPN prior to study (months) Mean/ Median (range)	Intervention (months)	Indication for HPN
Dahlan et al 1992 (118)	Randomised crossover	SO then SO-MCT Or SO-MCT then SO	5/5	29(4)	NI	NI	3	Inflammatory bowel disease (n=5)
Rubin et al 2000 (119)	Double blind randomised crossover	Structured SO-MCT then SO SO then structured SO-MCT	22/20	43.3(17.46)	NI	56.8	2 (1 per IVLE)	Short bowel syndrome (n=8) Crohn's disease (n=12) Other (n=2)
Vahedi et al 2005 (120)	Double blind RCT	SO-OO SO	13/13	50.7(21.68)	19.01 (2.42)	73.3	3	Short bowel syndrome (n=10) Obstruction (n=3)
Klek et al 2013 (22)	RCT	SMOF SO	73/62	48.9(14.54)	20.48 (4.48)	NI	1	Short bowel syndrome (n=39) Crohn's disease (n=8) Malabsorption (n=5) Fistula (n=4) Obstruction (n=2) Other (n=8)

Bohnert et al 2018 (121)	RCT	SO-MCT-FO SO-MCT	42/33	56.9(13.96)	21.1 (2.44)	NI	2	Malabsorption (n=42)
Klek et al 2018 (122)	RCT	SO-MCT SO-OO SMOF SO	88/65	54.5(14.9)	19.68 (4.64)	23.8 days	12	Vascular (n=28) Crohn's disease (n=12) Surgical (n=8) Radiation enteritis (n=4) Fistula (n=3) Motility disorders (n=2) Obstruction (n=1) Other (n=7)
Klek et al 2020 (23)	RCT	SO-MCT SO-OO SMOF	67/65	52.7(13.8)	19.02 (3.96)	22.7 days	60	Vascular (n=23) Crohn's disease (n=13) Surgical (n=9) Radiation enteritis (n=5) Fistula (n=3) Motility disorders (n=2) Obstruction (n=1) Other (n=9)
Klek et al 2024 (123)	Double-blind RCT	SO-MCT SO-MCT-FO	74/67	51.2(15.6)	NI	NI	2	Short bowel syndrome (n=50) Dysmotility (n=12) Fistula (n=6) Obstruction (n=2) Mucosal disease (n=2)

Reimund et al 2005 (124)	Prospective comparative cohort	SO or MCT/LCT then SO-OO	14/14	50(35-79)	20.1(12.3-30.8)	66	3	Crohn's disease (n=3) Radiation enteritis (n=3) Infarction (n=5) Ischaemia (n=1) Surgical (n=1) Other (n=1)
Osowska et al 2019 (125)	Prospective comparative cohort	SO then SMOF SO-OO	32/28	SMOF 57.4(34-69) SO-OO 63.8(29-79)	NI	4.5 years	2	Ischaemia (n=8) Crohn's disease (n=7) Obstruction (n=3) Mucosal dysfunction (n=4) Surgical (n=6)
Pironi et al 2017 (130)	Cross-sectional	SO SO-OO SMOF No-IVLE	31	OO 56(19-78) SMOF 44(19-73) No-IVLE 56(29-64)	OO 22(12-25) SMOF 20(17-23) No-IVLE 21(16-29)	OO 65(2-261) SMOF 29(5-53) No-IVLE 17(6-278)	N/A	Ischaemia (n=8) Obstruction (n=10) Crohn's disease (n=7) Other (n=6)
Weylandt et al 2022 (126)	Prospective, longitudinal cross-over	SO-MCT then SO-MCT-FO	8	49 (24)	22.8 (2.9)	48 (33)	2	Ischaemia (n=3) Inflammatory bowel disease (n=2) Obstruction (n=1) Trauma (n=2)
Sevela et al 2024 (127)	Prospective, cross-over	SMOF then SO-MCT-FO or SO-OO	12	58.3(17.6)	23.4(3.7)	Minimum three months	6	Short bowel syndrome (n=10) Other (n=2)

Clermont-Dejean et al 2023 (128)	Prospective, cross-over	SO SMOF	12	53.11(14.5)	22.4(3.0)	NI	13 (6 per IVLE)	Short bowel syndrome (n=7) Obstruction (n=1) Other (n=4)
Clermont-Dejean et al 2021 (129)	Prospective cohort	SO SMOF	120	50.5(40-59)	20.56(19.09-23.17)	NI	24	Short bowel syndrome (n=46) Dysmotility (n=20) Inflammatory bowel disease (n=5) GI Fistula (n=6) Obstruction (n=1) Surgical (n=3) Other (n=39)

SO, soybean oil; MCT, medium-chain triglycerides; NI, no information; IVLE, intravenous lipid emulsion; RCT, randomised controlled trial; OO, olive oil; SMOF, soybean-medium chain triglycerides-olive oil-fish oil; FO, fish oil

2.3.3: Risk of bias in selected studies

There was a high risk of bias in at least one domain in all but two of the RCTs included. Four studies lacked information on blinding of outcome assessors (detection bias) (118-120, 122) and six studies reported incomplete outcome data (attrition bias) (22, 118, 120-123). Only three cohort studies addressed potential confounding satisfactorily. One also failed to provide data for four participants (125) and the other reported combined results for both groups of participants (124). One cohort study was low risk across all domains except for selection of participants as no information was provided. There was no justification for the sample size in the cross-sectional study and overall it was judged as fair quality (130) (Table 2.3 & 2.4).

Table 2.2: Quality assessment of the included RCT studies based on reference (115)

Risk of Bias	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall quality
Dahlan et al. 1992 (118)	High – NI	High – method of concealment not described	High – NI	High – NI	Unclear – NI	Low	Unclear – no indication if PP or ITT analysis	Poor
Rubin et al. 2000 (119)	Low	Low	Low	Unclear – NI	Low	Low	Unclear - no indication of ITT or PP	Fair
Vahedi et al. 2005 (120)	Low	Low	Low	Unclear – NI	High – reduced sample size in results tables	High – some outcomes missing for some patients	Unclear	Poor
Klek et al. 2013 (22)	Low	Low	Low	Low	High – patients with lipid peroxidation were excluded from results table	Low	Low	Fair
Bohnert et al. 2018 (121)	Low	Low	Low	Low	High – reduced sample size in some results tables	Low	Low	Fair

Table 2.3: (continued).

Risk of Bias	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall quality
Klek et al 2018 (122)	Unclear – NI	Low	Low	Unclear – NI	High – reasons not provided for 7/23 patients who were lost to follow Lack of ITT analysis	Low	Low	Fair
Klek et al. 2020 (23)	Unclear – NI	Low	Low	Low	Low	Low	Low	Good
Klek et al. 2024 (123)	Low	Low	Low	Low	Some concerns – one patient not accounted for in Figure 1. Results were based on only half of the planned sample size in both treatment groups, leaving the study underpowered for the primary outcome.	High – missing sample sizes in results table. Not all secondary outcomes have been reported.	Low	Poor

Table 2.4: Quality assessment of the included observational studies based on references (116, 117)

ROBINS-I	Confounding	Selection of participants into the study	Classifications of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of the reported result	Risk of bias
Reimund et al. 2005 (124)	Serious – potential confounders not adjusted for	Low	Low	Low	Low	Low	Serious – results from both groups of participants combined	Serious
Osowska et al. 2019 (125)	Serious – potential confounders not adjusted for	Low	Low	Low	Serious – missing data for 4 participants	Low	Low	Serious
Weylandt et al 2022 (126)	Low	Unclear - NI	Low	Low	Low	Low	Low	Moderate
Sevela et al 2024 (127)	Serious – potential confounders not adjusted for	Low	Low	Low	Low	Low	Low	Serious
Clermont-Dejean et al 2023 (128)	Serious – potential confounders not adjusted for	Low	Low	Low	Serious - small sample size and only 57% retention rate	Low	Moderate – not all data available for all participants	Serious
Clermont-Dejean et al 2021 (129)	Low	Low	Low	Low	Serious – not all outcomes included in the protocol have been reported in the publication	Low	Low	Serious

Table 2.4: (continued).

Newcastle -Ottawa Scale	Selection: Representativeness of the sample	Selection: Sample size	Selection: Non-respondents	Selection: Ascertainment of the exposure	Comparability	Outcome: Assessment of the outcome	Outcome: Statistical test	Total score
Pironi et al. 2017 (130)	1/1	0/1 - not justified	N/A	1/1	1/2 – comparable across groups	1/1	1/1	5/8 - fair quality

2.3.4: Outcomes

A summary of results can be found in Table 2.5.

2.3.4.1: Safety/ tolerance

Five studies did not report on the safety or tolerance of HPN solutions (118, 125, 126, 129, 130) and one study reported that all LE tested were well tolerated with no clinical complications reported (127). Eight studies reported no significant difference between treatment groups in adverse events (AE) or serious adverse events (SAE) (23, 119-124, 128). One study (22) reported significantly more SAE in patients treated with SO compared with SMOF. In this study, eight patients experienced 10 SAE whereas two patients experienced two SAE in the SO (total n=39) and SMOF (total n=34) groups, respectively (p=0.03). Two and six patients in the SMOF and SO groups, respectively, discontinued treatment. In the same study, five AE in 2 patients in the SMOF group, and six AE in three patients in the SO group were assessed as possibly or probably related to study treatment. Reimund et al reported 3/5 patients presenting with migraine without aura, felt consistently better following 3 months of OO-SO.

2.3.4.2: Liver function

There were 11 studies that reported changes in liver function tests (22, 23, 119, 120, 122-127, 129). Seven studies found no significant changes between groups (119, 120, 123, 124, 126-129) and two studies reported positive changes associated with an OO-SO LE (122, 125). Osowska et al (125) reported a lower concentration of gamma-glutamyl transferase (GGT) after 60 days (p=0.044) and Klek et al (18) reported reduced bilirubin and GGT concentrations at the end of the 12-month intervention period (28.1±25.3umol/L at the beginning versus 11.1±4.5umol/L at the end; p=0.0023) and (222.5±205.8IU/L at the beginning versus 146.6±197.7IU/L at the end; p=0.0079), respectively. The changes in bilirubin and GGT were no longer significant at 60 months (23).

One study reported that mean concentrations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin were significantly lower in the SMOF group compared with SO group (p=0.049, 0.027 and 0.043, respectively) following a four-week intervention (22).

2.3.4.3: QoL

One study measured quality of life (QoL) using the EORTC-QLQ-C30 questionnaire (score range 0-100) (121). Scores for global health status increased similarly during the intervention period with both lipid emulsions (MCT/LCT/FO: 46.21±12.56 (baseline) vs 52.08±20.14 (visit two); MCT/LCT: 36.27±22.62 (baseline) vs 44.44±24.73 (visit two).

2.3.4.4: Anthropometry

One study measured body mass index (BMI) as the primary endpoint and reported no significant difference between treatment groups. (121). Four further studies reported weight +/- BMI as secondary endpoints and also found no significant changes between treatment groups (23, 120, 124, 129).

2.3.4.5: Micronutrients

One study reported significantly higher α-tocopherol concentrations in patients receiving SMOF versus SO after a four-week intervention (41.63(14.48) vs 30.35(12.54) □mol/L, p=0.0012). This is unsurprising since SMOF is enriched with vitamin E (22). In a different study comparing OO-SO with SO, there were non-significant differences in α-tocopherol concentrations between treatment groups (120).

2.3.4.6: Inflammation

In the cross-sectional study by Pironi et al., the inflammatory risk index (ω-6:ω-3 ratio) was lowest in patients receiving SMOF, and highest in the lipid free group (No-IVLE, ($p<0.001$). Additionally, the cardiovascular risk index (n-3 index) was higher in the SMOF group compared with all other HPN groups ($p<0.001$). Six studies reported non-significant changes in inflammatory markers (22, 121, 124-126, 128).

2.3.4.7: Fatty acids

The fatty acid (FA) profile of erythrocytes was reported in the study by Dahlan et al (118) where all patients were randomised to both treatment groups in a cross-over design. After three months of SO, linoleic acid (LA; 18:2n-6) increased whereas arachidonic acid (AA; 20:4n-6) and the ω-3:ω-6 ratio decreased. Conversely, infusion of MCT/LCT did not alter erythrocyte FA, and the increase in LA (18:2n-6) observed with SO disappeared following 12

weeks of MCT/LCT. In a similar cross-over study by Clermont-Dejean et al (128), the infusion of SMOF vs SO was associated with increased proportions of EPA and DHA.

Vahedi et al (120) reported statistically significant differences between treatment groups for plasma oleic acid (OA, C18:1n-9), y-linolenic acid (y-LA, 18:3n-6), and Mead acid (20:3n-9) with higher concentrations in the OO-SO versus the SO group. The difference in y-LA concentration observed in plasma was also evident in lymphocytes.

In the prospective comparative study by Osowska et al, patients were transferred from SO to OO-SO or SMOF (125). There were significant treatment differences between groups for palmitic acid (16:0), eicosatetraenoic acid (20:4n-3), eicosapentaenoic acid (EPA, 20:5n-3), docosapentaenoic acid (22:5n-3) and docosahexaenoic acid (DHA, 22:6n-3), which all increased with SMOF, and decreased with OO-SO. Conversely, myristic (14:0) and a-linolenic acid (18:3n-3) decreased with SMOF and increased with OO-SO. There were significantly larger increases in palmitoleic and oleic acid, and significantly greater decreases in stearic (18:0) and dihomo-y-linolenic (20:3n-6) acid in the OO-SO group. Reimund et al reported that plasma a-linolenic acid concentration decreased following three months of OO-SO (124).

Similar results were reported across studies in relation to fourth generation LEs. In one RCT comparing SO with SMOF in a four-week intervention (22), SMOF was associated with significant increases in plasma EPA and DHA and a significantly lower ω-6:ω-3 ratio in plasma and erythrocytes. Similar findings were reported in a comparative study whereby patients were transferred from SO to SMOF for 60-days (125). There were significant increases in the plasma proportions of EPA, docosapentaenoic acid (DPA; 22:5n-3) and DHA, and significant decreases in plasma LA, a-linolenic acid, eicosadienoic acid (20:2n-6), di-homo-g-linoleic acid (20:3n-6), and Mead acid. When comparing the SMOF group with the OO-SO group, participants prescribed SMOF had higher proportions of palmitic acid, stearic acid, di-homo-g-linolenic acid, arachidonic acid, and all ω-3 PUFAs including EPA and DHA. Conversely, the proportions of oleic acid, a-linolenic acid and eicosenoic acid (20:1n-9) were higher in the OO-SO group than the SMOF group.

Bohnert et al (121) measured erythrocyte, platelet and serum phospholipid FA and found significant increases in EPA, DHA and DPA, and significant decreases in LA, ARA, Di-homo-γ-linolenic acid (DGLA) and GLA following 8-weeks of MCT/LCT/FO. When compared with MCT/LCT, significant treatment differences for n-6 PUFAs were found in erythrocytes (ARA, DGLA and GLA), platelets (LA, DGLA and GLA) and serum phospholipids (LA, ARA) as each of these lipid classes decreased with MCT/LCT/FO. Similarly, in the study by Weylandt et al (126) in which all patients received FO following an 8-week washout period, there were significant increases in the Omega-3 index, and in the erythrocyte proportions of LA, EDA, ARA and AdA. Similar results were seen by Klek at al (123), with signficiant increases in the proportions of EPA and DHA in plasma and RBC following eight weeks of MCT/LCT/FO. The increase in EPA and DHA was accompanied by a decrease in the content of the AA.

When Sevela et al (127) compared SMOF with SO/OO, they observed lower di-homo-g-linoleic acid and total n-6 PUFAs, and conversely, higher EPA and total n-3 PUFAs proportions in the phospholipids with SMOF. Furthermore, the addition of FO further reduced the proportion of n-6 and increased the proportion of n-3 PUFAs in all IVLE.

In the cross-sectional study (130), vaccenic acid correlated positively with the weekly load of glucose in the SMOF and OO-SO groups ($p=0.053$ and 0.007). The SMOF group showed the highest EPA and DHA and the lowest AA percentages ($p<0.001$). EPA and DHA were positively correlated with the daily amount of SMOF ($p=0.044$), and the number of HPN infusions per week ($p=0.046$). In the OO-SO group, the percentage of oleic acid correlated positively with the weekly load of OO-SO ($p=0.043$

Table 2.5: Summary of results from the 10 included studies

Reference	Study detail	IVLEs	Safety/ tolerance	Inflammation/ peroxidation	Liver function	Fatty acids	Other
Dahlan et al 1992 (118)	Randomised crossover, n=5, 3 months	SO then SO-MCT Or SO-MCT then SO	NI	NI	NI	SO group: RBC PL FA: linoleic acid ↓ Arachidonic acid & n-3:n-6 ratio ↓ SO-MCT group: Did not alter RBC FA, and even tended to correct a pattern altered by the previous SO infusion.	NI
Rubin et al 2000 (119)	Double blind randomised crossover, n=22, 4 weeks	Structured SO-MCT then SO SO then structured SO-MCT	Vomiting: n=5 pts for SO/OO n=4 for SO	NS	↑ in serum AST, ALT, and GGT in 2 patients with SO in week 4, part 1. Levels returned to normal once changed to structured SO-MCT.	NS	Haematology & biochemical variables: NS Plasma lipids: NS
Vahedi et al 2005 (120)	Double blind RCT, n=13, 3 months	SO-OO SO	NS	NS	NS	SO-OO group: Plasma PL FA: oleic acid, gamma-linolenic acid & mead acid ↑	Haematology & biochemical variables: NS
Klek et al 2013 (22)	RCT, n=73, 4 weeks	SMOF SO	10 SAE in 8 pts with SO vs 2 in 2 pts with SMOF (p=0.03)	NS	ALT, AST & bilirubin were lower in the SMOF group (p=0.049, 0.027 & 0.043)	Plasma & RBC: EPA and DHA ↑ & n6:n3 ratio was significantly lower in the SMOF group versus the SO group	Serum a-tocopherol ↑ with SMOF (p<0.005)
Reference	**Study detail**	**IVLEs**	**Safety/ tolerance**	**Inflammation/ peroxidation**	**Liver function**	**Fatty acids**	**Other**

Bohnert et al 2018 (121)	RCT, n=42, 8 weeks	SO-MCT-FO SO-MCT	NI	NS	NS	SO-MCT-FO group: Erythrocytes, platelets & serum PL: EPA, DHA and DPA □ Linoleic acid, arachidonic acid, di-homo-g-linolenic acid, gamma linolenic acid □	Weight/BMI: NS QoL: NS
Klek et al 2018 (122)	RCT, n=67, 12 months	SO-MCT SO-OO SMOF SO	No AE recorded	NI	NS	NI	NI
Klek et al 2020 (23)	RCT, n=67, 60 months	SO-MCT SO-OO SMOF	No AE recorded	NI	Significant □ in median bilirubin concentration with SMOF (p=0.0138)	NI	NI
Klek et al 2024 (123)	RCT, n=72, 8 weeks	SO-MCT SO-MCT-FO	56 AEs in 28 pts. NS between groups	NI	NS	SO-MCT-FO group: Plasma & RBCs: EPA and DHA □□resulting in an increased n-3 index in RBCs Plasma triene:teraene ratio decreased in both groups with a lower mean value in the SO-MCT-FO group vs SO-MCT (p.048)	NI
Reference	**Study detail**	**IVLEs**	**Safety/ tolerance**	**Inflammation/ peroxidation**	**Liver function**	**Fatty acids**	**Other**

Reimund et al 2005 (124)	Cohort, n=14, 3 months	SO or MCT/LCT then SO-OO	3/5 patients presenting with migraine without aura during HPN infusion felt consistently better with OO/SO No AE recorded	NS	NS	SO-OO group: Significant ⍰ in a-linolenic acid	Weight/ BMI: NS Plasma lipids & fat soluble vitamins: NS Electrolytes & trace elements: NS
Osowska et al 2019 (125)	Cohort, n=28, 2 months	SO then SMOF SO-OO	NI	NS	Significantly lower GGT with SO-OO (p=0.044)	SMOF group: Linoleic acid, a-linolenic acid, eicosadienoic acid, di-homo-g-linolenic acid & mead acid ⍰. EPA, DPA & DHA ⍰. SO-OO group: Palmitic acid, stearic acid, linoleic acid, eicosadienoic acid, di-homo-g-linolenic acid, arachidonic acid, mead acid, EPA & DHA ⍰. Palmitoleic acid & oleic acid ⍰.	Blood lipids: NS
Reference	**Study detail**	**IVLEs**	**Safety/ tolerance**	**Inflammation/ peroxidation**	**Liver function**	**Fatty acids**	**Other**

Weylandt et al 2022 (126)	Prospective, longitudinal cross-over	SO-MCT then SO-MCT-FO	NI	NS	NS	Addition of FO: Median Omega-3-Index ⍰ from 9.57% to 12.75%. LA, EDA, ARA & AdA ⍰ EPA-derived and DHA-derived CYP-dependent and LOX-dependent metabolites ⍰ Absence of FO: EPA, DPA, DHA & OA ⍰	NI
Secvela et al 2024 (127)	Prospective cross-over	SMOF then SO-MCT-FO or SMOF then SO-OO All + FO	NS	FO significantly lowered SOD1 activities.	NS	Phospholipids: Lower dihomo-γ-linoleic acid and total *n*-6 PUFAs and, higher EPA and total *n*-3 PUFAs proportions in the SMOF vs the SO-OO regimen. NS difference between SMOF vs SO-MCT-FO or SO-MCT-FO vs SO-OO	NS differences in bile acids.
Clermont-Dejean et al (2023) (128)	Prospective cross-over	SO SMOF	NS	NS	NS	SMOF: EPA, DHA ⍰.	NS
Clermont-Dejean et al 2021 (129)	Prospective cohort	SO SMOF	NI	NI	NS	NS	Weight/ BMI: NS Line sepsis: NS SMOF: ⍰⍰hospitalisations (p.001)
Reference	**Study detail**	**IVLEs**	**Safety/ tolerance**	**Inflammation/ peroxidation**	**Liver function**	**Fatty acids**	**Other**

Pironi et al 2017 (130)	Cross-sectional	SO SO-OO SMOF No-IVLE	NI	CV risk: n-3 index - intermediate risk in OO/SO and NO-LE, low risk in SMOF Free radical stress index & %trans index = NS	NI	Percentage of oleic acid in RBCs positively correlated with the weekly load of SO-OO (p=0.043). RBC membrane EPA and DHA positively correlated with the daily amount of SMOF (p=0.044) and the no. HPN infusions/ week (p=0.046). Highest EPA and DHA and the lowest arachidonic acid percentages (p< 0.001) in the SMOF group Vaccenic acid positively correlated with the weekly HPN load of glucose with SO-OO (p=0.007) and SMOF (p=0.053)	Weight/ BMI: NS

Abbreviations: NI, no information; NS, non-significant; RBC, red blood cell; PL, phospholipids; FA, fatty acid; SAE, serious adverse events; ALT, alanine transaminase; AST, aspartate transaminase; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; BMI, body mass index; QoL, quality of life; GGT, gamma-glutamyltransferase; AE, adverse event; CV, cardiovascular; SOD, superoxide dismutase

2.4: Discussion

Fifteen studies involving a total of 519 participants were included in this review. There were 13 unique studies, since one study published initial results after 12 months and further outcomes after 5 years (23, 131). We included randomised controlled trials (RCTs), cohort and cross-sectional studies to provide all available evidence published in this area.
Our initial aim was to systematically review and evaluate the evidence for the differential effects of HPN solutions and to identify compositional features associated with differences in clinical endpoints. Except for one study including lipid-free HPN, only studies comparing lipid emulsions (LE) were identified and, consequently, the results, and much of this discussion, are focussed around LE. The included studies varied considerably with regards to length, sample size and interventions, reflecting the four generations of LE. Comparisons were made between SO and MCT/LCT or structured MCT/LCT (118, 119); SO and SMOF (22, 128, 129); MCT/LCT/FO and MCT/LCT (121, 123); SO, MCT/LCT, OO-SO and SMOF (122); MCT/LCT, OO-SO and SMOF (23); SO and OO/SO (124); SMOF and OO-SO (125); SO/MCT/FO, OO/SO and SMOF (127); and OO-SO, SMOF and No-IVLE (130). Due to the heterogeneity of the data, combining the data for statistical analysis was not feasible and therefore the reported findings were synthesised via a narrative summary.

With the exception of one study where a number of adverse events were assessed as possibly or probably related to SO (22), a major finding of our review is that all LE were reported to be well tolerated with no significant side effects. There were few differences in inflammatory biomarkers, although SMOF may be associated with a higher ω-3 cardiovascular risk index (represented by the sum of omega-3 PUFAs, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) (130). The higher the index, the lesser the risk of a cardiovascular event. These effects of additional EPA and DHA may be due to decreasing plasma triglycerides, inflammation, platelet aggregation and improving vascular reactivity (132) but, since these findings were reported in a cross sectional study, causality cannot be established.

A second significant finding of this systematic review is just how limited is the currently available evidence. Not a single study was found that compared the micronutrient or amino acid composition of HPN, possibly owing to a lack of universal consensus on the optimal

measures to use to assess micronutrient status in this patient group, and the unavailability of individual micronutrients for inclusion in HPN solutions in some countries. Much of the relevant evidence comes from case reports and retrospective epidemiological studies which have identified potentially toxic concentrations of copper, manganese and chromium, and signs of selenium and zinc deficiency in patients treated with HPN (74, 133). This highlights the priority of research to provide better understanding the need for reduced, or increased, doses of individual micronutrients in HPN patients with different underlying nutritional status and disease states.

Given that the aims of HPN include preventing or treating undernutrition and maximising quality of life (QoL) (13), it is surprising that only one study sought to understand the impact of HPN on QoL, and only 11 studies reported the weight or body mass index of the participants. The absence of QoL data may reflect the historical lack of validated HPN specific QoL tools. However, as research on, and clinical care for, patients with IF continues to progress, it is essential to investigate not only the effects of composition of HPN solutions on morbidity and mortality, but their impact on the QoL of patients.

In agreement with previous reports (113, 134), there were consistent findings across eight studies with regards to fish oil containing LEs and fatty acids (22, 121, 123, 125-128, 130). As anticipated, LEs containing fish oil were associated with increases in the proportions of omega-3 PUFAs EPA (20:5n-3) and DHA (22:6n-3). EPA and DHA are of particular clinical interest because these fatty acids compete with the omega-6 PUFA arachidonic acid (AA, C20:4) for incorporation into cellular membranes, and for metabolism by the enzymes that produce eicosanoids (132). Thus, EPA and DHA produce fewer pro-inflammatory mediators than AA. Furthermore, non-plant sources of lipid such as fish oil contain fewer phytosterols than SO. Theoretically this is advantageous as phytosterols inhibit the enzymes involved in the synthesis and metabolism of cholesterol and bile acids and, therefore, have been implicated in the development of IFALD when utilised long-term (135, 136). Whether these changes in patterns of fatty acids translate into clinical benefit has not been established.

Additional to the theoretical benefits discussed above, SMOF was associated with reductions in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin

following a four-week intervention (22). However, in other studies, these changes were not observed after an eight week (123) or 12-month intervention (122) but lower bilirubin was observed after 5 years (23). This suggests that any potential benefits of SMOF on liver enzymes may be transient. Alternatively, SMOF may be beneficial in patients with impaired liver function as suggested by a recent report on the largest case series of patients with intolerance to SO (137). Seventeen patients were transitioned to SMOF and followed up for a minimum of 12 months. Alkaline phosphatase (ALP) and triglyceride levels stabilised; AST, ALT and bilirubin levels decreased significantly; and vitamin E concentrations were significantly higher at 12 months. There was also a significant increase in the amount of energy provided by lipid and a subsequent decrease in energy from dextrose.

Essential fatty acid deficiency (EFAD) has been shown to occur in patients receiving lipid-free parenteral nutrition within two to four weeks (138-140). One study reported up to 30% of patients may develop symptoms of deficiency after one week, 66% at two weeks, 83% at three weeks, and 100% at four weeks (141). However, there have been no reports of EFAD in patients receiving the newer generations of LE and the findings of our systematic review suggest that these are sufficient to maintain normal EFA status in patients treated with HPN. There were no reports of EFAD in the three studies that measured EFA, each with a minimum follow up period of two months. These findings were further corroborated by Klek et al who reported no signs of EFAD following a 60-month intervention with SMOF (23).

Despite the scientific rigour in gathering, selecting, and summarising the data, the evidence in this review is limited by the paucity of RCTs, by the small sample sizes in most studies, and by a lack of interventions comparing the concentrations of micronutrients, amino acids and glucose in HPN solutions. The patient population in the included studies is heterogenous and, since very different LE were compared, meta-analyses was not feasible. IF patients treated with HPN are relatively rare with a prevalence of only 2500 people in England (9) and the management of such patients varies depending on geographical location. For example, in Europe patients are managed by major IF centres whereas, in America, providers who sign for HPN orders typically follow just one patient (142). This makes it difficult to gather data regarding the effectiveness of treatment and the associated complications and to run RCTs within the IF with HPN population. The inclusion of data from cohort and cross-sectional

studies in this review strengthens the evidence base, but with the proviso that causality cannot be established in such studies and directionality of associations cannot be seen in cross-sectional studies. Nine studies were identified that were not included in the systematic review published by Ahmed et al (113); two RCTs that were published since the previous literature search, six cohort, and one cross-sectional study. Comparison of outcomes across the different study types indicates that third and fourth generation lipids, SO-OO and SMOF, are safe and may exert favourable influences on liver function, fatty acid profiles and inflammation. The consistency in findings from different study designs supports the view of Shrier et al 'that excluding observational studies in systematic reviews a priori is inappropriate and internally inconsistent with an evidence-based approach".

2.5: Conclusion

This chapter provides an overview of the various intravenous lipid emulsions available for use in clinic practice. The main finding, however, is that despite the increasing use, and the complexity of, HPN, surprisingly few data are available to guide the provision of macro and micronutrients for adults requiring this therapy, highlighting the importance of the subsequent research reported in this thesis. Although LE containing olive and/or fish oil show promise with regards to liver function and blood and cell fatty acid profiles, further studies are required before drawing definitive conclusions on the clinical value of these emulsions.

Chapter 3: Clinician Survey

Quality of Life and Home Parenteral Nutrition: A Survey of Healthcare Professionals' Knowledge, Practice and Opinions

The research reported in this chapter has been published in *The Journal of Human Nutrition and Dietetics* and can be found using reference: **Kirk C,** Pearce MS, Mathers JC, Thompson NP, Gemmell L, and Jones DE. Quality of Life and Home Parenteral Nutrition: A Survey of UK Healthcare Professionals' Knowledge, Practice and Opinions. 2022. *J Hum Nutr Diet.* 36(3):687-696

3.1: Introduction

Quality of life (QoL) is a multi-dimensional concept that refers to 'an individuals perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations and standards' (143). QoL has been identified as the third most important outcome indicator that is essential for good quality of care in benign home parenteral nutrition (HPN) care in two multicentre, international studies. The first study was based on the opinions of healthcare professionals (HCPs) who identified incidence of catheter-related blood stream infections, incidence of rehospitalisations, and QoL as quality indicators (144). The second study was based on the opinions of patients. Their top three desired outcomes were incidence of catheter-related infection, survival and QoL (145). Consequently, current European guidelines recommend that 'QoL should be used as criteria to assess the quality of care of HPN program' (13) and 'quality of life for HPN patients be regularly measured using validated tools as part of standard clinical care' (35). However, little is known about whether healthcare professionals (HCPs) have embedded QoL assessment into routine clinical practice that would facilitate a more holistic approach to HPN care, the frequency of these assessments and the instruments of choice. Previous studies of HCPs using QoL assessments have focussed on doctors. For example, a study exploring knowledge and perception of importance of health-related QoL amongst physicians found that only 38% of respondents were aware of QoL literature and used the results in clinical practice, or for research purposes (146). In a survey of oncologists, 57% of participants felt that decisions were more difficult when they considered QoL issues, and despite 87% reporting QoL studies were useful for patient care, 69% reported that they would be more likely to base recommendations on experience rather than published literature (147).

Consequently, the first aim of this chapter was to assess the extent of QoL assessment in clinical practice among HCPs within multi-disciplinary teams with responsibility for HPN patients. In particular, I sought to understand why QoL is being measured, which instruments are being utilised, and the reasons for those choices. A second aim was to assess knowledge of QoL tools and the currently published literature on assessing QoL for patients receiving HPN. My final aim was to understand the opinions of HCPs on the contributors to poor QoL, and perceived importance of QoL assessment in clinical practice.

3.2: Method

An online survey was developed specifically for this study and therefore not previously validated. It was developed using a four-stage process. In the first instance, studies published in PubMed were screened to identify publications where surveys were used to understand knowledge and perception of importance of QoL. Key terms were combined as follows: physicians, questionnaire, survey, knowledge, perception of importance and quality of life. Only one relevant paper was returned titled 'Physicians knowledge of health-related quality of life and perception of its importance in daily clinical practice (2010) (146)'. Questions were extracted and used as a basis for my survey.

The second stage involved speaking with the nutrition team at the Freeman Hospital to get an insight into the language used when talking about quality of life. Clinicians were asked to describe a patient with good QoL and a patient with poor QoL. The answers and their choice of words were used to inform additional survey questions.

The third stage involved asking a working group of home parenteral nutrition (HPN) specialists to pilot the survey and score it out of 10 for ease of completion and clarity. This allowed a realistic estimate of time-to-complete. A small number of ambiguities were highlighted, which were corrected prior to implementation. Except those questions that were relevant to participants who actually measure QoL, all others were made mandatory.

The finalised survey (Appendix C) was uploaded to Crowdsignal; an online tool that can be used to create polls, surveys and quizzes, and was open for one month. Crowdsignal was chosen because Newcastle Hospitals provided a license free of charge and also because the software allows distribution of surveys via email, social media or on websites. Healthcare professionals (HCPs) throughout England, Scotland, Wales and Northern Ireland with responsibility for care of patients receiving HPN were invited to participate via an email. Participants were identified using a mailing list for the British Intestinal Failure Alliance (BIFA) which is a specialist group within the British Association for Parenteral and Enteral Nutrition. The email contained study information and a survey link. The link was printed in a newsletter produced by the Parenteral and Enteral Nutrition Group of the British Dietetic

Association and was also shared via the social media site Twitter. As responses were anonymous and did not include patient data, ethical approval was not required.

The four key focus areas for data collection were demographics, current practice, knowledge and opinions (Figure 3.1). The survey contained 24 closed questions and an 'additional comments' box at the end of the survey. There were also opportunities to write additional comments at the end of each closed question.

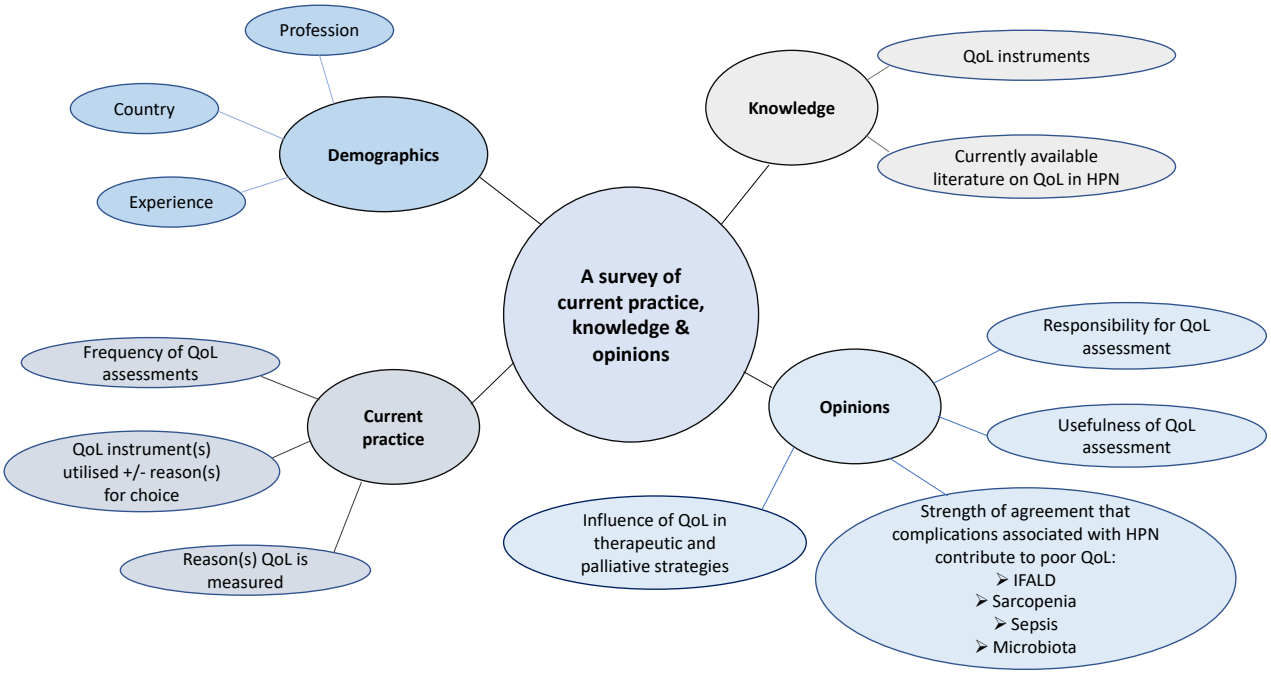


Figure 3.1: Conceptual diagram showing the four key areas of data collection

3.2.1: Statistical analysis

Results were exported from Crowdsignal to Microsoft® Excel and copied to Stata SE 17 statistical analysis software. A descriptive data analysis was performed to establish frequencies and proportions, and Pearson's chi-squared test was used to investigate differences between professions, centres, or lengths of experience. Due to the small number of responses from certain centres and professions, HPN centres (centres providing parenteral nutrition care to patients at home), intestinal failure centres (those providing support to inpatient surgical patients) and 'other' centres (hospitals not categorised as intestinal failure or HPN centres but that have responsibility for patients treated with HPN for example a patient's local hospital) were grouped together, as were pharmacists, surgeons and psychologists. A p-value of <0.05 was considered statistically significant. To

assess sample representation, each of the 23 centres providing HPN care in the UK was contacted to establish how many HCPs could have potentially participated in the survey.

3.3: Results

3.3.1: Demographics

The survey was completed by 67 healthcare professionals (HCPs). Their characteristics are summarised in Table 3.1.

Table 3.1: Demographics of survey participants

		N (%)
Country of workplace	England	53 (79)
	Scotland	7 (10)
	Northern Ireland	4 (6)
	Wales	3 (4)
Type of centre	Integrated HPN and IF centre	46 (69)
	HPN centre	7 (10)
	IF centre	3 (4)
	Other	11 (16)
Profession	Dietitian	24 (36)
	Nurse	17 (25)
	Gastroenterologist	14 (21)
	Pharmacist	6 (9)
	Surgeon	5 (7)
	Psychologist	1(2)
Years of experience of working with HPN patients	< 5	14 (21)
	5-10	14 (21)
	10-15	15 (23)
	15-20	9 (14)
	>20	14 (21)

Abbreviations: HPN, home parenteral nutrition; IF, intestinal failure

3.3.2: Sample representation

An estimated 41% of eligible participants completed the survey. With the exception of dietitians of whom 65% participated, this equates to approximately one third of each individual speciality with 34% of potential gastroenterologists participating, 30% of pharmacists, 34% of nurses, 42% of surgeons and 33% of psychologists.

3.3.3: Current practice

Over half of participants (57%) reported that quality of life (QoL) was never measured in their patients, 14% said it was measured ≤3 yearly, 6% every 2 years, 6% annually and 14% of

respondents were unsure (Figure 3.2). When the responses were separated by type of centre, 50% of participants from integrated intestinal failure/ home parenteral nutrition (IF/HPN) centres, and 86% of participants from HPN centres never measure QoL. Similarly, when the results were separated by participants that thought the measurement of QoL was useful, 50% reported never measuring QoL.

The HPN quality of life (HPN-QoL) instrument was the most frequently used tool, being chosen by 40% of the participants that measure QoL. This was followed by the short form 36 (SF-36) and EQ-5D, each used by 14% of those who measured QoL. Of these HCPs, 12% opted for the short bowel syndrome quality of life (SBS-QoL) questionnaire, 10% chose the parenteral nutrition impact questionnaire (PNIQ), 2% used the HPN patient reported outcomes questionnaire (HPN-PROQ) and 16% reported 'other' surveys such as the distress thermometer.

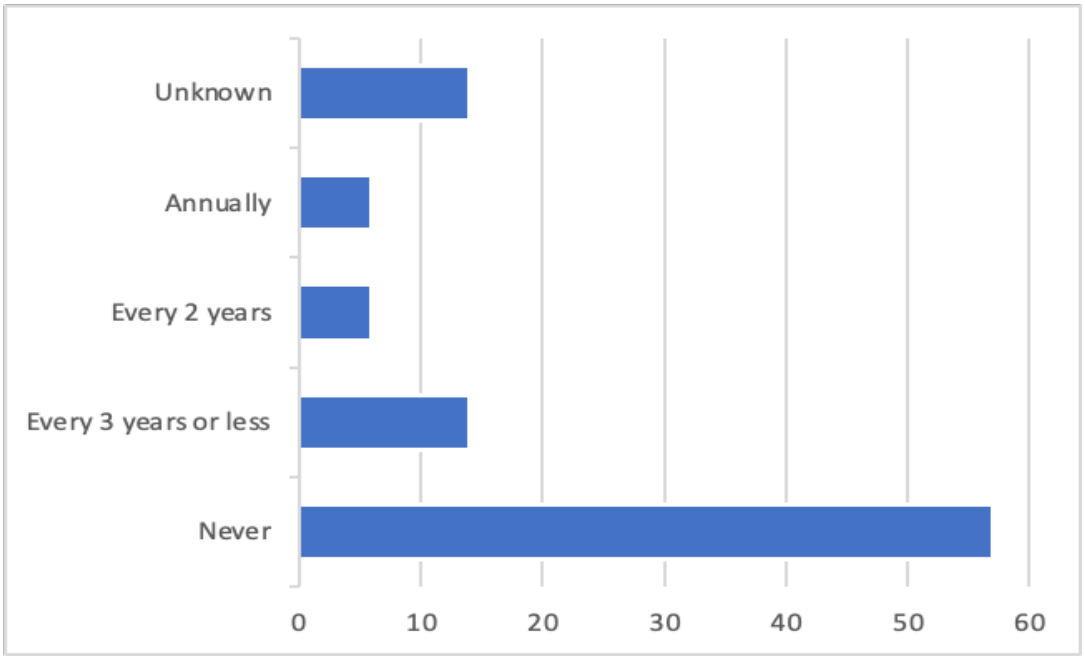


Figure 3.2: Frequency of QoL assessments (%)

The two most selected reasons for choosing a particular QoL instrument were the tool was an established unit of practice (36%) and familiarity (31%). Less popular reasons were ease of use (11%) and the instrument being part of a study (8%). 14% of HCPs were unsure why a QoL measure was chosen and no participants made a choice based on patient preferences. In terms of how the results of QoL assessments are shared, 29% of HCPs share with the

wider clinical team, 26% disseminate the results at conferences, 12% with patients, 12% in journals, 12% do not share results at all and 7% were unsure (Figure 3.3).

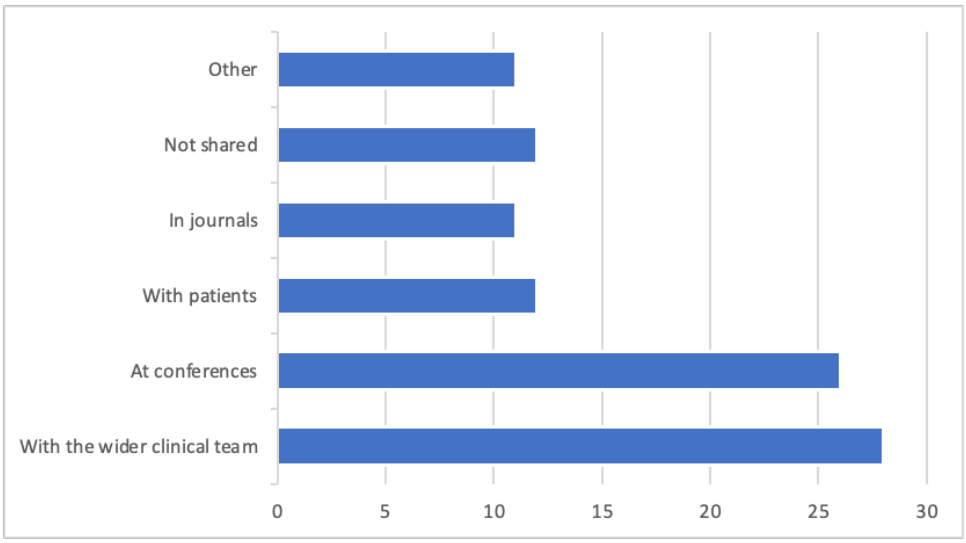


Figure 3.3: How the results of QoL assessments are shared (%)

*Respondents could give more than one answer to this question.

The reasons for measuring QoL included service evaluation (27%), research (21%), to inform decision making (13%), to identify patient preferences and help clinicians to make informed decisions (13%), because it is part of routine clinical care (10%), and to improve patient-provider communication and shared decision making (10%). A few participants (5%) were unsure why QoL is measured (Figure 3.4).

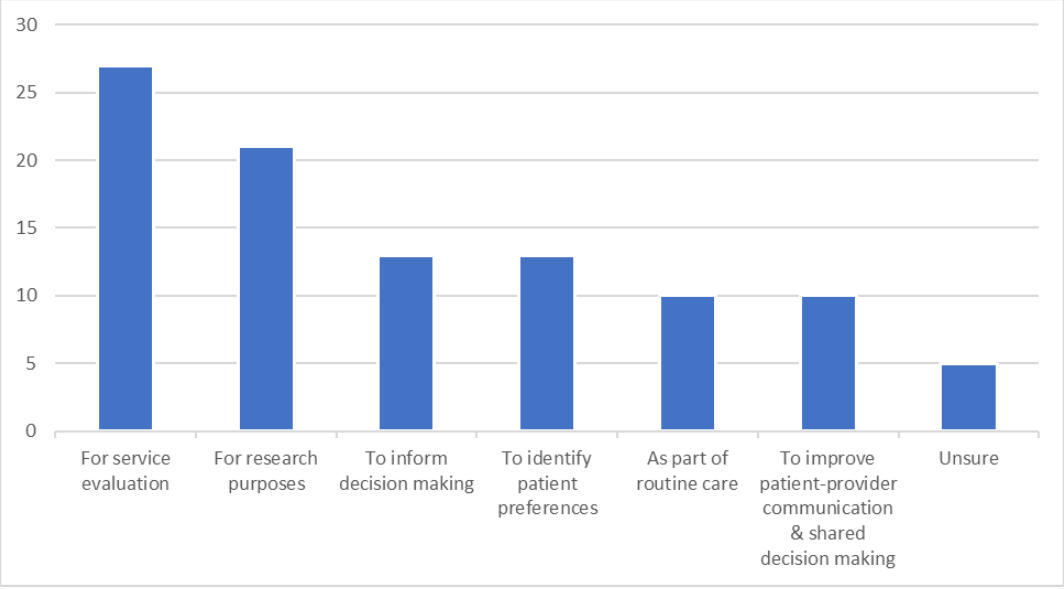


Figure 3.4: The reasons for measuring QoL (%)

*Respondents could give more than one answer to this question.

3.3.4: Knowledge

The HPN-QoL tool was the most familiar tool amongst HCP's with 23% of participants having knowledge of it. This was followed by the SF-36 (17%), PNIQ (14%), EQ-5D (12%), SBS-QoL (11%), HPN-PROQ (8%), and the New-QoL questionnaire. Other tools reported included the distress thermometer (1%), HAD score (1%) and the MSPSS (1%). Eleven percent of participants reported having knowledge of none of the tools. In terms of the currently available literature on QoL in HPN, 40% of participants reported having 'poor' or 'very poor' knowledge, 39% reported 'fair' knowledge and only 20% 'good' or 'very good' (Figure 3.5). Those with more experience (>20 years) were more likely to have knowledge of the SF-36 than those with 5, or fewer, years' experience (p=0.005) and gastroenterologists were more familiar with SF-36 than dietitians and nurses (p=0.014), and more familiar with the EQ-5D than all other professions (p=0.047).

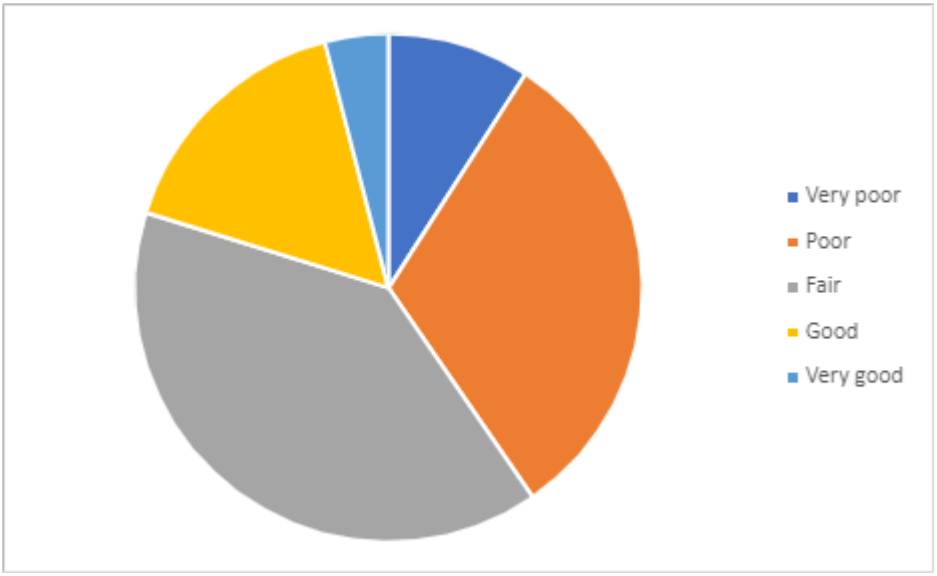


Figure 3.5: HCP's own rating of their knowledge of the currently available literature on QoL in HPN (%)

3.3.5: Opinions

Most respondents (86%) agreed or strongly agreed that intestinal failure associated liver disease (IFALD) and sarcopenia are contributors to poor QoL whereas 13% were undecided for both complications and only 1% disagreed. There was little consistency in opinions about the role of the gut microbiota with 57% of participants being undecided as to whether the gut microbiota impacts QoL, 42% agreed or strongly agreed, and 1% disagreed. All

participants agreed or strongly agreed that recurrent sepsis is a contributor to poor QoL (Figure 3.6).

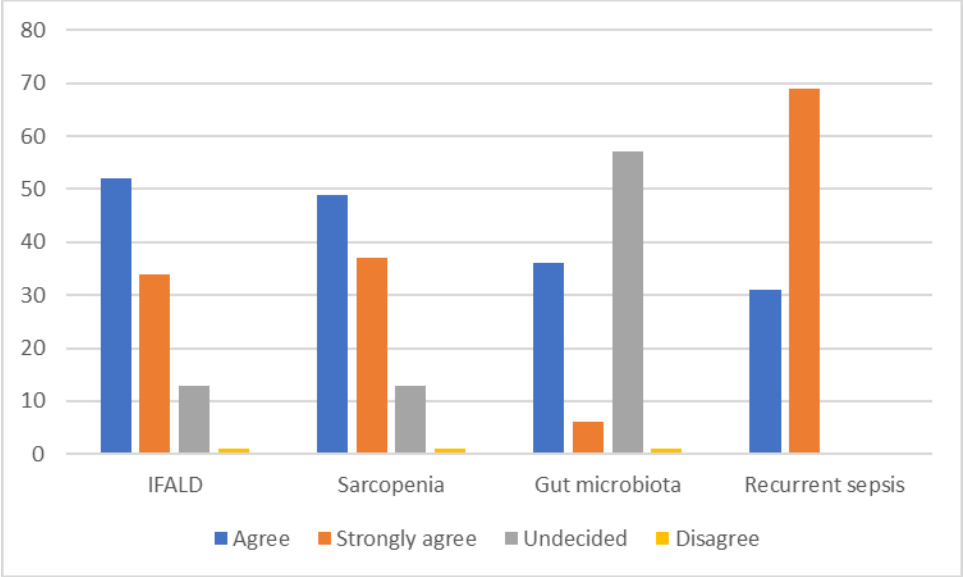


Figure 3.6: Strength of agreement that complications associated with HPN contribute to poor QoL (%)

When asked about the role of QoL in HPN treatment, 86% of participants agreed or strongly agreed that QoL should influence therapeutic strategies. Similarly, 81% and 91% of participants agreed or strongly agreed that QoL should influence the decision to commence HPN and palliative HPN, respectively. A minority (16%) of participants were undecided about the role of QoL in making a decision to commence HPN and 8% were undecided about palliative HPN (Figure 3.7).

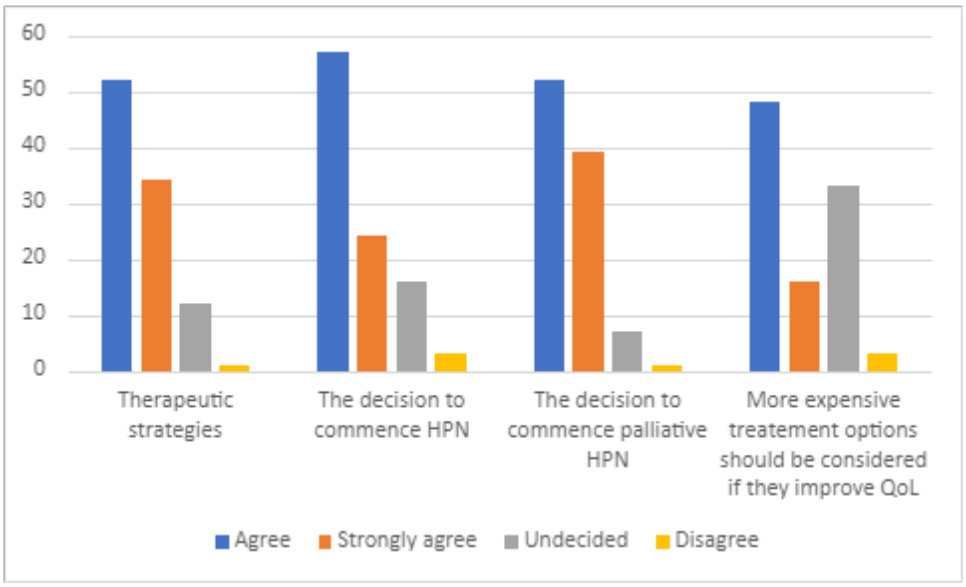


Figure 3.7: Strength of agreement that QoL should influence HPN therapy (%)

80% of participants agreed or strongly agreed that the measurement of QoL in HPN patients is useful and 20% were undecided.

When asked whether more expensive treatment options should be considered if they improved QoL, 64% of participants agreed or strongly agreed and 33% were undecided. The majority (75%) of participants agreed or strongly agreed that QoL assessments facilitate patient-clinician communication whereas 22% were undecided and 3% disagreed. When asked whether the idea of QoL is a flawed one, whose variables are very difficult for the clinician to analyse, to control, and therefore to integrate into clinical decision making, 26% of participants agreed or strongly agreed, 28% were undecided and 44% disagreed or strongly disagreed (Figure 3.8).

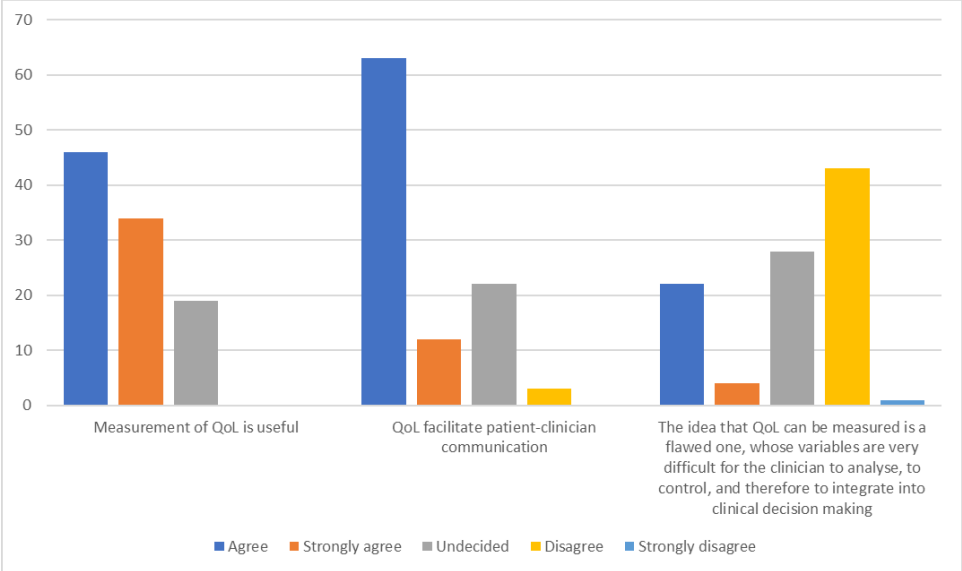


Figure 3.8: Strength of agreement of HCPs on benefit of QoL assessment (%)

For the different centre types, 98% of participants from integrated IF/HPN centres compared with 67% of participants from the other centres (HPN, IF, 'other') combined (p=0.024) agreed or strongly agreed that QoL should influence the decision to commence palliative HPN.

3.3.5: Free-text survey comments

Free-text comments to all survey questions can be seen in Appendix D. In summary, many HCPs questioned the relevance of existing QoL measurement tools, expressing a preference for patient-designed instruments that better reflect lived experience. There was concern that clinician-selected tools may lack sensitivity to the nuanced realities of life on HPN. Secondly, a recurring tension was noted between numerical scoring systems and narrative understanding. While some acknowledged the utility of quantified data for research and longitudinal comparison, others argued that rich narrative insights gained through patient dialogue are more meaningful for clinical decision-making. One respondent stated, *"Much better to evaluate QoL by talking to your patients… they can interpret the decisions required in the context of their quality of life.* Relatedly, respondents emphasised that QoL tools are most effective when they facilitate communication, particularly for less experienced clinicians, and support holistic, patient-centred care. *"It's not the measurement that makes the difference, it's the patient feeling they can express their concerns to the team,"* wrote

one participant. Another observed, *"They can be helpful where patients note things they haven't told the clinician. But this is sometimes just making up for poor communication."*

QoL was widely regarded as an important consideration in HPN-related decision-making, although its integration was described as challenging, particularly in acute or palliative scenarios. Many highlighted the importance of shared decision-making, weighing the potential for improved QoL against treatment burden and risks. One clinician commented, *"QoL should be considered alongside other medical decisions – not in isolation."* Another shared a memorable case: *"A young woman initially refused surgery due to fears about HPN, but changed her mind post-operatively. Three years later, she sent me a photo of herself diving into the sea. That image stays with me."*

Contributors to poor QoL identified by respondents included recurrent sepsis, sarcopenia, and social isolation. Conversely, some conditions such as IFALD, were perceived to have a less direct impact on daily wellbeing unless advanced. Finally, respondents recognised that QoL is inherently subjective and context-dependent, shaped by individual circumstances, expectations, and support networks. Despite concerns around measurement limitations, there was strong consensus that QoL should be regularly assessed and integrated into routine care planning wherever possible: *"We should probably use a formal method of assessing QoL… thanks for making me think about this more."*

3.4: Discussion

To my knowledge, this chapter presents the first survey that has investigated current practice, knowledge and the opinions of healthcare professionals (HCPs) with regards to quality of life (QoL) and home parenteral nutrition (HPN). There was consensus that the measurement of QoL in HPN patients is useful, yet over half of participants never assess QoL and 40% rated their knowledge of QoL literature poor or very poor. These findings are consistent with those reported by Morris et al who surveyed 260 oncologists and found that, although 80% believed that QoL should be measured prior to treatment, fewer than 50% of participants collected such information (148). Evidently, there is disparity between perceived utility of QoL assessment and its implementation in clinical practice. The reasons for this are likely multifactorial. For example, the absence of clinical guidelines, insufficient time, limited expertise of the QoL measure and possibly a lack of training and resources. These suggestions are supported by Skevington et al who investigated the barriers to using QoL

information in a cohort of general practitioners (149). They reported that time was the greatest barrier, identified by 43% of respondents. Additional reasons for non-use were lack of understanding about how QoL data can be used and lack of evidence supporting its use. Morris et al also found that time and resource constraints, perceived lack of an appropriate instrument and a belief that the measurement of QoL is unnecessary were barriers to collecting QoL data (7).

A major finding of this research is the inconsistency in QoL practice for patients treated with HPN. This includes the wide range of QoL instruments, both generic and disease-specific, that are being utilised and the variation in frequency of QoL assessments, if at all. The HPN-QoL tool was the most familiar and frequently used tool amongst participants. This is possibly because it is the only tool acknowledged in the ESPEN 2016 and 2021 clinical guidelines on chronic intestinal failure (35, 150). There are, of course, multiple disease-specific measures validated for use in patients on HPN and that makes comparison of the HPN population across different centres and countries very difficult. Very few participants reported using the EQ-5D and SF-36, which are generic QoL and health utility measures. They have been criticised for underrepresenting dimensions that may be specific to a particular condition such as intestinal failure (151). However, such measures should not be seen as alternatives to disease-specific questionnaires and instead, complementary. Further inconsistencies in QoL practice include the multitude of different reasons for assessing QoL and the variation in disseminating findings. Some HCPs do not disseminate findings, whereas others disseminate widely through conferences and journals. Further, 5% of HCPs did not know why QoL was being measured or why a particular tool was chosen (14%).

Perhaps surprisingly, no respondents reported choosing a QoL measure based on patient preferences and very few HCPs share the results of QoL assessments with their patients. QoL instruments are designed to enable patients' perspectives of the impact of health and healthcare interventions on their lives to be assessed and considered in clinical decision making and also in related research. Consequently, it is ironic that patients do not have an input on the choice of measure. One participant highlighted a similar point in the additional comments *'But-we use tools that we HCP have deemed suitable; in the age of PPI (patient and public involvement) I would like to see standardised rigorous tools that are PATIENT*

made. Why do we think we know what is a good reflector of QoL when we (usually) haven't actually lived the life?'. It is important to highlight that patients were involved in the development of the parenteral nutrition impact questionnaire (PNIQ) which was developed through unstructured qualitative interviews with 30 HPN patients and identifies as being the first patient centric HPN patient reported outcome measure (80). Similarly, nine and 12 patients from the Scottish Home Parenteral Nutrition Managed Clinical Network were involved in the development of the HPN-QoL tool at stages one and three, respectively (79).

No significant differences were found across different professionals in their opinions of QoL assessment, nor was this related to length of experience. It seems that the opinions of HCPs are independent of profession and length of time working with HPN patients. Similarly, there were no differences in opinions between those participants that do, and do not, measure QoL. Unsurprisingly, gastroenterologists and HCPs with more experience have better knowledge of the SF-36 QoL questionnaire. The SF-36 is a generic health measure that was developed in the 1980's and has since been used in thousands of research studies and it is likely that gastroenterologists have used this tool in other areas of their practice.

When participants were asked whether the complications associated with HPN treatment (intestinal failure associated liver disease, sarcopenia and sepsis) contribute to poor QoL, there was almost unanimous agreement that they did. However, there is an absence of published literature supporting these questions and, therefore, these opinions must arise from clinical experience alone. Only one study specific to the HPN population has measured QoL in relation to nutritional status, liver function and blood tests. Bluthner *et al* found that bioelectrical impedance of phase angle, citrulline and haemoglobin levels were independent risk factors for QoL in a cohort of 90 HPN patients (97).

The diverse range of HCPs who participated in the survey is a strength of this study. In addition, because the survey was completed by approximately 41% of the total cohort of professionals responsible for care of those undergoing HPN from different types of clinical unit and from all four countries in the UK, it is likely that I captured views of the relevant HCPs community. Furthermore, questions were mandatory meaning unit non-response and any associated bias did not occur. The study also has limitations. First, participant response

rate may have been influenced by the mode of survey distribution that included a newsletter and social media. It is possible that the knowledge and opinions of those that did not respond are different from those that did as these participants may have a personal interest in QoL. It is also possible that non-responders feel less confident in their knowledge of QoL measures and may use them less than those with better knowledge. If so, the frequency of QoL assessment across the UK is likely to be less than is suggested in our findings. Secondly, the survey provides evidence of QoL practice within HPN care in the UK, but did not explore the barriers and challenges that have led to such infrequent, or totally absent, QoL assessments for HPN patients.

3.5: Conclusion

This chapter summarises the first study of current practice, knowledge and the opinions of healthcare professionals (HCPs) with regards to quality of life (QoL) and home parenteral nutrition (HPN). The findings highlight significant variability in QoL practice for patients treated with HPN. This is clear in terms of the relative infrequency of QoL assessments, heterogeneity in methodology, and inconsistencies in how the results are utilised and disseminated. Evidently, there is a need for specific, evidence-based, clinical practice guidelines detailing how to define and measure QoL in this patient population. Despite the perceived usefulness and importance of QoL assessment, very few HCPs are embedding it into clinical practice and even fewer are sharing results with patients themselves.

3.6: Future chapters

Since healthcare professionals' perceptions of quality of life (QoL) may be at odds with those held by their patients, it is very important to ask patients to assess their own QoL using a reliable and valid measure. In the study reported in subsequent chapters of this thesis, QoL will be measured in relation to the life-threatening and life-debilitating complications of home parenteral nutrition such as sepsis, liver disease and sarcopenia.

Chapter 4: Methods

Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition

The protocol for this study has been published in BMJ Open and can be found using reference: **Kirk C,** Mathers J, Pearce M, Thompson NP, Jones D. Factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition: protocol for a multicentre, longitudinal observational study. *BMJ Open.* 2024 Jan 6;14(1):e082163. doi: 10.1136/bmjopen-2023-082163. The study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cohort studies (152).

4.1. Introduction

The aims of HPN are to increase survival and improve QoL. However, it is well documented that HPN patients have a decreased QoL, higher rates of depression and anxiety compared with the general population and most are unlikely to return to meaningful employment. Moreover, patients are affected not only by their intestinal disease, but also by decreased physical health due to multimorbidity and the threat of potentially life-threatening complications, such as intestinal failure associated liver disease (IFALD). Studies have focused primarily on the impact of HPN programmes and intestinal anatomy on the QoL of patients. Such studies fall short, since QoL is a rich multidimensional concept encompassing mental and physical health, and is likely affected by disease status, treatment, and the associated complications of treatment. To our knowledge, no studies have investigated the association between QoL and the complications of HPN treatment such as IFALD, sepsis, gut dysbiosis, sarcopenia and metabolic bone disease. The aim of this study was to therefore understand how HPN impacts on the QoL of patients, and the contribution played by the complications of treatment such as liver disease.

4.1.1 Study design

The study was designed as a prospective, longitudinal, observational cohort study. The Lead sponsor was Newcastle upon Tyne NHS Hospitals Foundation Trust.

4.1.2 Study setting

Patients were recruited from three participating centres: Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH), The Leeds Teaching Hospitals NHS Trust (LeedsTH), and Nottingham University Hospitals NHS Trust (NUH). LeedsTH and NUH are tertiary, integrated home parenteral nutrition/ intestinal failure (HPN/IF) centres and are of similar size to NuTH in terms of patient numbers. Together, the three centres provided a cohort of patients from a wide geographical area.

4.1.3. Study population

All adult patients treated with HPN for benign reasons from the three participating centres were invited to participate.

Table 4.1: Participant inclusion and exclusion criteria

Inclusion criteria	Adults (>18 years old) treated with HPN. Capacity to provide informed consent.
Exclusion criteria	Active Malignancy

4.1.4 Study outcomes

The primary outcome was mean change in quality of life (QoL) scores over 12 months. Secondary outcomes included factors, including liver function, gut microbiota, number of infusions of parenteral nutrition (PN) per week, nutritional composition of PN, and nutritional status, that may impact on QoL scores.

4.2. Ethical approval

Ethical approval was obtained from HRA and Health and Care Research Wales (HCRW) Research Ethics Committee on 25th October 2021 (21/SC/0316). Site specific capacity and capability was then obtained for each of the participating sites. Participants were recruited between March 2022 and March 2023. The study remained open until 31st March 2024. The study was eligible for portfolio adoption, Central Portfolio Management System (CPMS) ID 50506.

4.2.1. Ethical amendment

A non-substantial amendment request was sent to Hampshire Research Ethics Committee and received a favourable outcome on 26th August 2022. The amendment gave permission to change one of the participating sites from Southampton General Hospital to Nottingham University Hospital.

4.2.2. Funding

The research was supported by the National Institute of Health Research (grant number NIHR301591).

4.3. Recruitment strategy

4.3.1. Newcastle: Eligible study participants were identified using a database maintained by the Nutrition Team which includes all patients being treated with HPN from Newcastle Hospitals. One week prior to their routine clinic appointment, a participant information sheet explaining the study, an invitation to participate and the QoL questionnaires were sent to potential participants by post. Potential participants received a follow up phone call 24 hours prior to their appointment, providing them with an opportunity to ask questions. Participants were enrolled prospectively upon receipt of the signed consent form.

4.3.2. Leeds: Leeds Nutrition Team assessed eligibility and provided a list of patient names and contact details to the PI. As above, the PI sent an information sheet explaining the study, along with an invitation to participate through the post. Eligible participants received a follow up phone call one week later, providing them with an opportunity to ask questions. Enrolment followed successful screening and receipt of written informed consent.

4.3.3. Nottingham: The contract between NUH and NuTH stated that participant information could not be provided prior to study consent. Therefore, NUH Nutrition Team assessed eligibility and sent an information sheet explaining the study, along with an invitation to participate through the post. As telephone numbers were not provided, potential participants did not receive a follow up phone call from the PI. Enrolment followed successful screening and receipt of written informed consent.

4.4. Data collection

Data for LeedsTH and NUH patients that is recorded in medical notes during clinic visits was collected retrospectively during two research visits to each of the sites. Data collection for NuTH patients was collected prospectively by the PI, as a member of the clinical care team. Details of the study measures are provided in Table 3.

4.4.1. Demographic and clinical data

Demographic and clinical data were collected from the patients' medical notes prospectively. These data included past medical history, underlying diagnosis causing the need for HPN, gastrointestinal anatomy, and presence of a stoma.

4.4.2. Socioeconomic and deprivation data

Questions relating to socioeconomic status (SES) (education level, employment, household income, marital status, accommodation) were asked directly to the patient during clinic by me or a member of the nutrition team. Socioeconomic data is of interest because it has been shown repeatedly that individuals with lower SES have, on average, poorer health and die younger than those with a higher SES.

The Index of Multiple Deprivation (IMD) was used as an official measure of relative deprivation. IMD is part of a suite of outputs that form the Indices of Deprivation (IoD). The IoD2019 data were used for this study. It is based on seven distinct domains if deprivation (income (22.5%), employment (22.5%), healthy deprivation and disability (13.5%), education and skills training (13.5%), crime (9.3%), barriers to housing services (9.3%), and living environment (9.3%) which are combined and weighted to calculate the IMD 2019. It also incorporates census data in certain instances where there are gaps in the administrative data.

4.4.3. Anthropometric data

Body weight (kg) was measured to the closest 100g and standing height (cm) was measured to the closest 0.1cm using a stadiometer (SECA 799, SECA UK). These measures were performed by the clinic staff with outdoor wear, extra layers and shoes removed. Body mass index was calculated using body weight (kg)/ (height (m))2. Mid-arm circumference was measured on the patient's right arm according to the International Standards of Kinanthropometry, using a metal tape measure. Triceps skinfold thickness was also measured on the individual's right arm using a Harpenden skinfold calliper. Handgrip strength was measured using the right hand with Takei handgrip dynamometer. Three measurements were made with the participant standing upright. MAMC was calculated using the standard formula: MAMC = MAC–(3.14 x TSF thickness).

4.4.4. Whole body composition

To measure body composition, the Seca BIA mBCA 525 machine was used (SECA 515, Birmingham, UK). It is portable, easy-to-use, inexpensive and a non-invasive method. It uses

an 8-point BIA methodology that is accessible at the point of care and can be repeated frequently with minimal expense and no radiation exposure. Two electrodes, which are connected to a small machine that emits an imperceptible current which measures body composition, are placed on each hand and foot. Resistance (R) of the arms, legs and torso was measured at frequencies of 1, 2, 5, 10, 50, 100, 200, 500kHz and was performed with the patient lying supine either at their bedside or in clinic. BIA was not attempted in patients with oedema, ascites or lymphedema.

4.4.5. Nutritional requirements

The nutritional requirements of the participants were estimated prospectively by me using the most recent predictive equation recommended by the Parenteral and Enteral Nutrition Group (PENG) of the British Dietetic Association. Step one is to assess the patient's nutritional status including the measurement of actual body weight (BW) of fat free mass (FFM) in kg and collect other relevant data including age, diagnosis, degree of metabolic stress and current intake. Step two is to determine the patient's body mass index (BMI) and step three is to estimate resting energy expenditure according to the clinical condition, age and BMI:

REE (kcal/ day) = BW x kcal/kg BW

REE (kcal/ day) = FFM x kcal/kg FFM

Disease State	REE kcal/kg actual body weight (BW)						Comments	Studies (total number of subjects in each study)
	BMI < 18.5kg/m^2		BMI 18.5 - 30.0kg/m^2		BMI > 30.0kg/m^2			
	Age ≤ 65 years	Age > 65 years	Age ≤ 65 years	Age > 65 years	Age ≤ 65 years	Age > 65 years		
Burns								
Burns (spontaneously breathing)							See text and online resources	
Cardiac								
Chronic heart failure			25[A] (21-28)			18[A]		Riley *et al.* 1991 (n=28); Aquilani *et al.* 1994 (n=112); Aquilani *et al.* 1995 (n=36); Lommi *et al.* 1998 (n=14); Aquilani *et al.* 2003 (n=106); Savage *et al.* 2007 (n=109)
GI disease								
Crohn's disease	28[A]		25[A] (24-26)				In patients with low BMI, REE was 29 kcal/kg BW in active disease and 26 kcal/kg BW in remission (Gong *et al.* 2015)	Chan *et al.* 1986[T] (n=54); Stokes & Hill 1993[T] (n=13); Al-Jaouni *et al.* 2000 (n=40); Sasaki *et al.* 2010a (n=24); Gong *et al.* 2015 (n=75); Takaoka *et al.* 2015 (n=40)
Ulcerative colitis			26[A,B] (24-26)				REE decreased to ~ 23.5 kcal/kg BW following treatment. CRP, TNF-α and IL-6 were higher in patients with active disease (Inoue *et al.* 2015)	Sasaki *et al.* 2010b (n=23); Inoue *et al.* 2015 (n=13); Takaoka *et al.* 2015 (n=40)
Non-neoplastic GI disease							See **Table 3.2**	

Figure 4.1: Estimating resting energy expenditure (REE) using kcal/kg BW/day

For example, a 60kg, 50-year-old patient with Crohn's disease would have the following REE: 60 x 28 kcals = 1680 kcals/ day. The final (fourth) step is to assign a combined factor for physical activity and diet induced thermogenesis (PAL) according to likely activity level:

Table 4.2: Combined factor for physical activity and diet induced thermogenesis

PAL	Description	Examples
1.00 - 1.10	In bed and immobile	Acute illness or injury or post-surgery
1.10 - 1.20	In bed and/ or sitting out	Hospital ward, care home or at home
1.20 – 1.25	Limited mobility	Hospital ward or at home with full time care
1.25 – 1.40	Sedentary	Care home or at home

For example, using the patient from the previous scenario with a REE of 1680 kcals/ day. If there were in hospital, mostly in bed they would have a total energy expenditure estimated at: 1680 x 1.1 = 1848 kcals/ day.

4.4.6. Oral dietary energy intake

Oral diet energy and fluid intake was estimated using diet histories that were taken by a Registered Dietitian. Diet histories are a retrospective interview method consisting of questions about habitual food intakes and dietary behaviours.

4.4.7. HPN prescription

The nutritional composition of the HPN solution, type (compounded or multi-chamber bags (MCBs)), volume, frequency of infusions, total number of lipid and glucose feeds was recorded prospectively following the patient's clinic appointment.

4.4.8. Blood samples

Blood samples are taken routinely at every clinic appointment by a trained phlebotomist. A butterfly needle (BD Vacutainer Safety-Lok blood collection system) was inserted into the antecubital or dorsal hand vein using asceptic non-touch technique (ANTT). Samples were analysed in a Clinical Pathology Accredited laboratory (Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Clinical Biochemistry).

4.4.8.1. Micronutrients

Micronutrient (Vitamin B12, Folate, Copper, Zinc, Selenium, Manganese, Vitamins A, D and E) concentrations in blood are measured routinely in patients on HPN every 6-12 months. Blood for micronutrient analysis is taken into BD Vacutainer tubes and analysed by

inductively coupled plasma-mass spectrometry in standard mode; assay reproducibility is <5%. Results were recorded retrospectively and compared with reference intervals.

4.4.8.2. Full blood count (FBC)

To analyse FBC, a 4 ml ethylenediaminetetraacetic acid (EDTA) vacutainer® of whole blood was drawn. Variables of interest were: white cell count to identify possible infection, platelets as they were required for calculating non-invasive scores of liver function - specifically Fibrosis-4 scores, and haemoglobin. Samples were analysed using a Sysmex XN-9000 Blood cell processing system. Platelet levels were measured using a DC sheath flow detection method.

4.4.8.3. Blood lipids

Patients treated with HPN have blood lipid concentrations measured annually. A 5ml SST vacutainer® of whole blood was drawn and samples were analysed using a Roche Cobas C 311 automated chemistry analyser (Moss et al., 1987, Kaplan et al., 2003) to determine cholesterol, triglyceride, and lipoprotein levels (Apolipoprotein A-1 (the major protein constituent of high-density lipoproteins; HDL), and Apolipoprotein B (the major protein constituent of low-density lipoproteins; LDL)). The Roche cholesterol assay used meets the 1992 National Institutes of Health (NIH) goal of less than or equal to 3% for both precision and bias (Health, 1990). Triglyceride concentrations were determined with an enzymatic colorimetric test principle (Siedel et al., 1993) and apolipoproteins were determined using the Immunoturbidimetric assay principle (Siedel et al., 1988).

4.4.8.4. Electrolytes

To measure electrolyte (sodium, potassium, magnesium, phosphate, urea, and creatinine) concentrations, an EDTA vacutainer® of whole blood was obtained. Electrolyte concentrations are routinely measured at each clinic appointment and are of interest to identify hydration status, kidney function, and suitability of the HPN prescription.

4.4.9. Sepsis

Patients were recorded as having sepsis as per their medical notes and a ‘yes’ or ‘no’ recorded in the research database. The highest level of CRP during the patient's septic episode was also recorded.

4.4.10. Metabolic bone disease

Patients treated with HPN are recognised to be at high risk of metabolic bone disease (MBD) and therefore have Dual-energy X-ray absorptiometry (DEXA) scans performed every 3 years. Results were recorded retrospectively at baseline and 12 months.

4.4.11. Quality of life assessment

QoL for each patient was evaluated using three questionnaires, the Short Form 36 (SF-36), Home Parenteral Nutrition Quality of Life questionnaire (HPN-QoL) and Euro-QoL (EQ-5D-5L)). These were selected by patients themselves to maximise relevance and acceptability. The EQ-5D-5L was consistently reported as the preferred tool due to its brevity and ease of completion.

The SF-36 is the most frequently used non-disease specific questionnaire registered in clinical trials. It examines QoL in eight domains, scoring each between 0 and 100, and two summary scales (77).

The HPN-QoL is a disease-specific 48-item instrument that focuses on physical, emotional and symptomatic issues (79). It contains 7 multi-item functional scales and 1 single-item functional scale. There is also a 6 multi-item and 3-single item symptom scales. The symptom scales ask questions about body image, immobility, fatigue, sleeping pattern, gastrointestinal symptoms, other pain, stoma or bowel management, financial issues and body weight. The questionnaire also has three global health status/ QoL numerical rating scales seeking information on the effect of the underlying illness leading to the need for HPN, and the effect of HPN on QoL. The two single items relate to nutrition teams and the availability of an ambulatory pump for the infusion of HPN. A high score relates to a good outcome.

The EQ-5D-5L is a generic, self-assessed health related questionnaire that measures QoL on a 5-component scale: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (153). There are 5 response levels to each question (no problems, slight problems, moderate problems, severe problems, and extreme problems). The EQ-5D also contains a vertical visual analogue scale (VAS) where the participant rates their overall health. The endpoints are labelled 'The worst health you can imagine' (0) and 'The best health you can imagine' (100). It provides a quantitative measure of health outcome that reflects the participants own judgement.

4.4.12. Liver assessment

Liver assessment was based on laboratory tests, liver stiffness measurement, and where available, liver biopsy results. The gold standard method of diagnosing intestinal failure associated liver disease (IFALD) is to perform a liver biopsy. However, due to the invasive nature of this procedure, biopsies are not routinely done. Therefore, IFALD will be classified as a binary variable and diagnosed by elevation of one or more liver chemistry tests (bilirubin, alkaline phosphatase, gamma glutamyl transferase, aspartate transaminase, alanine transaminase) to greater than 1.5 times the upper limit of the reference range for at least six months in the absence of another cause. This is a generally accepted definition which encompasses the earliest and mildest liver dysfunction in IFALD (20).

4.4.12.1. Laboratory tests

A 5 ml SST vacutainer® of whole blood was drawn at each clinic visit. Samples were analysed using a Roche Cobas C 311 automated chemistry analyser to measure Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Gamma-Glutamyl Transferase (GGT), and Bilirubin (Bil) concentrations (154). ALT, AST, ALP, GGT, and Bil levels without pyridoxal phosphate activation were determined according to International Federation of Clinical Chemistry and Laboratory Medicine recommendations (Bergmeyer et al., 1986).

4.4.12.2. Liver stiffness measurement

Liver stiffness measurement (LSM) was carried out using the ultrasonographic Fibroscan Mini 430 (Echosens, Paris) which makes use of the transient elastography principle. The

examination was performed with the patients in supine position with their right arm in maximal abduction. An M-mode transducer was placed above the right lobe of the liver and scanned through the intercostal space (Sandrin et al). The LSM was represented by the median of 10 measurements and was considered reliable only if at least 10 successful acquisitions were obtained, and a success rate of 60%. Results are expressed as the median stiffness value in kilopascals (kPa). All Fibroscan measurements were performed by a trained and experienced nurse. Results were recorded retrospectively.

4.4.12.3. Liver biopsy

The results of liver biopsies were recorded where available as these are only performed depending on clinical need.

4.4.13. Experimental data

4.4.13.1. Lipidomics

To advance understanding of the contribution played by liver disease in QoL impairment, lipidomic analysis will be performed using blood samples from new patients (NuTH only) and an equal number of existing patients (matched by key characteristics). In collaboration with Aberdeen University, blood plasma (obtained at baseline and at 12 months following the infusion of a lipid and glucose-based feed) will undergo lipidomics analysis to elucidate mechanisms underlying specific changes in lipid metabolism.

De Novo Lipogenesis (DNL) will be estimated using the lipogenic index calculated as the ratio of palmitic acid (16:0) to linoleic acid (18:2n6) (155). An increase in DNL is indicated by an increased ratio of palmitate to linoleate. In addition, plasma free choline concentrations of HPN patients will be measured and compared with normal values of 11.4 +/- 3.7 nmol/ml (24).

4.4.13.2. Microbiota

Intestinal microbes play a fundamental role in the well-being of their host (156). Gut dysbiosis has been observed in adult and paediatric patients with IF and is associated with impaired outcome (58, 59, 157). To understand whether gut dysbiosis and impaired QoL are linked, either directly, or indirectly through the development of complications, stool or stomal samples were collected at baseline, 6 and 12 months and aliquots in 3ml cryovials stored at –80 degrees C within two hours. 16S rRNA sequencing will be used to identify the microbiome composition of these samples. Volume of stomal output, colour and consistency was also recorded.

4.5. Schedule of study measures

At baseline and 12 months, comprehensive data were collected across multiple domains including demographics, clinical background, anthropometry, nutritional requirements, dietary intake, parenteral nutrition composition, biochemical parameters, liver function, and QoL. Selected patients (Newcastle only) also provided biological samples for exploratory analyses (Table 4.3).

Table 4.3: Schedule of study measures

Variables		Baseline	12 months
Demographic & socioeconomic data	Gender, year of birth, ethnicity	√	
	Postcode	√	
	Smoking, activity	√	
	Education, household income, employment status, marital status	√	
Clinical data	Past medical history	√	
	Main underlying disease & reason for HPN	√	
	Gastrointestinal anatomy & presence of a stoma	√	
	Date HPN commenced	√	
Anthropometry	Weight, height & BMI	√	√
	MAC, TSF, MAMC & HGS	√	√
	Body composition analysis	√	
Nutritional requirements	Energy, nitrogen & lipid requirements	√	√
	Glucose oxidation rate	√	√
Oral dietary energy intake	Oral fluid and oral dietary energy intake	√	√
	Diet type	√	√
Parenteral nutrition prescription	No. of weekly infusions	√	√
	Volume +/- additional fluids	√	√
	Nutritional composition +/- micronutrients	√	√
Blood results	CRP, WCC	√	√
	Electrolytes (urea, creatinine, sodium, potassium, magnesium, phosphate, calcium)	√	√
	Micronutrients (vitamins A, D, E, B12 & folate, copper, zinc, manganese & selenium)	√	√
	Iron, Transferrin, Haemoglobin, Transferrin Saturations	√	√
	Cholesterol, Triglycerides, HDL cholesterol, Total/HDL cholesterol ratio, Non-HDL cholesterol	√	√
Liver markers	IFALD diagnosis (Y/N)	√	√
	Bilirubin, ALP, ALT, GGT, platelets, albumin	√	√
	Liver biopsy (Y/N) & result	√	√
	FibroScan (Y/N) & result	√	√
Admissions	Number of admissions & length of stay	√	√
	Sepsis during admission (Y/N) & CRP level	√	√
Experimental data*	Blood samples	√	√
	Stoma samples	√	√
QoL measures	EQ-5D, SF-36, HPN-QoL	√	√

* NuTH patients only

4.6. Sample size

Insufficient relevant data for HPN patients were available to inform a formal power calculation. The SF36 user guide (158) provides estimates of sample sizes necessary to detect differences over time within one group of participants, and between two experimental groups (Table 4 & 5). These estimates assume alpha of 0.05 (2-tailed), and power of 80%. The SF-36 outcome score ranges from 0-100. The sample size needed to detect a 10-point difference varies between each domain and the tables show the largest number of participants required for each domain. For this study there was an estimated pool of 500 participants from the three centres however it was anticipated that 45% would not meet the inclusion criteria. The remaining sample size was therefore likely to be 275. Based on a previous study at NuTH that evaluated the QoL of adult patients on HPN at a single time point (159), initial uptake was expected to be at least 80% (n=220).

Given the longitudinal nature of the study and allowing for a 20% drop-out rate at follow up, 10% of participants stopping HPN, and 10% data attrition, I anticipated complete data for 132 participants. This sample size would provide sufficient power to detect a 10-point difference in all domains of the SF-36.

Table 4.4: Sample size needed to detect a ten-point difference over time within one group in average SF-36 scores

Domain	Sample size required to detect a 10 – point difference
Physical Functioning	35
Role limitations (physical)	74
Bodily Pain	36
General Health	27
Vitality	28
Social Functioning	33
Role limitations (emotional)	69
Mental Health	21

Table 4.5: Sample size needed per group to detect a ten-point difference in change over time between two experimental groups in average SF-36 scores

Domain	Sample size required to detect a 10 – point difference
Physical Functioning	55
Role limitations (physical)	118
Bodily Pain	57
General Health	43
Vitality	45
Social Functioning	53
Role limitations (emotional)	111
Mental Health	34

4.7. Statistical analysis

Frequency statistics were calculated for each variable. Normality was assessed using the Shapiro-wilk test. As the data were not normally distributed, QoL scores at baseline and follow up were evaluated using Wilcoxon Signed-Rank Test. Difference in means between new and existing patients were analysed using the Mann-Whitney U Test (Willcoxon Rank-Sum). To compare data across the three study sites, the Kruskal-Wallis Test was used alongside pairwise comparisons with Bonferroni correction.

To explore the relationship between QoL scores and predictors, multivariable linear and ordinal, for EQ-5D, logistic regression analysis were used. First, collinearity amongst predictor variables was assessed using pairwise correlation matrices. Next, potential

confounders and mediators were identified using a Directed Acyclic Graph (DAG) (Figure 4.2).

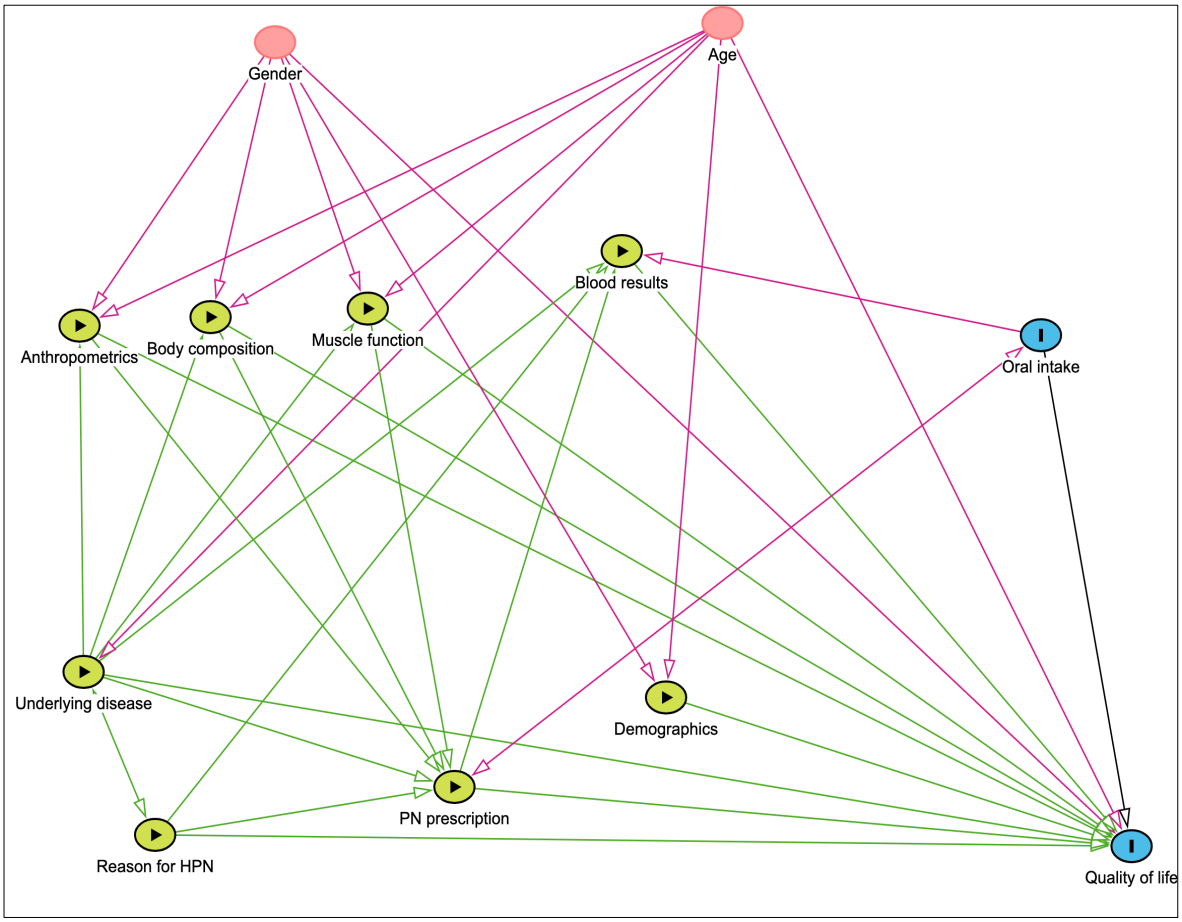


Figure 4.2: Directed Acyclic Graph

The DAG illustrates hypothesised causal pathways between variables influencing QoL in patients receiving HPN. Nodes represent variables grouped into key domains such as anthropometrics, bloods results. Arrows indicate assumed directional relationships based on prior evidence and clinical reasoning. For instance, age and gender influence multiple intermediate variables such as anthropometrics, body composition, and muscle function, which in turn impact QoL either directly or indirectly. The DAG was used to identify potential confounders, such as age and gender, which were accounted for in subsequent regression models to minimise bias and support causal interpretation. This process also ensures that mediators are not adjusted for, reducing the likelihood of collider bias.

Univariate regression models were then run with and without the suspected confounders. If the predictor coefficient changed significantly (by greater than 10%), confounding was confirmed. Where gender was confirmed as a confounder, multiplicative interaction terms

(exposure × sex) were incorporated into linear regression models. Interaction terms were tested using the ## operator in Stata, allowing for the inclusion of both main effects and interaction terms. Where statistically significant ($p < 0.05$) interactions were observed, further stratified analyses were conducted, and the regression models were run separately for males and females to interpret gender-specific associations.

In multivariable regression, predictor variables were added to the model in order of significance in the univariate regression analysis. Likelihood ratio tests were used to test the significance between the unadjusted and adjusted models. Individual QoL domains were handled as dependent variables and separate regression models were run for each. Regression assumptions were assessed via diagnostic plots and statistical tests. The assumptions were:

1. **Linearity**: The relationship between the independent variables and the dependent variable was linear.
2. **Homoscedasticity**: The variance of residuals was constant across all levels of the independent variables.
3. **No Multicollinearity**: Independent variables were not too highly correlated with each other.
4. **Normality of Residuals**: The residuals (errors) were approximately normally distributed.

Linearity and homoscedasticity were evaluated using residual versus fitted plots, while multicollinearity was assessed using variance inflation factors (VIFs). Normality of residuals was examined with quantile-normal plots and the Shapiro-Wilk test.

For the variables related to blood results, Principal Component Analysis (PCA) was conducted to reduce dimensionality and identify latent structures within related domains. PCA is a data-driven technique that transforms a set of possibly correlated variables into a smaller number of uncorrelated components (principal components), each representing a combination of the original variables that explains a portion of the total variance. Separate PCAs were performed for each blood domain (e.g., renal function, micronutrients, iron biomarkers, blood lipids, liver biomarkers), using the correlation matrix. Components with eigenvalues greater than 1 (Kaiser criterion) were retained, and component loadings were

used to interpret the underlying physiological patterns. The resulting principal component scores were standardised and used as independent variables in linear regression models assessing associations with QoL outcomes (EQ-5D, SF-36, and HPN-QoL domains).

Chapter 5: Results from the Longitudinal QoL Study

5.1 Introduction

This longitudinal study aimed to explore the impact of home parenteral nutrition (HPN) on patients' quality of life (QoL), with a particular focus on the role of liver disease. The primary outcome was the mean change in QoL scores over a 12-month period. Secondary outcomes included the influence of various factors on QoL scores, such as liver function, anthropometric measurements, the number of weekly PN infusions, the nutritional composition of PN, and overall nutritional status.

In accordance with the STROBE guidelines for cohort studies [150], this chapter begins with a summary of participant characteristics, followed by descriptive data analysis. Finally, inferential statistical results are presented, including any additional analyses such as principal component analysis (PCA).

A total of 199 participants were initially recruited, with 145 completing follow-up assessments (see Figure 5.1). Reasons for missing follow-up data included non-response (n = 25), discontinuation of HPN (n = 14), missing study identifiers on QoL questionnaires (n = 2), participants being too unwell to respond (n = 5), and participant death (n = 8).

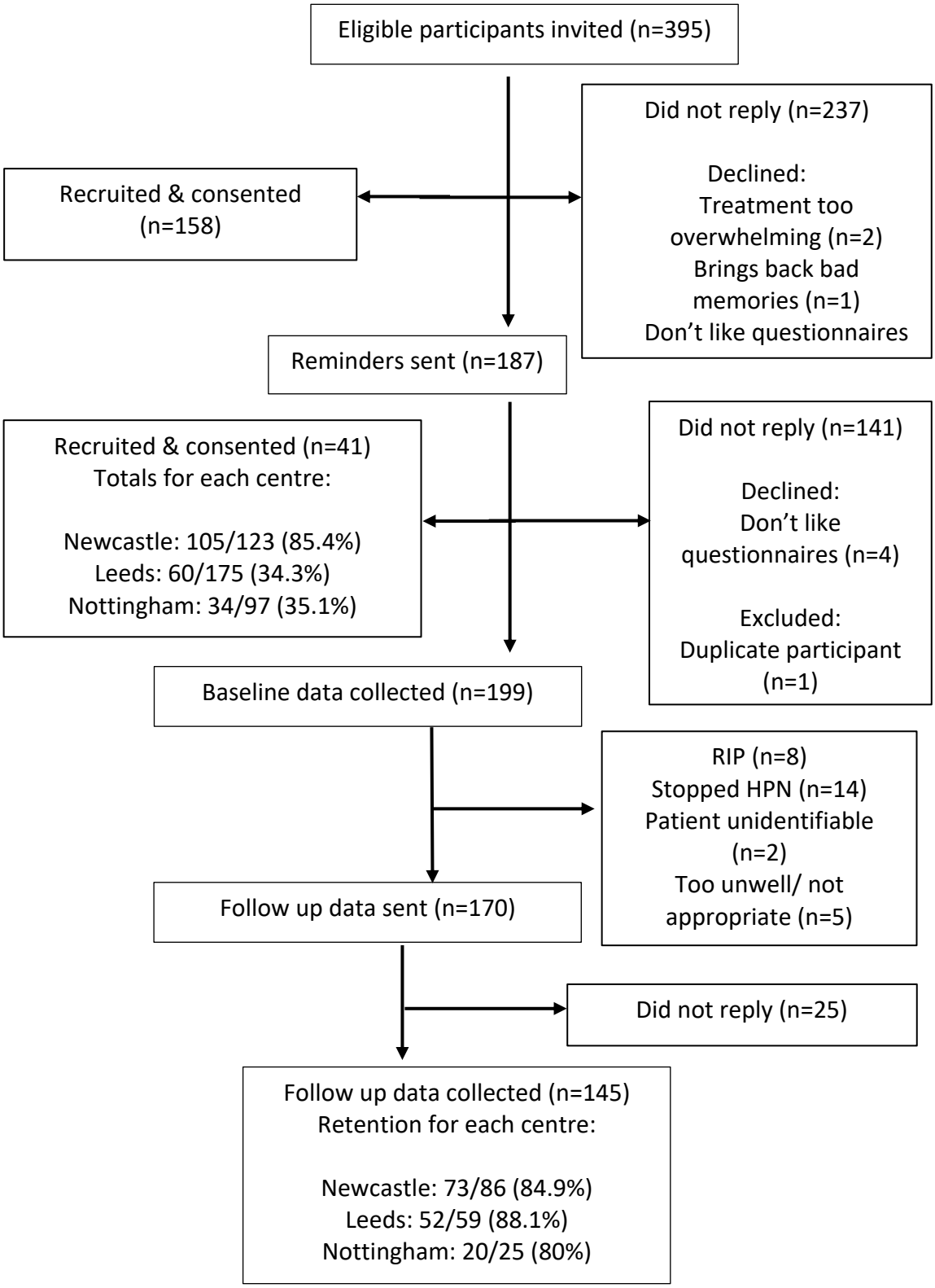


Figure 5.1: Flowchart showing the recruitment and retention of participants

5.2: Completeness of data collection

Data were collected from a total of 199 participants. Demographic details and blood results were available for almost all participants, as these are routinely recorded in clinical practice. In contrast, measures such as mid-arm circumference and handgrip strength were less frequently available, reflecting variability in practice between NHS sites; for example, Nottingham and Leeds do not routinely record anthropometry. Consequently, anthropometric data were available for only 78 participants at baseline.

Completeness of data collection is shown at baseline (Figure 5.2) and at 12-month follow-up (Figure 5.3). Certain measures, including DEXA scans, fibroscans, and liver biopsies, were collected opportunistically during the study period and reported in the baseline dataset only. These investigations were not repeated, as they are not part of routine follow-up practice.

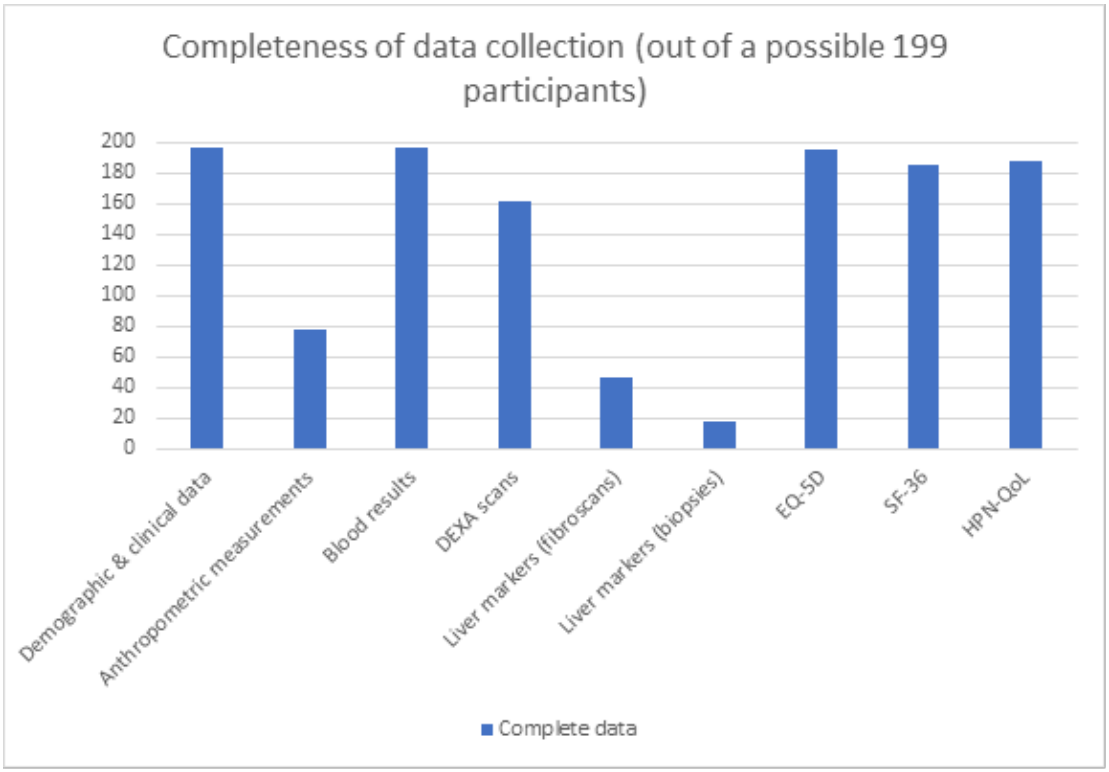


Figure 5.2: Completeness of data collection for each variable at baseline

At 12-month follow-up, data were available for 145 of the original 199 participants, reflecting attrition due to withdrawal, loss to follow-up, or death. Within this reduced cohort, completeness varied by variable: EQ-5D responses were returned by the majority, followed by SF-36 and HPN-QoL. Anthropometric and handgrip strength data showed the

lowest completeness, largely due to site differences in routine practice and the practical challenges of repeating these assessments. As a result, analyses involving anthropometry and muscle function were based on smaller subsamples, reducing statistical power and potentially introducing bias if missingness was not random.

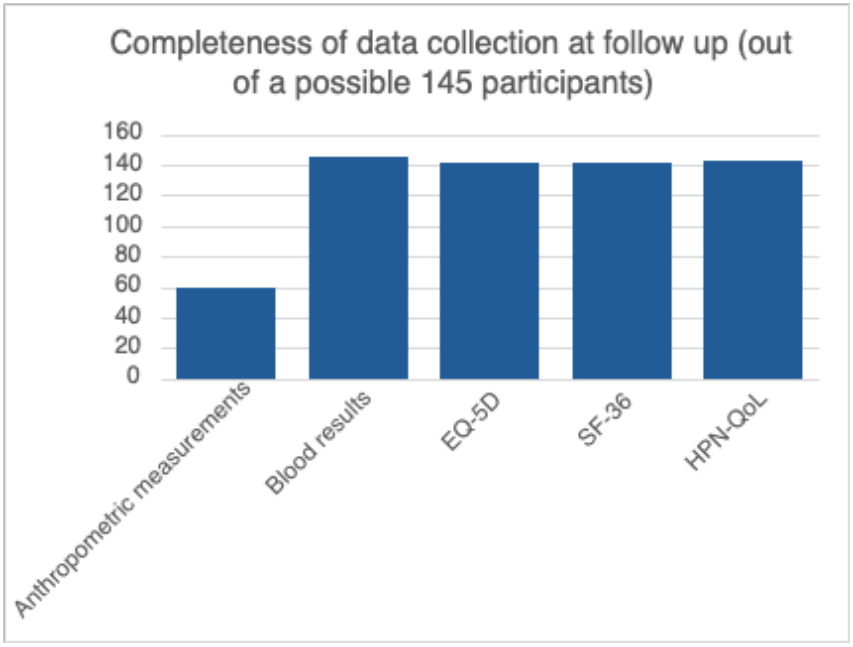


Figure 5.3: Completeness of data collection for each variable at follow up

5.3 Characteristics of study participants

Demographic and clinical data are shown in Table 5.1. The invited population was predominantly female (63%) and females were the majority among recruits (66%), retained participants (66%) and those lost to follow-up (65%). The most common underlying diseases were IBD (32%) and ischaemia (20%). Other conditions such as malignancy (9%), motility disorders (9%) and radiation enteritis (6%) represent fewer patients on HPN. SBS was the leading cause of HPN at baseline and follow up, accounting for 62% and 64% of cases, respectively. Most patients did not have their colon in continuity in the baseline (65%) or follow up groups (67%, respectively). There were no significant differences in the demographic and clinical characteristics at baseline between those participants who did, and did not, remain in the study.

Table 5.1: Demographic and clinical characteristics of study participants

	Baseline (n = 199)	Baseline for those lost to follow up (n = 54)	Follow up (n = 145)	p-value[1]
Age (years); (median (IQR))	60 (50-69)	58.5 (41.5-68)	61 (50-69)	0.307
Gender (n(%))				
Male	67 (34.2)	18 (35.3)	49 (33.8)	0.865
Female	129 (65.8)	33 (64.7)	96 (66.2)	
HPN duration (months); (median (IQR))	44.5 (13-80	32 (13-58)	47.5 (16-96)	0.145
Main underlying disease (n (%)):				
IBD	63 (32.3)	16 (29.6)	47 (32.6)	0.652
Ischaemia	40 (20.5)	13 (24.1)	27 (18.8)	
Malignancy	18 (9.2)	3 (5.6)	15 (10.4)	
Motility disorder/ radiation enteritis	25 (12.6)	5 (7.4)	20 (3.5)	
Other/ unknown	53 (26.6)	17 (25.9)	36 (24.3)	
Reason for HPN (N (%)):				
SBS	120 (62.2)	29 (53.7)	91 (64.1)	0.058
Obstruction	12 (6.1)	8 (14.8)	4 (2.8)	
Dysmotility	23 (11.8)	6 (11.1)	17 (12)	
Fistula	13 (6.7)	3 (5.6)	10 (7)	
Other/ unknown	31 (15.6)	8 (14.8)	26 (17.9)	
Type of stoma (N (%)):				
No stoma	59 (31.2)	18 (33.3)	41 (29.5)	0.066
Jejunostomy	45 (23.8)	11 (20.4)	34 (24.5)	
Ileostomy	66 (34.9)	15 (27.8)	51 (36.7)	
Colostomy	19 (10.1)	6 (11.1)	13 (9.4)	
Unknown	10 (5.3)	4 (7.4)	5 (3.6)	
Remaining SB length (cm) (N (%)):				
<50	22 (11.1)	9 (16.7)	13 (9)	0.217
51-100	22 (11.1)	3 (5.6)	19 (13.1)	
101-150	24 (12.1)	5 (9.3)	19 (13.1)	
151-200	9 (4.5)	1 (1.9)	8 (5.5)	
>200	57 (28.6)	14 (25.9)	43 (29.7)	
NK	65 (32.7)	2 (3.7)	43 (29.7)	
Colon in continuity (N (%))				
Yes	69 (34.7)	22 (40.7)	47 (32.4)	0.316
No	130 (65.3)	32 (59.3)	98 (67.6)	

Abbreviations: HPN, home parenteral nutrition; SB, small bowel. [1]*Wilcoxon Signed-Rank Test.*

The sociodemographic characteristics of study participants are summarised in Table 5.2. Data were collected at baseline only. In the baseline and follow up groups, over half of participants were married (51% and 57%, respectively) and 75% lived with family. Almost

90% of the cohort lived in a house or bungalow and upper secondary education was the most common level of education at baseline and follow up (38% and 35%, respectively). Just over one quarter of participants had an annual household income between £10,000 and £20,000 at baseline and follow up (29% and 26%, respectively). There were no significant differences between the two groups of participants except for marital status and the IMD rank. There was a significantly higher proportion of married participants in the follow up group, and the IMD rank was significantly lower in the lost to follow up group.

Table 5.2: Sociodemographic characteristics of study participants

	Baseline (n (%))	Baseline for those lost to follow up (n (%))	Follow up (n (%))	p-value[1]
Marital status:				
Single	42 (22.7)	18 (40.9)	24 (17.0)	**0.005**
Cohabiting	18 (9.7)	7 (15.9)	11 (7.8)	
Married	95 (51.4)	15 (34.1)	80 (56.7)	
Divorced/ separated	21 (11.4)	4 (9.1)	17 (12.1)	
Widowed	9 (4.9)	0 (0)	9 (6.4)	
Living status:				
Alone	41 (22.2)	11 (25.0)	30 (21.3)	0.678
Not alone	144 (77.8)	33 (75.0)	111 (78.7)	
Type of accommodation:				
House or bungalow	173 (88.7)	47 (90.4)	126 (88.1)	0.362
Self-contained flat/ room	22 (11.3)	5 (9.6)	17 (11.9)	
Level of education:				
Secondary	62 (40.3)	16 (55.2)	46 (36.8)	0.286
Post-secondary non-tertiary	22 (14.3)	4 (13.8)	18 (14.4)	
Short cycle tertiary	45 (29.2)	5 (17.2)	40 (32)	
Bachelors or higher	25 (16.2)	4 (13.8)	21 (16.8)	
Employment:				
Unemployed	61 (34.1)	17 (39.5)	44 (32.4)	0.500
Employed	26 (6.7)	5 (9.3)	22 (8.1)	
Retired	91 (50.8)	21 (48.8)	70 (51.5)	
Total household income (£, per annum):				0.837
<10,000	11 (7.1)	1 (3.5)	10 (8.0)	
10,001 - 20,000	44 (28.6)	11 (37.9)	33 (26.4)	
20,001 - 30,000	32 (20.8)	7 (24.1)	25 (20)	
30,001 - 40,000	13 (8.4)	2 (6.9)	11 (8.8)	
40,001 - 50,000	18 (11.7)	2 (6.9)	16 (12.8)	
>£50,000	17 (11)	2 (6.9)	15 (12.0)	
Prefer not to answer	19 (12.3)	4 (13.8)	15 (12.0)	
IMD decile (median (IQR))	5 (2-7)	4.5 (2-7)	5 (2-7)	0.773
IMD rank (median (IQR))	10545.5 (4871-20132)	7696 (2741.5-18803.5)	12616 (5976-21250	**0.031**

Abbreviations: IMD, Index of Multiple Deprivation. [1]*Wilcoxon Signed-Rank Test.*

5.4 Nutritional data

Nutritional data were available for 195 participants at baseline and 144 participants at follow up (Table 5.3). The type of HPN remained stable throughout the study with compounded

HPN being the most common at baseline (66%) and follow up (65%). The PN regime remained unchanged and there was very little differences in the composition of PN at follow up compared with baseline.

Table 5.3: Nutrition prescription of study participants, comparing between baseline and follow-up

	Baseline (n = 195)	**Baseline for those who completed follow up**	**Follow up (n = 144)**	**p-value[1]**
HPN type (n (%)):				
Multi-chamber bags	31 (15.9)	31 (21.5)	21 (14.6)	0.688
Compounded	128 (65.6)	94 (65.3)	94 (65.3)	
Fluids	36 (18.5)	19 (13.2)	29 (20.1)	
PN regime (median (IQR)):				
HPN volume (l)	2.0 (1.75-2.5)	2.0 (1.98-2.55)	2.0 (1.5-2.5)	0.833
Weekly infusions	6.0 (4-7)	5.5 (4-7)	6.0 (4-7)	0.316
Weekly lipid infusions	1.0 (0-3)	3.0 (1-7)	1.0 (0-3)	0.049
Weekly glucose infusions	3.0 (0-4)	4.0 (3-7)	2.0 (0-4)	0.567
PN composition (median (IQR)):				
Average energy (kcals/ day)	1262.5 (315-1600)	1048 (273-1522)	1000 (300-1523)	0.008
Average lipid (g/day)	12 (0-26)	10 (0-25)	10.5 (0-25)	0.023
Average glucose (g/day)	171 (40-250)	170 (25-250)	150 (35.5-250)	0.116
Average nitrogen (g/day)	8 (3-11)	8.0 (0-18)	7 (3-11)	0.050

Abbreviations: HPN, home parenteral nutrition; PN, parenteral nutrition; g, gram
[1]Wilcoxon signed-rank test

5.5 Anthropometrics, body composition and bone density

Table 5.4 displays the anthropometric measurements of study participants. There were no significant changes between baseline and follow up. The body composition data highlights a relatively low amount of visceral fat and varying levels of fat-free mass, skeletal muscle mass and total body water. There is a high prevalence of osteopenia (37%) and osteoporosis (40%) with less than one quarter of patients having normal bone density (23%).

Table 5.4: Anthropometric measurements of study participants

	Baseline Median (IQR)	Baseline for those who completed the study	Follow up	P-value[1]
Anthropometrics:				
Weight (kg); n=145)	65.1 (53.6-75.6)	65.0 (54.4-75.7)	64.3 (53.7-76.4)	0.221
BMI (kg/m2; n=141)	23.0 (20.5-26.4)	23.2 (20.8-26.4)	23.3 (20.3-27)	0.239
MAC (n= 58)	28.5 (25-32)	29.0 (26-32)	29.0 (25-32)	0.644
TSF (n= 42)	15.0 (11-20)	15.0 (10.5-20.0)	14.5 (11-20)	0.470
MAMC (n= 42)	23.4 (21.7-26)	24.1 (21.7-27.0)	23.0 (21-26.8)	0.912
HGS (n= 61)	22.5 (17.8-28.5)	22.8 (17.5-30.1)	22.4 (18.7-27.8)	**0.037**
Body composition (n=24):				
Visceral fat (l)	0.8 (0.2-2.6)	**N/A**	**N/A**	
FFM (kg)	42.4 (36.0-61.3)			
FFMI (kg/m2)	15.4 (14.1-19.1)			
SMM (kg)	17 (12.7-28.2)			
TBW (l)	31.7 (27.3-45.5)			
EBW (l)	15.1 (13.2-19.6)			
PA (degree)	4.9 (3.9-5.4)			
Bone density (n (%)):		**N/A**	**N/A**	
Normal	36 (22.8)			
Osteopenia	59 (37.3)			
Osteoporotic	63 (39.9)			
Total	**158**			

Abbreviations: BMI, body mass index; MAC, mid-arm circumference; TSF, tricep skinfold thickness; MAMC, mid-arm muscle circumference; HGS, handgrip strength, FFM, fat free mass; FFMI, fat free mass index; SMM, skeletal muscle mass; TBW, total body water; EBW, extracellular body water; PA, phase angle. [1]Wilcoxon signed-rank test

5.6 Blood results

Blood results are summarised in Table 5.5. Most median values were within the reference range at baseline and remained relatively stable at follow-up. Notably, vitamin B12 levels were elevated at both timepoints, while transferrin saturation remained low. Statistically significant changes were observed in creatinine (increased, $p < 0.001$) and vitamin D (decreased, $p = 0.002$); however, these changes are not considered clinically meaningful.

Table 5.5: Blood results of participants at baseline and follow up

	Reference range	Baseline (n=197)	Baseline for those who completed the study	Follow up (n=142)	p-value[1]
Kidney function (mmol/L):					
Sodium	133-146	139 (137-141)	139 (137-141)	139 (138-141)	0.970
Potassium	3.5-5.3	4.3 (4.0-4.7)	4.3 (4.0-4.7)	4.3 (4.0-4.6)	0.801
Creatinine	59-104	75 (61-95)	74 (61-92)	81 (64-101)	**0.001**
Urea	2.5-7.8	6.8 (4.9-8.9)	6.7 (4.9-8.6)	6.6 (4.9-9.5)	0.934
Adj. calcium	2.2-2.6	2.37 (2.31-2.44)	2.36 (2.31-2.43)	2.37 (2.31-2.43)	0.169
Phosphate	0.8-1.5	1.12 (0.94-1.28)	1.12 (0.93-1.28)	1.1 (0.99-1.25)	0.506
Magnesium	0.7-1.0	0.84 (0.78-0.90)	0.84 (0.78-0.90)	0.82 (0.77-0.88)	0.212
Vitamins:					
A (umol/L)	1.05-2.80	1.74 (1.34-2.43)	1.68 (1.34-2.40)	1.82 (1.38-2.49)	0.182
D (mmol/L)	>50	58 (38-80)	61 (43-82)	53 (35-71)	**0.002**
B12 (umol/L)	145-569	588 (387-895)	621 (415-900)	614 (397-828)	0.319
Folate (ug/L)	3.9-26.8	11.6 (7.5-19.4)	13.1 (7.5-20.0)	12.1 (7.7-20)	0.920
Trace elements (umol/L):					
Copper	11.0-25.1	16 (13.9-18.8)	16 (13.8-19.0)	16 (13.6-19.4)	0.278
Zinc	10.1-20.2	12 (7-14.3)	12.1 (10.7-14.3)	12.05 (10.6-14.7)	0.768
Selenium	0.66-1.57	1.04 (0.84-1.28)	1.07 (0.9 to 1.4)	1.07 (0.84-1.24)	0.773
Manganese (nmol/L)	80-260	219.5 (175-293)	182 (222-297)	231.2 (186-290.6)	0.709

Table 5.5: (continued).

	Reference range	Baseline (n=197)	Baseline for those who completed the study	Follow up (n=142)	p-value[1]
Blood lipids (mmol/L):					
Total cholesterol	<7.5	3.6 (3.1-4.3)	3.6 (3.2-4.3)	3.8 (3.1-4.4)	0.062
HDL cholesterol	<1.55	1.2 (0.9-1.5)	1.2 (0.9-1.6)	1.2 (0.9-1.5)	0.203
LDL cholesterol	<4.9	2.4 (1.9-2.9)	2.3 (1.9-2.9)	2.4 (1.9-2.9)	0.668
Triglycerides	0.5-1.7	1.3 0.9-2)	1.4 (1.0-2.1)	1.3 (0.9-1.9)	0.119
Iron markers:					
Serum iron (umol/L)	6-35	10 (6-16)	10.5 (7.0-15.0)	9 (2.4-9)	0.361
Transferrin (g/L)	2.0-3.6	2.7 (2.3-3.2)	2.8 (2.5-3.3)	2.6 (2.2-3.2)	0.158
Transferrin saturation (%)	20-50	16 (9-22)	16 (9-21)	15 (10.5-20)	0.675
Ferritin (ug/L)	>60	111 (51-286)	110 (51-218)	109.5 (50-266)	0.653
Inflammatory markers:					
WCC	4-11	6.9 (5.3-8.8)	8.0 (5.4-8.8)	6.9 (5.3-8.4)	0.501
CRP (mg/L)	0-5	5 (2-10)	8.1 5 (1-8)	5 (1-7)	0.222
Liver markers:					
Bilirubin (umol/L)	0-21	8 (5-13)	9 (5-13)	8 (5-14)	0.628
ALP (unit/L)	30-130	127 (91-199)	121 (90-179)	132 (95-183)	0.151
ALT (unit/L)	0-40	24 (17-42)	24 (17-44)	26 (18-45)	0.444
GGT (unit/L)	0-70	77 (25-158)	77 (37-158)	60 (23-128)	0.683
AST (unit/L)	0-40	43 (30-65)	41 (30-65)	29 (24-38)	0.179

All data are presented as median (IQR). Abbreviations: WCC, white cell count; CRP, C-reactive protein; ALP alkaline phosphatase; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; AST, aspartate aminotransferase. [1]Wilcoxon Signed-Rank Test.

5.7: Liver assessment

Limited data were available for liver imaging. AST levels are not routinely measured and were available for seven participants only (only one of whom was a new HPN patient). For that reason, Fib-4 scores could not be calculated. There were 47 fibroscans completed over the duration of the study with a median value of 7.1Kpa and a range of 2.9-18.4. A total of 17 liver biopsies were performed across the three centres. Biopsy data were included when available, either at baseline or follow-up. For baseline data, biopsies conducted within two years prior to the start of the study were eligible for inclusion. Results are summarised in Table 5.6.

Table 5.6: Overview of liver biopsy results

Findings	N	Further comments
Normal liver biopsy (no pathology)	2	No fibrosis, steatosis, inflammation, or necrosis
Mild portal inflammation	1	Non-specific; requires further clinical correlation, no specific liver disease
Portal hypertension and portal obstruction	1	Cavernous transformation and extensive varices formation
Mild steatosis, central venular fibrosis	1	Fibrosis score 1/6
Non-cirrhotic portal hypertension	1	Portal sinusoidal venopathy and signs of previous cholestasis
Mild steatosis, non-specific chronic cholangiopathy	1	
Florid steatohepatitis with incomplete cirrhosis	1	
Mild steatohepatitis with peri-venular/peri-cellular fibrosis	1	
Cirrhosis with extensive portal vein thrombosis	1	
Fatty liver with minimal fibrosis	1	
Fibrosis score 4/6	1	
Steatosis	1	
Significant fibrosis	1	
Perivenular fibrosis	1	
Steatohepatitis	1	
Mild steatosis	1	

5.8: Quality of life

5.8.1: EQ-5D-5L

5.8.1.1: Descriptive data analysis

The EQ-5D-5L questionnaire was returned by 196 participants at baseline and 142 participants at follow up (Table 5.7).

Among participants who completed both timepoints (n = 142), EQ-5D-5L scores showed minimal overall change. Mobility, self-care, and usual activity levels remained relatively stable, with a slight increase in those reporting no problems in self-care and a reduction in those unable to perform usual activities. In the pain/discomfort domain, moderate problems increased (27.6% to 40.9%), while severe problems decreased (29.0% to 17.6%). Anxiety/depression levels remained broadly consistent, with a slight increase in reports of mild symptoms. Median EQ-VAS scores remained unchanged at 50, and the health utility index also remained stable (0.50 at baseline vs. 0.49 at follow-up).

Table 5.7: EQ-5D-5L results at baseline and follow up

Dimension	Baseline (n = 196) N (%)	Baseline for those that completed follow up (n = 142)	Follow up (n = 142) N (%)
Mobility			
No problems	41 (20.9)	34 (23.5)	29 (20.4)
Slight problems	43 (21.9)	35 (24.1)	40 (28.2)
Moderate problems	68 (34.7)	47 (32.4)	46 (32.4)
Severe problems	35 (17.8)	24 (16.6)	19 (13.4)
Unable to walk about	9 (4.6)	5 (3.5)	8 (5.6)
Self care			
No problems	86 (43.9)	64 (44.1)	69 (48.6)
Slight problems	59 (30.1)	45 (31.0)	32 (22.5)
Moderate problems	30 (15.3)	22 (15.2)	29 (20.4)
Severe problems	15 (7.6)	11 (7.6)	9 (6.3)
Unable to wash or dress	6 (3.0)	3 (2.1)	3 (2.1)
Usual activities			
No problems	27 (13.8)	24 (16.6)	23 (16.2)
Slight problems	41 (20.9)	30 (20.7)	37 (26.1)
Moderate problems	67 (34.2)	50 (34.5)	45 (31.7)
Severe problems	36 (18.3)	25 (17.2)	26 (18.3)
Unable to do usual activities	25 (12.7)	16 (11.0)	11 (7.8)
Pain/ discomfort			
None	26 (13.3)	22 (15.2)	16 (11.3)
Slight	43 (21.9)	33 (22.8)	35 (24.7)
Moderate	58 (30.0)	40 (27.6)	58 (40.9)
Severe	56 (28.4)	42 (29.0)	15 (17.6)
Extreme	13 (6.6)	8 (5.5)	8 (5.6)
Anxiety/ depression			
None	51 (26.0)	39 (26.9)	37 (26.1)
Slight	46 (23.5)	32 (22.1)	45 (31.7)
Moderate	66 (33.7)	51 (35.2)	40 (28.2)
Severe	22 (11.2)	14 (9.7)	14 (9.9)
Extreme anxiety/ depression	11 (5.6)	9 (6.21)	6 (4.2)
EQ-5D-5L VAS (0-100)* Median (range)	50 (40-70)	50 (40-70)	50 (10-95)
Health utility index (-1 – 1) Median (IQR)	0.49 (0.22-0.67)	0.50 (0.22-0.68)	0.49 (0.22-0.68)

Abbreviations: VAS, visual analogue scale

Figure 5.4 shows the distribution of responses across the five EQ-5D-5L domains at baseline (n = 196). The most affected domains were pain/discomfort and usual activities**,** with most

patients reporting moderate or worse problems. Mobility and anxiety/ depression also showed considerable levels of impairment, with around 57% and 50% of patients, respectively, experiencing at least moderate difficulties. In contrast, self-care showed a more even distribution, with around 75% of patients reporting none or slight problems.

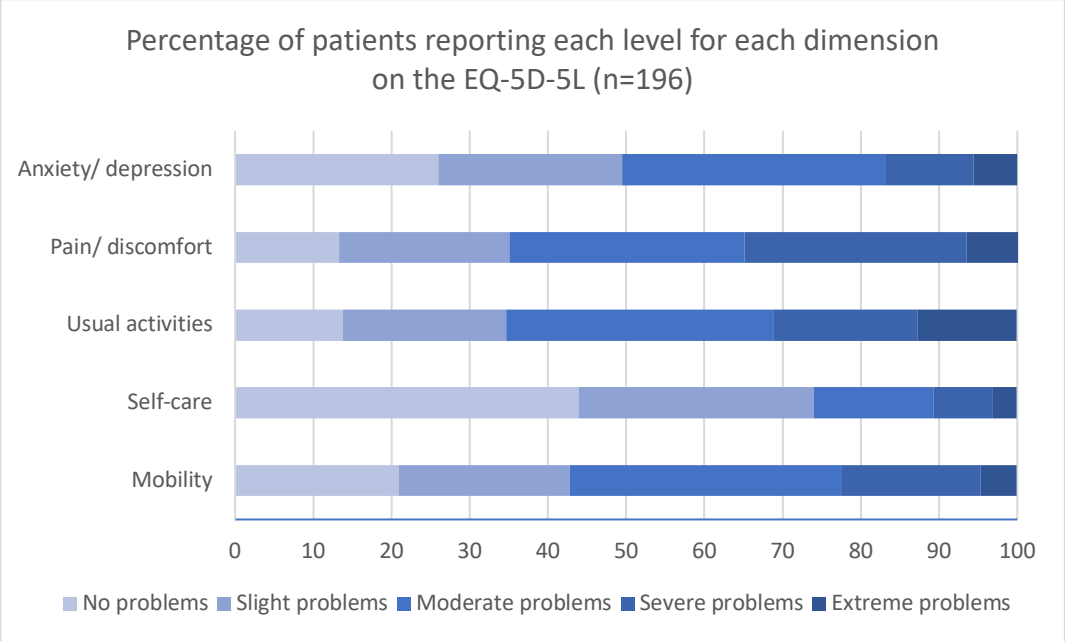


Figure 5.4: Health profile showing the percentage of patients reporting each level of problems for each domain on the EQ-5D-5L at baseline.

5.8.1.2: Inferential analysis to investigate factors associated with EQ-5D outcomes at baseline

5.8.1.2.1: Evaluation of collinearity between predictor variables

Prior to performing regression analysis, multicollinearity amongst potential predictor variables was assessed (Table 5.8). Length of SB was significantly associated with stoma type ($\chi^2 = 84.64$, $p < 0.001$), reason for HPN ($\chi^2 = 125.65$, $p < 0.001$), and underlying diagnosis ($\chi^2 = 71.64$, $p < 0.001$) (Table 5.13). Marital status was significantly associated with living status ($x2 = 88.85$, $p <0.001$) and household income was associated with education level ($x2 = 36.78$, $p=0.006$) and living status ($x2 = 36.18$, $p < 0.001$). Underlying diagnosis, length of SB, living status and education level were used in the univariate regression models and length of SB, living status and education levels were used in the multivariable models.

Table 5.8: Chi^2 test for categorical variables

Variables	Chi^2	p-value
Length of SB & stoma type	84.64	**<0.001**
Length of SB & reason for HPN	125.65	**<0.001**
Length of SB and underlying diagnosis	71.64	**<0.001**
Marital status & living status	88.85	**<0.001**
Household income & education level	36.78	**0.006**
Household income & living status	36.18	**<0.001**

Abbreviations: SB, small bowel; HPN, home parenteral nutrition

Pairwise correlations for markers of body composition and muscle function can be seen in Table 5.9. Strong positive correlations were observed between MAC and MAMC**,** and SMM and HGS**.** Similarly, significant correlations were seen between FFMI and MAC**,** FFMI and HGS**,** and between SMM and MAC**.** There were weak or non-significant correlations between TSF and all other variables. HGS, PA and SMM were used for regression analysis whereas the other variables were dropped.

Table 5.9: Pearson correlation coefficients (**r**) and p-values between anthropometric and muscle function parameters

	MAMC	MAC	TSF	HGS	FFMI	SMM
MAC	r = 0.883 **p <0.001**					
TSF	r = 0.132 p = 0.310	r = 0.499 **p <0.001**				
HGS	r = 0.436 **p <0.001**	r = 0.261 **p = 0.023**	r = -0.110 p = 0.405			
FFMI	r = 0.692 **p = 0.001**	r = 0.655 **p = 0.002**	r = -0.126 p = 0.609	r = 0.645 **p = 0.001**		
SMM	r = 0.705 **p <0.001**	r = 0.691 **p <0.001**	r = -0.084 p = 0.734	r = 0.803 **p <0.001**	r = 0.917 **p < 0.001**	
PA	r = 0.680 p =0.001	r = 0.596 **p = 0.006**	r = 0.029 p = 0.905	r = 0.486 **p = 0.022**	r = 0.559 **p = 0.005**	r = 0.620 **p = 0.001**

Abbreviations: MAC, mid-arm circumference (cm); TSF, tricep skinfold thickness (mm); HGS, handgrip strength (kg); FFMI, fat free mass index (kg/m2); SMM, skeletal muscle mass (kg); PA, phase angle (degree). Bold values indicate statistically significant correlations at p < 0.05.

Correlation coefficients for the PN composition and dietary intake variables are presented in Table 5.10. Significant positive correlations were observed between PN glucose and PN total energy and PN nitrogen and PN total energy. PN lipid showed a moderate positive

correlation with PN energy and PN nitrogen**.** Oral dietary energy intake was negatively associated with PN energy and PN glucose**.** Total PN energy, oral energy dietary intake and weekly PN infusions were taken forward into regression analysis.

Table 5.10: Correlation matrix for PN composition and dietary intake variables

	PN glucose	**PN energy**	**PN lipid**	**PN nitrogen**	**Weekly PN infusions**
PN energy	r = 0.895 **p <0.001**				
PN lipid	r = 0.424 **p <0.001**	r = 0.646 **p <0.001**			
PN nitrogen	r = 0.826 **p <0.001**	r = 0.907 **p <0.001**	r = 0.519 **p <0.001**		
Weekly PN infusions	r = 0.532 **p <0.001**	r = 0.600 **p <0.001**	r = 0.369 **p <0.001**	r = 0.644 **p <0.001**	
Oral energy dietary intake	r -0.482 **p <0.001**	r = -0.562 **p <0.001**	r = -0.420 **p <0.001**	r = -0.399 **p <0.001**	r = -0.364 **p <0.001**

Abbreviations: PN, parenteral nutrition; N, nitrogen (g).

5.8.1.2.2: Univariate ordinal regression analysis

Univariate ordinal logistic regression was conducted to explore the association between various predictors and the categorical outcomes of the EQ-5D, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Tables 5.11-5.15). Results are presented as odds ratios (OR) with 95% confidence intervals (CI) and p-values.

Table 5.11: Univariate logistic regression analysis for the mobility domain of the EQ5D

Predictor	OR	95% CI	Wald p-value	R^2	LRT p-value
Duration of HPN (months)	1.00	1.00 to 10.01	0.383	0.00	0.388
Living status	0.75	0.40 to 1.38	0.355	0.00	0.355
Education level				0.02	0.067
Secondary	1.00	Reference			
Post-secondary non-tertiary	0.67	0.27 to 1.69	0.399		
Short cycle tertiary	0.67	0.34 to 1.33	0.253		
Bachelors or higher	0.32	0.14 to 0.74	**0.008**		
Employment status				0.02	**0.010**
Unemployed	1.00	Reference			
Employed	0.31	0.14 to 0.69	**0.004**		
Retired	0.52	0.29 to 0.95	**0.033**		
SB length:				0.02	0.120
< 50cm	1.00	Reference			
51-100cm	1.30	0.55 to 3.82	0.635		
101-150cm	1.09	0.37 to 3.27	0.871		
151-200cm	3.80	0.97 to 14.94	0.056		
200cm	2.07	0.80 to 5.31	0.132		
Underlying disease				0.01	0.479
IBD	1.00	Reference			
Ischaemia	1.15	0.56 to 2.37	0.705		
Malignancy	2.00	0.85 to 4.70	0.110		
Motility disorder/ radiation enteritis	1.30	0.52 to 3.25	0.572		
Other/ unknown	1.59	0.81 to 3.12	0.175		
HGS (kg)	0.97	0.93 to 1.01	0.133	0.01	0.131
SMM (kg)	0.97	0.88 to 1.06	0.497	0.01	0.495
PA (degree)	0.62	-7.41 to 0.01	0.187	0.03	0.188
Oral dietary energy intake (kcal/d)	1.00	1.00 to 1.00	0.520	0.00	0.519
PN infusions/ wk	1.13	0.96 to 1.31	0.139	0.00	0.138
PN energy (kcal/d)	1.00	1.00 to 1.00	0.244	0.00	0.244

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Employed participants had 69% lower odds (p = 0.004), and retired participants 48% lower odds (p = 0.033) of mobility impairment compared to those unemployed. Similarly, participants with a bachelor's degree or higher had 68% lower odds of mobility problems compared to those with secondary education (p = 0.008) (Table 5.11).

Table 5.12: Univariate logistic regression analysis for the self-care domain of the EQ5D

Predictor	OR	95% CI	Wald p-value	R^2	LRT p-value
HPN length	1.00	1.00 to 1.01	0.886	0.00	0.887
Living status	0.79	0.43 to 1.47	0.466	0.00	0.467
Education level				0.01	0.288
Secondary	1.00	Reference			
Post-secondary non-tertiary	0.88	0.34 to 2.32	0.802		
Short cycle tertiary	0.62	0.31 to 1.24	0.174		
Bachelors or higher	0.47	0.20 to 1.12	0.090		
Employment status				0.02	**0.017**
Unemployed	1.00	Reference			
Employed	0.31	0.13 to 0.72	**0.007**		
Retired	0.58	0.32 to 1.06	0.075		
SB length:				0.01	0.693
< 50cm (constant)	1.00	Reference			
51-100cm	1.02	0.344 to 3.04	0.969		
101-150cm	1.06	0.35 to 3.15	0.922		
151-200cm	2.38	0.60 to 9.37	0.216		
200cm	1.41	0.55 to 3.57	0.474		
Underlying disease				0.01	0.291
IBD	1.00	Reference			
Ischaemia	1.72	0.83 to 3.57	0.146		
Malignancy	2.37	0.98 to 5.71	0.054		
Motility disorder/ radiation enteritis	1.23	0.47 to 3.22	0.669		
Other/ unknown	1.72	0.85 to 3.49	0.134		
HGS (kg)	0.96	0.92 to 1.01	0.088	0.02	0.079
SMM (kg)	0.96	0.88 to 10.06	0.419	0.01	0.415
PA (degree)	0.54	0.25 to 1.16	0.116	0.05	0.100
Oral dietary energy intake (kcal/d)	1.00	1.00 to 1.00	0.926	0.00	0.926
PN infusions/ wk	1.12	0.95 to 1.31	0.167	0.00	0.165
PN energy (kcal/d)	1.00	1.00 to 1.00	0.731	0.00	0.731

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Employed participants had 69% lower odds of experiencing self-care problems compared to those unemployed (p = 0.007). No other predictors were significantly associated with limitations in self-care (Table 5.12.

Table 5.13: Univariate logistic regression analysis for the usual activities domain of the EQ5D

Predictor	OR	95% CI	Wald p-value	R^2	LRT p-value
HPN length (months)	1.00	0.99 to 1.00	0.407	0.00	0.399
Living status	0.84	0.46 to 1.53	0.560	0.00	0.559
Education level				0.02	**0.013**
Secondary	1.00	Reference			
Post-secondary non-tertiary	0.73	0.30 to 1.75	0.477		
Short cycle tertiary	0.65	0.32 to 1.30	0.222		
Bachelors or higher	0.25	0.11 to 0.57	**0.001**		
Employment status				0.02	**0.003**
Unemployed	1.00	Reference			
Employed	0.29	0.13 to 0.68	**0.004**		
Retired	0.41	0.23 to 0.74	**0.003**		
SB length:				0.01	0.276
< 50cm	1.00	Reference			
51-100cm	0.65	0.22 to 1.96	0.443		
101-150cm	0.45	0.14 to 1.48	0.189		
151-200cm	2.60	0.61 to 11.11	0.198		
200cm	0.74	0.28 to 1.96	0.548		
Underlying disease				0.00	0.743
IBD	1.00	Reference			
Ischaemia	1.41	0.68 to 2.96	0.356		
Malignancy	1.43	0.62 to 3.27	0.398		
Motility disorder/ radiation enteritis	1.35	0.52 to 3.48	0.539		
Other/ unknown	1.55	0.80 to 2.99	0.195		
HGS (kg)	0.97	0.92 to 1.01	0.153	0.01	0.149
SMM (kg)	0.92	0.84 to 1.01	0.088	0.04	0.081
PA (degree)	0.60	0.31 to 1.16	0.126	0.03	0.125
Oral dietary energy intake (kcal/d)	1.00	1.00 to 1.00	0.167	0.01	0.165
PN infusions/ wk	1.19	1.02 to 1.40	**0.031**	**0.01**	**0.030**
PN energy (kcal/d)	1.00	1.00 to 1.00	0.161	0.01	0.160

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Participants who were employed had 71% lower odds of reporting problems with usual activities compared to those unemployed (p = 0.004), and retired participants had 59% lower odds (p = 0.003). Those with a bachelor's degree or higher had 75% lower odds of usual activity limitations compared to those with secondary education (p = 0.001). Additionally, a higher number of weekly PN infusions were associated with increased odds of usual activity impairment (p = 0.031) (Table 5.13).

Table 5.14: Univariate logistic regression analysis for the pain/ discomfort domain of the EQ5D

Predictor	OR	95% CI	Wald p-value	R^2	LRT p-value
HPN length (months)	1.00	0.10 to 1.01	0.590	0.00	0.588
Living status	1.04	0.56 to 1.93	0.897	0.00	0.897
Education level				0.01	0.441
Secondary	1.00	Reference			
Post-secondary non-tertiary	0.01	0.38 to 2.15	0.828		
Short cycle tertiary	1.00	0.50 to 2.03	0.994		
Bachelors or higher	0.53	0.24 to 1.20	0.127		
Employment status				0.00	**<0.001**
Unemployed	1.00	Reference			
Employed	0.27	0.12 to 0.60	0.001		
Retired	0.33	0.18 to 0.61	<0.001		
SB length:				0.02	0.054
< 50cm (constant)	1.00	Reference			
51-100cm	0.79	0.26 to 2.42	0.682		
101-150cm	0.47	0.16 to 1.39	0.173		
151-200cm	1.23	0.32 to 4.75	0.767		
200cm	1.44	0.57 to 3.59	0.439		
Underlying disease				0.01	0.075
IBD	1.00	Reference			
Ischaemia	0.54	0.26 to 1.12	0.098		
Malignancy	1.20	0.51 to 2.82	0.679		
Motility disorder/ radiation enteritis	0.53	0.21 to 1.32	0.173		
Other/ unknown	1.39	0.71 to 2.71	0.332		
HGS (kg)	0.96	0.93 to 1.00	0.085	0.01	0.085
SMM (kg)	0.95	0.87 to 1.05	0.333	0.01	0.339
PA (degree)	1.04	0.50 to 2.15	0.917	0.00	0.917
Oral dietary energy intake (kcal/d)	1.00	1.00 to 1.00	0.740	0.00	0.740
PN infusions/ wk	1.08	0.92 to 1.25	0.349	0.00	0.349
PN energy (kcal/d)	1.00	1.00 to 1.00	0.307	0.00	0.306

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Employed participants had 73% lower odds (p = 0.001), and retired participants 67% lower odds (p = 0.000) of reporting pain or discomfort compared to those unemployed. No significant associations were found (Table 5.14).

Table 5.15: Univariate logistic regression analysis for the anxiety/ depression domain of the EQ5D

Predictor	OR	95% CI	Wald p-value	R^2	LRT p-value
HPN length (months)	1.00	1.00 to 1.00	0.957	0.00	0.957
Living status	1.05	0.56 to 1.97	0.874	0.00	0.874
Education level				0.01	0.091
Secondary	1.00	Reference			
Post-secondary non-tertiary	1.52	0.63 to 3.70	0.353		
Short cycle tertiary	0.55	0.27 to 1.12	0.097		
Bachelors or higher	0.56	0.24 to 1.30	0.176		
Employment status				0.04	**<0.001**
Unemployed	1.00	Reference			
Employed	0.26	0.12 to 0.60	**0.002**		
Retired	0.24	0.13 to 0.45	**<0.001**		
SB length:				0.00	0.750
< 50cm	1.00	Reference			
51-100cm	0.77	0.26 to 2.28	0.636		
101-150cm	0.79	0.26 to 2.41	0.678		
151-200cm	2.28	0.52 to 9.93	0.274		
200cm	0.83	0.33 to 2.12	0.700		
Underlying disease				0.00	0.695
IBD	1.00	Reference			
Ischaemia	0.74	0.36 to 1.54	0.425		
Malignancy	1.06	0.45 to 2.49	0.897		
Motility disorder/ radiation	1.16	0.47 to 2.83	0.751		
enteritis	1.30	0.66 to 2.56	0.443		
Other/ unknown					
HGS (kg)	0.97	0.93 to -0.41	0.113	0.01	0.109
SMM (kg)	0.93	0.84 to 1.02	0.102	0.04	0.093
PA (degree)	0.65	0.33 to 1.27	0.210	0.02	0.209
Oral dietary energy intake (kcal/d)	1.00	1.00 to 1.00	0.317	0.00	0.317
PN infusions/ wk	1.08	0.93 to 1.26	0.302	0.00	0.302
PN energy (kcal/d)	1.00	1.00 to 1.00	0.900	0.00	0.899

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Employed participants had 74% lower odds of reporting anxiety or depression compared to those unemployed ($p = 0.002$), while retired participants had 76% lower odds ($p < 0.001$). No other variables were significantly associated with anxiety/depression (Table 5.15).

In summary, across all EQ-5D domains, employment status consistently emerged as a significant protective factor. Employed participants had significantly lower odds of reporting

problems with mobility, self-care, usual activities, pain/discomfort, and anxiety/depression compared to those unemployed. Retired participants similarly showed reduced odds in mobility, pain/discomfort and anxiety/depression**.** Those with a bachelor's degree or higher had lower odds of mobility and usual activity limitations**.** Additionally, a higher frequency of weekly PN infusions was associated with increased difficulties in usual activities.

Table 5.16: Univariate linear regression results for the EQ5D VAS scores

Predictor	Coefficient B	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.01	-0.07 to 0.04	0.680	0.00	0.680
Living status	3.03	-4.49 to 10.55	0.427	0.00	0.428
Education level				0.05	**0.043**
Secondary	Reference				
Post-secondary non-tertiary	-1.36	-12.20 to 9.47	0.804		
Short cycle tertiary	4.61	-3.85 to 13.07	0.284		
Bachelors or higher	13.74	3.57 to 23.90	**0.008**		
Employment status				0.08	**0.001**
Unemployed	Reference				
Employed	12.53	2.81 to 22.25	**0.012**		
Retired	12.71	5.81 to 19.62	**<0.001**		
SB length:				0.04	0.121
< 50cm	Reference				
51-100cm	9.30	-3.68 to 22.29	0.159		
101-150cm	10.40	-2.30 to 23.10	0.108		
151-200cm	-10.38	-27.06 to 6.30	0.221		
200cm	2.36	-8.43 to 13/16	0.666		
Underlying disease				0.04	0.102
IBD	Reference				
Ischaemia	3.63	-4.94 to 12.22	0.404		
Malignancy	-6.12	-15.98 to 3.74	0.223		
Motility disorder/ radiation enteritis	10.83	-0.31 o 21.97	0.057		
Other/ unknown	-0.74	-8.58 to 7.10	0.852		
HGS (kg)	0.56	0.12 to 1.00	**0.013**	0.08	0.083
SMM (kg)	1.43	0.44 to 2.43	**0.007**	0.29	**0.007**
PA (degree)	6.84	-0.98 to 14.68	0.083	0.13	0.083
Oral dietary energy intake (kcal/d)	0.01	0.00 to 0.01	**0.011**	0.07	**0.011**
PN infusions/ wk	-2.32	-4.13 to -0.50	**0.013**	0.03	**0.013**
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.195	0.01	0.195

Abbreviations: VAS, visual analogue scale; HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Univariate regression analyses showed that employment and retirement were associated with significantly higher EQ-5D VAS scores, with increases of 12.53 and 12.71 points, respectively, compared to unemployment. Higher education was also positively associated,

with those holding a bachelor's degree or higher scoring 13.74 points higher than those with secondary education. Physical measures, including handgrip strength and skeletal muscle mass, were significantly associated with improved VAS scores, with each unit increase corresponding to a 0.56- and 1.43-point increase, respectively. Additionally, higher oral dietary intake was linked to a modest increase in VAS scores, while each additional PN infusion per week was associated with a 2.32-point reduction. Overall, the model accounted for 8% of the variance in EQ-5D VAS scores (Table 5.16).

Employment status was significantly associated with health utility scores (Table 5.17). Compared with unemployment, being employed was linked to a 0.30-point increase in health utility, while retirement was associated with a 0.22-point increase. Education also showed a positive relationship with health utility, with individuals holding a bachelor's degree or higher reporting a 0.21-point increase compared to those with secondary education. HGS was a small but significant predictor, with a one-unit increase associated with a 0.01-point increase in health utility. The overall model explained 13% of the variance in health utility.

Table 5.17: Univariate linear regression results for the health utility scores

Predictor	Coefficient B	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.00	0.00 to 0.00	0.952	0.00	0.952
Living status	-0.00	-0.12 to 0.11	0.956	0.00	0.956
Education level				0.05	0.071
Secondary	Reference				
Post-secondary non-tertiary	0.05	-0.11 to 0.21	0.547		
Short cycle tertiary	0.07	-0.06 to 0.19	0.313		
Bachelors or higher	0.21	0.05 to 0.36	**0.008**		
Employment status				0.13	**<0.001**
Unemployed	Reference				
Employed	0.30	0.16 to 0.45	**<0.001**		
Retired	0.22	0.12 to 0.32	**<0.001**		
SB length:				0.01	0.460
< 50cm	Reference				
51-100cm	0.00	-0.20 to 0.20	0.966		
101-150cm	0.02	-0.18 to 0.21	0.873		
151-200cm	-0.16	-0.42 to 0.10	0.219		
200cm	-0.08	-0.24 to 0.09	0.359		
Underlying disease				0.04	0.138
IBD	Reference				
Ischaemia	0.06	-0.07 to 0.19	0.381		
Malignancy	-0.08	-0.23 to 0.07	0.311		
Motility disorder/ radiation enteritis	0.08	-0.09 to 0.26	0.334		
Other/ unknown	-0.08	-0.21 to 0.04	0.171		
HGS (kg)	0.01	0.00 to 0.02	**0.009**	0.09	**0.009**
SMM (kg)	0.01	-0.00 to 0.03	0.077	0.14	0.077
PA (degree)	0.06	-0.06 to 0.18	0.317	0.05	0.317
Oral dietary energy intake (kcal/d)	-8.46	-0.00 to 0.00	0.875	0.00	0.875
PN infusions/ wk	-0.03	-0.05 to 0.00	0.073	0.02	0.073
PN energy (kcal/d)	0.00	-0.00 to 0.00	0.608	0.00	0.608

Abbreviations: VAS, visual analogue scale; HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

5.8.1.2.3: Assessment of confounding variables

Age and gender were identified as potential confounders based on the DAG, which was supported by a change in the coefficient exceeding 10% upon adjustment (Table 5.18).

Table 5.18: Assessment of potential confounding variables for the mobility domain of the EQ-5D

Predictor	Coefficient (B)	95% CI	Wald p-value
Education level			
Secondary	1.00	Reference	
Post-secondary non-tertiary	0.67	0.27 to 1.69	0.399
Short cycle tertiary	0.67	0.34 to 1.33	0.253
Bachelors or higher	0.32	0.14 to 0.74	**0.008**
Adj. age			
Secondary	1.00	Reference	
Post-secondary non-tertiary	0.63	0.25 to 1.59	0.331
Short cycle tertiary	0.62	0.31 to 1.25	0.180
Bachelors or higher	0.26	0.11 to 6.26	**0.003**
*Adj. gender**			
Secondary	1.00	Reference	
Post-secondary non-tertiary	0.68	0.27 to 1.75	0.428
Short cycle tertiary	0.56	0.27 to 1.13	0.108
Bachelors or higher	0.27	0.12 to 0.64	**0.003**

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model. An asterisk indicates a change greater than 10% in the coefficient following adjustment*

The findings presented in Table 5.18 and Table 5.19 suggest that age and gender act as confounding variables in the relationship between sociodemographic factors and mobility and usual activities domains of the EQ-5D. Adjustments for these covariates resulted in notable changes in effect sizes, particularly for education level and employment status in the mobility and usual activities domains. For example, the odds ratios for higher education became stronger and more statistically significant after adjusting for gender. Similarly, adjusted models for employment status showed consistently lower odds of functional limitations. These observed shifts support the inclusion of age and gender as covariates in the subsequent multivariable analyses.

Table 5.19: Assessment of potential confounding variables for the usual activities domains of the EQ-5D

Predictor	Coefficient (B)	95% CI	Wald p-value
Education level			
Secondary	1.00	Reference	
Post-secondary non-tertiary	0.73	0.30 to 1.75	0.477
Short cycle tertiary	0.65	0.32 to 1.30	0.222
Bachelors or higher	0.25	0.11 to 0.57	**0.001**
Adj. age			
Secondary	1.00		
Post-secondary non-tertiary	0.67	0.28 to 1.62	0.373
Short cycle tertiary	0.63	0.31 to 1.26	0.190
Bachelors or higher	0.21	0.09 to 0.59	**<0.001**
*Adj. gender**			
Secondary	1.00	Reference	
Post-secondary non-tertiary	0.71	0.30 to 1.72	0.450
Short cycle tertiary	0.52	0.25 to 1.06	0.074
Bachelors or higher	0.22	0.09 to 0.51	**<0.001**
Employment status			
Unemployed	1.00	Reference	
Employed	0.29	0.13 to 0.68	**0.004**
Retired	0.41	0.23 to 0.74	**0.003**
Adj. age			
Unemployed	1.00	Reference	
Employed	0.29	0.12 to 0.71	**0.006**
Retired	0.40	0.18 to 0.87	**0.021**
Adj. gender			
Unemployed	1.00	Reference	
Employed	0.28	0.12 to 0.66	**0.004**
Retired	0.42	0.23 to 0.77	**0.005**

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model. An asterisk indicates a change greater than 10% in the coefficient following adjustment*

The findings in Table 5.20 demonstrate that both age and gender also acted as confounders in the associations between sociodemographic, functional measures and EQ-5D VAS scores. After adjustment for age and gender, the association between having a bachelor's degree or higher and higher VAS scores remained significant and became more pronounced. The association between employment and VAS scores also strengthened after adjusting for age, although significance was reduced when adjusting for both age and gender. Similarly, HGS and SMM remained significantly associated with higher VAS scores after adjustment for age alone, though adjustment for gender reduced the effect estimates.

Table 5.20: Assessment of potential confounding variables for the EQ-5D VAS

Predictor	Coefficient (B)	95% CI	p-value
Education level			
Secondary	Reference		
Post-secondary non-tertiary	-1.36	-12.20 to 9.47	0.804
Short cycle tertiary	4.61	-3.85 to 13.07	0.284
Bachelors or higher	13.74	3.57 to 23.90	**0.008**
*Adj. age**			
Secondary	Reference		
Post-secondary non-tertiary	-0.45	-11.00 to 10.11	0.933
Short cycle tertiary	5.58	-2.67 to 13.83	0.183
Bachelors or higher	16.03	6.03 to 26.03	**0.002**
*Adj. age, gender**			
Secondary	Reference		
Post-secondary non-tertiary	-1.04	-11.25 to 9.18	0.842
Short cycle tertiary	7.76	-0.32 to 15.84	0.060
Bachelors or higher	15.68	5.87 to 25.49	**0.002**
Employment status			
Unemployed	Reference		
Employed	12.53	2.81 to 22.25	**0.012**
Retired	12.71	5.81 to 19.62	**<0.001**
*Adj. age**			
Unemployed	Reference		
Employed	14.58	4.49 to 24.66	**0.005**
Retired	8.49	-0.52 to 17.49	0.065
*Adj. age, gender**			
Unemployed	Reference		
Employed	14.50	4.82 to 24.18	**0.004**
Retired	7.11	-1.55 to 15.79	0.107
HGS	0.56	0.12 to 1.00	**0.013**
*Adj. age**	0.63	0.19 to 1.07	**0.006**
Adj. age, gender	0.61	-0.09 to 1.32	0.086
SMM (kg)	1.43	0.44 to 2.43	**0.007**
Adj. age	1.43	0.45 to 2.41	**0.006**
Adj. gender	1.32	-0.42 to 3.05	0.130

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model. An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.21 shows that age and gender confounded the relationships between sociodemographic and functional factors and health utility scores. Higher education and employment remained significant predictors after adjustment, although the effect of employment was slightly reduced when adjusting for both age and gender. HGS remained positively associated with utility scores after age adjustment.

Table 5.21: Assessment of potential confounding variables for the EQ-5D healthy utility scores

Predictor	Coefficient (B)	95% CI	p-value
Education level			
Secondary	Reference		
Post-secondary non-tertiary	0.05	-0.11 to 0.21	0.547
Short cycle tertiary	0.07	-0.06 to 0.19	0.313
Bachelors or higher	0.21	0.05 to 0.36	**0.008**
Adj. age			
Secondary	Reference		
Post-secondary non-tertiary	0.06	-0.09 to 0.22	0.427
Short cycle tertiary	0.08	-0.04 to 0.20	0.203
Bachelors or higher	0.24	0.09 to 0.39	**0.002**
Adj. gender			
Secondary	Reference		
Post-secondary non-tertiary	0.04	-0.12 to 0.20	0.592
Short cycle tertiary	0.09	-0.03 to 0.22	0.142
Bachelors or higher	0.21	0.06 to 0.37	**0.006**
Employment status			
Unemployed	Reference		
Employed	0.30	0.16 to 0.45	**<0.001**
Retired	0.22	0.12 to 0.32	**<0.001**
*Adj. age**			
Unemployed	Reference		
Employed	0.35	0.21 to 0.50	**<0.001**
Retired	0.12	-0.02 to 0.25	0.084
*Adj. age, gender**			
Unemployed	Reference		
Employed	0.35	0.21 to 0.50	**<0.001**
Retired	0.10	-0.03 to 0.23	0.130
HGS (kg)	0.01	0.00 to 0.02	**0.009**
Adj. age	0.01	0.00 to 0.02	**0.002**
Adj. gender	0.01	0.00 to 0.02	0.080

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

5.8.1.2.4: Multivariable regression analysis

Logistic regression was conducted to examine the association between education level, employment status, and gender and mobility (Table 5.22). In the initial model including education level and employment status only, both predictors were significantly associated with mobility (LR $\chi^2(5) = 16.39$, $p = 0.006$). A second model including gender as a covariate showed improved model fit (LR $\chi^2(6) = 21.19$, $p = 0.002$). A LRT comparing the two models

confirmed that the addition of gender significantly improved the model fit (LR $\chi^2(1) = 4.80$, p = 0.029). In the final model, male gender was associated with significantly higher odds of greater mobility, after adjusting for education level and employment status.

Table 5.22: Ordered logistic multivariable regression for the EQ-5D domains

Outcome	Predictor	OR	95% CI	Wald p-value	LRT p-value	R^2
Mobility	**Employment**				**0.010**	
	Unemployed	1.00	Reference			0.05
	Employed	0.40	0.17 to 0.95	**0.039**		
	Retired	0.46	0.24 to 0.91	**0.025**		
	Education:				**0.010**	
	Secondary	1.00	Reference			
	Post-secondary non-tertiary	0.75	0.29 to 1.94	0.557		
	Short cycle tertiary	0.68	0.32 to 1.41	0.302		
	Bachelors or higher	0.35	0.15 to 0.84	**0.018**		
	Gender	2.03	1.07 to 3.84	**0.030**	**0.029**	
Self-care	N/A: Univariate only					
Usual activities	**Education:**				**0.010**	0.06
	Secondary	1.00	Reference			
	Post-secondary non-tertiary	0.76	0.31 to 1.85	0.543		
	Short cycle tertiary	0.61	0.29 to 1.26	0.182		
	Bachelors or higher	0.27	0.11 to 0.67	**0.005**		
	Employment				**0.010**	
	Unemployed	1.00	Reference			
	Employed	0.42	0.17 to 1.04	0.061		
	Retired	0.40	0.21 to 0.77	**0.006**		
	Gender	2.09	1.11 to 3.93	**0.023**	**0.022**	
Pain	N/A: Univariate only					
Anxiety/ depression	N/A: Univariate only					

For the usual activities outcome, the initial regression model showed that education level was significantly associated with greater difficulty performing usual activities (LR $\chi^2(3) = 11.74$, p = 0.008), with individuals in the highest education category having notably lower odds of activity limitations (OR = 0.23, 95% CI: 0.09–0.53, p = 0.001). Model fit improved significantly upon adding employment status (LR $\chi^2(2) = 9.14$, p = 0.010), revealing that both unemployed and retired individuals had higher odds of limitations compared to those employed. The inclusion of gender further strengthened the model (LR $\chi^2(1) = 5.26$, p =

0.0219), with females showing increased odds of experiencing limitations (OR = 2.09, 95% CI: 1.11–3.93, p = 0.023). In contrast, adding weekly PN infusions did not yield a significant contribution (p = 0.78) and did not enhance model fit (LR $\chi^2(1) = 0.08$, p = 0.78).

Table 5.23: Linear multivariable regression for the EQ-5D VAS and health utility scores

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
VAS	**Employment**				**0.001**	0.19
	Unemployed	Reference				
	Employed	12.15	-0.89 to 25.21	0.067		
	Retired	11.20	1.35 to 21.05	**0.026**		
	HGS (kg)	0.55	0.09 to 1.00	**0.019**	**0.020**	
Health utility	**Employment**				**<0.001**	0.23
	Unemployed	Reference				
	Employed	0.19	-0.04 to 0.41	0.100		
	Retired	0.09	-0.10 to 0.29	0.341		
	Age (years)	0.01	-0.00 to 0.02	0.054	**0.016**	
	Gender	0.12	-0.10 to 0.34	0.287	**0.003**	
	HGS (kg)	0.01	0.00 to 0.02	**0.016**	**0.011**	

Abbreviations: VAS, visual analogue scale; HGS, handgrip strength

In linear regression models examining predictors of the EQ-5D VAS, employment status was initially associated with VAS scores (p = 0.013), with both employed groups reporting significantly higher scores than the unemployed (Table 5.23). Adding HGS significantly improved model fit (LR $\chi^2(1) = 5.81$, p = 0.016), and higher HGS was associated with better VAS scores (β = 0.55, p = 0.020). Inclusion of age, gender, SMM, education level, oral dietary intake and the number of weekly infusions did not significantly improve the model (all p > 0.05) and were therefore excluded. The final model retained employment status and HGS only.

For the health utility outcome, being employed was initially marginally associated with higher scores (β = 0.23, p = 0.051), whereas age and gender were not significant predictors. Upon inclusion of HGS, it became a significant positive predictor (β = 0.014, p = 0.016), and the effect of employment status was attenuated. The overall model fit improved significantly with the addition of HGS (LR $\chi^2(1) = 6.43$, p = 0.011). As a result, because age and gender were confirmed confounders, they were retained in the final model along with employment status and HGS.

5.8.1.2.5: Model assumption checks for EQ-5D regression analyses

Regression diagnostics were conducted for all final multivariable regression models for the EQ-5D. Overall, diagnostics indicated that key assumptions were reasonably met (Table 5.24). For health utility, mild non-normality of residuals was present but as the sample size of that model was reduced to n=72 (compared with n=151 for the other domains), the model was still robust and therefore no adjustments were made.

Table 5.24: Multivariable regression diagnostics for the EQ-5D

SF-36 domain	Residual normality (p-value)	Heteroskedasticity (Breusch-Pagan; p-value)	Mean VIF	Notes
Mobility	0.204	0.164	1.24	Assumptions met
Usual activities	0.194	0.584	1.24	Assumptions met
VAS	0.867	0.541	1.21	Assumptions met
Health utility	0.036	0.624	2.54	Mild non-normality of residuals

Regression diagnostics confirmed the following assumptions: linearity between predictors and outcome, normally distributed residuals, homoscedasticity (constant variance), no multicollinearity (VIF < 10). Abbreviations: VAS, visual analogue scale; VIF, variance inflation factor.

5.8.2: Short Form-36 questionnaire

5.8.2.1: Descriptives

The SF-36 questionnaire was returned by 186 participants at baseline and 138 participants at follow up (Table 5.25).

Table 5.25: SF-36 results at baseline and follow up

	Baseline (n=186)	**Baseline results for follow up participants only (n=141)**	**Follow up (n = 141)**	**p-value**
Physical functioning	30 (10-55)	30 (10-60)	30 (10-55)	0.771
Role limitations (physical)	0 (0-25)	0 (0-25)	0 (0-25)	0.330
Role limitations (emotional)	0 (0-100)	0 (0-100)	33 (0-100)	0.482
Energy/ fatigue*	30 (5-40)	30 (10-40)	30 (15-50)	**0.041**
Emotional wellbeing	56 (40-76)	56 (46.5-76)	60 (44-72)	0.179
Social functioning	38 (22-62)	50 (12-50)	50 (25-64)	0.998
Pain	45 (22-68)	45 (22-68)	45 (22-58)	0.459
General health	25 (10-40)	25 (10-40)	25 (10-35)	0.304

All data are presented as median (IQR)

Many domains remained consistent over time such as PF, RLPH, pain and general health. There was a slight increase in the emotional role limitations score, emotional well-being and social functioning scores, although these were not significant. The median score for energy/ fatigue remained unchanged, however, the IQR was higher and statistical significance was reached (p.041). The spread of the data for each domain can be seen in Figure 5.5. The plot highlights the variation in scores, the median, and the presence of outliers for each domain.

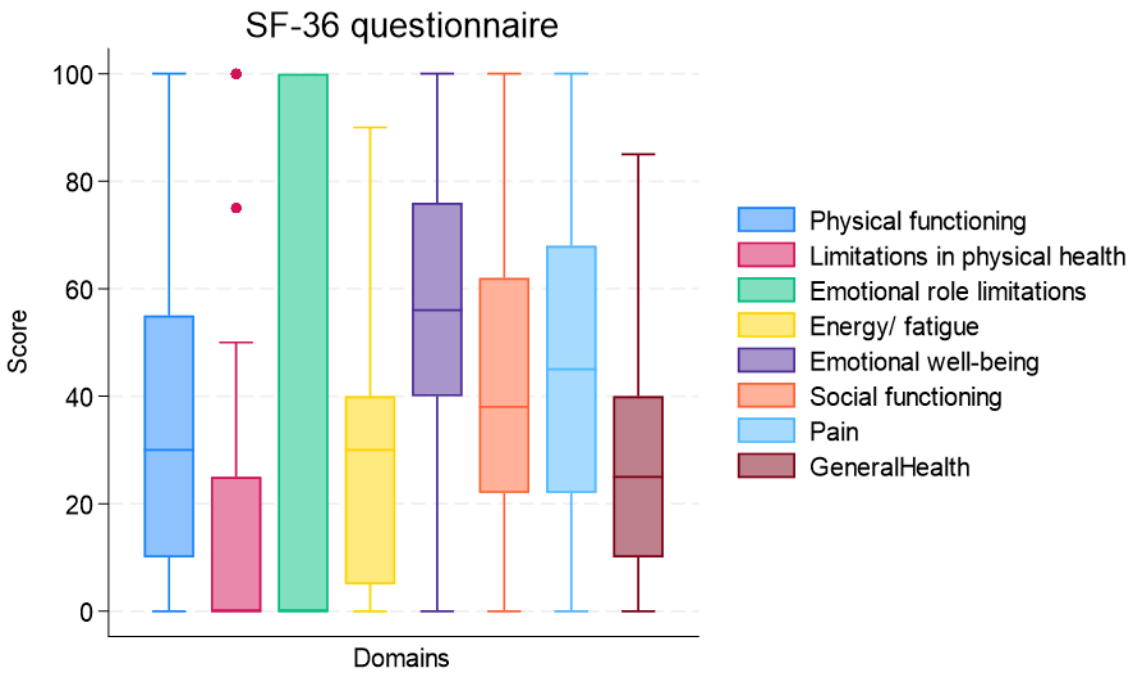


Figure 5.5: Boxplot displaying the distribution of scores at baseline across all domains of the SF-36 questionnaire.

5.8.2.2: Use of inferential statistics to investigate factors associated with SF-36 outcomes at baseline

5.8.2.2.1: 5.8.1.2.2: Univariate linear regression analysis

Results in Table 5.26 are reported as regression coefficients (B) with 95% CI, p-values, and the proportion of variance explained (R^2).

Table 5.26: Univariate linear regression analysis for the physical functioning domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.03	-0.04 to 0.11	0.389	0.00	**0.004**
Living status	11.49	1.20 to 21.79	0.029	0.03	**0.029**
Education level				0.06	**0.042**
Secondary	Reference				
Post-secondary non-tertiary	4.34	-10.51 to 19.18	0.564		
Short cycle tertiary	4.00	-7.67 to 15.66	0.499		
Bachelors or higher	19.93	6.25 to 33.63	**0.005**		
Employment status				0.10	**<0.001**
Unemployed	Reference				
Employed	28.09	14.95 to 41.24	**<0.001**		
Retired	8.05	-1.37 to 17.47	0.093		
SB length:				0.04	0.174
< 50cm	Reference				
51-100cm	-6.67	-18.23 to 18.23	1.000		
101-150cm	8.47	-9.13 to 26.07	0.344		
151-200cm	-16.23	-38.97 to 6.51	0.161		
200cm	-6.04	-21.03 to 8.95	0.427		
Underlying disease				0.02	0.428
IBD	Reference				
Ischaemia	-8.89	-20.97 to 3.20	0.148		
Malignancy	-10.45	-24.70 to 3.79	0.149		
Motility disorder/ radiation enteritis	-6.39	-21/74 to 8.96	0.412		
Other/ unknown	-8.82	-19.76 to 2.12	0.113		
HGS (kg)	1.00	0.43 to 1.56	**0.001**	0.15	**0.001**
SMM (kg)	0.86	-0.43 to 2.15	0.181	0.08	0.181
Phase angle (degree)	8.95	0.04 to 17.86	**0.049**	0.17	**0.049**
Oral dietary energy intake (kcal/d)	0.01	-0.00 to 0.01	0.169	0.02	0.169
PN infusions/ wk	-1.31	-3.86 to 1.25	0.314	0.01	0.314
PN energy (kcal/d)	0.00	-0.01 to 0.01	0.935	0.00	0.935

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was strongly associated with better PF, with employed participants scoring 28.09 points higher compared to those who were unemployed ($p < 0.001$). Higher education was also associated with improved PF scores, with participants holding a bachelor's degree or higher scoring 19.93 points higher than those with secondary education

only (p = 0.005). Living with others was associated with an 11.49-point increase in PF scores compared to living alone (p = 0.029). HGS was positively associated with PF, with each 1 kg increase in HGS corresponding to a 1-point increase in PF scores (p = 0.001) (Table 5.26).

Table 5.27: Univariate linear regression analysis for the physical role limitations domain of the SF-36

Predictor	**Coefficient (B)**	**95% CI**	**p-value**	**R^2**	**LRT p-value**
HPN length (months)	0.07	-0.03 to 0.16	0.167	0.01	0.167
Living status	9.98	-3.13 to 23.09	0.135	0.01	0.135
Education level				0.03	0.277
Secondary	Reference				
Post-secondary non-tertiary	10.15	-9.37 to 29.67	0.306		
Short cycle tertiary	7.07	-8.27 to 22.41	0.364		
Bachelors or higher	17.30	-0.71 to 35.30	0.060		
Employment status				0.04	**0.026**
Unemployed	Reference				
Employed	17.57	0.16 to 34.98	**0.048**		
Retired	16.25	3.77 to 28.72	**0.011**		
SB length:				0.08	**0.012**
< 50cm	Reference				
51-100cm	-15.26	-37.72 to 7.19	0.181		
101-150cm	10.65	-11.03 to 32.32	0.334		
151-200cm	-30.26	-58.27 to -2.26	**0.034**		
200cm	-17.76	-36.22 to 0.70	0.059		
Underlying disease				0.02	0.464
IBD	Reference				
Ischaemia	-1.39	-16.57 to 13.79	0.857		
Malignancy	-11.36	-29.26 to 6.54	0.212		
Motility disorder/ radiation enteritis	-6.94	-26.23 to 12.33	0.478		
Other/ unknown	-11.08	-24.82 to 2.67	0.114		
HGS (kg)	1.08	0.25 to 1.90	**0.011**	0.09	**0.011**
SMM (kg)	1.58	0.29 to 2.87	**0.018**	0.24	**0.019**
Phase angle (degree)	16.24	8.51 to 23.98	**<0.001**	0.48	**<0.001**
Oral dietary energy intake (kcal/d)	0.01	0.00 to 0.02	**0.013**	0.07	**0.013**
PN infusions/ wk	-1.25	-4.47 to 1.98	0.447	0.00	0.447
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.512	0.00	0.512

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was significantly associated with better physical role limitations scores, with employed participants scoring 17.57 points higher and retired participants scoring 16.25 points higher than unemployed participants ($p = 0.048$ and $p = 0.011$, respectively). HGS ($p = 0.011$), SMM ($p = 0.018$), PA ($p < 0.001$), and higher oral dietary energy intake ($p = 0.013$) were also significantly associated with improved physical role functioning. SB length (101–150 cm) was associated with lower scores compared to those with <50 cm ($p = 0.034$). Living status, education, underlying disease, weekly PN infusions, and PN energy were not significantly associated with this domain (Table 5.27).

Table 5.28: Univariate linear regression analysis for the emotional role limitations domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.06	-0.06 to 0.18	0.330	0.01	0.330
Living status	4.40	-12.65 to 21.45	0.611	0.00	0.611
Education level				0.03	0.287
Secondary	Reference				
Post-secondary non-tertiary	8.88	-15.63 to 33.38	0.475		
Short cycle tertiary	11.06	-8.19 to 30.32	0.258		
Bachelors or higher	21.53	-1.07 to 44.13	0.062		
Employment status				0.09	**0.001**
Unemployed	Reference				
Employed	36.61	14.76 to 58.45	**0.001**		
Retired	26.60	10.94 to 42.25	**0.001**		
SB length:				0.05	0.140
< 50cm	Reference				
51-100cm	14.05	-15.95 to 44.05	0.357		
101-150cm	2.87	-26.09 to 31.83	0.845		
151-200cm	-30.85	-68.27 to 6.56	0.105		
200cm	-4.89	-29.55 to 19.77	0.696		
Underlying disease				0.01	0.618
IBD	Reference				
Ischaemia	3.76	-16.15 to 23.66	0.710		
Malignancy	-3.41	-26.88 to 20.06	0.775		
Motility disorder/ radiation enteritis	13.95	-11.33 to 39.23	0.278		
Other/ unknown	-5.77	-23.80 to 12.25	0.528		
HGS (kg)	0.87	-0.22 to 1.96	0.117	0.03	0.117
SMM (kg)	1.35	-1.03 to 3.72	0.251	0.06	0.251
Phase angle (degree)	13.06	-3.72 to 29.84	0.121	0.11	0.121
Oral dietary energy intake (kcal/d)	-0.00	-0.02 to 0.02	0.971	0.00	0.971
PN infusions/ wk	-2.57	-6.76 to 1.62	0.228	0.01	0.228
PN energy (kcal/d)	0.00	-0.01 to 0.01	0.757	0.00	0.757

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was significantly associated with better emotional role functioning, with employed participants scoring 36.61 points higher and retired participants scoring 26.60 points higher than unemployed participants (both p = 0.001). No other predictors showed statistically significant associations with emotional role limitations in univariate analysis (Table 5.28).

Table 5.29: Univariate linear regression analysis for the energy/ fatigue domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.02	-0.07 to 0.04	0.583	0.00	0.583
Living status	4.91	-2.90 to 12.73	0.216	0.01	0.216
Education level				0.04	0.107
Secondary	Reference				
Post-secondary non-tertiary	-1.05	-12.08 to 9.98	0.851		
Short cycle tertiary	-5.77	-14.44 to 2.90	0.190		
Bachelors or higher	7.80	-2.37 to 19.98	0.132		
Employment status				0.04	**0.033**
Unemployed	Reference				
Employed	10.77	0.63 to 20.90	**0.037**		
Retired	8.71	1.45 to 15.98	**0.019**		
SB length:				0.07	**0.021**
< 50cm	Reference				
51-100cm	-3.68	-17.12 to 9.76	0.589		
101-150cm	9.25	-3.73 to 22.22	0.161		
151-200cm	-16.64	-33.40 to 0.12	0.052		
200cm	-7.04	-18.09 to 4.00	0.210		
Underlying disease				0.04	0.133
IBD	Reference				
Ischaemia	3.00	-5.97 to 11.97	0.511		
Malignancy	-7.74	-18.31 to 2.84	0.151		
Motility disorder/ radiation enteritis	9.11	-2.29 to 20.50	0.116		
Other/ unknown	-1.63	-9.76 to 6.49	0.692		
HGS (kg)	0.61	0.16 to 1.06	**0.009**	0.09	**0.009**
SMM (kg)	0.90	0.33 to 1.76	**0.042**	0.18	**0.043**
Phase angle (degree)	5.73	-0.67 to 12.14	0.077	0.14	0.077
Oral dietary energy intake (kcal/d)	0.01	0.00 to 0.02	**0.008**	0.08	**0.008**
PN infusions/ wk	-1.54	-3.46 to 0.37	0.114	0.01	0.353
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.353	0.00	0.353

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was significantly associated with better energy/fatigue scores, with employed participants scoring 10.77 points higher and retired participants scoring 8.71 points higher than unemployed participants (p = 0.037 and p = 0.019, respectively). HGS (p = 0.009), SMM (p = 0.042), and higher oral dietary energy intake (p = 0.008) were also significantly associated with improved energy/fatigue scores. No significant associations

were observed for living status, education, SB length, underlying disease, PA, PN infusions, or PN energy (Table 5.29).

Table 5.30: Univariate linear regression analysis for the emotional wellbeing domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.01	-0.05 to 0.07	0.726	0.00	0.726
Living status	-1.14	-9.46 to 7.18	0.787	0.00	0.787
Education level				0.03	0.281
Secondary	Reference				
Post-secondary non-tertiary	-1.73	-13.44 to 9.98	0.771		
Short cycle tertiary	5.12	-4.08 to 14.33	0.273		
Bachelors or higher	8.90	-1.90 to 19.70	0.106		
Employment status				0.13	**<0.001**
Unemployed	Reference				
Employed	14.50	4.29 to 24.72	**0.006**		
Retired	17.89	10.57 to 25.21	**<0.001**		
SB length:				0.02	0.721
< 50cm	Reference				
51-100cm	9.89	-4.76 to 24.55	0.184		
101-150cm	9.47	-4.67 to 23.62	0.188		
151-200cm	2.36	-15.91 to 20.64	0.799		
200cm	5.05	-7.00 to 17.10	0.410		
Underlying disease				0.01	0.685
IBD	Reference				
Ischaemia	1.57	-8.05 to 11.20	0.747		
Malignancy	-5.59	-16.94 to 5.76	0.333		
Motility disorder/ radiation enteritis	-1.65	-13.87 to 10.57	0.790		
Other/ unknown	-4.18	-12.89 to 4.54	0.345		
HGS (kg)	0.40	-0.11 to 0.91	0.121	0.03	0.121
SMM (kg)	0.86	-0.06 to 1.79	0.066	0.15	0.066
Phase angle (degree)	7.50	1.06 to 13.94	**0.024**	0.22	**0.025**
Oral dietary energy intake (kcal/d)	0.00	-0.00 to 0.01	0.391	0.01	0.391
PN infusions/ wk	-1.93	-3.94 to 0.07	0.059	0.02	0.059
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.138	0.01	0.138

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was significantly associated with higher EWB scores, with employed participants scoring 14.50 points higher and retired participants scoring 17.89 points higher

than unemployed participants (p = 0.006 and p < 0.001, respectively). PA was also significantly associated with better EWB (p = 0.024) (Table 5.30).

Table 5.31: Univariate linear regression analysis for the social functioning domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.06	-0.03 to 0.14	0.175	0.01	0.175
Living status	3.65	-7.66 to 14.96	0.525	0.00	0.525
Education level				0.05	0.067
Secondary	Reference				
Post-secondary non-tertiary	3.30	-12.67 to 19.26	0.684		
Short cycle tertiary	10.82	-1.72 to 23.37	0.090		
Bachelors or higher	18.65	3.92 to 33.37	**0.013**		
Employment status				0.10	**<0.001**
Unemployed	Reference				
Employed	25.87	11.60 to 40.14	**<0.001**		
Retired	18.67	8.44 to 28.90	**<0.001**		
SB length:				0.04	0.174
< 50cm	Reference				
51-100cm	18.42	-1.42 to 38.26	0.069		
101-150cm	20.83	1.68 to 39.97	**0.033**		
151-200cm	7.39	-17.36 to 31.12	0.557		
200cm	5.37	-10.94 to 21.68	0.517		
Underlying disease				0.03	0.271
IBD	Reference				
Ischaemia	5.45	-7.21 to 18.10	0.397		
Malignancy	4,62	-10.30 to 19.54	0.542		
Motility disorder/ radiation enteritis	4.03	-12.04 to 20.10	0.621		
Other/ unknown	-6.83	-18.29 to 4.62	0.241		
HGS (kg)	0.72	-0.03 to 1.47	0.059	0.05	0.059
SMM (kg)	1.32	-0.17 to 2.81	0.080	0.14	0.080
Phase angle (degree)	14.73	5.19 to 24.27	**0.004**	**0.33**	**0.004**
Oral dietary energy intake (kcal/d)	0.02	0.01 to 0.028	**<0.001**	0.14	**<0.001**
PN infusions/ wk	-2.02	-4.70 to 0.67	**0.030**	0.01	**0.030**
PN energy (kcal/d)	-0.01	-0.01 to 0.00	0.070	0.02	0.070

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was significantly associated with better SF scores, with employed participants scoring 25.87 points higher and retired participants 18.67 points higher than those unemployed (both $p < 0.001$). Higher education (bachelor's degree or above) was also associated with improved SF ($p = 0.013$). SB length of 51–100 cm was linked to better scores compared to <50 cm ($p = 0.033$). PA ($p = 0.004$) and oral dietary energy intake ($p < 0.001$) were both significantly associated with higher SF (Table 5.31).

Table 5.32: Univariate linear regression analysis for the pain domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.04	-0.04 to 0.12	0.335	0.01	0.335
Living status	-3.73	-14.67 to 7.21	0.502	0.00	0.502
Education level				0.03	0.170
Secondary	Reference				
Post-secondary non-tertiary	5.66	-10.06 to 21.39	0.478		
Short cycle tertiary	-1.92	-14.28 to 10.44	0.760		
Bachelors or higher	14.26	-0.24 to 28.77	0.054		
Employment status				0.06	**0.004**
Unemployed	Reference				
Employed	16.99	2.79 to 31.18	**0.019**		
Retired	16.37	6.19 to 26.54	**0.002**		
SB length:				0.05	0.071
< 50cm	Reference				
51-100cm	4.37	-14.62 to 23.36	0.650		
101-150cm	13.75	-4.58 to 32.09	0.141		
151-200cm	-14.05	-37.73 to 9.64	0.244		
200cm	-3.12	-18.74 to 12.49	0.694		
Underlying disease				0.03	0.330
IBD	Reference				
Ischaemia	0.76	-12.34 to 13.87	0.909		
Malignancy	-9.24	-24.69 to 6.21	0.240		
Motility disorder/ radiation enteritis	-2.82	-19.47 to 13.82	0.738		
Other/ unknown	-11.33	-23.19 to 0.54	0.061		
HGS (kg)	0.64	-0.11 to 1.39	0.092	0.04	0.092
SMM (kg)	1.65	0.27 to 3.02	**0.021**	**0.23**	**0.021**
Phase angle (degree)	5.58	-5.48 to 16.64	0.306	0.05	0.306
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0..01	0.344	0.01	0.344
PN infusions/ wk	-2.02	-4.70 to 0.67	0.140	0.01	0.140
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.535	0.00	0.535

Employment status was associated with lower scores in the pain domain, with employed participants scoring 16.99 points higher and retired participants 16.37 points higher than those unemployed (p = 0.019 and p = 0.002, respectively). Higher SMM was also significantly associated with lower scores for pain (p = 0.021) (Table 5.32).

Table 5.33: Univariate linear regression analysis for the general health domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.04	-0.10 to 0.01	0.148	0.01	0.148
Living status	5.25	-2.31 to 12.82	0.172	0.01	0.172
Education level				0.03	0.241
Secondary	Reference				
Post-secondary non-tertiary	-3.37	-14.26 to 7.52	0.542		
Short cycle tertiary	-3.58	-12.14 to 4.98	0.409		
Bachelors or higher	6.88	-3.16 to 16.93	0.178		
Employment status				0.09	**0.001**
Unemployed	Reference				
Employed	16.80	7.04 to 26.56	**0.001**		
Retired	11.71	4.73 to 18.71	**0.001**		
SB length:				0.03	0.423
< 50cm	Reference				
51-100cm	-2.63	-16.05 to 10.79	0.699		
101-150cm	6.28	-6.67 to 19.23	0.340		
151-200cm	-4.50	-21.24 to 12.23	0.596		
200cm	-5.15	-16.18 to 5.88	0.358		
Underlying disease				0.05	0.063
IBD	Reference				
Ischaemia	6.37	-2.32 to 15.06	0.150		
Malignancy	-5.74	-15.99 to 4.51	0.270		
Motility disorder/ radiation enteritis	6.23	-4.81 to 17.27	0.267		
Other/ unknown	-4.46	-12.33 to 3.41	0.265		
HGS (kg)	0.39	-0.07 to 0.84	0.093	0.04	0.093
SMM (kg)	0.92	-0.11 to 1.96	0.077	0.14	0.077
Phase angle (degree)	6.07	-1.55 to 13.68	0.112	0.12	0.112
Oral dietary energy intake (kcal/d)	0.01	-0.00 to 0.01	0.086	0.04	0.086
PN infusions/ wk	-1.78	-3.64 to 0.08	0.061	0.02	0.061
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.365	0.00	0.365

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Employment status was associated with better GH scores, with employed participants scoring 16.80 points higher and retired participants 11.71 points higher than unemployed participants (both p = 0.001). No other predictors were significantly associated with GH in univariate analysis (Table 5.33).

In summary, across all SF-36 domains, employment status consistently emerged as a significant predictor of better QoL with employed and retired participants reporting higher scores than those unemployed. Higher education was associated with better outcomes in select domains, including physical and social functioning. Physical measures such as HGS, SMM and PA showed significant associations with physical functioning, energy/fatigue, and SF. Oral dietary energy intake was positively associated with energy/ fatigue and SF, while PN variables showed no consistent relationship with any domain.

5.8.2.2.2: Assessment of confounding variables

Age and gender were identified as potential confounders, and this was confirmed by a change in the coefficient (B) of greater than 10%, identified with an asterisk.

Table 5.34 confirms age and gender as confounders between several predictors and SF-36 PF scores. The association between higher education and better PF remained significant and slightly strengthened after adjustment. In contrast, the effect of employment was attenuated and became non-significant. HGS remained a strong predictor across models, with slightly increased effect estimates after adjustment.

Table 5.34: Assessment of confounding for the physical functioning domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value
Phase angle (degree)	8.95	0.04 to 17.86	**0.049**
Adj. age	*8.76*	*-0.37 to 17.89*	*0.059*
Adj. gender	*8.38*	*-0.97 to 17.72*	*0.076*
Education:			
Secondary	Reference		
Post-secondary non-tertiary	4.34	-10.51 to 19.18	0.564
Short cycle tertiary	4.00	-7.67 to 15.66	0.499
Bachelors or higher	19.93	6.25 to 33.36	0.005
Adj. age			
Secondary	*Reference*		
Post-secondary non-tertiary	*5.05*	*-9.77 to 19.86*	0.502
Short cycle tertiary	*4.54*	*-7.09 to 16.18*	0.442
Bachelors or higher	*21.50*	*7.71 to 35.30*	**0.002**
Adj. gender			
Secondary	*Reference*		
Post-secondary non-tertiary	*3.86*	*-10.69 to 18.42*	0.601
Short cycle tertiary	*6.32*	*-5.30 to 17.95*	0.284
Bachelors or higher	*21.89*	*8.28 to 35.51*	**0.002**
Employment status			
Unemployed	Reference		
Employed	28.09	14.95 to 41.24	**<0.001**
Retired	8.05	-1.37 to 17.47	0.093
*Adj. age**			
Unemployed	Reference		
Employed	*31.42*	*17.97 to 44.87*	***<0.001***
Retired	*0.20*	*-1201 to 12.40*	*0.975*
*Adj. age, gender**			
Unemployed	Reference		
Employed	*31.17*	*17.95 to 44.39*	***<0.001***
Retired	*-1.05*	*-13.06 to 10.95*	*0.863*
Handgrip strength	1.00	0.43 to 1.56	**0.001**
Adj. age	*1.05*	*0.48 to 1.63*	***0.001***
*Adj. gender**	*1.24*	*0.43 to 1.04*	***0.003***

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment.*

Table 5.35 shows that age and gender were confounders in the relationship between employment, functional measures, and role limitations. For physical role limitations, the effect of employment became non-significant after adjustment, while associations with HGS,

SMM, and PA strengthened. For emotional role limitations, employment remained significant after adjusting for age, but weakened after adjusting for gender.

Table 5.35: Assessment of confounding for the role limitations domains of the SF-36

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Physical	Employment status			
	Unemployed	Reference		
	Employed	17.57	0.16 to 34.98	**0.048**
	Retired	16.25	3.77 to 28.72	**0.011**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*21.60*	*3.75 to 39.45*	***0.018***
	Retired	*6.73*	*-9.47 to 22.92*	*0.413*
	*Adj. age, gender**			
	Unemployed	*Reference*		
	Employed	*21.67*	*3.88 to 39.45*	***0.017***
	Retired	*5.74*	*-10.40 to 21.89*	*0.483*
	Handgrip strength (kg)	1.08	0.25 to 1.90	**0.011**
	*Adj. age**	*1.33*	*0.54 to 2.13*	***0.001***
	*Adj. age, gender**	*2.04*	*0.79 to 3.29*	***0.002***
	Phase angle (degree)	16.24	8.51 to 23.98	**<0.001**
	Adj. age	*15.95*	*8.14 to 23.77*	***<0.001***
	Adj. gender	*15.90*	*7.75 to 24.05*	***0.001***
	SMM (kg)	1.58	0.29 to 2.87	**0.018**
	Adj. age	*1.59*	*0.31 to 2.88*	***0.018***
	*Adj. gender**	*2.90*	*0.78 to 5.01*	***0.010***
Emotional	Employment status			
	Unemployed	Reference		
	Employed	36.61	14.76 to 58.45	**0.001**
	Retired	26.60	10.94 to 42.25	**0.001**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*39.90*	*17.37 to 62.43*	***0.001***
	Retired	*18.82*	*-1.63 to 39.26*	*0.071*
	*Adj. gender**			
	Unemployed	*Reference*		
	Employed	*39.91*	*17.77 to 62.06*	***<0.001***
	Retired	*16.99*	*-3.12 to 37.10*	*0.097*

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ***** *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.36 shows that age and gender acted as confounders in the associations between employment, physical measures, and both energy/fatigue and EWB. For energy/fatigue, the association with employment was attenuated and became non-significant after adjusting for both age and gender, while HGS remained significant across models. For EWB the effect of employment remained significant after adjustment, with only modest changes in coefficients. PA remained significantly associated with EWB after adjusting for age and gender.

Table 5.36: Assessment of confounding for the energy/ fatigue and emotional wellbeing domains of the SF-36

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Energy/ fatigue	Employment status			
	Unemployed	Reference		
	Employed	10.77	0.63 to 20.90	**0.037**
	Retired	8.71	1.45 to 15.98	**0.019**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*12.51*	*2.07 to 22.94*	***0.019***
	Retired	*4.60*	*-4.87 to 14.07*	*0.339*
	*Adj. age, gender**			
	Unemployed	*Reference*		
	Employed	*12.32*	*2.15 to 22.48*	***0.018***
	Retired	*3.50*	*-5.73 to 12.73*	*0.455*
	HGS (kg)	0.61	0.16 to 1.06	**0.009**
	Adj. age	*0.66*	*0.20 to 1.12*	***0.005***
	Adj. gender	*0.67*	*0.03 to 1.32*	***0.041***
	SMM (kg)	0.90	0.33 to 1.76	**0.042**
	Adj. age	*0.91*	*0.11 to 1.71*	***0.028***
	Adj. gender	*0.53*	*-0.96 to 2.03*	*0.464*
Emotional wellbeing	Employment status			
	Unemployed	Reference		
	Employed	14.50	4.29 to 24.72	**0.006**
	Retired	17.89	10.57 to 25.21	**<0.001**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*18.04*	*7.69 to 28.38*	***0.001***
	Retired	*9.56*	*0.17 to 18.94*	***0.046***
	*Adj. age, gender**			
	Unemployed	*Reference*		
	Employed	*19.19*	*9.13 to 29.26*	***<0.001***
	Retired	*9.74*	*0.61 to 18.88*	***0.037***
	Phase angle (degree)	7.50	1.06 to 13.94	**0.024**
	Adj. age	7.82	1.43 to 14.23	**0.019**
	Adj. gender	6.91	0.21 to 13.62	**0.044**

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.37 shows that age and gender confounded the associations between social functioning, education, and employment. The association with higher education remained significant and strengthened after adjustment, particularly for those with a bachelor's degree or higher. The effect of employment attenuated after adjustment and became non-significant for retired participants. Phase angle remained significantly associated with social functioning across all models, indicating a robust independent effect.

Table 5.37: Assessment of confounding for the social functioning domain of the SF-36

Predictor	Coefficient (B)	95% CI	p-value
Education level:			
Secondary	Reference		
Post-secondary non-tertiary	3.30	-12.67 to 19.26	0.684
Short cycle tertiary	10.82	-1.72 to 23.37	0.090
Bachelors or higher	18.65	3.92 to 33.37	**0.013**
*Adj. age**			
Secondary	*Reference*		
Post-secondary non-tertiary	*4.81*	*-10.75 to 20.37*	*0.542*
Short cycle tertiary	*11.99*	*-0.24 to 24.22*	*0.055*
Bachelors or higher	*21.98*	*7.49 to 36.47*	***0.003***
*Adj. age, gender**			
Secondary	*Reference*		
Post-secondary non-tertiary	*4.37*	*-11.10 to 19.84*	*0.577*
Short cycle tertiary	*13.57*	*1.23 to 25.91*	***0.031***
Bachelors or higher	*23.35*	*8.76 to 37.94*	***0.002***
Employment status			
Unemployed	Reference		
Employed	25.87	11.60 to 40.14	**<0.001**
Retired	18.67	8.44 to 28.90	**<0.001**
*Adj. age**			
Unemployed	*Reference*		
Employed	*29.53*	*14.93 to 44.13*	***<0.001***
Retired	*10.03*	*-3.22 to 23.28*	*0.137*
*Adj. age, gender**			
Unemployed	*Reference*		
Employed	*29.36*	*14.74 to 43.98*	***<0.001***
Retired	*9.26*	*-4.01 to 22.54*	*0.170*
Phase angle (degree)	14.73	5.19 to 24.27	**0.004**
Adj. age	*13.91*	*5.16 to 22.66*	***0.003***
Adj. gender	*14.66*	*4.58 to 24.75*	***0.007***

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model. An asterisk indicates a change greater than 10% in the coefficient following adjustment.*

For the pain and general health domains of the SF-36, age and gender confounded the relationship between employment and better scores weakened after adjustment, becoming non-significant for retired participants (Table 5.38). The effect of employment on pain scores was notably attenuated after adjustment, while associations with general health followed a similar pattern. In contrast, SMM remained significantly associated with pain after age adjustment, but the effect was negated after adjusting for gender.

Table 5.38: Assessment of confounding for the pain and general health domains of the SF-36

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Pain	Employment status:			
	Unemployed	Reference		
	Employed	16.99	2.79 to 31.18	**0.019**
	Retired	16.37	6.19 to 26.54	**0.002**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*22.87*	*8.64 to 37.09*	***0.002***
	Retired	*2.49*	*-10.42 to 15.41*	*0.703*
	*Adj. age, gender**			
	Unemployed	*Reference*		
	Employed	*23.29*	*9.06 to 37.53*	***0.001***
	Retired	*2.16*	*-10.76 to 15.09*	*0.741*
	SMM (kg)	1.65	0.27 to 3.02	**0.021**
	Adj. age	*1.65*	*0.24 to 3.06*	***0.024***
	*Adj. gender**	*0.02*	*-2.19 to 2.22*	*0.988*
General health	Employment status:			
	Unemployed	Reference		
	Employed	16.80	7.04 to 26.56	**0.001**
	Retired	11.71	4.73 to 18.71	**0.001**
	*Adj. age**			
	Unemployed	*Reference*		
	Employed	*20.49*	*10.66 to 30.32*	***<0.001***
	Retired	*3.01*	*-5.91 to 11.94*	*0.506*
	*Adj. age, gender**			
	Unemployed	*Reference*		
	Employed	*20.26*	*10.45 to 30.06*	***<0.001***
	Retired	*2.31*	*-6.58 to 11.21*	*0.608*

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model. An asterisk indicates a change greater than 10% in the coefficient following adjustment*

5.8.2.2.3: Multivariable regression analysis for the SF-36

Multivariable linear regression analyses were conducted for each of the SF-36 domains to identify the strongest predictors of HRQoL. Table 5.39 summarises the predictors that were retained in the final models along with their regression coefficients, CI, p-values and the LRT p-values.

Among the models predicting PF, the model including HGS alone demonstrated the best fit, with HGS emerging as a statistically significant predictor (β = 0.99, *p* = 0.001). Adding gender to the model did not significantly improve model performance and gender was non-

significant. A third model incorporating HGS, gender, and phase angle yielded higher overall variance of 19% but none of the predictors reached statistical significance, and the small sample size (n = 22) limited its reliability. Therefore, the model with HGS alone was retained.

For the RLPH domain, the initial model with employment status alone showed that both employed and retired participants reported significantly better scores compared to those unemployed (p = 0.048 and p = 0.011, respectively). Adding age slightly improved model fit (LRT χ^2 = 3.30, p = 0.069), and the effect of employment status remained evident. Including gender further improved the model, with gender becoming a significant predictor (p = 0.041), although only the employed group retained a significant association. A final model incorporating phase angle (based on a smaller subsample n = 23), explained a substantially greater proportion of variance (R^2 = 0.53). In this model, phase angle emerged as the only significant predictor (p = 0.035), while the effects of employment status, age, and gender were no longer significant.

For the energy/fatigue domain, oral dietary energy intake alone was a significant predictor, with higher intake associated with improved scores (p = 0.001). Adding HGS to the model significantly improved model fit (LRT χ^2 = 4.89, p = 0.027), with both oral energy dietary intake (p = 0.001) and HGS (p = 0.032) emerging as significant predictors.

For the SF domain, oral dietary energy intake was a significant predictor, with higher intake associated with better scores (B = 0.018, p <0.001), explaining approximately 15% of the variance. Adding employment status significantly improved model fit (LRT $\chi^2(2)$ = 9.39, p = 0.009), with employed individuals scoring significantly higher than those unemployed (B = 25.21, p = 0.003). A further model including SB length did not improve the model fit (LR $\chi^2(5)$ = 3.91, p = 0.562), and none of the SB length categories were significant predictors. Thus, the model including oral dietary energy intake and employment status was retained as the final model.

For the pain domain, initial univariate analysis showed that employment status was a significant predictor of pain scores (p = 0.004), with employed and retired participants reporting significantly less pain than unemployed individuals. Adding age to the model significantly improved model fit (LRT $\chi^2(1)$ = 10.76, p = 0.001), with increasing age associated with higher pain scores (p = 0.001). The addition of gender did not result in a significant

improvement (LRT $\chi^2(1) = 2.77$, $p = 0.096$), and the gender coefficient was not statistically significant. Therefore, the model including employment status and age was selected as the final model, explaining approximately 12.4% of the variance in pain scores. Among participants with available body composition data, adding SMM to the model increased the explained variance from 18.8% to 27.1%. However, this improvement was not statistically significant (LRT $\chi^2(1) = 2.47$, $p = 0.116$), and SMM was not a significant predictor in the model ($p = 0.170$).

Lastly, for the GH domain, the initial model including only employment status significantly predicted GH scores ($p < 0.001$), explaining approximately 8.7% of the variance. Adding age to the model significantly improved model fit (LRT $\chi^2(1) = 8.92$, $p = 0.003$), with both employment status and age emerging as significant predictors. The addition of gender did not further improve the model fit with gender being non-significant ($p = 0.068$). The final model including employment status and age explained approximately 14% of the variance in GH scores.

Table 5.39: Final multivariable regression models for each domain of the SF-36

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
PF	N/A: Univariate only					
RLPH	Employment:				**0.026**	0.53
	Unemployed	Reference				
	Employed	11.08	-17.26 to 39.43	0.421		
	Retired	-5.44	-24.21 to 13.33	0.549		
	Age (years)	0.03	-1.12 to 1.17	0.958	0.069	
	Gender	-4.10	-24.36 to 16.14	0.674	**0.038**	
	PA (degree)	13.93	1.13 to 26.72	**0.035**	**0.001**	
RLEH	N/A: Univariate only					
Energy/ fatigue	Oral dietary energy intake (kcal/d)	-0.01	-0.01 to 0.00	0.076	**0.008**	0.25
	HGS (kg)	0.62	0.18 to 1.06	**0.007**	**0.027**	
EWB	Employment:				**<0.001**	0.21
	Unemployed	Reference				
	Employed	19.19	9.13 to 29.26	**<0.001**		
	Retired	9.74	0.61 to 18.88	**0.037**		
	Age (years)	0.42	0.12 to 0.71	**0.006**	**0.006**	
	Gender	-8.46	-15.02 to -1.89	**0.012**	**0.011**	
SF	Oral dietary energy intake (kcal/d	0.02	0.01 to 0.03	**<0.001**	**<0.001** **0.009**	0.25
	Employment:	Reference				
	Unemployed	25.21	8.84 to 41.58	**0.003**		
	Employed	10.68	-3.06 to 24.42	0.126		
	Retired					
Pain	Employment:				**0.004**	0.19
	Unemployed	Reference				
	Employed	32.17	-0.29 to 64.63	0.052		
	Retired	5.35	-28.96 to 39.66	0.748		
	Age (years)	0.41	-0.78 to 1.59	0.483	**0.001**	
GH	Employment:				**0.001**	0.14
	Unemployed	Reference				
	Employed	20.49	10.66 to 30.32	**<0.001**		
	Retired	3.0.1	-5.91 to 11.94	0.506		
	Age (years)	0.43	0.15 to 0.72	**0.003**	**0.003**	

Abbreviations: PF, physical functioning; RLPH, role limitations due to physical health; RLEH, role limitations due to emotional health; EWB, emotional wellbeing; SF, social functioning; GH, general health; HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; PA, phase angle

5.8.2.2.4: Model assumption checks for SF-36 regression analyses

Regression diagnostics were conducted for all final multivariable linear regression models for the SF-36. Overall, diagnostics indicated that key assumptions of linear regression were reasonably met. Where assumption violations were identified (e.g., heteroskedasticity), appropriate statistical adjustments (e.g., robust standard errors) were made (Table 5.40).

Table 5.40: Multivariable regression diagnostics for the SF-36

SF-36 domain	Residual normality (p-value)	Heteroskedasticity (Breusch-Pagan; p-value)	Mean VIF	Notes
Role limitations (physical)	0.648	**0.023**	1.69	Heteroskedasticity - robust SE used
Energy/ fatigue	0.392	0.380	1.01	Assumptions met
Emotional wellbeing	0.851	0.858	1.69	Assumptions met
Social functioning	0.132	0.647	1.45	Assumptions met
Pain	0.216	0.167	3.11	Assumptions met
General health	0.035	**0.004**	1.67	Mild non-normality, heteroskedasticity - robust SE used

Abbreviations: VIF, Variance inflation factor. Regression diagnostics confirmed the following assumptions: linearity between predictors and outcome, normally distributed residuals, homoscedasticity (constant variance), no multicollinearity (VIF < 10).

Two models predicting RLPH and GH showed evidence of heteroskedasticity (Breusch–Pagan test: $\chi^2(1) = 5.14$, $p = 0.023$ and $\chi^2(1) = 8.28$, $p = 0.004$, respectively), for which robust standard errors were applied. The residuals for GH also showed mild non-normality (Skewness–Kurtosis test: $p = 0.035$), although this was not considered problematic given the large sample size (n = 165). VIF (mean VIF = 1.67) indicated no multicollinearity.

5.8.3: Home parenteral nutrition QoL questionnaire

5.8.3.1: Descriptive data analysis

There were 189 participants who returned the HPN-QoL questionnaire at baseline and 143 participants who returned it at follow up (Table 5.41). All results relate to median scores (IQR).

Table 5.41: HPN-QoL results at baseline and follow up

	Baseline (n=189)	**Baseline for follow up participants (n = 143)**	**Follow up (n = 143)**	**p-value[1]**
Functional scales (high score = good functioning)				
General health	75 (50-75)	75 (50-75)	75 (50-75)	**0.043**
Ability to holiday	25 (0-37.5)	25 (0-37.5)	25 (0-50)	**0.030**
Physical functioning	41.6 (16.6-50)	41.6 (16.6-50)	41.6 (16.6-50)	0.860
Coping	56 (44-67)	56 (44-67)	56 (44-67)	0.928
Ability to eat and drink	50 (33.3-83.3)	50 (33.3-83.3)	66.6 (50-83.3)	**0.014**
Employment	0 (0-33.3) *16.7 (0-50)	0 (0-33.3)	0 (0-33.3) *16.6 (0-50)	0.524
Sexual function	0 (0-16.6) *0 (0-66.6)	0 (0-16.6)	0 (0-16.6) *0 (0-16.7)	0.167
Emotional functioning	50 (29-75)	50 (25-67)	50 (25-67)	0.776
HPN items				
Nutrition team	100 (67-100)	100 (67-100)	100 (67-100)	0.337
Ambulatory pump	**n=156** 66.6 (33.3-100)	**n=116** 66.6 (33.3-100)	**n=116** 66.6 (66.6-100)	0.091
Symptom scales (high score = worse symptoms)				
Body image	33 (17-50)	33 (17-50)	33 (0-50)	0.917
Weight	33 (0-67)	33 (0-67)	33 (0-67)	0.283
Immobility	47 (33-67)	47 (30-67)	47 (27-67)	0.928
Fatigue	67 (33-100)	67 (33-100)	67 (33-100)	0.755
Sleep pattern	67 (33-100)	67 (33-100)	67 (33-100)	0.621
GI symptoms	22 (11-44)	22 (11-44)	22.5 (11-44)	0.778
Other pain	67 (33-83)	67 (33-83)	50 (33-83)	0.629
Stoma management**	**n=136** 33.3 (16.6-66.6)	**n=106** 33.3 (16.6-66.6)	**n=106** 33.3 (0-50)	**0.001**
Bowel management**	**n=62** 33 (22-44)	**n=53** 44 (22-61.5)	**n=53** 33 (22-55)	0.470
Financial issues	0 (0-33.3)	0 (0-33.3)	0 (0-33.3)	0.886
QoL numerical rating scale	0 (-10-10)	0 (-10-10)	0 (-10-11.5)	0.213

**excluding participants over 67 years old*

***participants may have a stoma and open their bowels and therefore answer both questions.*

[1]*Wilcoxon-Signed-Rank Test.*

There were non-significant changes between baseline and follow up across most domains. In terms of the functional scales, general health scores decreased, despite the median score not changing (p.043). Median scores for ability to holiday remained unchanged but were statistically worse at follow up (p.030). Scores for ability to eat and drink were better at follow up compared with baseline (p.014). For stoma management where high scores are associated with worse symptoms, the median score reduced and reached statistical significance (p.001). Further statistical analysis was carried out excluding participants of retirement age to understand the impact on employment and sexual function scores. The median employment score improved but remained low at 16.7/100 and the median score for sexual function did not change.

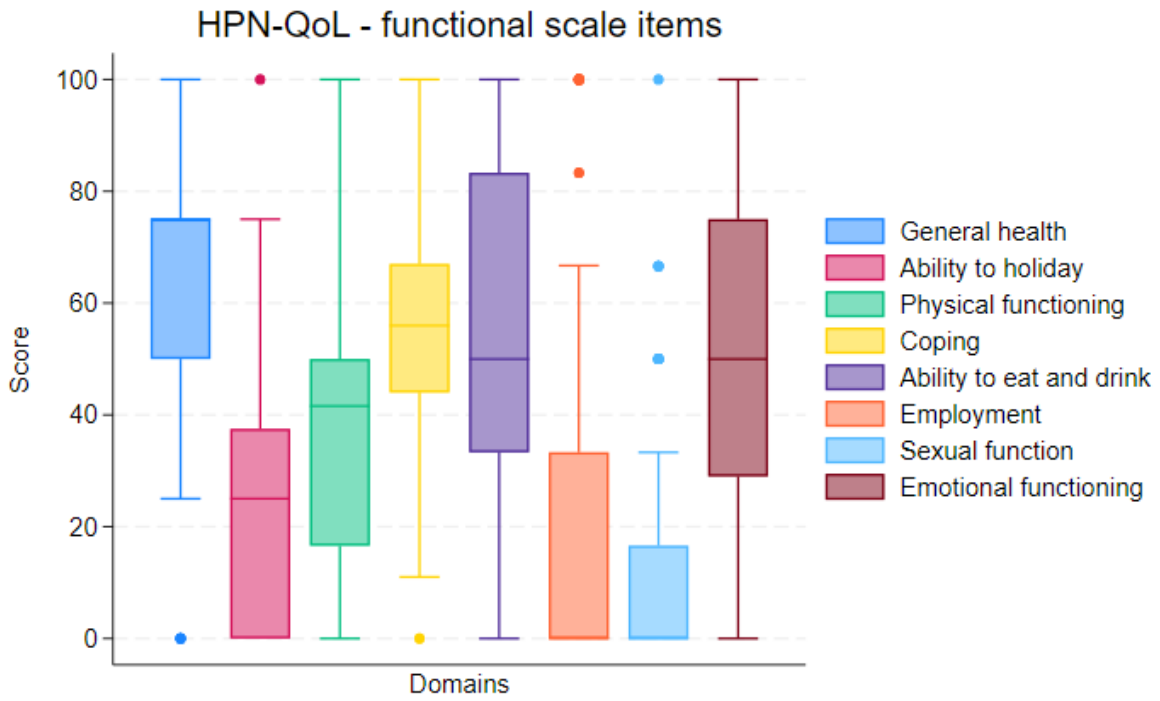


Figure 5.6: Boxplot showing the distribution of scores across the eight functional scale items of the HPN-QoL questionnaire

The spread of the data for each functional scale domain can be seen in Figure 5.6 and for each symptom scale domain in Figure 5.7. Both plots highlight variation in scores, the median, and the presence of outliers for each domain.

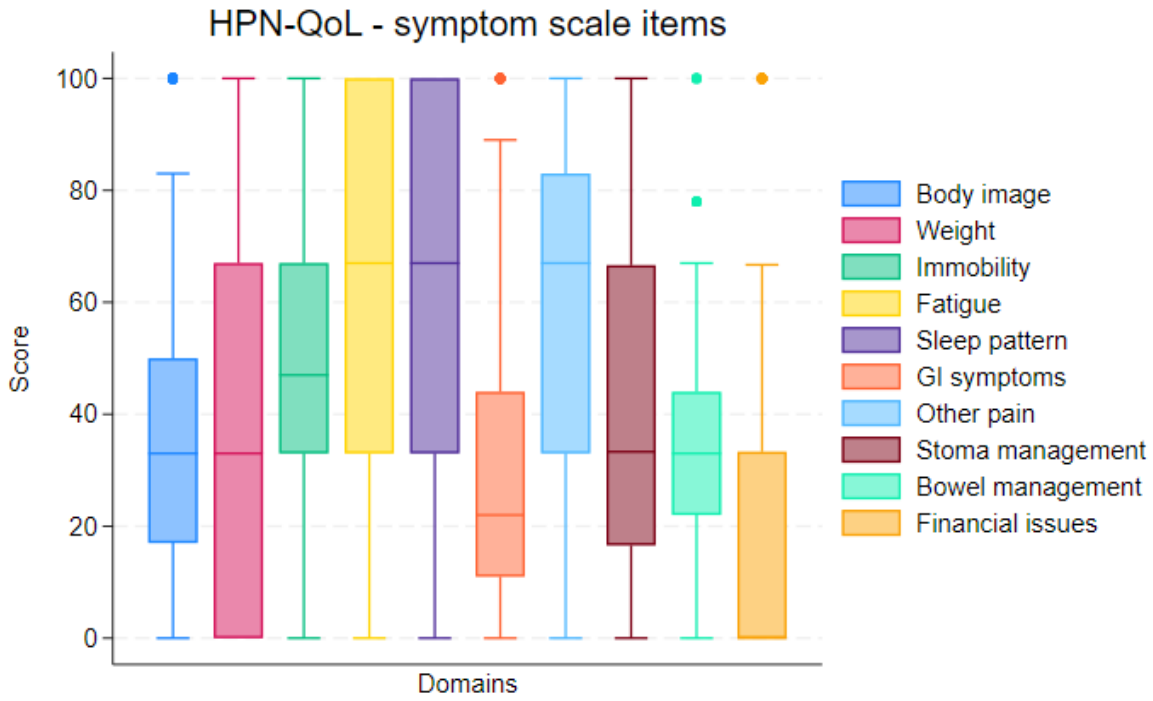


Figure 5.7: Boxplot showing the distribution of scores across the 10 symptom scale items of the HPN-QoL questionnaire

5.8.3.2: Use of inferential statistics to investigate factors associated with HPN-QoL at baseline

5.8.3.2.1: 5.8.1.2.2: Univariate linear regression analysis

The results in Table 5.42 are presented as regression coefficients (B) with 95% CI, p-values, and the proportion of variance explained (R^2). In the GH domains, where higher scores indicate better GH, HGS and oral dietary energy intake were positively associated with GH scores. Participants with IBD reported significantly lower GH compared to those with other underlying conditions. No significant associations were found.

Table 5.42: Univariate regression results for the general health domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.02	-0.09 to 0.04	0.425	0.00	0.425
Living status	-0.59	-9.21 to 8.03	0.893	0.00	0.893
Education level				0.02	0.380
Secondary	Reference				
Post-secondary non-tertiary	-0.63	-12.57 to 11.31	0.918		
Short cycle tertiary	3.99	-5.59 to 13.57	0.412		
Bachelors or higher	9.09	-2.13 to 20.31	0.112		
Employment status				0.03	0.095
Unemployed	Reference				
Employed	9.72	-1.67 to 21.11	0.094		
Retired	-2.08	-10.08 to 5.93	0.609		
SB length:				0.04	0.160
< 50cm	Reference				
51-100cm	-11.39	-26.58 to 3.80	0.141		
101-150cm	2.42	-12.30 to 17.13	0.746		
151-200cm	1.74	-18.13 to 21.60	0.863		
200cm	4.75	-7.95 to 17.44	0.461		
Underlying disease				0.08	**0.007**
IBD	Reference				
Ischaemia	-14.53	-24.17 to -4.88	**0.003**		
Malignancy	-8.18	-19.79 to 3.43	0.166		
Motility disorder/ radiation enteritis	-9.79	-22.77 to 2.80	0.127		
Other/ unknown	2.42	-6.34 to 11.17	0.586		
HGS (kg)	**0.60**	**0.06 to 1.14**	**0.030**	0.07	**0.030**
SMM (kg)	0.54	-0.54 to 1.63	0.303	0.06	0.303
PA (degree)	2.62	4.95 to 10.18	0.476	0.03	0.476
Oral dietary energy intake (kcal/d)	**0.01**	**0.00 to 0.02**	**0.016**	0.07	**0.016**
PN infusions/ wk	-0.95	-3.07 to 1.16	0.376	0.00	0.376
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.349	0.00	0.349

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Table 5.43 shows no significant associations between the ability to holiday and all predictors. Overall, the model explained little variance, indicating limited predictive value from the examined variables.

Table 5.43: Univariate regression results for the ability to holiday domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.03	-0.02 to 0.09	0.250	0.01	0.250
Living status	0.18	-7.24 to 7.59	0.963	0.00	0.963
Education level				0.01	0.715
Secondary	Reference				
Post-secondary non-tertiary	-1.03	-11.60 to 9.54	0.847		
Short cycle tertiary	4.34	-4.14 to 12.82	0.314		
Bachelors or higher	0.71	-9.23 to 10.64	0.888		
Employment status				0.01	0.400
Unemployed	Reference				
Employed	4.64	-5.39 to 14.67	0.362		
Retired	-1.79	-8.85 to 5.25	0.615		
SB length:				0.02	0.559
< 50cm	Reference				
51-100cm	-5.56	-18.93 to 7.82	0.414		
101-150cm	3.96	-9.00 to 16.92	0.548		
151-200cm	-6.25	-23.06 to 10.56	0.464		
200cm	-0.02	-11.26 to 11.21	0.997		
Underlying disease				0.02	0.367
IBD	Reference				
Ischaemia	7.02	-1.65 to 15.69	0.112		
Malignancy	2.89	-7.37 to 13.14	0.579		
Motility disorder/ radiation enteritis	-4.23	-15.53 to 7.07	0.461		
Other/ unknown	3.09	-4.79 to 10.97	0.440		
HGS (kg)	0.07	-0.47 to 0.61	0.792	0.00	0.792
SMM (kg)	0.67	-0.69 to 2.02	0.314	0.06	0.314
PA (degree)	8.27	-0.47 to 17.00	0.062	0.18	0.062
Oral dietary energy intake (kcal/d)	0.01	-0.00 to 0.01	0.159	0.02	0.159
PN infusions/ wk	-0.96	-2.80 to 0.87	0.301	0.01	0.301
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.178	0.01	0.178

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Table 5.44 shows that education, employment, HGS, and SMM were significantly associated with better PF scores on the HPN-QoL. Participants with higher education or employment had higher functioning scores, with the strongest effect observed for those employed. HGS and SMM were also significant predictors.

Table 5.44: Univariate regression results for the HPN-QoL physical functioning domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.01	-0.05 to 0.07	0.650	0.00	0.650
Living status	7.66	-0.44 to 15.75	0.064	0.02	0.064
Education level				0.06	**0.024**
Secondary	Reference				
Post-secondary non-tertiary	10.12	-1.08 to 21.32	0.076		
Short cycle tertiary	10.97	2.06 to 19.88	**0.016**		
Bachelors or higher	13.58	3.06 to 24.10	**0.012**		
Employment status				0.08	**0.001**
Unemployed	Reference				
Employed	19.18	8.65 to 29.72	**0.006**		
Retired	10.35	2.98 to 17.72	**<0.001**		
SB length:				0.04	0.138
< 50cm	Reference				
51-100cm	-2.72	-17.37 to 11.92	0.714		
101-150cm	9.58	-4.61 to 23.76	0.184		
151-200cm	-12.05	-30.45 to 6.35	0.198		
200cm	-3.40	-15.64 to 8.84	0.584		
Underlying disease				0.02	0.522
IBD	Reference				
Ischaemia	2.23	-7.38 to 11.83	0.647		
Malignancy	0.56	-10.81 to 11.92	0.923		
Motility disorder/ radiation enteritis	-4.40	-16.94 to 8.13	0.489		
Other/ unknown	-5.60	-14.27 to 3.07	0.204		
HGS (kg)	0.80	0.25 to 1.34	**0.005**	0.11	**0.005**
SMM (kg)	1.66	0.37 to 2.95	**0.014**	0.28	**0.014**
PA (degree)	7.84	-2.02 to 17.69	0.112	0.13	0.112
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0.01	0.711	0.00	0.711
PN infusions/ wk	0.45	-1.59 to 2.48	0.665	0.00	0.665
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.907	0.00	0.907

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Table 5.45 indicates that none of the demographic or clinical variables were significantly associated with coping scores. Among the physical and nutritional markers, only oral dietary energy intake showed a weak positive association.

Table 5.45: Univariate regression results for the coping domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.01	-0.05 to 0.07	0.771	0.00	0.771
Living status	0.21	-8.17 to 8.60	0.960	0.00	0.960
Education level				0.02	0.426
Secondary	Reference				
Post-secondary non-tertiary	2.33	-9.32 to 13.97	0.693		
Short cycle tertiary	2.35	-6.91 to 11.62	0.617		
Bachelors or higher	9.25	-1.69 to 57.68	0.097		
Employment status				0.02	0.184
Unemployed	Reference				
Employed	9.44	-1.51 to 20.39	0.091		
Retired	5.39	-2.27 to 13.05	0.167		
SB length:				0.03	0.334
< 50cm	Reference				
51-100cm	1.56	-13.36 to 16.47	0.837		
101-150cm	9.43	-5.02 to 23.87	0.200		
151-200cm	-12.00	-30.74 to 6.74	0.208		
200cm	2.65	-9.82 to 15.11	0.676		
Underlying disease				0.00	0.982
IBD	Reference				
Ischaemia	-0.24	-10.03 to 9.55	0.962		
Malignancy	-3.52	-15.10 to 8.06	0.550		
Motility disorder/ radiation enteritis	-0.66	-13.43 to 12.12	0.919		
Other/ unknown	-1.28	-10.12 to 7.55	0.775		
HGS (kg)	0.40	0.13 to 0.94	0.138	0.03	0.138
SMM (kg)	0.72	-0.53 to 1.97	0.244	0.07	0.244
PA (degree)	4.68	-4.07 to 13.43	0.277	0.06	0.277
Oral dietary energy intake (kcal/d)	0.01	0.00 to 0.02	**0.034**	0.01	**0.034**
PN infusions/ wk	-1.81	-3.84 to 0.23	0.081	0.02	0.081
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.307	0.01	0.307

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Table 5.46 presents univariate regression results for the ability to eat and drink domain. While education level showed no significant associations, retired participants had significantly higher scores than unemployed participants. SB length (101–150 cm) and malignancy as underlying disease were also positively and negatively associated with scores, respectively. Among physical and nutritional predictors, HGS, SMM, and oral dietary energy intake were positively associated with higher scores. In contrast, both weekly PN infusions and PN energy were inversely associated with ability to eat and drink.

Table 5.46: Univariate regression results for the ability to eat and drink domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.00	-0.07 to 0.08	0.922	0.00	0.922
Living status	-0.25	-10.53 to 10.02	0.961	0.00	0.961
Education level				0.02	0.461
Secondary	Reference				
Post-secondary non-tertiary	-8.42	-22.89 to 6.05	0.252		
Short cycle tertiary	-2.86	-14.37 to 8.65	0.624		
Bachelors or higher	4.63	-8.96 to 18.22	0.502		
Employment status				0.05	**0.012**
Unemployed	Reference				
Employed	11.97	-1.35 to 25.29	0.078		
Retired	13.99	4.67 to 23.31	**0.003**		
SB length:				0.13	**<0.001**
< 50cm	Reference				
51-100cm	2.57	-10.50 to 23.65	0.448		
101-150cm	20.80	4.26 to 37.34	**0.014**		
151-200cm	10.19	-11.27 to 31.64	0.350		
200cm	-7.29	-21.56 to 6.98	0.315		
Underlying disease				0.06	**0.028**
IBD	Reference				
Ischaemia	3.23	-8.26 to 14.72	0.580		
Malignancy	-17.47	-31.06 to -3.87	**0.012**		
Motility disorder/ radiation enteritis	2.08	-12.91 to 17.08	0.784		
Other/ unknown	-8.70	-19.07 to 1.68	0.100		
HGS (kg)	0.66	0.09 to 1.23	**0.023**	0.07	**0.023**
SMM (kg)	1.31	0.03 to 2.59	**0.045**	0.19	**0.045**
PA (degree)	7.89	-1.29 to 17.06	0.088	0.15	0.088
Oral dietary energy intake (kcal/d)	0.02	0.02 to 0.03	**<0.001**	0.34	**<0.001**
PN infusions/ wk	-5.11	-7.47 to -2.74	**<0.001**	0.09	**<0.001**
PN energy (kcal/d)	-0.1	-0.02 to -0.01	**<0.001**	0.13	**<0.001**

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the employment domain, having a bachelor's degree or higher was associated with a 22.34-point higher score compared to secondary education (Table 5.47). Employment status was the strongest predictor, with employed participants scoring 39.7 points higher than those unemployed. HGS was also positively associated with employment scores. No other significant associations were observed.

Table 5.47: Univariate regression results for the employment domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.00	-0.07 to 0.08	0.922	0.00	0.922
Living status	-0.03	-0.10 to 0.04	0.424	0.00	0.424
Education level				0.08	**0.006**
Secondary	Reference				
Post-secondary non-tertiary	0.75	-13.26 to 14.76	0.916		
Short cycle tertiary	1.15	-10.01 to 12.32	0.838		
Bachelors or higher	22.34	9.17 to 35.50	**0.001**		
Employment status				0.31	**<0.001**
Unemployed	Reference				
Employed	39.70	28.58 to 50.83	**<0.001**		
Retired	-5.60	-13.40 to 2.20	0.158		
SB length:				0.02	0.658
< 50cm	Reference				
51-100cm	-3.14	-20.82 to 14.55	0.727		
101-150cm	-9.37	-26.50 to 7.76	0.282		
151-200cm	-10.18	-32.41 to 12.04	0.367		
200cm	-0.92	-15.74 to 13.89	0.902		
Underlying disease				0.01	0.604
IBD	Reference				
Ischaemia	-7.01	-18.45 to 4.43	0.228		
Malignancy	-8.06	-21.60 to 5.48	0.242		
Motility disorder/ radiation enteritis	-6.55	-21.48 to 8.38	0.388		
Other/ unknown	-6.88	-17.27 to 3.51	0.193		
HGS (kg)	0.98	0.36 to 1.59	**0.002**	**0.13**	**0.002**
SMM (kg)	1.53	-0.26 to 3.32	0.090	0.14	0.090
PA (degree)	8.30	-4.58 to 21.19	0.193	0.09	0.193
Oral dietary energy intake (kcal/d)	-0.00	-0.01 to 0.01	0.852	0.00	0.852
PN infusions/ wk	-0.20	-2.64 to 2.25	0.874	0.00	0.874
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.330	0.01	0.330

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the sexual function domain of the HPN-QoL, employment was significantly associated with better sexual function scores, while retired status showed no significant difference. SB length (<150 cm) was associated with lower scores, particularly among those with 101–150 cm. HGS was positively associated with sexual function (Table 5.48).

Table 5.48: Univariate regression results for the sexual function domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.02	-0.02 to 0.07	0.367	0.00	0.367
Living status	2.13	-4.05 to 8.32	0.497	0.00	0.497
Education level				0.01	0.829
Secondary	Reference				
Post-secondary non-tertiary	2.31	-5.84 to 10.47	0.576		
Short cycle tertiary	2.10	-4.34 to 8.53	0.520		
Bachelors or higher	3.15	-4.38 to 10.69	0.409		
Employment status				0.09	**<0.001**
Unemployed	Reference				
Employed	10.71	3.53 to 17.90	**0.004**		
Retired	-3.04	-8.11 to 2.03	0.238		
SB length:				0.06	**0.047**
< 50cm	Reference				
51-100cm	-13.51	-24.36 to -2.65	**0.015**		
101-150cm	-9.08	-19.59 to 1.43	0.090		
151-200cm	-16.42	-30.61 to -2.22	**0.024**		
200cm	-6.65	-15.79 to 2.48	0.152		
Underlying disease				0.01	0.725
IBD	Reference				
Ischaemia	0.81	-6.39 to 8.01	0.824		
Malignancy	-4.53	-13.04 to 3.99	0.296		
Motility disorder/ radiation enteritis	-3.95	-13.34 to 5.44	0.408		
Other/ unknown	-0.27	-6.91 to 6.38	0.937		
HGS (kg)	0.40	0.09 to 0.71	**0.013**	0.09	**0.013**
SMM (kg)	0.77	-0.06 to 1.60	0.067	0.17	0.067
PA (degree)	4.30	-1.62 to 10.21	0.144	0.11	0.144
Oral dietary energy intake (kcal/d)	0.00	-0.00 to 0.00	0.973	0.00	0.973
PN infusions/ wk	0.47	-1.05 to2.00	0.541	0.00	0.541
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.082	0.02	0.082

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the emotional functioning domain of the HPN-QoL, employment status was significantly associated with better emotional functioning, with employed and retired participants reporting higher scores than those unemployed. Lastly, HGS was also positively associated with emotional functioning scores (Table 5.49).

Table 5.49: Univariate regression results for the emotional functioning domain (high scores = good functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.00	-0.07 to 0.07	0.991	0.00	0.991
Living status	1.59	-8.53 to 11.70	0.757	0.00	0.757
Education level				0.01	0.665
Secondary (constant)	Reference				
Post-secondary non-tertiary	-2.19	-16.25 to 11.86	0.758		
Short cycle tertiary	1.12	-10.06 to 12.30	0.844		
Bachelors or higher	7.22	-5.98 to 20.42	0.282		
Employment status				0.06	**0.004**
Unemployed	Reference				
Employed	17.78	4.93 to 30.64	**0.007**		
Retired	13.66	4.66 to 22.65	**0.003**		
SB length:				0.04	**0.232**
< 50cm	Reference				
51-100cm	-15.99	-33.62 to 1.63	0.075		
101-150cm	-8.01	-25.08 to 9.07	0.356		
151-200cm	-16.56	-38.71 to 5.60	0.142		
200cm	-2.10	-16.83 to 12.63	0.779		
Underlying disease				0.00	0.980
IBD	Reference				
Ischaemia	-0.45	-12.03 to 11.13	0.939		
Malignancy	-2.99	-16.69 to 10.71	0.668		
Motility disorder/ radiation enteritis	-0.03	-15.14 to 15.07	0.997		
Other/ unknown	-2.82	-13.27 to 7.63	0.596		
HGS (kg)	0.98	0.36 to 1.59	**0.012**	0.09	**0.012**
SMM (kg)	1.19	-0.28 to 2.67	0.106	0.13	0.107
PA (degree)	8.50	-1.73 to 18.73	0.098	0.14	0.098
Oral dietary energy intake (kcal/d)	-0.00	-0.01 to 0.01	0.476	0.01	0.476
PN infusions/ wk	-2.13	-4.54 to 0.29	0.084	0.02	0.084
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.479	0.00	0.479

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

HGS and SMM were both predictors of perceived support from the nutrition team and the use of an ambulatory pump (Tables 5.50 & 5.51). A one-unit increase in HGS was linked to a 1.05-point increase in nutrition team support, whereas a one-unit increase in SMM was associated with a 2.15-point increase. Phase angle was also associated with nutrition team support.

Table 5.50: Univariate regression results for the nutrition team support domain

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.01	-0.07 to 0.09	0.820	0.00	0.820
Living status	-0.66	-11.58 to 10.27	0.906	0.00	0.906
Education level				0.02	0.437
Secondary	Reference				
Post-secondary non-tertiary	-0.85	-15.86 to 14.16	0.911		
Short cycle tertiary	-0.85	-12.81 to 11.11	0.889		
Bachelors or higher	-11.21	-25.32 to 2.89	0.118		
Employment status				0.01	0.487
Unemployed	Reference				
Employed	3.09	-11.31 to 17.49	0.673		
Retired	6.13	-3.98 to 16.23	0.233		
SB length:				0.04	0.179
< 50cm	Reference				
51-100cm	-7.17	-25.93 to 11.60	0.452		
101-150cm	10.44	-7.73 to 28.62	0.258		
151-200cm	5.61	-17.97 to 29.19	0.639		
200cm	6.69	-9.00 to 22.37	0.401		
Underlying disease				0.04	0.103
IBD	Reference				
Ischaemia	-8.69	-20.86 to 3.48	0.161		
Malignancy	-17.57	-31.96 to -3.19	**0.017**		
Motility disorder/ radiation enteritis	-0.39	-16.25 to 15.47	0.962		
Other/ unknown	-0.39	-11.38 to 10.60	0.945		
HGS (kg)	1.05	0.47 to 1.62	**0.001**	0.16	**0.001**
SMM (kg)	2.15	0.39 to 3.90	**0.019**	0.26	**0.019**
PA (degree)	12.92	0.17 to 25.66	**0.047**	0.19	**0.047**
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0.01	0.577	0.00	0.578
PN infusions/ wk	-2.96	-5.55 to -0.37	**0.025**	0.03	**0.025**
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.199	0.01	0.199

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

For pump use, a one-unit increase in HGS was associated with a 1.55-point increase in pump use, and a one-unit increase in SMM was linked to a 2.86-point increase.

Table 5.51: Univariate regression results for the ambulatory pump domain

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.07	-0.02 to 0.17	0.146	0.01	0.146
Living status	0.39	-13.37 to 14.16	0.955	0.00	0.955
Education level				0.05	0.116
Secondary	Reference				
Post-secondary non-tertiary	18.94	-0.69 to 38.57	0.058		
Short cycle tertiary	13.28	-1.98 to 28.54	0.087		
Bachelors or higher	-0.16	-17.48 to 17.15	0.985		
Employment status				0.01	0.641
Unemployed	Reference				
Employed	6.53	-10.79 to 23.85	0.457		
Retired	-1.22	-14.12 to 11.69	0.853		
SB length:				0.05	0.149
< 50cm	Reference				
51-100cm	-5.28	-29.71 to 19.15	0.670		
101-150cm	9.58	-14.28 to 33.45	0.429		
151-200cm	-2.20	-33.18 to 28.88	0.889		
200cm	9.08	-11.75 to 29.90	0.391		
Underlying disease				0.02	0.435
IBD	Reference				
Ischaemia	-4.70	-20.23 to 10.83	0.550		
Malignancy	2.89	-14.44 to 20.22	0.742		
Motility disorder/ radiation enteritis	0.04	-19.60 to 19.86	0.997		
Other/ unknown	10.48	-3.72 to 24.67	0.147		
HGS (kg)	1.55	0.68 to 2.41	**0.001**	0.20	**0.001**
SMM (kg)	2.86	0.97 to 4.75	**0.006**	0.43	**0.006**
PA (degree)	14.23	-0.35 to 28.82	0.055	0.24	0.055
Oral dietary energy intake (kcal/d)	0.01	-0.00 to 0.02	0.184	0.03	0.184
PN infusions/ wk	-1.25	-4.51 to 2.01	0.449	0.00	0.449
PN energy (kcal/d)	-0.00	-0.01 to 0.01	0.536	0.00	0.537

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition.

Table 5.52 shows univariate regression results for the body image concerns domain of the HPN-QoL, where higher scores indicate more concerns. All associations were non-significant.

Table 5.52: Univariate regression results for the body image concerns domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.06	-0.13 to -0.01	0.088	0.02	0.088
Living status	4.01	-5.90 to 13.92	0.425	0.00	0.425
Education level				0.03	0.262
Secondary	Reference				
Post-secondary non-tertiary	1.64	-11.73 to 15.01	0.809		
Short cycle tertiary	8.83	-1.82 to 19.48	0.103		
Bachelors or higher	9.88	-2.68 to 22.44	0.122		
Employment status				0.01	0.340
Unemployed	Reference				
Employed	8.93	-3.97 to 21.82	0.174		
Retired	0.48	-8.57 to 9.53	0.916		
SB length:				0.02	0.716
< 50cm	Reference				
51-100cm	-3.98	-21.49 to 13.53	0.654		
101-150cm	-1.40	-18.36 to 15.56	0.871		
151-200cm	4.72	-17.28 to 26.73	0.672		
200cm	-8.31	-22.94 to 6.33	0.264		
Underlying disease				0.01	0.759
IBD	Reference				
Ischaemia	-2.34	-13.69 to 9.00	0.684		
Malignancy	-5.48	-18.88 to 7.93	0.421		
Motility disorder/ radiation enteritis	-8.71	-23.49 to 6.07	0.246		
Other/ unknown	-0.48	-10.72 to 9.77	0.927		
HGS (kg)	-0.05	-0.63 to 0.54	0.875	0.00	0.875
SMM (kg)	0.81	-0.51 to 2.12	0.216	0.08	0.216
PA (degree)	2.85	-6.61 to 12.31	0.536	0.02	0.536
Oral dietary energy intake (kcal/d)	-0.00	-0.01 to 0.00	0.321	0.01	0.321
PN infusions/ wk	-0.31	-2.71 to 2.10	0.802	0.00	0.802
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.787	0.00	0.787

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Similarly, no variables reached statistical significance for the weight concerns domain (Table 5.53.

Table 5.53: Univariate regression results for the weight concerns domains (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.11	-0.11 to 0.08	0.814	0.00	0.814
Living status	4.40	-8.83 to 17.64	0.512	0.00	0.512
Education level				0.00	0.943
Secondary	Reference				
Post-secondary non-tertiary	4.37	-14.10 to 22.84	0.640		
Short cycle tertiary	3.54	-11.15 to 18.23	0.635		
Bachelors or higher	0.12	-17.23 to 17.47	0.989		
Employment status				0.01	0.614
Unemployed	Reference				
Employed	-6.22	-23.96 to 11.52	0.490		
Retired	-5.89	-18.30 to 6.51	0.350		
SB length:				0.03	0.317
< 50cm	Reference				
51-100cm	-1.41	-24.92 to 22.10	0.906		
101-150cm	2.63	-20.15 to 24.40	0.820		
151-200cm	-0.11	-29.65 to 29.43	0.994		
200cm	-15.31	-34.96 to 4.34	0.126		
Underlying disease				0.01	0.681
IBD	Reference				
Ischaemia	-5.32	-20.67 to 10.04	0.495		
Malignancy	-2.95	-21.11 to 15.20	0.749		
Motility disorder/ radiation enteritis	-9.08	-29.09 to 10.93	0.372		
Other/ unknown	3.84	-9.96 to 17.63	0.584		
HGS (kg)	0.07	-0.76 to 0.91	0.860	0.00	0.860
SMM (kg)	0.02	-15.07 to 15.10	0.998	0.00	0.998
PA (degree)	0.75	-1.39 to 2.89	0.472	0.03	0.472
Oral dietary energy intake (kcal/d)	-0.00	-0.02 to 0.01	0.643	0.00	0.643
PN infusions/ wk	3.07	-0.14 to 6.27	0.060	0.02	0.060
PN energy (kcal/d)	0.01	-0.00 to 0.01	0.105	0.01	0.105

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Table 5.54 summarises univariate regression results for the immobility domain (higher scores = worse symptoms). Education and employment emerged as significant predictors. Holding a bachelor's degree or higher was associated with significantly lower immobility scores, and being employed was linked to reduced symptoms. SB length was also associated

with worse immobility. Among physical measures, HGS showed a strong inverse relationship, while associations for SMM and PA did not reach significance.

Table 5.54: Univariate regression results for the immobility domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.02	0.06 to 0.09	0.643	0.00	0.643
Living status	-3.64	-13.82, 6.54	0.481	0.00	0.481
Education level				0.06	**0.040**
Secondary	Reference				
Post-secondary non-tertiary	-5.34	-19.43 to 8.74	0.454		
Short cycle tertiary	-4.58	-15.79 to 6.62	0.420		
Bachelors or higher	-19.49	-32.73 to -6.26	**0.004**		
Employment status				0.05	**0.007**
Unemployed	Reference				
Employed	-21.3	-34.54 to -8.06	**0.002**		
Retired	-8.49	-17.75 to 0.78	0.072		
SB length:				0.05	0.111
< 50cm	Reference				
51-100cm	4.87	-13.04 to 22.79	0.592		
101-150cm	-1.78	-19.13 to 15.57	0.840		
151-200cm	23.33	0.82 to 45.84	**0.042**		
200cm	6.53	-8.44 to 21.50	0.391		
Underlying disease				0.03	0.327
IBD	Reference				
Ischaemia	4.93	-6.83 to 16.69	0.410		
Malignancy	12.55	-1.35 to 26.46	0.077		
Motility disorder/ radiation enteritis	5.94	-9.39 to 21.27	0.446		
Other/ unknown	9.44	-1.12 to 20.02	0.080		
HGS (kg)	-1.18	-1.78 to -0.58	**<0.001**	0.18	**<0.001**
SMM (kg)	-1.14	-2.77 to 0.49	0.161	0.10	0.161
PA (degree)	-9.21	-20.36 to 1.94	0.100	0.14	0.100
Oral dietary energy intake (kcal/d)	-0.0	-0.01 to 0.01	0.398	0.01	0.398
PN infusions/ wk	0.55	-1.97 to 3.06	0.669	0.00	0.669
PN energy (kcal/d)	-0.0	-0.01 to 0.01	0.341	0.01	0.341

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the fatigue domain, participants with short-cycle tertiary education reported significantly greater symptoms, compared to those with secondary education. Additionally, lower HGS was associated with increased fatigue. Other variables were not associated with fatigue scores (Table 5.55).

Table 5.55: Univariate regression results for the fatigue domain (high score = worse symptoms)

Predictor	**Coefficient (B)**	**95% CI**	**p-value**	**R^2**	**LRT p-value**
HPN length (months)	0.03	-0.05 to 0.12	0.424	0.00	0.424
Living status	72.05	62.07 to 82.03	**<0.001**	0.01	**<0.001**
Education level				0.09	**0.003**
Secondary	Reference				
Post-secondary non-tertiary	3.24	-12.32 to 18.79	0.682		
Short cycle tertiary	16.76	4.38 to 29.14	**0.008**		
Bachelors or higher	-11.51	-26.13 to 3.11	0.122		
Employment status				0.01	0.417
Unemployed	Reference				
Employed	-2.32	-17.81 to 13.17	0.768		
Retired	-7.09	-17.90 to 3.72	0.197		
SB length:				0.05	0.089
< 50cm	Reference				
51-100cm	1.71	-18.24 to 21.65	0.866		
101-150cm	-14.20	-33.5- to 5.10	0.148		
151-200cm	20.22	-4.98 to 45.41	0.115		
200cm	5.09	-11.48 to 21.65	0.545		
Underlying disease				0.01	0.763
IBD	Reference				
Ischaemia	-1.51	-14.87 to 11.85	0.824		
Malignancy	9.14	-6.66 to 24.94	0.255		
Motility disorder/ radiation enteritis	-2.17	-19.59 to 15.25	0.806		
Other/ unknown	0.84	-11.11 to 12.79	0.889		
HGS (kg)	-0.97	-1.71 to -0.23	**0.011**	0.09	**0.011**
SMM (kg)	-1.21	-2.79 to 0.36	0.124	0.12	0.124
PA (degree)	-4.87	-16.35 to 6.61	0.386	0.04	0.386
Oral dietary energy intake (kcal/d)	-0.01	0.02 to 0.01	0.286	0.01	0.286
PN infusions/ wk	0.61	-2.22 to 3.44	0.670	0.00	0.670
PN energy (kcal/d)	0.00	-0.01 to 0.01	0.664	0.00	0.664

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the sleep disturbances domain, most predictors showed no significant associations. However, lower HGS was associated with increased sleep disturbances (Table 5.56).

Table 5.56: Univariate regression results for the sleep disturbances domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.00	-0.9 to 0.10	0.937	0.00	0.937
Living status	-0.29	-13.73 to 13.14	0.966	0.00	0.966
Education level				0.05	0.078
Secondary	Reference				
Post-secondary non-tertiary	-7.46	-26.09 to 11.17	0.430		
Short cycle tertiary	9.22	-5.50 to 23.94	0.218		
Bachelors or higher	-13.85	-31.35 to 3.65	0.120		
Employment status				0.02	0.232
Unemployed	Reference				
Employed	-8.60	-26.39 to 9.18	0.341		
Retired	-10.84	-23.42 to 1.74	0.091		
SB length:				0.03	0.310
< 50cm	Reference				
51-100cm	-3.39	-27.28 to 20.50	0.780		
101-150cm	-20.35	-43.48 to 2.77	0.084		
151-200cm	-11.35	-41.53 to 18.84	0.459		
200cm	-18.95	-38.75 to 0.85	0.061		
Underlying disease				0.01	0.855
IBD	Reference				
Ischaemia	-4.77	-20.68 to 11.15	0.555		
Malignancy	-7.73	-26.25 to 10.78	0.411		
Motility disorder/ radiation enteritis	-3.63	-24.38 to 17.11	0.730		
Other/ unknown	-7.55	-21.79 to 6.68	0.296		
HGS (kg)	-0.87	-1.72 to -0.01	**0.048**	0.04	**0.048**
SMM (kg)	-1.06	-2.91 to 0.79	0.246	0.07	0.246
PA (degree)	-0.82	-14.18 to 12.54	0.900	0.00	0.900
Oral dietary energy intake (kcal/d)	-0.00	-0.02 to 0.01	0.632	0.00	0.632
PN infusions/ wk	1.20	-2.12 to 4.53	0.476	0.00	0.476
PN energy (kcal/d)	0.01	-0.00 to 0.01	0.081	0.02	0.081

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the GI symptoms domain (Table 5.57), retired participants reported significantly higher GI symptom burden than those unemployed. SB length >200 cm and an underlying diagnosis

of IBD were also associated with worse symptoms. Other predictors showed no significant associations.

Table 5.57: Univariate regression results for the gastrointestinal symptoms domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.01	-0.08 to 0.07	0.874	0.00	0.874
Living status	4.13	-5.84 to 14.11	0.415	0.00	0.415
Education level				0.01	0.557
Secondary	Reference				
Post-secondary non-tertiary	3.47	-10.15 to 17.09	0.615		
Short cycle tertiary	7.90	-2.92 to 18.72	0.151		
Bachelors or higher	3.61	-9.18 to 16.40	0.577		
Employment status				0.13	**<0.001**
Unemployed	Reference				
Employed	-12.12	-24.50 to 0.27	0.055		
Retired	-21.47	-30.09 to -12.85	**<0.001**		
SB length:				0.10	**0.002**
< 50cm	Reference				
51-100cm	-1.88	-18.83 to 15.07	0.475		
101-150cm	-5.95	-22.35 to 10.46	0.421		
151-200cm	8.76	-12.65 to 30.17	**0.014**		
200cm	17.75	3.67 to 31.83	0.969		
Underlying disease				0.10	**0.001**
IBD	Reference				
Ischaemia	-14.98	-26.12 to -3.84	**0.009**		
Malignancy	13.10	-0.08 to 26.28	**0.051**		
Motility disorder/ radiation enteritis	-9.25	-23.79 to 5.28	0.211		
Other/ unknown	4.44	-5.51 to 14.40	0.380		
HGS (kg)	-0.45	-1.09 to 0.19	0.162	0.03	0.162
SMM (kg)	-1.29	-2.65 to 0.06	0.060	0.17	0.060
PA (degree)	-5.99	-15.95 to 3.97	0.224	0.08	0.224
Oral dietary energy intake (kcal/d)	0.00	-0.00 to 0.01	0.327	0.01	0.327
PN infusions/ wk	2.06	-0.39 to 4.51	0.099	0.01	0.099
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.327	0.01	0.327

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

Table 5.58 presents univariate regression findings for the 'other' pain domain. Employed and retired participants reported significantly lower pain scores than unemployed individuals,

with reductions of 23.16 and 18.43 points, respectively. Higher HGS and SMM were also associated with significantly reduced pain scores. Other sociodemographic, clinical, and PN-related variables showed no significant associations.

Table 5.58: Univariate regression results for the other pain domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	0.04	-0.04 to 0.13	0.300	0.01	0.300
Living status	0.24	-11.27 to 11.74	0.967	0.00	0.967
Education level				0.03	0.213
Secondary	Reference				
Post-secondary non-tertiary	2.23	-14.09 to 18.54	0.788		
Short cycle tertiary	2.94	-10.03 to 15.90	0.655		
Bachelors or higher	-13.44	-28.77 to 1.88	0.085		
Employment status				0.08	**0.001**
Unemployed	Reference				
Employed	-23.16	-38.08 to -8.23	**0.003**		
Retired	-18.43	-28.81 to -8.04	**0.001**		
SB length:				0.05	0.084
< 50cm	Reference				
51-100cm	3.33	-16.74 to 23.41	0.743		
101-150cm	-10.58	-30.00 to 8.85	0.284		
151-200cm	8.91	-16.45 to 34.26	0.489		
200cm	7.72	-8.95 to 24.39	0.362		
Underlying disease				0.05	**0.043**
IBD	Reference				
Ischaemia	-9.12	-22.25 to 4.01	0.172		
Malignancy	1.25	-14.29 to 16.79	0.874		
Motility disorder/ radiation enteritis	-11.83	-28.97 to 5.31	0.175		
Other/ unknown	9.42	-2.31 to 21.16	0.115		
HGS (kg)	-1.13	-1.85 to -0.41	**0.003**	0.12	**0.003**
SMM (kg)	-1.95	-3.71 to -0.20	**0.031**	0.22	**0.031**
PA (degree)	-3.88	-17.62 to 9.85	0.561	0.02	0.561
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0.01	0.745	0.00	0.745
PN infusions/ wk	2.80	-0.01 to 5.61	0.051	0.02	0.051
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.244	0.01	0.244

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the stoma management domain, retired participants had significantly lower scores than the unemployed. SB length (<200cm) and PA were also associated with lower stoma management scores. Other predictors showed non-significant associations (Table 5.59).

Table 5.59: Univariate regression results for the stoma management domain (high score = worse symptoms)

Predictor	**Coefficient (B)**	**95% CI**	**p-value**	**R^2**	**LRT p-value**
HPN length (months)	-0.01	-0.10 to 0.08	0.791	0.00	0.791
Living status	-7.07	-19.55 to 5.41	0.264	0.01	0.264
Education level				0.02	0.560
Secondary	Reference				
Post-secondary non-tertiary	-6.16	-24.74 to 12.41	0.512		
Short cycle tertiary	-2.65	-16.20 to 10.89	0.698		
Bachelors or higher	-11.34	-27.49 to 4.81	0.167		
Employment status				0.06	0.023
Unemployed	Reference				
Employed	-10.43	-27.88 to 7.02	0.239		
Retired	-16.42	-28.08 to -4.76	**0.006**		
SB length:				0.10	**0.019**
< 50cm	Reference				
51-100cm	4.17	-16.13 to 24.47	0.685		
101-150cm	-15.00	-34.54 to 4.55	0.132		
151-200cm	-12.50	-37.74 to 12.74	0.329		
200cm	-23.36	-42.34 to -4.39	**0.016**		
Underlying disease				0.01	0.890
IBD	Reference				
Ischaemia	0.93	-13.42 to 15.28	0.898		
Malignancy	8.28	-12.68 to 29.24	0.436		
Motility disorder/ radiation enteritis	7.03	-10.30 to 24.35	0.424		
Other/ unknown	2.93	-11.09 to 16.94	0.680		
HGS (kg)	-0.53	-1.24 to 0.17	0.134	0.05	0.134
SMM (kg)	-0.78	-2.49 to 0.93	0.344	0.06	0.344
PA (degree)	-13.66	-24.27 to -3.06	**0.015**	0.35	**0.015**
Oral dietary energy intake (kcal/d)	-0.01	-0.02 to 0.00	0.054	0.06	0.054
PN infusions/ wk	1.56	-1.58 to 4.69	0.329	0.01	0.329
PN energy (kcal/d)	0.01	-0.00 to 0.01	0.061	0.03	0.06§

For the bowel management domain (Table 5.60), SB length of 101–150 cm was significantly associated with worse outcomes. Other predictors showed non-significant associations.

Table 5.60: Univariate regression results for the bowel management domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.09	-0.22 to 0.04	0.189	0.03	0.189
Living status	5.18	-13.69 to 24.04	0.584	0.01	0.584
Education level				0.10	0.225
Secondary	Reference				
Post-secondary non-tertiary	13.82	-8.35 to 35.98	0.215		
Short cycle tertiary	16.61	-4.19 to 37.42	0.114		
Bachelors or higher	21.42	-2.73 to 45.57	0.081		
Employment status				0.03	0.437
Unemployed	Reference				
Employed	11.28	-9.84 to 32.40	0.288		
Retired	9.44	-7.49 to 26.37	0.268		
SB length:				0.22	**0.015**
< 50cm	Reference				
51-100cm	22.00	-10.93 to 54.93	0.186		
101-150cm	14.75	-20.82 to 50.32	0.410		
151-200cm	77.75	25.68 to 129.82	**0.004**		
200cm	18.81	-5.81 to 43.43	0.132		
Underlying disease				0.07	0.361
IBD	Reference				
Ischaemia	6.46	-17.95 to 30.87	0.598		
Malignancy	-13.41	-35.40 to 8.58	0.227		
Motility disorder/ radiation enteritis	1.13	-38.59 to 40.84	0.955		
Other/ unknown	-8.62	-28.84 to 11.61	0.397		
HGS (kg)	-0.59	-1.39 to 0.22	0.146	0.08	0.146
SMM (kg)	-2.56	-5.63 to 0.52	0.082	0.57	0.082
PA (degree)	-9.41	-27.13 to 8.30	0.214	0.35	0.214
Oral dietary energy intake (kcal/d)	0.00	-0.12 to 0.02	0.721	0.00	0.721
PN infusions/ wk	-3.79	-7.66 to 0.08	0.055	0.06	0.055
PN energy (kcal/d)	-0.00	-0.1 to 0.01	0.495	0.01	0.495

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For the financial concerns domain retired participants reported significantly fewer financial concerns compared to unemployed individuals (Table 5.61). Underlying disease type also demonstrated some variation, with participants with ischaemia reporting lower financial burden compared to those with IBD. No other variables reached significance.

Table 5.61: Univariate regression results for the financial concerns domain (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.03	-0.10 to 0.05	0.514	0.00	0.514
Living status	-2.20	-13.11 to 8.71	0.691	0.00	0.691
Education level				0.01	0.568
Secondary	Reference				
Post-secondary non-tertiary	-6.26	-20.91 to 8.39	0.400		
Short cycle tertiary	-4.15	-15.89 to 7.58	0.485		
Bachelors or higher	-9.28	-23.05 to 4.48	0.184		
Employment status				0.11	**<0.001**
Unemployed	Reference				
Employed	-10.32	-23.41 to 2.77	0.121		
Retired	-20.82	-30.00 to -11.64	**<0.001**		
SB length:				0.02	0.629
< 50cm	Reference				
51-100cm	-6.48	-25.44 to 12.48	0.501		
101-150cm	-11.17	-29.54 to 7.19	0.231		
151-200cm	-6.47	-31.27 to 18.32	0.607		
200cm	-7.78	-23.62 to 8.07	0.334		
Underlying disease				0.04	0.090
IBD	Reference				
Ischaemia	-15.67	-27.76 to -3.58	**0.011**		
Malignancy	-3.51	-17.82 to 10.80	0.629		
Motility disorder/ radiation enteritis	-13.88	-29.66 to 1.90	0.084		
Other/ unknown	-8.89	-19.87 to 2.08	0.112		
HGS (kg)	0.36	-0.27 to 1.00	0.259	0.02	0.259
SMM (kg)	-0.29	-1.59 to 1.01	0.645	0.01	0.645
PA (degree)	-6.08	14.60 to 2.43	0.151	0.11	0.151
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0.01	0.937	0.00	0.937
PN infusions/ wk	0.54	-2.08 to 3.16	0.685	0.00	0.685
PN energy (kcal/d)	0.00	-0.01 to 0.01	0.897	0.00	0.897

Abbreviations: HPN, home parenteral nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PN, parenteral nutrition.

For overall QoL, retirement was significantly associated with higher QoL scores compared to unemployment. Other variables were not significantly associated with overall QoL scores (Table 5.62).

Table 5.62: Univariate regression results for the overall QoL domain

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.03	-0.02 to 0.09	0.261	0.01	0.261
Living status	-0.70	-8.21 to 6.82	0.855	0.00	0.855
Education level				0.01	0.343
Secondary	Reference				
Post-secondary non-tertiary	2.45	-7.65 to 12.55	0.633		
Short cycle tertiary	-0.51	-8.50 to 7.59	0.901		
Bachelors or higher	8.06	-1.58 to 17.71	0.101		
Employment status				0.05	**0.016**
Unemployed	Reference				
Employed	9.29	-0.43 to 19.01	0.061		
Retired	9.86	2.94 to 16.77	**0.005**		
SB length:				0.02	0.508
< 50cm	Reference				
51-100cm	-10.91	-24.54 to 2.72	0.116		
101-150cm	0.19	-13.01 to 13.40	0.977		
151-200cm	-7.10	-24.61 to 10.41	0.425		
200cm	-3.01	-14.35 to 8.32	0.601		
Underlying disease				0.01	0.610
IBD	Reference				
Ischaemia	3.66	-5.46 to 12.78	0.430		
Malignancy	-5.89	-16.43 to 4.66	0.272		
Motility disorder/ radiation enteritis	0.17	-11.57 to 11.01	0.978		
Other/ unknown	0.07	-8.15 to 8.29	0.986		
HGS (kg)	0.51	-0.02 to 1.03	0.059	0.05	0.059
SMM (kg)	0.66	-0.39 to 1.72	0.206	0.08	0.206
PA (degree)	3.54	-3.69 to 10.77	0.318	0.05	0.318
Oral dietary energy intake (kcal/d)	0.01	-0.00 to 0.01	0.058	0.04	0.058
PN infusions/ wk	-1.43	-3.24 to 0.37	0.120	0.01	0.120
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.177	0.01	0.177

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition, GI, gastrointestinal; QoL, quality of life

5.8.3.2.2: Assessment of confounding variables

Table 5.63 demonstrates that age and gender were confounders in the associations between physical measures, education, and the GH and PF domains of the HPN-QoL. HGS and SMM remained significant predictors of PF after adjustment. The association between education and PF strengthened with gender adjustment, especially for those with a bachelor's degree or higher.

Table 5.63: Assessment of confounding for the general health and physical functioning domains

Outcome	Predictor	Coefficient (B)	95% CI	p-value
General health	HGS (kg)	0.60	0.06 to 1.14	**0.030**
	Adj. age	0.55	-0.01 to 1.10	0.053
	*Adj. gender**	0.97	0.06 to 1.87	**0.036**
Physical functioning	HGS (kg)	0.80	0.25 to 1.34	**0.005**
	Adj. age	0.79	0.23 to 1.35	**0.007**
	Adj. gender	0.84	0.03 to 1.64	**0.041**
	SMM (kg)	1.66	0.37 to 2.95	**0.014**
	Adj. age	1.67	0.35 to 2.99	**0.016**
	Adj. gender	1.62	-1.15 to 4.39	0.236
	Education level			
	Secondary	Reference		
	Post-secondary non-tertiary	10.12	-1.08 to 21.31	0.076
	Short cycle tertiary	10.97	2.06 to 19.88	**0.016**
	Bachelors or higher	13.58	3.06 to 24.10	**0.012**
	Adj. age			
	Secondary	Reference		
	Post-secondary non-tertiary	10.47	-0.74 to 21.69	0.067
	Short cycle tertiary	11.14	2.23 to 20.05	**0.015**
	Bachelors or higher	14.46	3.82 to 25.10	**0.008**
	*Adj. gender**			
	Secondary	Reference		
	Post-secondary non-tertiary	9.63	-1.34 to 20.59	0.085
	Short cycle tertiary	12.62	3.81 to 21.43	**0.005**
	Bachelors or higher	14.36	3.92 to 24.81	**0.007**

Abbreviations: HGS, handgrip strength; SMM, skeletal muscle mass. ***Adj. age:*** *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.64 indicates that age and gender were confounders in the associations between HGS, employment status, and the employment and sexual function domains. HGS remained significantly associated with both outcomes after age adjustment, though significance was lost after adjusting for both age and gender in the employment model. The association between employment and sexual function weakened slightly after adjustment, but remained significant for employed participants after adjusting for age or gender individually.

Table 5.64: Assessment of confounding for the employment and sexual function domains

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Employment	HGS (kg)	0.98	0.36 to 1.59	**0.002**
	*Adj. age**	0.73	0.18 to 1.27	**0.010**
	Adj. age, gender	0.76	-0.12 to 1.65	0.091
Sexual function	HGS (kg)	0.40	0.09 to 0.71	**0.013**
	*Adj. age**	0.29	0.00 to 0.58	**0.049**
	*Adj. age, gender**	0.38	-0.10 to 0.85	0.118
	Employment status			
	Unemployed	Reference		
	Employed	10.71	3.53 to 17.90	**0.004**
	Retired	-3.04	-8.11 to 2.03	0.238
	*Adj. age**			
	Unemployed	Reference		
	Employed	7.69	0.64 to 14.74	**0.033**
	Retired	5.55	-0.96 to 12.06	0.094
	*Adj. gender**			
	Unemployed	Reference		
	Employed	7.07	0.20 to 13.95	**0.044**
	Retired	4.07	-2.31 to 10.46	0.209

Abbreviations: HGS, handgrip strength. ***Adj. age:*** *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Both age and gender acted as confounders in the associations between HGS, education, employment, and immobility symptoms. HGS remained significantly and inversely associated with immobility after adjustment, with only minor changes in the coefficient (Table 5.65). The negative association between higher education (particularly bachelor's or higher) and immobility symptoms was strengthened after adjusting for age and gender. Similarly, the significant association between employment and reduced immobility was attenuated and became non-significant after adjustment.

Table 5.65: Assessment of confounding for the immobility symptom scale domain

Predictor	Coefficient (B)	95% CI	p-value
HGS (kg)	-1.18	-1.78 to -0.58	**<0.001**
Adj. age	-1.26	-1.87 to -0.66	**<0.001**
Adj. gender	-1.21	-2.09 to -0.33	**0.008**
Education level			
Secondary	Reference		
Post-secondary non-tertiary	-5.34	-19.43 to 8.73	0.454
Short cycle tertiary	-4.58	-15.79 to 6.62	0.420
Bachelors or higher	-19.49	-32.73 to -6.26	**0.004**
Adj. age			
Secondary	Reference		
Post-secondary non-tertiary	-5.93	-19.98 to 8.13	0.406
Short cycle tertiary	-4.85	-16.02 to 6.32	0.392
Bachelors or higher	-20.95	-34.29 to -7.61	**0.002**
Adj. gender			
Secondary	Reference		
Post-secondary non-tertiary	-4.86	-18.72 to 9.00	0.489
Short cycle tertiary	-6.20	-17.34 to 4.93	0.272
Bachelors or higher	-21.00	-34.21 to -7.79	**0.002**
Employment status			
Unemployed	Reference		
Employed	-21.30	-34.54 to -8.06	**0.002**
Retired	-8.49	-17.75 to 0.78	0.072
Adj. age			
Unemployed	Reference		
Employed	-23.07	-36.64 to -9.51	**0.001**
Retired	-3.63	-16.01 to 8.76	0.564
Adj. gender			
Unemployed	Reference		
Employed	-20.08	-33.19 to -6.98	**0.003**
Retired	-6.53	-15.80 to 2.73	0.166

Abbreviations: HGS: Handgrip strength. ***Adj. age:*** *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.66 indicates that age and gender acted as confounders in several associations within the symptom scale domains. HGS remained significantly associated with lower fatigue and sleep disturbance scores after adjustment, with effect sizes slightly increasing when both age and gender were controlled. Employment was consistently associated with reduced stoma management and financial concerns, and these associations remained statistically significant

after adjusting for age and gender. Similarly, PA remained significantly associated with fewer stoma management problems, with a stronger effect after gender adjustment

Table 5.66: Assessment of confounding for symptom scale domains

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Fatigue	HGS (kg)	-0.97	-1.71 to -0.23	**0.011**
	*Adj. age**	-1.12	-1.86 to -0.37	**0.004**
	*Adj. age, gender**	-1.58	-2.77 to -0.39	**0.010**
Sleep pattern	HGS (kg)	-0.87	-1.72 to -0.01	**0.048**
	Adj. age	-0.89	-1.77 to -0.01	**0.049**
	Adj. gender	-0.75	-2.18 to 0.67	0.295
Stoma management	Employment status			
	Unemployed	Reference		
	Employed	-10.43	-27.88 to 7.02	0.239
	Retired	-16.42	-28.08 to -4.76	**0.006**
	*Adj. age**			
	Unemployed	Reference		
	Employed	-10.16	-27.70 to 7.37	0.254
	Retired	-19.28	-35.57 to -2.98	**0.021**
	*Adj. age, gender**			
	Unemployed	Reference		
	Employed	-10.18	-27.80 to 7.44	0.255
	Retired	-19.36	-36.08 to -2.63	**0.024**
	Phase angle (degree(	-13.66	-24.27 to -3.06	**0.015**
	Adj. age	-13.64	-24.70 to -2.59	**0.019**
	*Adj. gender**	-15.50	-27.39 to -3.60	**0.015**
Financial	Employment status			
	Unemployed	Reference		
	Employed	-10.32	-23.41 to 2.77	0.121
	Retired	-20.82	-30.00 to 11.64	**<0.001**
	*Adj. age**			
	Unemployed	Reference		
	Employed	-13.64	-26.91 to -0.37	**0.044**
	Retired	-11.76	-23.88 to 0.35	0.057
	*Adj. age, gender**			
	Unemployed	Reference		
	Employed	-13.86	-27.24 to -0.48	**0.042**
	Retired	-12.36	-24.67 to -0.06	**0.049**

Abbreviations: HGS; handgrip strength. Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

Table 5.67 shows that the relationship between employment and overall QoL remains significant after adjusting for age and persisted after adjusting for both age and gender.

Table 5.67: Assessment of confounding for the overall QoL domain

Outcome	Predictor	Coefficient (B)	95% CI	p-value
Overall QoL	Employment status			
	Unemployed	Reference		
	Employed	9.29	-0.43 to 19.01	0.061
	Retired	9.86	2.94 to 16.77	**0.005**
	*Adj. age**			
	Unemployed	Reference		
	Employed	10.34	0.25 to 20.42	**0.045**
	Retired	7.49	-1.65 to 16.63	0.108
	*Adj. age, gender**			
	Unemployed	Reference		
	Employed	10.44	0.34 to 20.54	**0.043**
	Retired	6.98	-2.23 to 16.19	0.137

Adj. age: *Results are adjusted for age as a covariate in the regression model.* ***Adj. gender:*** *Results are adjusted for gender as a covariate in the regression model.* ***Adj. age, gender:*** *Results are adjusted for age and gender as a covariate in the regression model.* ******* *An asterisk indicates a change greater than 10% in the coefficient following adjustment*

5.8.3.3.4 Multivariable regression analysis

5.8.3.3.4.1: HPN-QoL: functional scale domains

Table 5.68 presents the final multivariable regression models for each functional scale domain of the HPN-QoL. In the initial model, HGS significantly predicted GH (β = 0.60, p = 0.030), explaining approximately 6.6% of the variance. Adding gender improved the overall model fit (R^2 = 0.096), and HGS remained a significant predictor (β = 1.03, *p* = 0.011). However, the gender coefficient itself was not statistically significant (p = 0.143), and the LRT did not indicate a significant improvement in model fit ($\chi^2(1) = 2.25$, p = 0.133). Therefore, the univariate model with HGS alone was retained.

For the PF domain, employment status was a significant predictor, with both employed (p = 0.001) and retired (p = 0.008) individuals reporting better scores than those unemployed. Adding gender significantly improved model fit (LRT χ^2 = 6.45, p = 0.011), with male gender associated with lower scores (p = 0.012). A further model including education level showed a marginal improvement in model fit (LRT $\chi^2(3) = 7.77$, p = 0.051), with higher education levels

(short-cycle tertiary and bachelor's or higher) significantly associated with improved PF ($p = 0.019$ and $p = 0.049$, respectively). Thus, the final model included employment status, gender, and education, explaining approximately 15.7% of the variance in PF.

For the ability to eat and drink, as expected, oral dietary energy intake was a significant independent predictor, with higher intake associated with improved scores ($B = 0.025$, $p < 0.001$), explaining approximately 34% of the variance. Adding HGS to the model significantly improved model fit (LRT $\chi^2 = 4.19$, $p = 0.041$), and HGS also emerged as a statistically significant predictor. However, the addition of SMM did not enhance the model and resulted in loss of significance for both HGS and SMM, possibly due to reduced sample size ($n = 18$). The simpler model including oral dietary energy intake and HGS was therefore retained and explained 39% of the variance in ability to eat and drink scores.

Table 5.68: Multivariable regression results for the HPN-QoL functional scale domains (high score = better functioning)

Outcome	Predictor	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
General health	N/A: Univariate only					
Ability to holiday	N/A: Univariate only					
Physical functioning	Employment: Unemployed	Reference			**0.001**	0.16
	Employed	14.44	3.30 to 25.58	**0.011**		
	Retired	8.14	0.15 to 16.14	**0.046**		
	Gender	-8.98	-16.54 to -1.42	**0.020**	**0.011**	
	Education: Secondary	Reference			0.051	
	Post secondary non-tertiary	8.91	-1.86 to 19.69	0.104		
	Short cycle tertiary	10.57	1.80 to 19.34	**0.019**		
	Bachelors or higher	10.69	0.06 to 21.32	**0.049**		
Ability to E&D	Diet intake (kcal/d)	0.02	0.01 to 0.03	**<0.001**	**<0.001**	0.39
	HGS (kg)	0.46	0.00 to 0.91	**0.048**	**0.040**	
Employment	HGS (kg)	0.72	0.18 to 1.27	**0.010**	**0.002**	0.35
	Age (years)	-0.86	-1.22 to -0.50	**<0.001**	**<0.001**	
Sexual function	Employment: Unemployed	Reference			**<0.001**	0.23
	Employed	7.07	0.20 to 13.95	**0.044**		
	Retired	4.07	-2.31 to 10.46	0.209		
	Age (years)	-0.41	-0.61 to -0.20	**<0.001**	**<0.001**	
	Gender	-7.72	-12.23 to -3.21	**0.001**	**<0.001**	
Emotional functioning	HGS (kg)	0.95	0.34 to 1.56	**0.003**	**0.012**	0.16
	Age (years)	0.49	0.07 to 0.90	**0.021**	**0.018**	

Abbreviations: HGS, handgrip strength; NK, not known; SB, small bowel

For the employment domain of the HPN-QoL, HGS alone was a significant predictor, with higher HGS associated with better scores ($\beta = 0.98$, $p = 0.002$), explaining approximately 13% of the variance. Introducing age into the model substantially improved its explanatory power, increasing the variance explained to 35% (Table 5.68). In this model, both HGS and age were significant predictors. The LRT confirmed that the model including age was significantly better than the HGS only model ($\chi^2 = 20.21$, $p < 0.001$). Although education level was initially explored as a potential predictor, it was not retained in the final model, as it did

not significantly improve model fit once age and HGS were included and all levels of education were non-significant.

For the sexual function domain, the initial model including SB length categories alone was statistically significant ($p = 0.047$), with several SB length categories showing reduced scores relative to the reference group. Adding employment status improved model fit, with employed participants reporting significantly higher sexual function scores compared to the unemployed ($\beta = 10.87$, $p = 0.003$), while SB length associations were attenuated. Introducing age further improved model performance ($\chi^2 = 12.00$, $p = 0.001$), and in this model, both employment ($p = 0.031$) and age ($\beta = -0.39$, $p = 0.001$) were significant predictors, indicating better scores among employed and younger participants. The final model, which also included gender, showed the highest explanatory power ($R^2 = 0.23$). In this model, younger age, male gender, and employment remained significant predictors of better sexual function, while SB length categories no longer showed significant effects. Therefore, the model including age, gender, and employment was retained as the final model (Table 5.68).

For emotional functioning, HGS was a significant predictor in the initial model ($\beta = 0.80$, $p = 0.012$), explaining approximately 9% of the variance in scores. Adding age significantly improved model fit (LRT $\chi^2(1) = 5.63$, $p = 0.018$), and both HGS and age were significant predictors, with better emotional functioning associated with higher HGS and older age. Although a third model including employment status explained more variance ($R^2 = 0.22$), the improvement in fit was not statistically significant (LRT $\chi^2(2) = 4.55$, $p = 0.103$), and the coefficients for employment were not significant. Therefore, the model including HGS and age was retained as the most appropriate model for predicting emotional functioning.

5.8.3.3.4.2: HPN-QoL: HPN item domains

For the nutrition team support domain, higher HGS was significantly associated with better scores ($\beta = 1.05$, $p = 0.001$), explaining approximately 16% of the variance. Adding the number of weekly infusions significantly improved model fit (LRT $\chi^2(1) = 6.19$, $p = 0.013$), increasing the explained variance to approximately 23%. In this model, both HGS and infusions per week were significant predictors, with more frequent infusions associated with

lower nutrition support scores. Thus, the final model including both HGS and weekly PN infusions was retained (Table 5.69).

Table 5.69: Multivariable regression results for the HPN-QoL HPN item domains (high score = better perceived support)

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
Nutrition team support	HGS (kg) Infusions/wk	0.95 -4.83	0.39 to 1.51 -8.71 to -0.96	**0.001** **0.015**	**0.013**	0.23
Ambulatory pump use	N/A: univariate analysis only					

Abbreviations: HGS, handgrip strength; NK, not known

5.8.3.3.4.3: HPN-QoL: symptom scale domains

Higher HGS was significantly associated with lower immobility scores, explaining 18% of the variance. Neither employment nor education were independently associated with immobility, and adding them did not significantly improve model fit (LR $\chi^2(2) = 3.45$, $p = 0.178$). Therefore, the final model retained HGS alone and can be seen in the univariate regression table (Table 5.54).

In relation to the fatigue domain, higher HGS was significantly associated with lower scores, accounting for approximately 9% of the variance. Adding age to the model significantly improved model fit (LRT $\chi^2(1) = 3.88$, $p = 0.049$), increasing the explained variance to 13%. In this adjusted model, HGS remained a significant predictor ($p = 0.004$), while age was non-significant ($p = 0.055$). Adding gender did not significantly improve the model ($p = 0.31$), therefore HGS and age were retained only (Table 5.70).

Table 5.70: Multivariable regression results for the HPN-QoL symptom scale domains (high score = worse symptoms

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
Body image	N/A: Univariate only (Table 5.52)					
Weight	N/A: Univariate only (Table 5.53)					
Immobility	N/A: Univariate only (Table 5.54)					
Fatigue	HGS	-1.12	-1.86 to -0.37	0.004	0.05	0.13
	Age	-0.49	-0.99 to 0.01	0.055		
Sleeping pattern	N/A: Univariate only (Table 5.56)					
GI symptoms	Employment:				**0.011**	0.20
	Unemployed	Reference				
	Employed	-11.26	-23.07 to 0.55	0.062		
	Retired	-20.27	-29.63 to -10.90	**<0.001**		
	SB length:					
	< 50cm	Reference				
	51-100cm	-0.51	-16.86 to 15.85	0.951		
	101-150cm	-0.94	-17.34 to 15.45	0.910		
	151-200cm	16.68	-4.79 to 38.15	0.127		
	>200cm	17.10	3.12 to 31.08	**0.017**		
Other pain	Employment:				**0.002**	0.21
	Unemployed	Reference				
	Employed	0.90	-21.24 to 23.22	0.929		
	Retired	-20.56	-36.83 to -4.30	**0.014**		
	HGS (kg)	-1.20	-1.95 to -0.45	**0.002**		
Stoma management	PA (degree)	-20.89	-30.55 to -11.23	**0.001**	**0.006**	0.74
	SB length:					
	< 50cm	Reference				
	51-100cm	20.88	-13.09 to 54.86	0.201		
	151-200cm	-12.48	-46.23 to 21.28	0.429		
	>200cm	-47.99	-84.00 to -11.97	**0.014**		
Bowel management	N/A: Univariate only (Table 5.60)					
Financial concerns	N/A: Univariate only (Table 5.61)					

Abbreviations: HGS, handgrip strength; GI, gastrointestinal; SB, small bowel; PA, phase angle

In the initial model, employment status significantly predicted GI symptom scores, with retired participants reporting significantly fewer symptoms compared to those unemployed (B = –21.47, p < 0.001). Adding SB length significantly improved model fit (LRT $\chi^2(5) = 14.82$, p = 0.011), increasing the explained variance to 20%. In this model, the retired group remained a strong predictor, while SB length >200cm was also significantly associated with higher GI symptom scores. Other SB length categories were not statistically significant.

For other pain, employment status significantly predicted scores in the univariate analysis (R^2 = 0.08, p<0.001*),* with both employed (*B* = –23.16, p = 0.003) and retired (B = –18.43, *p* = 0.001) participants reporting significantly lower pain compared to those unemployed. In the second model (n = 69), HGS emerged as a strong independent predictor (B = –1.20, p = 0.002). The effect of retirement remained significant (B = –20.56, p = 0.014), but the effect of employment was no longer significant (p = 0.929). The model explained a substantially larger proportion of variance (R^2 = 0.21). When SMM was added in a smaller subsample (n = 19), neither employment nor SMM remained significant, and HGS showed only a trend (β = –1.68, p = 0.064) despite increased variance explained (R^2 = 0.40). The simpler model including employment and HGS was retained.

An initial model including only employment status did not significantly predict stoma-related outcomes (p = 0.359). A subsequent model including employment status and phase angle showed improved fit (R^2 = 0.37), but employment status remained non-significant. A final model including phase angle and SB length explained a substantially greater proportion of variance (R^2 = 0.74), with phase angle emerging as a significant predictor. The addition of SB length significantly improved model fit (LRT $\chi^2(4)$ = 14.36, p = 0.006). Given the non-significance of employment status across all models it was excluded from the final model**.**

5.8.3.3.5: Effect modification by gender on the association between muscle strength and QoL outcomes

Where gender was identified as a potential confounder, interaction tests were performed to look at effect modification. In the domains of GH, employment, sexual function, stoma management, financial concerns and overall QoL, there were no significant differences between males and females. In contrast, significant differences were observed in the domains of immobility, fatigue and sleep disturbances (Figures 5.8 and 5.9).

Among females, HGS was strongly and significantly associated with reduced immobility (B = –2.84, 95% CI: –4.05 to –1.62, p < 0.001, R^2 = 0.36) and fewer sleep disturbances (B = –2.22, 95% CI: –4.15 to –0.30, p = 0.025, R^2 = 0.11). In contrast, these associations were not observed in males, where HGS was not significantly related to immobility (B = –0.05, 95% CI: –1.25 to 1.15, p = 0.930) or sleep disturbances (B = 0.40, 95% CI: –1.20 to 2.01, p = 0.610) (Figure 5.8).

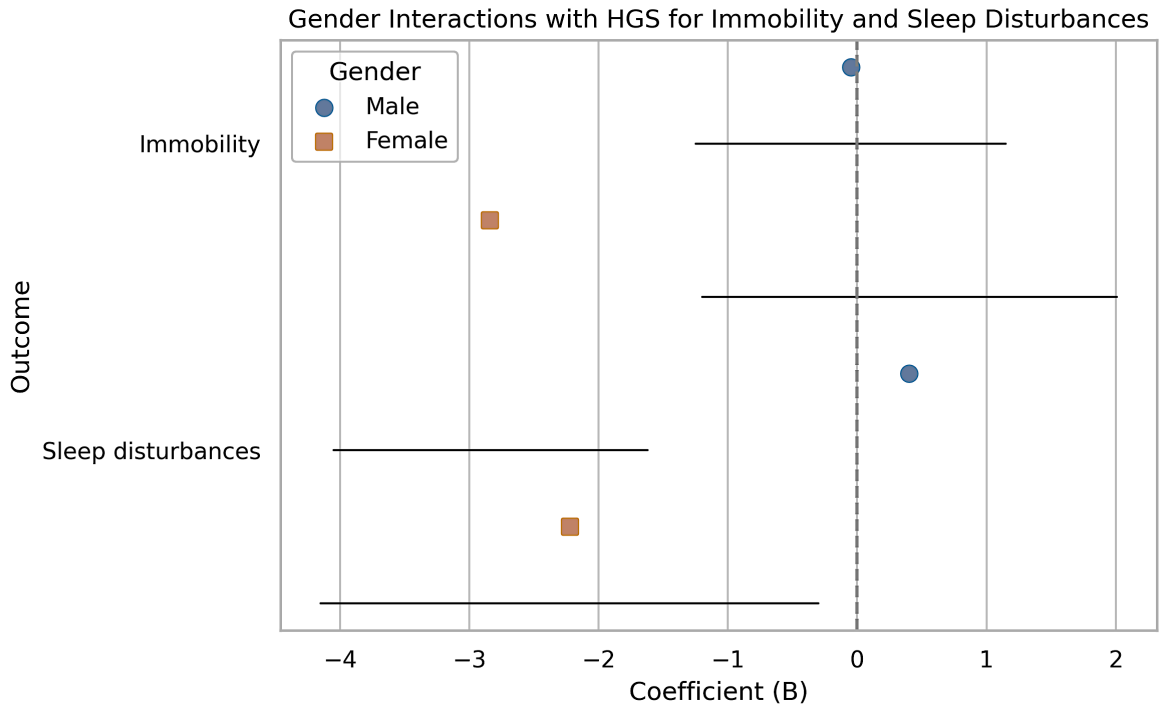


Figure 5.8: Association between handgrip strength (HGS) and immobility and sleep disturbances, stratified by gender. Error bars represent 95% confidence intervals.

For the fatigue domain, there were multiple predictors (HGS and age). Therefore, separate regression models were conducted for males and females using HGS and age as predictors of fatigue scores (Figure 5.9). Among males, the model was not statistically significant ($F(2, 27) = 1.10$, $p = 0.347$), with HGS and age failing to predict fatigue, and accounting for only 8% of the variance. In contrast, the model for females was statistically significant ($F(2, 40) = 7.19$, $p = 0.002$), explaining 26% of the variance. Higher HGS was significantly associated with lower fatigue whilst age was non-significant.

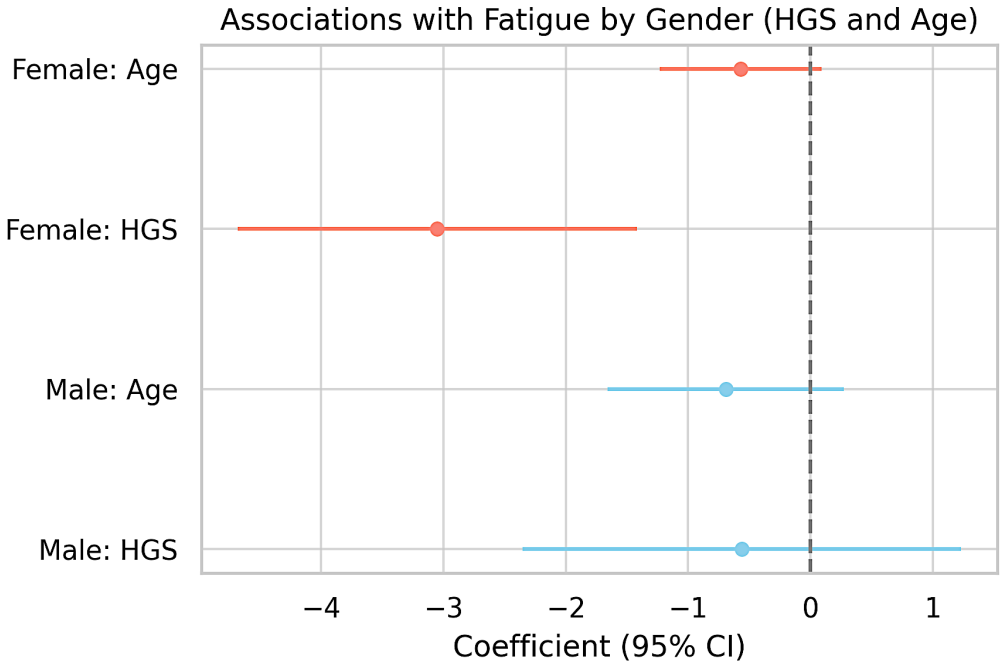


Figure 5.9: Coefficient plot showing the association between fatigue and handgrip strength (HGS) and age, stratified by gender. Error bars represent 95% confidence intervals.

5.8.3.3.6: Model assumption checks for HPN-QoL regression analyses

Regression diagnostics were performed for each multivariable regression model for the HPN-QoL. The assumption of normality of residuals was generally met across most models, except for employment (p = 0.008), sexual function (p = <0.001), nutrition team support (p = 0.006), and GI symptoms (p = 0.008), where evidence of skewness was present. Heteroskedasticity, was also detected in the same domains (employment, sexual function, nutrition team support, and GI symptoms; all $p \leq 0.001$). Robust SE were applied in these models to address the violation of homoscedasticity. All models demonstrated low multicollinearity, with mean VIF values below 2.1. The assumptions for the remaining models were met (Table 5.71).

Table 5.71: Multivariable regression diagnostics for the HPN-QoL functional scale domains

Domain	Residual normality (p-value)	Heteroskedasticity (Breusch-Pagan; p-value)	Mean VIF	Notes
General health	0.392	0.920	1.00	Assumptions met
Physical functioning	0.070	0.718	1.24	Slight skewness
Ability to E&D	0.430	0.911	1.01	Assumptions met
Employment	0.008	0.001	1.16	Skewness and heteroskedasticity – robust SE used
Sexual function	0.000	<0.001	2.06	Skewness and heteroskedasticity – robust SE used
Emotional functioning	0.372	0.363	1.04	Assumptions met
Nutrition team support	0.006	0.000	1.02	Skewness and heteroskedasticity
Fatigue	0.050	0.606	1.04	Assumptions met
GI symptoms	0.008	0.001	1.95	Skewness and heteroskedasticity
Other pain	0.683	0.302	1.21	Assumptions met
Stoma management	0.099	0.966	1.85	Assumptions met

Abbreviations: GH, general health; PF, physical functioning; E&D, eat and drink; GI, gastrointestinal symptoms, VIF, variance inflation factor. Regression diagnostics confirmed the following assumptions: linearity between predictors and outcome, normally distributed residuals, homoscedasticity (constant variance), no multicollinearity (VIF < 10).

5.8.4: Summary of biomarker domains and associations with HRQoL

Principal Component Analysis (PCA) was performed across five sets of variables corresponding to blood results. These related to kidney function (sodium, potassium, urea, creatinine, Adj. Ca; n = 164), micronutrients (vitamins A, B12, D, copper, zinc, folate, manganese, selenium; n = 124), iron biomarkers (iron, ferritin, haemoglobin, transferrin, transferrin saturation; n = 72), blood lipids (cholesterol, triglycerides, HDL, non-HDL, total:HDL ratio; n = 123), and liver function (bilirubin, ALP, ALT, GGT, platelet count; n = 89). Components with eigenvalues >1 were retained. These components were then entered into linear regression models to assess their associations with HRQoL outcomes.

5.8.4.1: EQ-5D outcomes and biomarker domains

For markers of kidney function, there were no significant associations with either HRQoL outcome ($p > 0.05$). Similarly, micronutrients were not significantly associated with EQ-VAS (all $p > 0.05$). For iron biomarkers, PC1 (iron, transferrin saturation) was significantly associated with higher EQ-5D utility index scores ($\beta = 0.07$, $p = 0.014$). The model explained 10.4% of the variance. There was a positive, non-significant association with EQ-VAS ($\beta = 3.17$, $p = 0.079$).

There were no significant associations between any of the components relating to blood lipids and the VAS or utility index scores ($p> 0.05$). For liver function, while no significant association was observed for the VAS ($p = 0.165$), PC2 (Bil, ALT) was significantly associated with higher utility scores ($\beta = 0.08$, $p = 0.018$) and the model explained 8.3% of the variance.

5.8.4.2: SF-36 outcomes and biomarker domains

For the kidney function profile**,** PC1 (characterised by high loadings on urea, creatinine, and potassium), was significantly associated with better pain scores ($\beta = 3.82$, $p = 0.035$) and greater EWB ($\beta = 3.29$, $p = 0.019$). No other SF-36 domains showed significant associations.

For the micronutrient profile**,** PC1 (high loadings on folate, zinc, selenium, vitamin B12, and manganese), was significantly associated with lower pain ($\beta = 4.54$, $p = 0.033$). Associations with other domains were not statistically significant ($p > 0.05$).

In the iron-related biomarker profile**,** PC1 (with high contributions from iron, ferritin, and transferrin saturation) was significantly associated with higher pain scores ($\beta = 7.09$, $p = 0.029$), while no other domains reached statistical significance.

For the lipid profile**,** PC1 (characterised by high HDL and an inverse association with the total:HDL ratio) was significantly associated with better GH **(**$\beta = 3.26$, $p = 0.040$). No other SF-36 domains showed significant associations.

Finally, within the liver profile**,** PC1 (high ALP, ALT, GGT, platelets; inverse bilirubin) was significantly associated with lower PF ($\beta = –5.33$, $p = 0.012$) and showed a trend toward higher pain ($\beta = –4.66$, $p = 0.052$). PC2 (high bilirubin and ALT; low platelets) was significantly

associated with RLPH (β = 6.83, *p* = 0.033) and emotional role limitations (β = 14.46, *p* = 0.002).

5.8.4.3: HPN-QoL outcomes and biomarker domains

For markers of kidney function, PC2 (characterised by sodium, magnesium, and selenium) was positively associated with GH (β = 3.45, p = 0.038) and PF (β = 3.43, p = 0.038), and negatively associated with fatigue (β = -5.39, p = 0.017), and other pain (β = -6.12, p = 0.008). PC1 (reflecting higher levels of urea, creatinine, and potassium), was inversely associated with GI symptoms (β = -4.42, p = 0.008), stoma-related issues (β = -6.97, p = 0.002), and bowel management scores (β = -6.16, p = 0.022).

The only statistically significant finding in relation to micronutrients was for the nutrition team support domain where PC3 (vitamins A, D, and copper) showed a positive association (β = 6.33, p = 0.012). For the iron related biomarkers, there was a positive association between PC2 (with a strong positive loading on haemoglobin and negative loading on ferritin) and coping (β = 5.73, p = 0.026), and between PC2 and sexual function (β = 3.42, *p* = 0.013). There was a significant negative association between PC1 (high positive loadings on iron and transferrin saturation) and the ability to eat and drink (β = –5.02, p = 0.035). Other pain was inversely associated with PC1 (β = –6.08, p = 0.038).

In relation to blood lipids, coping was significantly and positively associated with PC2 (strong positive loading on HDL and a negative loading on the total/HDL ratio) (β = 3.34, p = 0.031). The nutrition team support domain was significantly associated with PC2 (β = 5.86, *p* = 0.002), and stoma-related concerns were inversely associated with PC1 (high positive loadings on total cholesterol, triglycerides, non-HDL, and the total/HDL ratio) (β = –4.64, p = 0.033).

Lastly, for the liver biomarkers, ambulatory pump use was negatively associated with PC1 (high positive loadings on ALP, ALT, GGT, and platelets, and a negative loading on bilirubin) (β = –9.88, *p* = 0.003), and PC2 was negatively associated with body image (β = –5.40, p = 0.036), GI symptoms (β = –6.16, p = 0.033), and other pain (β = –9.52, p = 0.005).

5.8.5: Change in QoL at follow up

5.8.5.1: Follow up SF-36 scores

5.8.5.1.1: Univariate analysis of domains with significant change

Univariate linear regression was conducted for follow-up data on SF-36 domains that showed significant change over time. Energy/fatigue was the only domain with a statistically significant change, and was therefore the focus of this analysis (Table 5.72).

Table 5.72: Univariate linear regression for energy/ fatigue domain of the SF-36 at follow up

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
HPN length (months)	-0.04	-0.10 to 0.02	0.188	0.01	0.188
Living status	2.83	-5.88 to 11.55	0.521	0.00	0.521
Education level				0.03	0.309
Secondary	Reference				
Post-secondary non-tertiary	-8.52	-20.13 to 3.07	0.148		
Short cycle tertiary	-7.74	-16.81 to 1.34	0.094		
Bachelors or higher	-4.72	-15.72 to 6.82	0.397		
Employment status				0.03	0.171
Unemployed	Reference				
Employed	5.02	-5.69 to 15.73	0.355		
Retired	7.61	-0.35 to 15.58	0.061		
SB length:				0.10	**0.011**
< 50cm	Reference				
51-100cm	-14.89	-29.41 to -0.38	**0.044**		
101-150cm	-3.23	-17.74 to 11.29	0.661		
151-200cm	-30.33	-49.03 to -11.63	**0.002**		
200cm	-14.96	-27.59 to -2.34	**0.021**		
HGS (kg)	0.77	0.12 to 1.41	**0.021**	0.11	**0.020**
Adj. age	0.75	0.10 to 1.40	**0.025**		
Adj. gender	1.01	0.14 to 1.87	**0.024**		
SMM (kg)	0.38	-1.01 to 1.76	0.571	0.02	0.571
PA (degree)	-2.84	-12.35 to 6.68	0.563	0.09	0.563
Oral dietary energy intake (kcal/d)	-0.00	-0.01 to 0.01	0.575	0.01	0.575
PN infusions/ wk	-1.25	-3.22 to 0.73	0.214	0.01	0.214
PN energy (kcal/d)	0.00	-0.00 to 0.01	0.381	0.01	0.381

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition

Table 5.72 demonstrates that SB length was strongly associated with fatigue, with significantly lower scores observed among those with longer small bowels i.e. 51–100 cm, 151–200 cm, and > 200cm remaining, relative to those with <50 cm. HGS was a significant independent predictor, even after adjusting for age and gender. Other variables including length of time on HPN, phase angle, oral dietary energy intake and total PN energy were not significantly associated with energy/fatigue scores.

5.8.5.1.2: Multivariable regression modelling of energy/ fatigue outcomes

Multivariable linear regression was performed on the energy/ fatigue domain using SB length and HGS as predictors.

Table 5.73: Final multivariable regression model for the energy/ fatigue domain of the SF-36

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
Energy/ fatigue	SB length:				**0.011**	
	< 50cm	Reference				0.24
	51-100cm	-21.47	-40.91 to -2.02	**0.031**		
	101-150cm	10.94	-28.12 to 50.00	0.575		
	151-200cm	-15.83	-40.84 to 9.19	0.209		
	200cm	-10.53	-26.97 to 5.90	0.203		
	HGS (kg)	0.87	0.22 to 1.51	**0.009**	**0.005**	

Abbreviations: SB, small bowel; NK, not known

When HGS was added to the unadjusted model for energy/fatigue, it emerged as a significant independent predictor of reduced fatigue (β = 0.87, p = 0.009), and the association between SB length <50 cm and lower fatigue scores became statistically significant (β = –21.47, p = 0.031). A LRT confirmed that inclusion of HGS significantly improved model fit. However, the 95% CIs for SB length categories were notably wide, particularly for the 101–150 cm and 151–200 cm groups, reflecting substantial uncertainty in these estimates. This likely stems from the small number of participants within each SB length subgroup (see Table 5.1). Adjusting further for age did not improve model fit, and age itself was not a significant predictor (p = 0.780).

5.8.5.2: Follow up HPN-QoL scores

5.8.5.2.1: Univariate analysis of domains with significant change

For the HPN-QoL questionnaire, there were significant changes at follow up in the following domains – general health, ability to eat and drink, ability to holiday and stoma management. Table 5.74 presents univariate linear regression results for the GH domain of the HPN-QoL. Most predictors showed no statistically significant associations, however, the number of weekly PN infusions was associated with a 2.59-point reduction in GH scores.

Table 5.74: Univariate linear regression for the general health domain of the HPN-QoL (high score = better functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
Time on HPN (months)	-0.06	-0.13 to 0.02	0.124	0.02	0.124
Living status	4.03	-6.03 to 14.10	0.430	0.00	0.430
Education level				0.02	0.528
Secondary	Reference				
Post-secondary non-tertiary	-8.51	-21.76 to 4.73	0.206		
Short cycle tertiary	0.03	-10.27 to 10.32	0.996		
Bachelors or higher	-4.94	-17.49 to 7.60	0.437		
Employment status				0.02	**0.025**
Unemployed	Reference				
Employed	10.80	-1.89 to 23.47	0.095		
Retired	0.57	-8.78 to 9.91	0.904		
SB length:				0.04	0.297
< 50cm	Reference				
51-100cm	-0.51	-17.93 to 16.92	0.954		
101-150cm	11.34	-6.09 to 28.76	0.200		
151-200cm	1.37	-21.32 to 24.07	0.905		
200cm	10.51	-4.81 to 25.83	0.177		
HGS (kg)	0.54	-0.41 to 1.49	0.257	0.03	0.257
SMM (kg)	-0.94	-2.80 to 0.92	0.300	0.07	0.300
PA (degree)	-5.47	-18.39 to 7.46	0.383	0.05	0.383
Oral dietary energy intake (kcal/d)	0.00	-0.01 to 0.02	0.414	0.01	0.414
PN infusions/ wk	-2.59	-4.88 to -0.31	**0.026**	0.03	**0.026**
PN energy (kcal/d)	0.01	-0.01 to 0.00	0.073	0.02	0.073

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition

Table 5.75 indicates that each additional weekly PN infusion was linked to a 5.14-point decrease in the ability to eat and drink score. Retired participants scored 15.04 points higher than those who were unemployed, while having a small bowel length of 101–150 cm was associated with a 25.28-point increase. As anticipated, greater oral dietary energy intake improved scores by 0.02 points per kcal, whereas each additional PN kcal corresponded to a 0.02-point decrease.

Table 5.75: Univariate linear regression for the ability to eat and drink domain of the HPN-QoL (high score = better functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
Time on HPN (months)	-0.02	-0.10 to 0.07	0.708	0.00	0.708
Living status	0.33	-11.09 to 11.76	0.954	0.00	0.954
Education level				0.06	0.060
Secondary	Reference				
Post-secondary non-tertiary	-20.72	-35.93 to -5.05	**0.008**		
Short cycle tertiary	-5.48	-17.31 to 6.35	0.361		
Bachelors or higher	-1.92	-16.33 to 12.49	0.792		
Employment status				0.06	**0.015**
Unemployed	Reference				
Employed	13.65	-0.47 to 27.77	0.058		
Retired	15.04	4.63 to 25.44	**0.005**		
SB length:				0.22	**<0.001**
< 50cm (constant)	Reference				
51-100cm	-0.17	-18.05 to 17.70	0.985		
101-150cm	25.28	7.40 to 43.15	**0.006**		
151-200cm	2.96	-20.32 to 26.24	0.802		
200cm	-12.53	-28.25 to 3.19	0.117		
HGS (kg)	0.21	-0.77 to 1.20	0.665	0.00	0.665
SMM (kg)	0.85	-0.83 to 2.53	0.301	0.07	0.301
PA (degree)	10.39	-0.21 to 21.00	0.054	0.21	0.054
Oral dietary energy intake (kcal/d)	0.02	0.01 to 0.03	**<0.001**	0.25	**<0.001**
PN infusions/ wk	-5.14	-7.65 to -2.64	**<0.001**	0.10	**<0.001**
PN energy (kcal/d)	-0.2	-0.02 to -0.01	**<0.001**	0.20	**<0.001**

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition

Table 5.76 shows no significant association between any of the predictors and the ability to holiday score.

Table 5.76: Univariate linear regression for the ability to holiday domain of the HPN-QoL (high score = better functioning)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
Time on HPN (months)	-0.01	-0.07 to 0.06	0.863	0.00	0.863
Living status	-0.35	-8.87 to 8.17	0.936	0.00	0.936
Education level				0.03	0.352
Secondary	Reference				
Post-secondary non-tertiary	4.41	-7.21 to 16.03	0.454		
Short cycle tertiary	7.88	-1.16 to 16.92	0.087		
Bachelors or higher	1.03	-9.97 to 12.04	0.853		
Employment status				0.01	0.462
Unemployed	Reference				
Employed	-0.28	-11.14 to 10.57	0.959		
Retired	-4.58	-12.59 to 3.41	0.259		
SB length:				0.08	0.054
< 50cm	Reference				
51-100cm	-7.59	-22.18 to 7.00	0.305		
101-150cm	8.86	-5.74 to 23.45	0.232		
151-200cm	-7.97	-26.97 to 11.04	0.409		
200cm	7.36	-5.48 to 20.19	0.259		
HGS (kg)	0.14	-0.61 to 0.89	0.708	0.00	0.708
SMM (kg)	-0.38	-1.66 to 0.90	0.535	0.02	0.535
PA (degree)	-1.84	-10.68 to 6.99	0.664	0.01	0.664
Oral dietary energy intake (kcal/d)	-0.00	-0.01 to 0.00	0.313	0.02	0.313
PN infusions/ wk	-0.90	-2.88 to 1.07	0.367	0.01	0.367
PN energy (kcal/d)	-0.00	-0.01 to 0.00	0.112	0.00	0.112

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition

Table 5.77 indicates that lower education and employment status were significantly associated with lower stoma management scores. Specifically, participants with post-secondary non-tertiary education had stoma scores 22.13 points lower than those with secondary education (p = 0.030), and those who were employed or retired reported 19.28 and 17.11 points lower scores, respectively, compared to unemployed individuals.

Table 5.77: Univariate linear regression for the stoma management domain of the HPN-QoL (high score = worse symptoms)

Predictor	Coefficient (B)	95% CI	p-value	R^2	LRT p-value
Time on HPN (months)	0.03	-0.06 to 0.12	0.554	0.00	0.554
Living status	-2.61	-15.59 to 10.36	0.690	0.00	0.690
Education level				0.05	0.182
Secondary	Reference				
Post-secondary non-tertiary	-22.13	-42.04 to -2.21	**0.030**		
Short cycle tertiary	-4.78	-18.43 to 8.87	0.489		
Bachelors or higher	-2.43	-18.83 to 13.96	0.768		
Employment status				0.09	**0.012**
Unemployed (constant)	Reference				
Employed	-19.28	-35.30 to -3.26	**0.019**		
Retired	-17.11	-29.28 to -4.93	**0.006**		
SB length:				0.01	**0.026**
< 50cm (constant)	Reference				
51-100cm	13.81	-7.84 to 35.46	0.209		
101-150cm	-7.75	-29.40 to 13.90	0.479		
151-200cm	-6.09	-34.15 to 21.96	0.667		
200cm	-12.55	-33.78 to 8.67	0.243		
HGS (kg)	-0.46	-1.79 to 0.86	0.483	0.01	0.483
SMM (kg)	-0.27	-1.72 to 1.18	0.696	0.01	0.696
PA (degree)	-3.26	-13.75 to 7.23	0.516	0.03	0.516
Oral dietary energy intake (kcal/d)	-0.01	-0.02 to 0.00	0.214	0.03	0.214
PN infusions/ wk	0.83	-2.24 to 3.90	0.592	0.00	0.592
PN energy (kcal/d)	0.00	-0.01 to 0.01	0.480	0.00	0.480

Abbreviations: HPN, Home Parenteral Nutrition, SB, small bowel; NK, not known; HGS, handgrip strength; SMM, skeletal muscle mass; PA, phase angle; PN, parenteral nutrition

5.8.5.2.2: Multivariable regression analysis

A series of regression models were conducted to identify predictors of the ability to eat and drink, and stoma management domains (Table 5.78).

Table 5.78: Multivariable linear regression for the follow up predictors of the HPN-QoL

Outcome	Exposure	Coefficient (B)	95% CI	p-value	LRT p-value	R^2
Ability to E&D	Dietary intake, Average PN kcals	0.01 -0.01	0.00 to 0.02 -0.02 to 0.00	**0.026** 0.060	**<0.001** **0.003** **0.030**	0.47
	SB length:					
	<50cm	Reference				
	51-100cm	-4.47	-24.42 to 15.47	0.655		
	101-150cm	11.27	-16.07 to 38.61	0.412		
	151-200cm	0.58	-28.88 to 30.04	0.969		
	>200cm	-17.53	-35.72 to 0.66	0.059		
Stoma management	**Education:**				0.182	0.12
	Secondary	Reference				
	Post secondary	-21.90	-41.34 to -2.45	**0.028**		
	Short cycle tertiary	-1.12	-14.71 to 12.47	0.870		
	Bachelors or higher	0.48	-15.79 to 16.74	0.953		
	Employment:				**0.029**	
	Unemployed	Reference				
	Employed	-16.08	-33.06 to 0.90	0.063		
	Retired	-16.58	-29.61 to -3.55	**0.013**		

In the initial model, oral dietary energy intake was positively associated with the ability to eat and drink (β = 0.022, p < 0.001), explaining 23.5% of the variance. Adding total PN energy improved model fit, with oral dietary energy intake remaining positively associated (β = 0.017, p = 0.003) and PN energy negatively associated (β = –0.011, p = 0.035). A LRT confirmed a significant improvement (LR χ^2 = 4.68, p = 0.030). A third model included weekly PN infusion frequency, but this did not further improve the model (R^2 = 0.275; LR χ^2 = 0.91, p = 0.340), and only oral dietary energy intake remained significant (β = 0.018, p = 0.002). The final model included SB length, oral dietary energy intake, and total PN energy. Oral dietary energy intake again remained significant, and while not all SB length categories reached significance, its inclusion substantially improved model fit.

For stoma management, the first model looked at education level as a predictor and was not statistically significant overall (p = 0.182). Individuals with post-secondary non-tertiary

education had significantly lower symptom scores for stoma management compared to those with secondary education only (β = –22.13, p = 0.030). In the second model, employment status was added and the model became statistically significant. The association with post-secondary non-tertiary education remained significant, and being retired was also significantly associated with lower symptom scores for stoma management (Table 5.78).

5.8.6: Subgroup analyses

This section explores how QoL outcomes varied across specific subgroups within the cohort.

5.8.6.1: Centre-based variability in QoL outcomes

5.8.6.1.1: EQ-5D outcomes by participating centre

Table 5.79 and 5.80 presents EQ-5D domain scores at baseline stratified by participating centre (recruitment site). Significant differences were observed in the EQ-5D VAS scores ($p < 0.001$), with pairwise comparisons indicating that patients from Leeds and Nottingham reported significantly higher VAS scores compared with those from Newcastle (both $p < 0.001$). Health utility scores also varied significantly across sites ($p = 0.001$), with Newcastle participants showing lower scores than those from Leeds ($p = 0.012$) and Nottingham ($p = .0001$). Next, data for Leeds and Nottingham were combined and compared against Newcastle. Among the EQ-5D domains, only usual activities remained significantly different, with more Newcastle patients reporting limitations in this area ($p = 0.028$). Additionally, Newcastle patients reported significantly lower VAS scores than the combined Leeds/Nottingham group ($p = <0.001$).

Table 5.79: EQ-5D-5L results for the mobility, self-care and usual activities domains at baseline, stratified by participating centre and for Leeds and Nottingham combined

Dimension	Newcastle 1; N = 101	Leeds 2; N = 60	Nottingham 3; N = 35	Leeds & Nottingham combined	P-value[1]	1 vs 2 & 3 combined p-value
Mobility						
No problems	17 (16.8)	13 (21.7)	11 (31.4)	24 (25.3)	**<0.001, site 1 vs 3 <0.001, 2 vs 3 0.002**	0.295
Slight problems	21 (20.8)	12 (20)	10 (28.6)	22 (20.9)		
Moderate problems	41 (40.6)	20 (33.3)	7 (20)	27 (25.7)		
Severe problems	17 (16.8)	12 (20)	6 (17.1)	18 (17.1)		
Unable walk about	5 (5)	3 (5)	1 (2.9)	4 (3.8)		
Self-care						
No problems	43 (42.6)	24 (40)	19 (54.3)	43 (40.9)	**0.010, 1 vs 3 0.002, 2 vs 3 0.001**	0.648
Slight problems	31 (30.7)	19 (31.7)	9 (25.7)	28 (26.6)		
Moderate problems	13 (12.9)	11 (18.3)	6 (17.1)	17 (16.2)		
Severe problems	11 (10.9)	4 (6.7)	0 (0)	4 (3.8)		
Unable wash or dress	3 (3)	2 (3.3)	1 (2.9)	3 (2.9)		
Usual activities						
No problems	10 (9.9)	13 (21.7)	4 (11.4)	17 (16.2)	**<0.001, 1 vs 2 <0.001, 1 vs 3 <0.001, 1 vs 3 0.040**	**0.028**
Slight problems	20 (19.8)	10 (16.7)	11 (31.4)	21 (20)		
Moderate problems	35 (34.7)	22 (36.7)	10 (28.6)	32 (30.4)		
Severe problems	18 (17.8)	11 (18.3)	7 (20)	18 (17.1)		
Unable to do usual activities	18 (17.8)	4 (6.7)	3 (8.6)	7 (6.7)		

All data are presented as number (%). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

Table 5.80: EQ-5D-5L results for the pain, anxiety/ depression, VAS and health utility domains at baseline, stratified by participating centre and for Leeds and Nottingham combined

Dimension	**Newcastle 1; N = 101**	**Leeds 2; N = 60**	**Nottingham 3; N = 35**	**Leeds & Nottingham combined**	**P-value[1]**	**1 vs 2 & 3 combined p-value**
Pain/ discomfort						
None	11 (10.9)	12 (20)	3 (8.6)	15 (14.3)	**0.004, 1 vs 2 0.001**	0.130
Slight	19 (18.8)	14 (23.3)	10 (28.6)	24 (25.3)		
Moderate	33 (32.7)	14 (23.3)	11 (31.4)	25 (23.8)		
Severe	29 (28.7)	16 (26.7)	11 (31.4	27 (25.7)		
Extreme	9 (8.9)	4 (6.7)	0 (0)	4 (3.8)		
Anxiety/ depression						
None	23 (22.8)	16 (26.7)	12 (34.3)	28 (26.6)	**0.020, 1 vs 3 0.002**	0.256
Slight	23 (22.8)	14 (23.3)	7 (20)	21 (20)		
Moderate	23 (22.8)	21 (35)	12 (34.3)	33 (31.4)		
Severe	12 (11.9)	7 (11.7)	3 (8.6)	10 (9.5)		
Extreme	8 (7.9)	2 (3.3)	1 (2.9)	3 (2.9)		
EQ-5D-5L VAS (0-100)* Median (range)	45 (0-90)	52.5 (10-100)	60 (10–95)	55 (40-75)	**0.001, 1vs 2 and 1 vs 3 <0.001**	**<0.001**
Health utility index (-1 – 1) Median (range)	0.47 (-0.34 - 0.99)	0.48 (-0.40 – 0.99)	0.57 (-0.26 – 0.99)	0.52 (0.24-0.71)	**0.001, 1 vs 2 0.012, 1 vs 3 <0.001**	0.153

All data are presented as number (%). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

5.8.6.4.1.2: SF-36 outcomes by participating centre

SF-36 results stratified by participating centre revealed notable site differences. Patients from Nottingham had the highest median scores in physical functioning, emotional role limitations, energy/fatigue, pain, and general health, while Leeds patients scored highest in social functioning. In contrast, Newcastle patients had the lowest median scores in emotional wellbeing, social functioning, and pain, and did not lead in any SF-36 domain. Across all centres, physical role limitations had a median score of zero. When Leeds and Nottingham were combined and compared with Newcastle, the latter had significantly lower median scores for physical functioning (p = 0.001), emotional wellbeing (p = 0.038), and pain (p = 0.024) (Table 5.81).

Table 5.81: SF-36 results at baseline, stratified by participating centre

	Newcastle (1; n=91)	**Leeds (2; n=60)**	**Nottingham (3; n=34)**	**Leeds & Nottingham combined**	**p-value[1]**	**1 vs 2&3 combined**
	Median (range)					
PF	30 (10-50)	25 (5-65)	42.5 (15-65)	30 (10-65)	0.215	0.295
RLPH	0 (0-0)	0 (0-100)	0 (0-0)	0 (0-50)	0.137	0.192
RLEH	0 (0-100)	0 (0-100)	67 (0-100)	16.5 (0-100)	0.189	0.074
Energy/ fatigue	25 (10-35)	22.5 (4-47.5)	35 (25-45)	30 (5-45)	0.062	0.228
EWB	52 (40-68)	60 (42-80)	60 (48-80)	60 (48-80)	0.107	**0.038**
SF	25 (12-50)	62 (25-75)	50 (25-62)	50 (25-75)	**0.001 1&2 <0.001 1&3 0.038**	**0.001**
Pain	35 (10-58	45 (22-78)	45 (22-68)	45 (22-68)	**0.074**	**0.024**
GH	25 (10-40)	20 (5-45)	35 (20-45)	25 (5-45)	0.189	0.462

Abbreviations: PF, physical functioning; RLPH, role limitations due to physical health; RLEH, role limitations due to emotional health; EWB, emotional wellbeing; SF, social functioning; GH, general health. All data are presented as medians (IQR). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

5.8.6.1.2: HPN-QoL outcomes by participating centre

HPN-QoL outcomes varied significantly across participating centres (Table 5.82). Patients in Leeds and Nottingham had significantly higher PF scores compared to those in Newcastle (p < 0.001), and those in Nottingham also had higher EF scores (p = 0.015 overall; Newcastle vs Nottingham p = 0.018). Ability to eat and drink was higher in Leeds and Nottingham than

Newcastle (p = 0.037), and GH scores showed a modest but significant difference between Newcastle and the combined group (p = 0.047). No other significant differences were found.

Table 5.82: HPN-QoL functional scale score results at baseline, stratified by participating centre (high score = better functioning)

	Newcastle (1; n=94)	**Leeds (2; n=60)**	**Nottingham (3; n=35)**	**Leeds & Nottingham combined**	**p-value[1]**	**1 vs 2 & 3 combined**
General health	75 (50-75)	75 (50-75)	75 (50-75)	75 (50-75)	0.128	**0.047**
Ability to holiday	25 (0-43.8)	25 (0-37.5)	25 (0-50)	25 (0-37.5)	0.987	0.876
Physical functioning	25 (16.6-50)	41.6 (33.3-62.5)	37.5 (16.6-58.3)	41.6 (33.3-41.6)	**0.001 1&2 <0.001**	**0.001**
Coping	54.5 (43-67)	56 (44-67)	56 (33-78)	56 (44-67)	0.149	0.149
Ability to eat and drink	50 (33.3-66.7)	66.6 (33.3-100)	66.6 (50-83.3)	66.6 (33.3-100)	**0.109**	**0.037**
Employment	0 (0-33.3)	0 (0-33.3)	0 (0-16.7)	0 (0-33.3)	0.391	0.803
Sexual function	0 (0-0)	0 (0-16.7)	0 (0-16.7)	0 (0-16.7)	0.177	0.093
Emotional functioning	42 (17-67)	54 (37.5-75)	58 (33-75)	58 (33-75)	**0.015 1&2 0.019 1&3 0.018**	**0.004**

All data are presented as medians (IQR). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

Table 5.83 shows no significant differences between centres in patient-reported outcomes related to the nutrition team or ambulatory pump.

Table 5.83: HPN-QoL HPN-item results at baseline, stratified by participating centre (high score = better outcome)

	Newcastle (1; n=94)	Leeds (2; n=60)	Nottingham (3; n=35)	Leeds & Nottingham combined	p-value[1]	1 vs 2 & 3 combined
Nutrition team	100 (67-100)	100 (67-100)	100 (67-100)	100 (67-100)	0.516	0.536
Ambulatory pump	66.6 (33.3-100) n=74	66.6 (33.3-100) n=50	66.6 (66.6-100) n=32	66.6 (33.3-100)	0.253	0.268

All data are presented as medians (IQR). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

Table 5.84 shows that Newcastle participants reported significantly worse symptom-related QoL scores compared to those from Leeds and Nottingham in several domains. Specifically, immobility scores were higher in Newcastle versus Leeds and Nottingham. Scores for other pain were also worse in Newcastle. Similarly, the QoL numerical rating scale was markedly lower in Newcastle compared to Leeds and Nottingham.

Table 5.84: HPN-QoL symptom scale results at baseline, stratified by participating centre (high score = worse symptoms)

	Newcastle (1; n=94)	**Leeds (2; n=60)**	**Nottingham (3; n=35)**	**Leeds & Nottingham combined**	**p-value[1]**	**1 vs 2 & 3 combined**
Body image	33 (17-50)	33 (17-50)	33 (0-50)	33 (17-50)	0.516	0.615
Weight	33 (0-67)	33 (0-67)	33 (0-67)	33 (0-67)	0.560	0.339
Immobility	53 (33-80)	40 (33-67)	47 (20-67)	47 (27-67)	0.073	**0.022**
Fatigue	67 (33-100)	67 (33-100)	67 (33-100)	67 (33-100)	0.396	0.175
Sleep pattern	67 (33-100)	67 (33-100)	50 (33-67)	67 (33-100)	0.589	0.331
GI symptoms	23 (5.5-44)	22 (5.5-44)	37.5 (11.44)	22 (11-44)	0.532	0.735
Other pain	67 (33-83)	50 (17-83)	50 (33-83)	50 (17-83)	0.055	**0.017**
Stoma management	33.3 (16.6-66.6) n=65	33.3 (16.6-50) n=46	33.3 (16.6-50) n=26	33.3 (16.6-50)	0.492	0.328
Bowel management	33 (11-44) n=35	44 (33-67) n=14	33 (33-44) n=9	44 (33-61.5)	0.130	0.084
Financial issues	33.3 (0-33.3)	0 (0-33.3)	0 (0-33.3)	0 (0-33.3)	0.203	0.118
QoL numerical rating scale	-7 (-20-7)	3 (-8.5-17)	5 (-10-13)	3(-10-13)	**0.008 1&2 0.005 1&3 0.035**	**0.002**

All data are presented as medians (IQR). [1]Overall p-value from Kruskal–Wallis test comparing distributions across Newcastle, Leeds, and Nottingham.

5.8.6.2: QoL for new patients only

Table 5.85 presents SF-36 domain scores at baseline and follow-up among newly established HPN patients. Overall, patients reported low scores across all domains at both timepoints, with minimal change observed. The only domain reaching statistical significance was energy/fatigue (p = 0.004). Although the median fatigue scores at baseline and follow-up were identical, the Wilcoxon signed-rank test showed a statistically significant reduction in fatigue over time (z = -2.878, p = 0.004). The direction of the difference was driven by a greater number of participants reporting improved fatigue at follow-up, as reflected by the higher sum of negative ranks (166.5 vs. 23.5).

Table 5.85: Longitudinal changes in SF-36 scores, for new HPN patients only (n=25)

	Baseline	**Follow up**	**p-value[1]**
	Median (IQR)		
Physical functioning	35 (5-45)	35 (10-50)	0.469
Role limitations (physical)	0 (0-0)	0 (0-0)	0.250
Role limitation (emotional)	0 (0-33)	0 (0-100)	0.359
Energy/ fatigue	30 (13-35)	30 (10-55)	**0.003**
Emotional wellbeing	56 (40-64)	52 (40-60)	0.627
Social functioning	25 (0-25)	38 (12-62)	0.137
Pain	32 (10-45)	35 (20-58)	0.101
General health	25 (20-40)	30 (20-35)	0.524

All data are presented as medians (IQR). [1]Wilcoxon Signed-Rank Test.

5.8.6.2.1: New patient QoL versus existing patient QoL

At baseline, new patients were classified as those who had been on HPN for six months or less (n = 25) and existing patients were those who had been on HPN for seven months or greater (n = 146; Table 5.86).

Table 5.86: Baseline QoL scores measured by the SF-36 questionnaire for new versus existing HPN patients

	Existing patients (n=146)	**New patients (n=25)**	**p-value[1]**
Baseline			
Physical functioning	30 (10-60)	35 (5-45)	0.573
Role limitations (physical)	0 (0-35)	0 (0-0)	**0.025**
Role limitation (emotional)	0 (0-100)	0 (0-33)	0.088
Energy/ fatigue	30 (4-45)	30 (13-35)	0.885
Emotional wellbeing	56 (40-76)	56 (40-64)	0.524
Social functioning	50 (25-75)	25 (0-25)	**0.001**
Pain	45 (22-68)	32 (10-45)	0.084
General health	25 (10-40)	25 (20-40)	0.353
Follow up			
Physical functioning	30 (10-55)	35 (10-50)	0.878
Role limitations (physical)	0 (0-25)	0 (0-0)	0.268
Role limitation (emotional)	33 (0-100)	0 (0-100)	0.387
Energy/ fatigue	30 (15-50)	30 (10-55)	0.697
Emotional wellbeing	60 (44-72)	52 (40-60)	0.129
Social functioning	50 (25-75)	38 (12-62)	0.128
Pain	45 (22-67)	35 (20-58)	0.453
General health	25 (10-35)	30 (20-35)	0.596

All data are presented as medians (IQR). [1]Mann-Whitney U Test.

For the SF-36, baseline comparisons between new and existing patients revealed no significant differences across domains, except for physical role limitations (p = 0.030) and social functioning (p = <0.001), with new patients reporting poorer social functioning. At follow-up, no significant differences were observed between groups for any SF-36 domain. Similarly, there were no group differences in EQ-5D-5L domain scores, VAS, or health utility index. However, the HPN-QoL showed significant differences in three domains: new patients reported greater difficulty with eating and drinking (p = 0.042), perceived less benefit from ambulatory pumps (p = 0.007), and rated their overall quality of life lower (p = 0.007).

5.8.7.3: Evaluation of QoL at baseline in participants who died before follow-up compared with survivors who completed follow-up

This section outlines the QoL outcomes for a small group of participants within the study who sadly passed away before study completion (n=8). For that reason, only baseline data were available.

5.8.7.3.1: QoL measured by the EQ-5D-5L

All eight participants in this subgroup returned the EQ-5D questionnaire at baseline. VAS scores ranged from 10 to 60 with a median of 39 (Figure 5.10). Their health utility scores ranged from -0.26 to 0.73 with a median of 0.10.

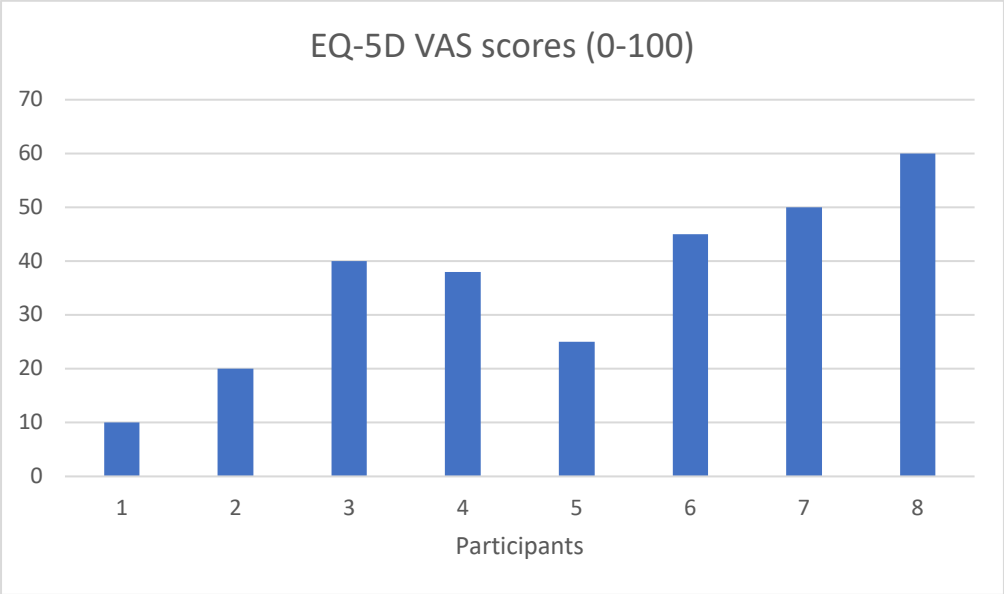


Figure 5.10: Individual participant EQ-5D VAS scores

The percentage of patients reporting each level of the five domains can be seen in Figure 5.11. There were 37.5% and 25% of participants, respectively, that reported no problems for anxiety/ depression and self-care. In contrast, 100% of participants reported some level of problem in the pain/discomfort, usual activities and mobility domains. The domains most affected were pain/discomfort and mobility whereby 75% of participants reported severe or extreme problems.

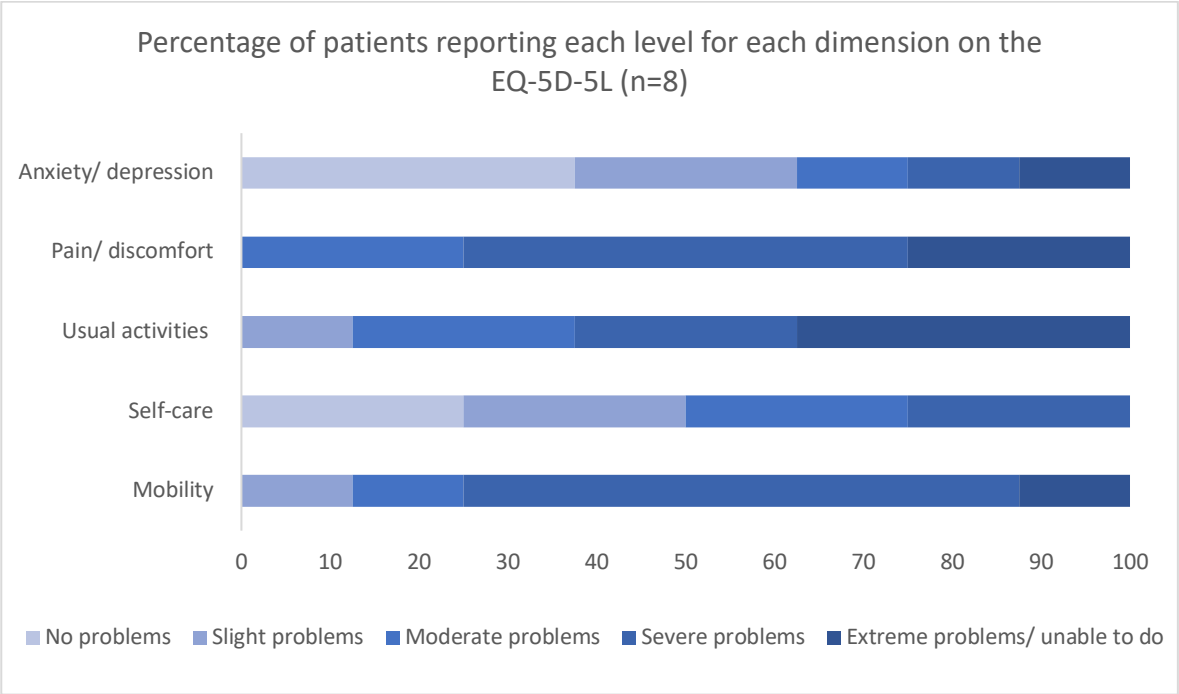


Figure 5.11: Percentage of patients reporting each level of the five dimensions of the EQ-5D questionnaire.

A comparison of EQ-5D-5L responses between participants who died during follow-up (n=8) and the wider cohort (n=196) showed that while QoL was impaired across the full group, those who died experienced more severe limitations across key domains. In the RIP group, the majority reported moderate to extreme problems with mobility, pain/discomfort, and usual activities, compared to around 58% and 65% of the wider cohort, respectively, who reported similar levels of difficulty in these domains. Self-care difficulties were reported by approximately half of the RIP group, versus around one-quarter of the broader cohort. Emotional distress was the least affected domain among RIP participants, with only one-third reporting moderate or worse anxiety or depression, compared to around 50% of the wider group.

5.8.7.3.2: QoL measured by the SF-36 questionnaire

There were six participants who returned the SF-36 questionnaire at baseline. Their individual scores for each domain can be seen in Table 5.87. Scores were low for all domains with 'role emotional' and 'role physical' being the most affected. Almost all participants scored zero. The highest scores were seen for emotional wellbeing.

Table 5.87: Individual participant scores for each domain of the SF-36

	Participants					
	1	**2**	**3**	**4**	**5**	**6**
Physical functioning	15	40	5	5	0	5
Role physical	0	100	0	0	0	0
Role emotional	0	0	0	0	0	0
Energy/ fatigue	30	25	0	0	5	0
Emotional wellbeing	52	80	32	28	20	44
Social functioning	12	75	0	38	38	12
Pain	10	78	0	22	0	22
General health	0	30	20	5	5	0

When comparing SF-36 domain scores between participants who died during follow-up (RIP group, n=6) and the wider cohort (n=186), notable differences emerged in both the severity and distribution of QoL impairments. In the RIP group, the most affected domains were role limitations (physical and emotional), social functioning, and pain, with the majority of participants scoring at or near zero. Physical functioning and general health were also substantially impaired, with most RIP participants scoring below the cohort median of 30 and 25, respectively. The least affected domain in the RIP group was emotional wellbeing, where scores, though lower than the wider cohort (median 56), still ranged between 20 and 80. Similarly, energy/fatigue scores varied but were slightly less impaired relative to role-based domains.

5.8.7.3.3: QoL measured by the HPN-QoL questionnaire

All eight participants completed the HPN-QoL questionnaire at baseline. Individual scores for each domain can be seen in Table 5.88.

Table 5.88: Individual participant scores for each domain of the HPN-QoL questionnaire

	Participants							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Functional scales (0-100; high score = good functioning)								
General health	50	50	25	50	50	75	75	75
Ability to holiday	0	0	25	50	0	0	50	12.5
Physical functioning	0	0	75	50	8.3	0	41.6	33.3
Coping	0	22	58	56	22	67	67	56
Ability to eat and drink	33.3	16.6	66.7	83	50	83.3	66.6	33.3
Employment	33.3	0	0	0	16.6	50	0	0
Sexual function	0	0	0	0	0	0	0	0
Emotional functioning	83	100	67	42	67	8	42	58
HPN items								
Nutrition team	67	33	67	100	33	100	100	100
Ambulatory pump	66.6	NA	66.6	100	0	NA	100	100
Symptom scales (0-100; high score = worse symptoms)								
Body image	0	33	0	50	33	83	100	67
Weight	0	100	0	100	67	100	100	33
Immobility	33	27	27	47	80	80	87	53
Fatigue	33	67	67	100	67	100	83	33
Sleep pattern	0	67	67	100	67	67	22	67
GI symptoms	11	11	33	0	100	44	67	22
Other pain	83	33	67	83	67	67	83	83
Stoma management	33.3	66.6	16.6	33.3	33.3	33.3	33.3	NA
Bowel management	0	NA	NA	NA	NA	NA	NA	44
Financial issues	33.3	0	0	0	33.3	33.3	0	0

The functional scales which appear to be most affected are ability to holiday, physical functioning, employment and sexual function. The symptom scale items most affected are weight, fatigue, sleep pattern and other pain.

At baseline, the RIP group (n=8) consistently reported lower functional HPN-QoL scores than the broader cohort (n=189). Median general health scores in the full cohort were 75 (IQR 50–75), while in the RIP group scores ranged from 25 to 75. Ability to holiday scores were 25 (0–37.5) in the cohort and ranged from 0 to 50 in the RIP group. Physical functioning scores were lower among RIP participants (0–75) compared to the cohort median of 41.6 (16.6–50).

Coping scores were also lower in the RIP group (0–67) than the cohort median of 56 (44–67). The ability to eat and drink was similar across groups, with RIP scores ranging from 16.6 to 83.3 versus 50 (33.3–83.3) in the cohort. Employment and sexual function scores were uniformly low in both groups. Emotional functioning in the RIP group ranged from 8 to 100, compared to a cohort median of 50 (29–75).

For HPN-specific items, nutrition team scores were similar across groups (100 [67–100] in the cohort; 33–100 in RIP). Ambulatory pump scores ranged from 0 to 100 in the RIP group and 66.6 (33.3–100) in the cohort. On symptom scales (higher scores indicate worse symptoms), RIP participants reported higher values in most domains. Fatigue ranged from 33 to 100 (cohort median 67 [33–100]); immobility 27 to 87 (cohort median 47 [33–67]); and other pain 67 to 83 (cohort median 67 [33–83]). GI symptoms ranged from 0 to 100 in RIP versus 22 (11–44) in the cohort. Body image and weight concerns were also higher in the RIP group, ranging up to 100, compared to whole cohort medians of 33 (17–50) and 33 (0–67), respectively.

Chapter 6: General discussion

6.1: Introduction

This thesis set out to address a major evidence gap in understanding the quality of life (QoL) in adults receiving home parenteral nutrition (HPN), combining a systematic review, a national survey of healthcare professionals (HCPs), and an observational study to explore how clinical, nutritional, and psychosocial factors interact to shape patient experiences. The findings reveal a consistent pattern across all three components, highlighting a gap between clinical practice and the lived realities of patients. They highlight the need for greater standardisation, patient involvement, and multidimensional care.

The systematic review revealed a striking paucity of high-quality evidence to guide macronutrient and micronutrient provision in HPN, and few studies included patient-centred outcomes. Lipid emulsions, particularly those containing fish oil, showed promise in modifying biochemical markers, but their impact on QoL remains underexplored. This gap in patient-reported outcomes was echoed in the survey, where HCPs described inconsistent use of QoL tools, limited integration of results into care, and scepticism regarding the relevance of existing instruments. Despite broad agreement on the importance of QoL assessment, many clinicians highlighted practical barriers such as time constraints, tool validity, and lack of training, and called for patient-led approaches. One respondent noted: “Why do we think we know what is a good reflector of QoL when we haven’t lived the life?”

These concerns provided important context and justification for the final component of this thesis: a longitudinal, multicentre study designed to evaluate QoL among adults receiving HPN. This study sought to move beyond clinician perception and tool limitations by directly assessing the lived experiences of patients over time, using a combination of generic and disease-specific patient reported outcome measures (PROMs). The remainder of this discussion will therefore focus on the findings, interpretations, and implications of the longitudinal QoL study, and how they relate to the broader context established by the previous work.

6.2: Longitudinal effects of HPN on QoL

This study utilised the largest cohort of HPN patients assessed using the SF-36 questionnaire to date, enabling a comprehensive evaluation of health-related quality of life (HRQoL). This was further strengthened by the inclusion of the EQ-5D and the HPN-QoL, a disease-specific instrument. The primary aim of the longitudinal analysis was to assess changes in QoL over a 12-month period, with the hypothesis that scores would improve during the first year of HPN. However, this hypothesis was not supported, as no significant changes were observed in seven of the eight SF-36 domains. A notable proportion of participants recorded the lowest possible scores in areas such as physical and emotional role limitations, suggesting a potential floor effect. Such a floor effect may prevent detection of changes in HRQoL over the 12-month follow-up and suggests that the SF-36 may lack the sensitivity to detect subtle variations in health status among individuals with IF. Additionally, modelling HPN duration as a continuous variable revealed no significant associations with QoL in any domain. This suggests that there is no overall improvement (or detriment) over time in QoL of IF patients on long-term HPN. However, the current study did not investigate the possibility of potential sub-groups of IF patients whose QoL improved (or deteriorated) with increasing duration of HPN.

The longitudinal findings align closely with those of Schönenberger et al., who evaluated HRQoL in a cohort of 70 HPN patients at six-month intervals over a two-year period (102). They used a non-disease-specific version of the SF-36 (SF-36v2) and reported no significant changes in the mental health-related domains (vitality, social functioning, emotional role limitations, and mental health) and only trends toward improvement in the physical health domains (physical functioning, physical role limitations, bodily pain, and general health). A critical limitation of their study, however, was substantial attrition: 32 patients discontinued HPN during follow-up, five died, and an additional 24 either withdrew consent, were lost to follow-up, or joined late. As a result, only nine participants completed the study, making it highly unlikely that the analysis was adequately powered to detect meaningful changes in HRQoL over time.

Using the HPN-QoL tool, significant improvements were observed from baseline to follow-up in domains such as general health, ability to go on holiday, ability to eat and drink, and

stoma management. However, interpretation of these findings is limited by the novelty of the tool, as there are currently no published longitudinal studies using the HPN-QoL questionnaire. Only one prior conference abstract has reported similar data, based on 33 patients (median age 57) with IF assessed three years apart, which showed no significant changes over time, apart from a decline in employment (160).

More recently, Jones et al. (2023) (103) conducted a large longitudinal study of 572 patients using the Parenteral Nutrition Impact Questionnaire (PNIQ), where lower scores indicate better QoL. They found that reductions in weekly home parenteral support (HPS) infusions were associated with improved QoL, with both unadjusted and adjusted models showing significant improvements (−1.10 and −1.34, respectively). These findings are consistent with some of our results, where higher infusion frequency was linked to decreased ability to perform usual activities (EQ-5D) and lower VAS scores. However, Jones et al. also reported no linear dose-response relationship when infusion frequency was modelled as a continuous variable, suggesting that reductions in infusion days do not lead to proportionate improvements in QoL.

6.3: Cross sectional analysis of QoL

Descriptive analysis across multiple QoL measures indicates that QoL is significantly impaired among individuals receiving HPN. The most affected domains were those related to physical functioning, pain, general health, role limitations (both physical and emotional), employment, sexual function, ability to take holidays, fatigue, and sleep. In contrast, while scores in other domains were also suboptimal, areas such as emotional wellbeing, coping, body image, concerns about weight, gastrointestinal (GI) symptoms, and financial issues appeared comparatively less affected. These findings highlight a notable discrepancy between preserved emotional resilience and compromised physical functioning. While emotional coping strategies remain relatively intact, physical limitations and lifestyle constraints significantly impair the ability to fulfil valued life roles and maintain independence.

These findings closely align with those of Richards and Irving (1997) (161), who assessed QoL in 51 patients with IF on HPN using the SF-36 and EQ-5D instruments. Despite being over

two decades old, their study revealed a similar pattern of marked impairments in physical functioning, bodily pain, general health, and role limitations, alongside comparatively better-preserved scores in emotional wellbeing and mental health. The mean health utility score in the present study (EQ-5D index = 0.49) is similar to the 0.51 reported by Richards and Irving, further highlighting the significant reduction in perceived health status in this population. Both studies also identified low employment rates and younger age as important effect modifiers in QoL outcomes. Together, these results suggest that while HPN enables survival and community-based living, it continues to impose a considerable burden on daily functioning and subjective health, particularly in domains linked to physical independence and social participation.

Employment and higher education were linked consistently to better QoL across all QoL measures, with employed individuals and those holding a bachelor's degree or higher reporting better health utility and VAS scores, mobility, self-care, usual activities, physical, emotional, and social functioning. However, these relationships may be bidirectional. It is possible that individuals with better physical and psychological health are more likely to maintain employment or pursue further education, rather than employment or education directly improving QoL. This reverse causality is particularly relevant in the context of HPN, where symptom burden, fatigue, and frequent medical care may limit capacity to work. Therefore, although these socioeconomic factors appear protective, it is also plausible that better health enables individuals to remain socially and economically active. Although this was a longitudinal study, sociodemographic data were collected only at baseline, limiting the ability to determine the direction of these associations. Further longitudinal research is needed to clarify these relationships and to assess whether interventions aimed at improving employment opportunities or access to education can enhance QoL in individuals receiving HPN.

For individual QoL measures, the EQ-5D results in this study reveal health utility and VAS scores that align with values observed in some of the most debilitating chronic diseases. A comprehensive systematic review by Van Wilder et al. (2019) reported EQ-5D index scores across a wide range of chronic non-communicable conditions (162). Within this catalogue, mean EQ-5D healthy utility scores ranged from as low as –0.20 in severe Alzheimer's disease

to values approaching 1.00 in milder conditions such as hypertension or early-stage metabolic disorders. In the category of digestive diseases, which includes IF and related conditions, scores ranged from 0.49 to 0.92, with liver dysfunction and pancreatic disease at the lower end. Similarly, patients undergoing haemodialysis for renal failure showed scores around 0.44, and individuals with chronic respiratory diseases such as COPD had scores near 0.47.

These comparisons position HPN patients within a cohort of individuals with the most significant QoL impairments. While many chronic conditions are associated with physical limitations or disease burden, HPN introduces a unique combination of physical, nutritional, social, and psychological challenges that appear to translate into markedly reduced self-perceived health status. The alignment of HPN utility scores with those reported in advanced kidney disease, liver disease, and pancreatic dysfunction reinforces the argument for recognising HPN as a high-burden therapy requiring comprehensive, multidisciplinary support. Furthermore, these findings provide a strong foundation for informing economic evaluations, service planning, and resource allocation in HPN care, as they reflect a level of disability comparable to some of the most burdensome chronic illnesses.

The SF-36 scores in our study were consistently lower across all domains compared with those reported by Bluthner et al., who assessed QoL in 90 German patients receiving HPN (97). Differences in patient characteristics may partly explain this variation; our cohort was slightly older (mean age 57.7 vs 51.1 years), included a higher proportion of individuals with IBD (32.2% vs 18.9%) and motility disorders (11.8% vs 5.6%), and fewer with ischaemia (20.5% vs 32.3%). While PN regimens were largely similar, in the German study, all PN was individually compounded, whereas in our cohort, 16% received pre-prepared ‘off-the-shelf’ bags and 19% were on fluid-only prescriptions. Another contributing factor may be the duration on HPN, as Bluthner et al. only included patients who had been receiving HPN for at least six months. That being said, both the cross-sectional and longitudinal analyses in our study found little association between HPN duration and QoL outcomes.

Furthermore, the German study did not report a response rate, limiting the ability to assess the representativeness of their findings within the wider German IF population. In alignment

with findings from Bluthner's study, I observed that phase angle was positively associated with physical functioning, and that oral dietary energy intake (kcals/ day) was associated with better scores for social functioning, energy/ fatigue and RLPH. Bluthner et al categorised patients into two groups depending on whether they consumed oral food. In addition to improvements in the physical components of the SF-36 (general health, energy/ fatigue, bodily pain), they found that oral food intake was associated with better scores for mental health.

With regard to the HPN-QoL measure, our findings largely differ from those reported by Baxter et al (163) who conducted an international study on QoL in 699 HPN patients. They reported that QoL scores were significantly associated with HPN duration (improving with longer duration), underlying diagnosis (higher in patients with IBD and ischaemia), and living status (lower when living alone). In contrast, we found no association between living status and QoL across all domains, except for fatigue, where individuals living alone reported more severe symptoms. Likewise, QoL scores did not significantly differ across underlying conditions, apart from general health which was better in those with IBD compared with ischaemia, and GI symptoms, which were more favourable in those with ischaemia compared with IBD. Several factors may account for the differences observed between our findings and those reported by Baxter et al. While their study was international in scope and included a broader, potentially more heterogeneous population, our cohort was limited to three centres within the UK. Additionally, the larger sample size in the Baxter study may have afforded greater statistical power to detect associations that were not apparent in our smaller cohort. Differences in patient characteristics, such as the distribution of underlying diseases or duration on HPN, may also contribute to the contrasting outcomes. Although both cohorts appear similar in terms of gender distribution, living status, and underlying diagnosis, it is worth noting that the Baxter study had substantial missing data on key sociodemographic and clinical variables. For instance, underlying disease was unknown for 89 patients, and living status was unreported for 149 patients which may impact the reliability and comparability of their findings.

A noteworthy observation in this study is the difference in QoL results between participating centres with higher QoL among patients in Leeds and Nottingham compared with Newcastle.

These differences are unlikely to reflect genuine disparities in patient outcomes and are more plausibly attributed to nonresponse bias, particularly among participants from Leeds and Nottingham. Recruitment procedures differed between sites (see Methods, page 81), and as a member of the clinical team in Newcastle, my existing rapport with patients may have enhanced engagement and response rates at that site. Indeed, Newcastle achieved an 85% response rate, compared to just 34% in Leeds and 35% in Nottingham. It is therefore plausible that the data from Newcastle offer a more accurate reflection of HRQoL among individuals receiving HPN, whereas the lower response rates at other centres may be skewed toward healthier or more motivated participants. This highlights the potential for selection bias in QoL research, particularly in studies with low response rates. Notably, many published studies do not report response rates (97, 102, 163), however, where stated, they are typically in line with those seen in Leeds and Nottingham. For example, the largest longitudinal study to date reported a 35% response rate at baseline, with only 38% of those respondents completing follow-up (103).

6.4: Relationship between QoL and clinical factors

A key finding from our study is the strong association between body composition, measured by BIA, muscle function (as assessed by handgrip strength (HGS)), and QoL. Irrespective of the specific QoL instrument used, both body composition and muscle strength consistently correlated with multiple QoL domains, including energy/fatigue, physical functioning, general health, emotional and social functioning, emotional wellbeing, perceived pain, immobility, sleep disturbances, stoma management, VAS scores, and health utility. These findings suggest that diminished muscle strength and unfavourable body composition are important contributors to poorer QoL outcomes.

Despite this, there is limited published research specifically exploring the relationship between body composition, HGS, and QoL in patients receiving HPN. However, previous studies have demonstrated the clinical relevance of unfavourable body composition, such as low phase angle and reduced fat-free mass index, linking these markers to prolonged hospitalisation, higher hospital readmission rates, and increased mortality risk. For instance, Kohler et al. (164) reported that phase angle below normal predicted adverse outcomes, with low fat-free mass index acting as an independent risk factor for mortality. Similarly,

Stack et al. (165) examined the role of HGS in patients with IBD, finding a significant correlation between HGS and SF-36 fatigue scores. This highlights sarcopenia as a potentially important driver of fatigue and supports the use of HGS as a practical, objective tool for assessing muscle function and fatigue in IBD populations.

In contrast to these findings, Giesler et al (99) reported no association between HGS and the physical function or fatigue domains of the HPN-QoL instrument, possibly due to the small sample size used in their study (n = 31). While such studies emphasise the broader importance of muscle strength and body composition, our study is among the first to directly link these factors to QoL in patients on HPN. These findings highlight the potential for interventions aimed at improving muscle mass and muscle strength to enhance QoL in this population. Further research is needed to explore the role of HGS as a predictive marker for QoL outcomes in patients receiving HPN and to develop and test interventions designed to improve muscle mass and function.

This study revealed gender-specific differences in the association between HGS and domains such as immobility, fatigue, and sleep disturbances. HGS was significantly associated with reduced symptom burden in females, but not in males, suggesting that physical strength may play a more critical role in shaping functional and symptomatic QoL outcomes for women receiving HPN. These differences may reflect both physiological and psychosocial mechanisms. For example, lower baseline muscle strength in females may lead to more impactful variations in HGS, or women may be more acutely affected by functional limitations in how they experience fatigue and sleep disturbances. Additionally, gender-role expectations around independence and caregiving may influence how such symptoms are perceived and reported. Understanding these gender-specific associations is essential for developing targeted interventions aimed at improving muscle strength and, consequently, enhancing QoL, particularly among female patients. Research examining gender differences in the relationship between HGS and QoL is scarce, particularly in chronic conditions. In 2024, a study of HGS and QoL in Korean cancer patients reported findings similar to those in the present study. The authors reported that lower relative HGS was associated with decreased HRQoL in female patients, while no significant association was found in male patients (166).

This study collected comprehensive biochemical data via blood tests, revealing several significant associations between biomarker profiles and QoL in patients receiving HPN. The findings suggest that QoL in this population may be influenced by underlying biochemical and nutritional status. Among the profiles examined, iron-related biomarkers and liver function markers showed the most consistent associations across both generic and disease-specific QoL measures. For instance, higher levels of iron and transferrin saturation were associated with improved EQ-5D utility scores and reduced pain on the HPN-QoL, indicating that iron sufficiency may contribute to better overall vitality. In terms of liver function, two distinct principal components (PCs) emerged. PC1 (elevated ALP, ALT, GGT, and platelets with low bilirubin) was linked to reduced physical functioning on the SF-36 and a reduction in ambulatory pump use on the HPN-QoL, suggesting functional limitations related to liver dysfunction. PC2, dominated by bilirubin and ALT, was associated with poorer scores in body image, gastrointestinal symptoms, and pain domains, pointing to a broader psychosomatic impact of hepatic abnormalities.

These findings are consistent with those of Bluthner et al. (2020) (97), who reported that elevated liver enzymes, specifically ALT and GGT, were independently associated with lower scores in the physical components of the SF-36. These findings, and those from the current study, suggest that liver dysfunction adversely affects physical QoL in patients on HPN. By using PCA to identify clinically relevant biomarker patterns, the present study builds on this work and offers more nuanced insights into how specific liver profiles contribute not only to physical impairment but also to psychosocial and symptomatic burden. Together, these results emphasise the importance of early detection and proactive management of liver-related complications in HPN to mitigate their impact on patient well-being.

Kidney function markers were not significantly associated with EQ-5D scores but did show specific associations with several QoL domains, including pain, emotional wellbeing, fatigue, gastrointestinal symptoms, and stoma-related concerns. Notably, PC1 (comprising urea, creatinine, and potassium) was negatively associated with multiple symptom scores, potentially reflecting the influence of hydration status or renal clearance on symptom burden. There were few significant associations with micronutrients. However, PC1 (zinc,

folate, selenium, vitamin B12, and manganese) was positively associated with pain on the SF-36, while PC3 (vitamins A, D, and copper) was linked to greater perceived support from the nutrition team on the HPN-QoL, potentially reflecting increased clinical engagement in patients with nutritional deficiencies. Although these findings suggest that biochemical status may influence QoL in specific ways, direct comparisons with the existing literature are not possible due to a lack of published studies examining these relationships in the HPN population. Most current research does not include patient-reported QoL outcomes or does not assess renal and micronutrient markers in this context. Therefore, these results offer a novel contribution and emphasise the need for further investigation into the role of nutritional and biochemical profiles in shaping QoL for individuals receiving HPN. However, these findings should be interpreted with caution due to the limited sample size and missing data across some biomarker domains. Nonetheless, the use of PCA helped reduce collinearity and facilitated the identification of meaningful biochemical patterns, providing novel insights into the relationship between physiological status and QoL in this complex patient population. Collectively, these results highlight the value of integrating biochemical markers into holistic assessments of QoL. While the observed associations do not imply causality, they highlight potentially modifiable targets for intervention and monitoring. Importantly, the findings also suggest that biological measures interact with QoL in nuanced ways, varying by domain and context.

6.5: QoL in new HPN patients

This was the first study of its kind to investigate the QoL of patients newly established on HPN (≤6 months on HPN). Analysis revealed persistently low SF-36 scores across all domains at both baseline and follow-up, with minimal change over time. While a statistical difference was noted in the energy/fatigue domain, the median value remained unchanged, suggesting that the finding may reflect small individual improvements rather than a meaningful clinical shift. No notable changes were observed over time for EQ-5D or HPN-QoL scores, indicating that QoL remains substantially compromised in the early months of HPN, with limited short-term improvement across both generic and disease-specific measures.

When compared with existing HPN patients (>6 months on HPN), new patients reported poorer social functioning and greater limitations in physical roles at baseline. These findings

are perhaps unsurprising, as patients newly initiated on HPN are likely still adapting to the physical and psychosocial demands of treatment. At follow-up, differences between new and existing patients on the SF-36 were no longer apparent, suggesting potential early adaptation. However, baseline scores on the HPN-QoL highlighted additional challenges for new patients, including greater difficulty with eating and drinking, lower perceived benefit from ambulatory pump use, and overall lower quality of life ratings. These findings likely reflect the complex physical and emotional adjustment required during the initial stages of HPN, a period often marked by strict oral dietary restrictions to manage fluid balance and uncertainty about long-term outcomes. Together, these findings highlight the importance of tailored support for patients during the early phase of HPN, particularly with regard to nutritional adaptation and psychosocial adjustment. Targeted interventions aimed at supporting social reintegration and functional independence may be especially beneficial during this critical period.

6.6: Revisiting the hypotheses

At the outset of this thesis, six hypotheses were proposed (Chapter 1). Here, each is revisited in light of the findings, with reference to the relevant chapters and acknowledgment of data not yet analysed but collected for future work.

1. There will be significant variability between clinicians in the assessment and management of QoL. This hypothesis was supported by the findings of Chapter 3, which demonstrated marked heterogeneity in how QoL is assessed and applied in clinical practice. Responses from healthcare professionals highlighted inconsistent use of validated tools, variation in whether and how QoL results are integrated into care planning, and scepticism regarding the utility of existing measures. These findings confirm that variability remains a significant barrier to standardised practice.

2. QoL scores will improve during the first year of HPN therapy and plateau thereafter. This hypothesis was not supported. Longitudinal analyses in Chapters 4–6 found no consistent improvement in QoL over 12 months of HPN therapy. In several SF-36 domains, floor effects were observed, indicating persistent impairments in physical and emotional role functioning that may limit the ability of this tool to

detect change. The findings therefore do not support the expectation of initial improvement followed by plateau.

3. QoL scores will be influenced by the underlying disease, gastrointestinal anatomy, and HPN regime. This hypothesis was also not supported. Analyses in Chapters 4–6 found no strong or consistent associations between these clinical characteristics and QoL outcomes across SF-36, EQ-5D, or HPN-QoL domains. While some differences were observed in subgroup comparisons, these were limited in scope and did not demonstrate a clear pattern.

4. QoL scores will be influenced adversely by co-morbidities, for example, the presence of intestinal failure–associated liver disease (IFALD). This hypothesis received partial support. Subgroup analyses suggested that certain liver function profiles were associated with lower QoL, consistent with the notion that IFALD and other comorbidities may exacerbate symptom burden and functional impairment. However, the evidence was limited and further investigation is required to substantiate these findings.

5 & 6. Parenteral nutrition causes an upregulation of de novo lipogenesis (DNL), and, parenteral nutrition causes alterations in phospholipid metabolism with reductions in plasma free choline. These hypotheses were not directly tested within this PhD, but they were developed to extend the mechanistic insights gained in Chapter 2. Both hypotheses will be addressed using the biological samples collected prospectively as part of the study protocol outlined in Chapter 4. This will allow investigation of whether PN induces upregulation of de novo lipogenesis and whether it alters phospholipid metabolism with reductions in plasma free choline. While beyond the scope of the current thesis, these hypotheses provide an important translational bridge between the biochemical findings in Chapter 2 and the clinical outcomes in Chapters 3–6. They will form the foundation of future postdoctoral work, enabling deeper mechanistic understanding of how HPN may influence metabolic pathways and, ultimately, patient QoL.

In summary, hypotheses 1 and 4 received partial or full support, while hypotheses 2 and 3 were not supported by the data. Hypotheses 5 and 6 remain to be tested, with appropriate

samples collected for future investigation. Together, this iterative evaluation underscores both the contributions and limitations of the current work and sets a clear trajectory for ongoing research.

6.7: Strengths and weaknesses

A strength of the research discussed in this chapter is the multidimensional assessment of QoL, allowing for a comprehensive evaluation of QoL across multiple relevant domains. While the SF-36 and EQ-5D captured overall health status, the HPN-QoL offered more sensitive measurement of factors directly relevant to patients receiving HPN, such as fatigue, infusion-related burden, and body image concerns. This dual approach enhanced the clinical and interpretive value of the findings. Similarly, strong recruitment and retention enabled development of the largest known longitudinal cohort of HPN patients assessed with the combined use of SF-36, HPN-QoL, and EQ-5D instruments. This enhances the reliability of the results, allows for meaningful subgroup analyses, and improves the generalisability of findings to similar patient populations. It also provides a valuable contribution to the limited longitudinal data available in this complex and under-researched group.

Another strength is the inclusion of objective measures of physical function such as HGS and body composition which adds clinical relevance and strengthens the interpretation of associations with QoL outcomes. Similarly, sociodemographic variables such as employment and education were considered as were blood biomarker data, enabling identification of patterns while managing collinearity which is an advanced analytical approach that is rarely seen in HPN research.

Furthermore, the study population was drawn from three UK centres with a good geographical spread, enhancing generalisability of findings to other NHS Trusts. Lastly, the investigation of gender differences uncovered important sex-specific differences in the relationship between HGS and QoL, an unexplored area in the intestinal failure and HPN populations.

This study also has important limitations. QoL was assessed at two time points only (baseline and 12 months), which allowed for evaluation of overall change over time but limited the ability to explore intermediate trends, short-term fluctuations, or the timing of change. This

design may have missed more nuanced patterns of improvement or decline and constrained the modelling of longitudinal trajectories. Similarly, demographic and socioeconomic variables were collected at baseline only, under the assumption that key characteristics such as age, sex, education, and employment status would remain relatively stable over the course of the study. However, this approach does not fully capture dynamic socioeconomic changes (e.g., job loss, income shifts) that could influence HRQoL, potentially leading to residual confounding or exposure misclassification.

There was also variability in the number of variables collected per participant. While some individuals had complete datasets including biochemical, anthropometric, and clinical data, others lacked one or more data types due to differences in routine clinical assessments or participant burden. Missing data were not imputed, and analyses were conducted using available case data only. This approach may have reduced statistical power and introduced bias if the data were not missing completely at random. Consequently, some multivariable models may be based on smaller, potentially non-representative subsamples, limiting the generalisability of specific findings. The impact of missing data was particularly relevant for analyses involving biochemical and anthropometric predictors of QoL. For example, some domains such as physical functioning, role limitations, or fatigue were hypothesised to be associated with markers such as HGS, skeletal muscle mass (SMM) or micronutrient status. However, due to incomplete data, these predictors could not be included in all multivariable models. As a result, the strength or presence of associations in certain domains, particularly those reflecting physical or nutritional status, may have been underestimated or not detected. This limits the ability to draw definitive conclusions about the role of specific physiological factors in shaping domain-specific QoL outcomes.

This study explored the impact of liver dysfunction on QoL using PCA of liver-related biomarkers, identifying distinct biochemical profiles that were significantly associated with both physical and psychosocial QoL domains. While this approach provided meaningful insights, the absence of consistent formal diagnoses of liver disease or hepatic complications limited the ability to interpret these findings in the context of clinical liver pathology. The incomplete availability of liver function tests also reduced the sample size for some models, highlighting the need for more comprehensive clinical data in future research.

This study did not compare QoL scores to UK general population norms, as reference data for instruments such as the SF-36 and EQ-5D are already available in the literature (97, 161, 167). Instead, the focus was placed on within-cohort variability and the associations between clinical, nutritional, and biochemical factors and patient-reported outcomes. While normative comparisons can be useful for contextualising absolute scores, this study aimed to explore potential drivers of QoL variation specifically within the HPN population.
Lastly, my dual role as both researcher and member of the clinical care team, particularly at the Newcastle centre, may have influenced participant responses and study dynamics. While this facilitated recruitment and improved questionnaire return rates, it may also have introduced response bias. Patients may have felt inclined to provide more favourable responses due to familiarity or perceived expectations, and some may have felt a sense of obligation to participate. Additionally, my direct access to patients in hospital or clinic settings may have led to over-recruitment of more engaged or stable individuals, compared to the postal recruitment methods used at the other sites (Leeds and Nottingham). These factors may affect the representativeness and generalisability of findings.

6.8: Unanswered questions and future research

While this study provides valuable insights into the complex interplay between clinical, nutritional, and psychosocial factors influencing QoL in HPN patients, several important questions remain unanswered. The cross-sectional and observational nature of many analyses limits the ability to draw causal inferences. For instance, it remains unclear whether improvements in nutritional biomarkers or liver function directly lead to better QoL, or whether these associations reflect underlying health status or reverse causality. Similarly, the consistently strong associations between employment, education, and QoL raise questions about directionality, whether social participation enhances well-being, or whether healthier individuals are more likely to remain employed or pursue further education.

Another area requiring further exploration is the observed gender-specific differences in the association between physical strength and QoL, particularly the stronger relationship between HGS and symptom burden in women. These findings suggest potential physiological or psychosocial differences that warrant dedicated investigation. Furthermore, while this

study used PCA to identify liver function patterns associated with QoL outcomes, the lack of formal diagnoses for liver disease or PN-associated hepatic complications limited interpretation. Standardised diagnostic data would strengthen future analyses of hepatic burden in this population.

Future research should build on these findings through larger, multicentre longitudinal studies incorporating multiple timepoints and standardised clinical assessments. Qualitative or mixed-methods approaches could further enrich understanding by capturing the lived experience of patients adjusting to HPN, particularly in the early stages of treatment. Interventional studies targeting modifiable factors, such as muscle strength, nutritional deficiencies, or psychosocial support may also help clarify causal pathways and guide multidisciplinary care strategies. Complementary strategies to enhance muscle mass and function through tailored physical activity programmes, such as physiotherapy or resistance training, could support improvements in fatigue, mobility, and independence.

In addition, future work will test two mechanistic hypotheses arising from this programme of research. First, that parenteral nutrition causes an upregulation of de novo lipogenesis (DNL), contributing to hepatic lipid accumulation and dysfunction. Second, that parenteral nutrition alters phospholipid metabolism, leading to reductions in plasma free choline, with potential implications for liver health and systemic inflammation. These hypotheses will be evaluated in a subsequent postdoctoral study using advanced metabolic and lipidomic techniques. Together, these investigations will enhance our understanding of the systemic effects of parenteral nutrition and their impact on patient well-being.

6.9: Implications for clinicians and policymakers

The findings of this study have several important implications for both health policymakers and clinicians involved in the care of patients receiving HPN.

6.9.1: For Clinicians

- **Routine use of PROMs:** The strong associations between clinical, nutritional, and psychosocial variables and QoL outcomes support the integration of routine PROMs into clinical practice. PROMs can help identify unmet needs, track changes over time, and guide more person-centred care.

- **Multidisciplinary care planning:** The observed impacts of liver function, micronutrient status, and physical strength on QoL highlight the need for coordinated, multidisciplinary care that includes dietitians, pharmacists, psychologists, physiotherapists, gastroenterologists and liver specialists.
- **Tailored support for new patients**: Newly initiated HPN patients reported lower QoL and more difficulty adjusting to key lifestyle factors. This underlines the importance of early-stage interventions that focus on education, psychosocial support, and dietary adaptation during the critical transition to care at home.
- **Gender-specific considerations**: The finding that HGS was more strongly associated with QoL outcomes in women suggests the need for gender-sensitive assessments and interventions, particularly around physical rehabilitation and symptom management.
- **Standardising QoL measurement in HPN**: Evidence from this thesis shows that EQ-5D-5L yields results comparable to SF-36 and HPN-QoL while being faster to complete and preferred by patients**.** We recommend the EQ-5D-5L as the core QoL measure for routine national IF practice**,** with disease-specific instruments (e.g., HPN-QoL/PNIQ) used where additional granularity is needed (research, complex case review).

6.9.2: For Policymakers

- **Commissioning of holistic HPN services**: The findings reinforce the need to design and fund HPN services that go beyond basic provision of nutrition support. Services should integrate psychosocial care, functional rehabilitation, and ongoing monitoring of clinical and nutritional status.
- **Prioritising integrated, multidisciplinary care:** The associations between nutritional, physical, and biochemical factors and QoL outcomes suggest that comprehensive, multidisciplinary care, including dietetics, physiotherapy, and psychosocial support, is essential. Policy-level support for integrated HPN services may improve patient outcomes beyond clinical metrics.
- **Resource allocation based on patient-reported outcomes:** As QoL scores can reveal hidden burdens not captured by lab values or clinical status, funding decisions should

reflect the value of PROMs in assessing treatment impact and guiding personalised care planning.

- **Addressing centre-level inequalities:** Differences in recruitment and response rates across centres suggest variability in patient engagement or access. This may reflect broader issues in service delivery, pointing to a need for policy interventions to ensure more equitable support and follow-up across regions.
- **Targeted interventions for physical and psychosocial wellbeing:** Domains such as physical functioning, fatigue, pain, and physical role limitations were notably impacted. These findings support investment in targeted rehabilitation and mental health services for the HPN population, which may be currently under-resourced.
- **Data infrastructure:** Improved systems for routinely collecting and linking PROMs with clinical data would enhance service evaluation, enable benchmarking, and support research on outcomes that matter most to patients.
- **Workforce and training investment:** Multidisciplinary HPN teams should be adequately resourced and trained to deliver comprehensive care, particularly in recognising and responding to patient-reported concerns.
- **Support for employment and social participation:** Given the strong relationship between employment and QoL, policy efforts should focus on professional rehabilitation, flexible work arrangements, and social integration strategies for HPN recipients.

6.10: Conclusion

This thesis presents a comprehensive, multi-method investigation into the QoL of adults receiving HPN, combining a systematic review, a national survey of HCPs, and a longitudinal patient cohort study. Together, these studies offer new insights into both the current evidence base and the real-world implementation of QoL assessment and support in HPN care.

The systematic review identified a lack of high-quality evidence to guide macro- and micronutrient composition in HPN solutions, with few studies evaluating patient-reported outcomes. While some lipid emulsions, particularly those containing fish oil, showed potential clinical benefits, their impact on patient QoL remains largely unmeasured. This absence of patient-centred research highlights a major gap in the existing literature and

reinforces the importance of outcome measures that reflect the lived experience of those on HPN.

The national survey revealed that although HCPs widely value the concept of QoL assessment, its implementation remains inconsistent. Many clinicians reported rarely using QoL tools in practice, citing barriers such as time constraints, tool limitations, and a lack of training. Notably, there was a clear call for more patient-informed measures and greater integration of PROMs into routine care. These findings highlight a disconnect between clinical recognition of QoL's importance and its actual use to guide decision-making.

Building on these gaps, the longitudinal cohort study provided the most detailed evaluation of QoL in the HPN population to date. Using both generic (EQ-5D, SF-36) and disease-specific (HPN-QoL) instruments, it identified persistent impairments in physical functioning, fatigue, pain, and role limitations. Importantly, the study demonstrated that QoL is not simply a function of diagnosis, but is closely associated with nutritional status, body composition, physical strength, and sociodemographic factors such as employment and education. These findings suggest that routine QoL assessment can offer actionable insights into patient wellbeing and identify modifiable contributors to poor outcomes.

Taken together, the three studies reinforce a central message: that QoL in HPN is shaped by a complex and interrelated set of clinical, nutritional, functional, and psychosocial factors. They highlight the urgent need for integrated, multidisciplinary approaches to care that place patient-reported outcomes at the heart of decision-making. For clinicians, this means routine use of validated PROMs and targeted support for physical rehabilitation, nutritional optimisation, and psychosocial wellbeing. For policymakers, it means investing in services that are not only clinically effective but also responsive to what matters most to patients - function, autonomy, and QoL.

This thesis thus contributes meaningful evidence to an under-researched field, offering both a critique of the current evidence base and a practical roadmap for improving care delivery and outcomes for adults living with HPN.

Appendices

Appendix A: List of search terms for all databases

Table 1: Medline search terms

"Quality of Life"/
exp Patient Satisfaction/
patient reported outcome measures/
clinical outcomes.mp.
clinical markers.mp.
Biomarkers/
biochemical markers.mp.
Nutritional Status/
weight.mp.
"body weights and measures"/ or exp body fat distribution/ or body mass index/ or exp body size/ or body surface area/ or skinfold thickness/ or waist-hip ratio/
Sarcopenia/
liver function.mp.
intestinal failure associated liver disease.mp.
IFALD.mp.
parenteral nutrition associated liver disease.mp.
PNALD.mp.
laboratory markers.mp.
(parenteral nutrition adj4 (home or nursing care)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
HPN.mp.
parenteral feed*.mp.
(Parenteral adj4 (All-in-one multi-chamber bags or solution*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
intravenous feed*.mp.
parenteral nutrition solutions/
18 or 19 or 20 or 21 or 22 or 23
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
24 and 25

limit 26 to (english language and humans)

Table 2: Embase search terms

"Quality of Life"/
exp Patient Satisfaction/
patient reported outcome measures/
clinical outcomes.mp.
clinical markers.mp.
Biomarkers/
biochemical markers.mp.
Nutritional Status/
weight.mp.
"body weights and measures"/ or exp body fat distribution/ or body mass index/ or exp body size/ or body surface area/ or skinfold thickness/ or waist-hip ratio/
Sarcopenia/
liver function.mp.
intestinal failure associated liver disease.mp.
IFALD.mp.
parenteral nutrition associated liver disease.mp.
PNALD.mp.
laboratory markers.mp.
(parenteral nutrition adj4 (home or nursing care)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
HPN.mp.
parenteral feed*.mp.
(Parenteral adj4 (All-in-one multi-chamber bags or solution*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
intravenous feed*.mp.
parenteral nutrition solutions/
18 or 19 or 20 or 21 or 22 or 23
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
24 and 25
limit 26 to (english language and humans)

Table 3: Scopus search terms

(TITLE-ABS ("parenteral nutrition") OR TITLE-ABS ("intravenous nutrition") OR TITLE-ABS (hp n) OR TITLE-ABS (tpn)) AND TITLE-ABS ("quality of life") O R TITLE-ABS ("patient satisfaction") OR TITLE-ABS ("patient re ported outcome") OR TITLE-AB S ("clinical outcome*") OR TIT LE-ABS ("clinical marker*") OR TITLE-ABS (biomarker*) OR TI TLE-ABS ("nutritional status") OR TITLE-ABS (weight) OR TI TLE-ABS (sarcopenia) OR TITL E-ABS ("liver function") OR TIT LE-ABS ("intestinal failure associated liver disease") OR TITLE-A BS (ifald) OR TITLE-ABS (pnald) OR TITLE-ABS ("parenteral nutrition associated liver disease") OR TITLE-ABS ("laboratory markers") AND (LIMIT-TO (DOC TYPE , "ar")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Humans"))

Table 4: Web of Science search terms

(TS="parenteral nutrition" OR TS="home parenteral nutrition" OR TS="total parenteral nutrition" OR TS="intravenous nutrition" OR TS="HPN" TS="TPN") AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
(AK="quality of life" OR AK="patient satisfaction" OR AK="patient reported outcome*" OR AK="clinical outcome*" OR AK="clinical marker*" AK="biomarker*" OR AK="Nutritional status" OR AK="weight" OR AK="sarcopenia" OR AK="liver function" OR AK="intestinal failure associated liver disease" OR AK="IFALD" OR AK="parenteral nutrition associated liver disease" OR AK="PNALD" OR AK="laboratory marker*") AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
#2 AND #1 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years

Appendix B: Data extraction form

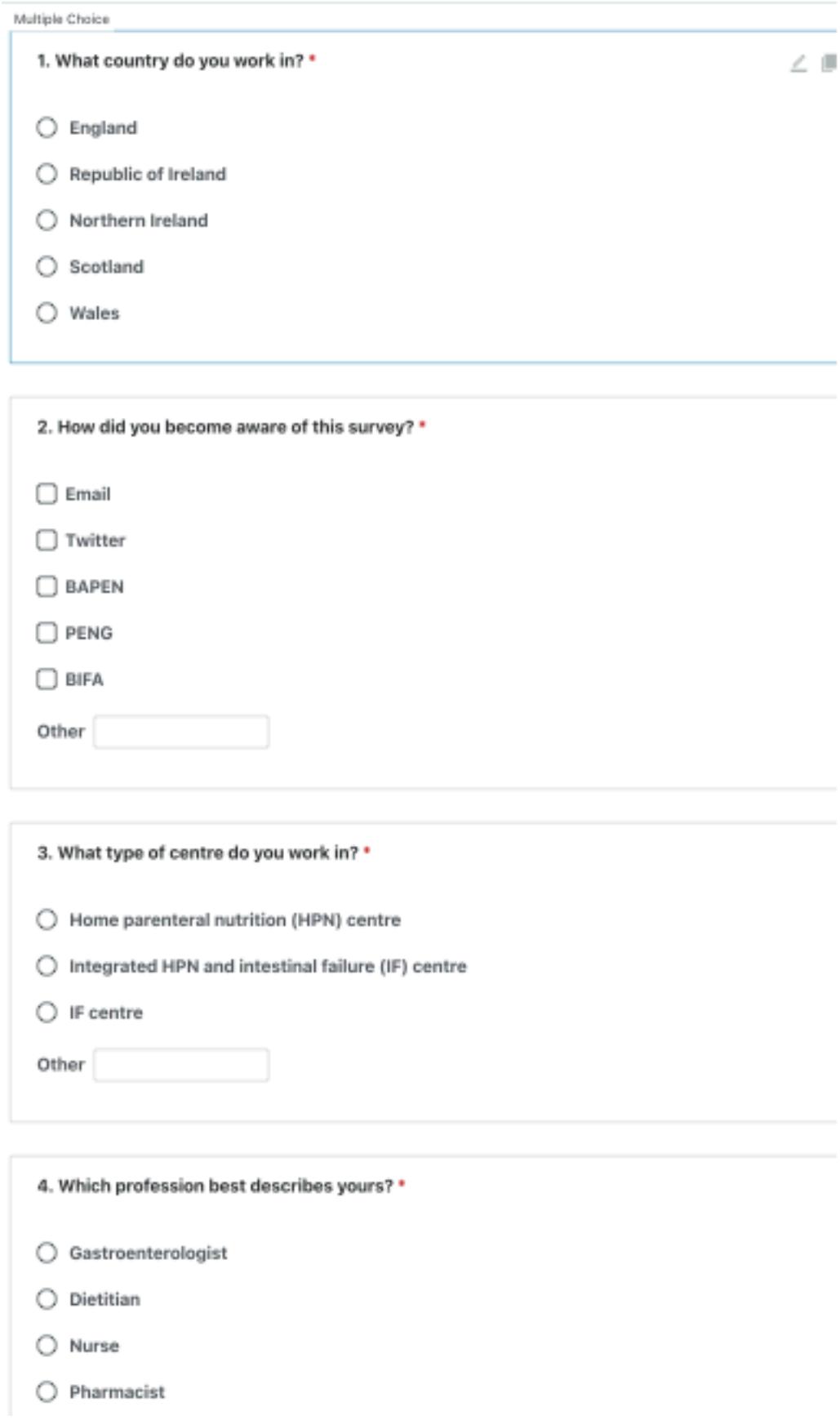
Study title	
Main author, year	
Study ID	
Country	
Study funding source/ conflicts of interest	

Study Characteristics	**Eligibility criteria**	Yes	No	Unclear	**Location in text or source**
Type of study	Controlled Trial	☐	☐	☐	
	Prospective cohort	☐	☐	☐	
	Cross-sectional	☐	☐	☐	
Participants		☐	☐	☐	
Intervention feed		☐	☐	☐	
Comparator feed(s)		☐	☐	☐	
Outcomes		☐	☐	☐	
INCLUDE X☐			**EXCLUDE** ☐		
Reason for exclusion					
Methods	**Description**				**Location in text or source**
Aim of study					
Design					
Start date					
End date					
Study duration					
Notes:					
Population/ setting	**Description**				**Location in text or source**
Population description					
Setting/ location/ country					
Inclusion criteria					
Exclusion criteria					
Method of recruitment of participants					
Total no. participants					
Baseline imbalances					
Withdrawals/ exclusions					
Age: Mean (SEM)					
Sex					

Race/Ethnicity		
Underlying diagnosis		
Co-morbidities		
Other relevant sociodemographics		
Subgroups measure		
Subgroups reported		
Notes:		
Intervention/ comparison	**Description**	**Location in text or source**
Group name		
No. Randomised/ included		
Description		
Duration of treatment period Mean (SEM)		
Timing		
Delivery		
Providers		
Co-interventions		
Economic information		
Compliance		
Notes:		
Intervention/ comparison	**Description**	**Location in text or source**
Group name		
No. Randomised/ included		
Description		
Duration of treatment period Mean (SEM)		
Timing		
Delivery		
Providers		
Co-interventions		
Economic information		

Compliance		
Notes:		
Outcome:	**Description**	**Location in text or source**
Time points collected/ reported		
Results		
Is outcome/tool validated?	☐ Yes ☐ No ☐ Unclear	
Imputation of missing data & reason		
Statistics/ appropriateness		
Notes:		
Outcome:	**Description**	**Location in text or source**
Time points collected/ reported		
Results		
Is outcome/tool validated?	☐ Yes ☐ No ☐ Unclear	
Imputation of missing data & reason		
Statistics/ appropriateness		
Notes:		

Appendix C: E-survey instrument



Multiple Choice

1. What country do you work in? *

- ○ England
- ○ Republic of Ireland
- ○ Northern Ireland
- ○ Scotland
- ○ Wales

2. How did you become aware of this survey? *

- ☐ Email
- ☐ Twitter
- ☐ BAPEN
- ☐ PENG
- ☐ BIFA

Other

3. What type of centre do you work in? *

- ○ Home parenteral nutrition (HPN) centre
- ○ Integrated HPN and intestinal failure (IF) centre
- ○ IF centre

Other

4. Which profession best describes yours? *

- ○ Gastroenterologist
- ○ Dietitian
- ○ Nurse
- ○ Pharmacist

Other

5. How many years have you worked with HPN or intestinal failure patients?

- ◯ < 5 years
- ◯ 5-10 years
- ◯ 10-15 years
- ◯ 15-20 years
- ◯ > 20 years

6. Which of the following quality of life (QoL) tools are you familiar with? *

- ☐ EQ-5D
- ☐ HPN-QoL
- ☐ SF-36
- ☐ New quality of life questionnaire (New QoL)
- ☐ Parenteral nutrition impact questionnaire (PNIQ)
- ☐ Home parenteral nutrition patient reported outcome questionnaire (HPN-PROQ)
- ☐ Short bowel syndrome-QoL (SBS-QoL)
- ☐ None of the above

Other

7. How often is the QoL of HPN patients measured in your department? *

- ◯ Never, move to question 12
- ◯ Bi-annually
- ◯ Annually
- ◯ Every 2 years
- ◯ Every 3 years
- ◯ Less than every 3 years

Other

Comments:

8. Which of the following tools are used to measure QoL in your department? (Tick all that apply

- [ ] EQ-5D
- [ ] HPN-QoL
- [ ] SF-36
- [ ] New QoL
- [ ] PNIQ
- [ ] HPN-PROQ
- [ ] SBS-QoL

Other

Comments:

9. What is the reason the above QoL measure(s) is/are used? (Tick all that apply)

- [ ] Established unit of practice
- [ ] Ease of use
- [ ] Patient preference
- [ ] Familiarity

Other

Comments:

10. How are the results of QoL assessments in your department shared? (Tick all that apply)

- [ ] With patients
- [ ] With the wider clinical team
- [ ] In journals
- [ ] At conferences
- [ ] None

Other

Comments:

11. QoL is measured in your department: (tick all that apply)

- [ ] For research purposes
- [ ] For service evaluation
- [ ] As part of routine clinical care
- [ ] To inform decision making
- [ ] To identify patient preferences and help clinicians to make informed decisions
- [ ] As a means to improve patient-provider communication and shared decision making

Other

Comments:

12. How would you rate your knowledge of the currently available literature on QoL in HPN? *

- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor
- ◯ Very poor

Comments:

13. Intestinal Failure Associated Liver Disease (IFALD) is a contributor to poor QoL? *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

14. Sarcopenia is a contributor to poor QoL? *

- ◯ Strongly agree
- ◯ Agree

- ◯ Disagree
- ◯ Strongly disagree

Comments:

15. The gut microbiota plays a role in QoL *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

16. Recurrent sepsis is a contributor to poor QoL *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

17. QoL should influence therapeutic strategies *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

18. QoL should influence the decision to commence HPN *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

19. QoL should influence the decision to commence palliative HPN *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

20. The measurement of QoL in HPN patients is useful *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

21. More expensive treatment options should be considered if they improve QoL *

- ◯ Strongly agree
- ◯ Agree

- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

22. The idea that QoL can be measured is a flawed one, whose variables are very difficult for the clinician to analyse, to control, and therefore to integrate into clinical decision making *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

Comments:

23. QoL assessments facilitate patient-clinician communication *

- ◯ Strongly agree
- ◯ Agree
- ◯ Undecided
- ◯ Disagree
- ◯ Strongly disagree

24. Who should be responsible for measuring QoL? (Tick all that apply) *

- [ ] Physicians
- [ ] Allied health professionals
- [ ] Nurses

Other

Comments:

Please leave any additional comments here

Thank you very much for taking the time to complete my survey.

Please enter your question here

Appendix D: Table of free text comments from the survey

The measurement of QoL is useful: 1. But-we use tools that we HCP have deemed suitable; in the age of PPI (patient and public involvement) I would like to see standardised rigorous tools that are PATIENT made. Why do we think we know what is a good reflector of QoL when we (usually) haven't actually lived the life?' 2. Does it (QoL) need formal measurement on a scale? or are these decisions part of holistic care between the pt (patient) and their clinician/s? 3. None of the tools really work for me. Why does the medical profession persist on translating narrative into numbers? Much better to evaluate the QOL by talking to your patients....as they can interpret the decisions required in the context of their quality of life!
QoL assessments facilitate patient-clinician communication: 1. It's not the measurement that makes the difference – it's the patient feeling that they can express their concerns/ priorities etc to the team looking after them 2. This can be more down to the individual clinician. One that is very well versed in the care of these patients and is a natural communicator this will have little contribution but one that is new to the area or not naturally a communicator will find it helpful to construct their conversations with the families. 3. They can do where patients note things that they haven't told the clinician. But this is just making up for poor communication skills by the clinician in many cases. 4. can assess QOL without formal scoring system with detailed history however I appreciate that scoring systems quantify data and make future comparisons easier 5. gives a starting place BUT we needs standards of care to make the discussion of the QoL measure a routine one 6. If used appropriately 7.

QoL should influence the decision to commence HPN/ therapeutic strategies:

1. Baseline QOL should not influence as difficult to assess potential for QOL improvement at time commencing HPN but potential to improve QOL should be considered and be patient focussed - assumption should be that patient engaged with seeking improvement in QOL that this can be achieved
2. yes, though the decision whether to resect ischaemic gut at 3am is a difficult one and QoL almost impossible to assess in the emergency situation
3. the effect of managing HPN must be considered in QoL
4. Difficult. Very heterogeneous population and decisions may change. I remember a young girl with a large desmoid and FAP who had infarcted her small intestine and told her surgeon that if he had to take out all her gut and leave her on PN for the rest of her life, she would rather die. He opened and closed her abdomen as per her wishes, but as soon as she woke up from the GA she told him that she had no choice and he had to take her straight back to theatre to do the enterectomy. The picture she gave me of her diving into the sea off Corfu three years later is one of my most treasured memories of any of my IF patients.
5. to a degree with detailed discussion with patient and MDT
6. Dependent on patient population. Evidence from previous studies suggest that there is at least an initial improvement in QoL in patients with apparent gut dysmotility although there is also evidence of increased risk of line infections in this patient cohort. I suspect longer time scales may show a reduction in QoL over time
7. Always, if HPN could increase QoL then why not?
8. For type 2/3 patients I think it is more difficult as their acute QoL after a catastrophic event may not reflect what their long term QoL could be
9. We do not use QOL enough in our decision making. Many people with IF have an appalling QOL and longevity is not the most important factor for many!
10. I don't think QoL should be the single factor in decision making, but should be considered as a factor alongside other medical decisions
11. But not if risks>benefits i.e. not purely for visceral pain, unless BMI leaves us with little choice

12. For palliative patients I absolutely agree that QoL is a strong influencer For type 2/3 patients I think it is more difficult as their acute QoL after a catastrophic event may not reflect what their long term QoL could be
13. Shared decision making key. Potential to improve QOL needs to be considered vs burden of treatment
14. Who decides quality of life? Performance status much more important and relevant...
15. as above- with detailed discussion of risks and benefits and MDT discussion
16. Important to very carefully weigh up the significant risks as well as benefits.2
17. Cost should not come in to it but in reality it does
18. I.e. when deciding to commence palliative PN
19. Should be part of the discussion regarding risk and benefits of treatment
20. the effect of managing HPN must be considered in palliative pts as well as the management of expectations / outcomes

Recurrent sepsis is a contributor to poor QoL

1. The physical effects of sepsis impact massively on QoL. For example, enjoyment of daily activities, independence with tasks, time with family, ability to work and finances.
2. Recurrent admissions associated with this and associated morbidity

The gut microbiota plays a role in QoL

1. For a minority of patients i.e. those with SIBO.
2. Not sure that there is much evidence to support this statement
May have indirect impact by influencing bacterial overgrowth and stomal output
3. Insufficient evidence
4. I am not aware of any work in this area
5. Not enough knowledge to answer accurately

Sarcopenia is a contributor to poor QoL:

1. Poor function expected with sarcopenia and therefore impact on QOL
2. I am not sure that sarcopenia has been measured in relation to QoL but would be interesting to see if is a contributing factor
3. Not aware of it

Intestinal Failure Associated Liver Disease (IFALD) is a contributor to poor QoL:

1. Depends on patient, their perception/approach and if treatable.
2. IFALD per se unlikely to be. More likely to be the factors that predispose to IFALD including ultrashort bowel necessitating multiple day infusions etc.
IFALD itself I would expect to be 'asymptomatic' until advanced state
3. Given that many patients have cirrhosis without their doctors or them even being aware of it, then clearly not - until they know they have it
4. Have only seen very few patients with IFALD

The idea of QoL is a flawed one, whose variables are very difficult for the clinician to analyse, to control, and therefore to integrate into clinical decision making:

1. Agree it's imperfect but doesn't mean it lacks utility if properly understood and contextualised in terms of its limitations
2. QoL tools are the patients interpretation of their experience therefor cannot be flawed
3. Quality of life is a subjective one and this can differ depending on many factors which include parents/carers, prognosis for the patient, class back ground and the families quality of life pre the HPN. We are professionals need to not let our own bias cloud our view of quality of life and impose this on others. There are of course more obvious things which will have a huge impact on QoL
4. Scoring systems turn narrative (and all its subtleties) into numbers that are then translated back for interpretation - much is lost in the process. There are some benefits for clinical research (but in a very coarse way), but if numerical scoring systems are used to try to direct complex decision making - sorry, health professionals and patients are much better off without them

5. It may be difficult to measure and variable depending on the specific feelings of the patient on the day QoL is measured, however, it is important to assess QoL and integrate this into the care we provide.
6. Difficult to assess accurately, hard not to let personal opinions factor in decision making/assessments
7. Some aspects are very difficult to analysis or control and difficult to unpick issues related solely to HPN and to other factors such as reason for intestinal failure but the tools do help to ensure we as clinicians are consistency considering the impact of key issues for patients
8. Does anyone need to measure QOL? All team members should consider these issues when dealing with pt
9. QoL has so many different meanings to different people. Thus, measuring it and then generalising the findings is difficult.

Additional comments:

1. Whilst QoL is an important measurement and consideration in a patient's wellbeing it also needs to be balanced with the risk of interventions eg I don't believe HPN should be a lifestyle choice. However, I acknowledge that it is very difficult for clinicians/HCPs to "imagine" being in a patient's shoes, particularly with intractable symptoms or chronic pain. QoL measurements can help to give insight into this.
2. REALLY looking forward to seeing this research written up and published. Thank you for doing it
3. Very interesting
4. Not currently used in my place of work. I have used them previously and were very useful when I worked within rheumatology. However, if a Pt has a poor QoL due to IF there are very few tools available to us to help improve that.
5. We should probably use a formal method of assessing qol . thanks for making me think about this more

Appendix E: REC approval

Mrs C Kirk
Senior Dietitian/ Training Fellow Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk
The Newcastle upon Tyne Hospitals NHS Foundation
Trust
Nutrition and Dietetics
Freeman Hospital
NE7 7DN

25 October 2021

Dear Mrs Kirk

HRA and Health and Care

Study title:	**A longitudinal study of factors that impact on the quality of life of intestinal failure patients treated with home parenteral nutrition**
IRAS project ID:	**297366**
Protocol number:	**9816**
REC reference:	**21/SC/0316**
Sponsor	**The Newcastle Joint Research Office**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **297366**. Please quote this on all correspondence.

Yours sincerely,
Natasha Bridgeman

Approvals Specialist

Email: approvals@hra.nhs.uk

Copy to: Mr Aaron Jackson, The Newcastle Joint Research Office **List of Documents**

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
IRAS Application Form [IRAS_Form_31082021]		31 August 2021
Letter from funder [Letter from funder]	1	09 April 2021
Organisation Information Document [Organisation Information Document]	1	20 September 2021
Other [Good Clinical Practice]	1	23 June 2021

Other [Responsibilities of investigators form]	1	23 June 2021
Other [Site agreement]	1	06 October 2021
Other [Site agreement]	1	06 October 2021
Participant consent form [Consent form]	1	23 June 2021
Participant consent form [Consent form]	1	06 October 2021
Participant information sheet (PIS) [PIS]	1	23 June 2021
Participant information sheet (PIS) [Participant information document]	2	06 October 2021
Participant information sheet (PIS) [Participant information document]	2	06 October 2021
Referee's report or other scientific critique report [Funder feedback]	1	01 January 2021
Research protocol or project proposal [Research protocol]	1	26 May 2021
Schedule of Events or SoECAT [SoECAT]	1	20 October 2020
Summary CV for Chief Investigator (CI) [Chief Investigator CV]	1	26 May 2021
Validated questionnaire [HPN QOL]	1	23 June 2021
Validated questionnaire [EQ-5D-5L]	1	20 September 2021
Validated questionnaire [SF 36]	1	20 September 2021

Appendix F: Invitation to participate letter – group 1

THE BIOLOGICAL DETERMINANTS OF QUALITY OF LIFE IN HOME PARENTERAL NUTRITION
PARTICIPANT INFORMATION SHEET (Group 1)

INVITATION TO PARTICIPATE IN A RESEARCH PROJECT

We would like to invite you to take part in a research study which is a collaboration between Newcastle University, Newcastle Hospitals, Leeds Teaching Hospitals and Southampton General Hospital. Before you decide whether to volunteer or not it is important for you to understand why the research is being carried out and what it involves. Please take the time to read the enclosed information carefully and do not hesitate to contact us if there is anything you are not sure about, or if you would like more information.
The study is funded by the National Institute of Health Research (NIHR) and *has been approved by the XXXX Research Ethics Committee*

The Principle Investigator is **Mrs Colette Kirk, Senior Dietitian and PhD student**
The research team also consists of:

Nick Thompson Consultant Gastroenterologist Freeman Hospital	**Dave Jones** Professor of Liver Immunology Newcastle University	**John Mathers** Professor of Human Nutrition Newcastle University
Mark Pearce Professor in Applied Epidemiology Newcastle University	**Peter Mooney** Consultant Gastroenterologist St James University Hospital	**Trevor Smith** Consultant Gastroenterologist University Hospital Southampton NHS Foundation Trust

To contact the study team: **Tel:** 0191 2231231 **Email:** c.kirk3@newcastle.ac.uk

THANK YOU

What is the purpose of the study?

We would like to find out whether biological factors such as liver function/ weight/ dehydration etc. affect the quality of life of patients receiving home parenteral nutrition (HPN).

How will we use information about you?

We will need to use information from you and your medical records for this research project and entered into a research database.
This information will include your:

- NHS number
- Lifestyle data (smoking, alcohol, physical activity)
- Socioeconomic data (employment),

- Clinical data (diagnosis, reason for HPN, gastrointestinal anatomy, surgical history)
- Anthropometric measures (weight, height, body mass index, mid-arm circumference, tricep skinfold thickness, grip strength, bioelectrical impedance)
- Nutritional data (oral intake, number of infusions of HPN/week, composition of HPN)
- Medication history
- Blood test results

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

- You can find out more about how we use your information https://newcastlejro.com/research-in-newcastle/new-study/data-security/
- by asking one of the research team
- by sending an email to nuth.genericqueries@nhs.net
- Or by ringing us on 0191 2231231.

Why have I been invited?

We are contacting patients who are currently receiving HPN from Newcastle Hospitals, Leeds Teaching Hospitals NHS Trust and Southampton General Hospital, to ask them to participate.

Do I have to take part?

The decision to take part is entirely up to you. If you decide to participate you will be free to withdraw at any time and without giving a reason. Your decision whether to take part will not affect any care or support you may be receiving at this time.

What will happen to the data collected?

The data will be examined at Newcastle University. We will look for links between the data collected from your routine clinic appointments to the information provided in the quality of life questionnaires.

Expenses and payments

No payments are available. However all postage will be free and freepost envelopes will be provided.

What are the possible disadvantages and risks of taking part?

There are no risks in taking part in the questionnaires. You do not have to answer any of the questions included in the survey if you do not want to.

What are the possible benefits of taking part?

We do not believe there will be any direct benefit to you as an individual. However, the study will help us to find out more about what factors affect quality of life in patients receiving HPN and, in the longer term, may help to improve the service offer to such patients. In particular, the findings will be used to design an intervention that will aim to improve the factors identified as affecting quality of life.

What will happen to the results of the study?

- All anonymised data will be analysed by the research team. The results will be:
- Shared amongst participants in the form of a patient information leaflet
- Shared through the charity PINNT
- Written up for publication in scientific and medical journals

Anonymous direct quotes from the questionnaires may be written up in an anonymised form as part of the results. However the identities of all participants will be kept confidential.

Will my taking part in this study be kept confidential?

Yes. All information about you will be handled in confidence and we will adhere to all relevant legal and ethical processes. Patients contacted will be logged anonymously by the clinical team at the corresponding hospital and assigned a unique ID number. This number will be written on the front of the questionnaires. The ID number will be used to track which patients have returned the questionnaires and then we can send out the follow up questionnaires. All information collected about you will be anonymous and will be kept strictly confidential.

What if there is a problem?

You are free to participate or not in the study and this will in no way affect your care at the hospital. If you have a minor complaint then please contact the research team in the first instance. If you prefer to raise your concerns with someone not involved in your care, you can contact the Patient Advise and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department through any of the details below:

Telephone: 0191 223 1382 or 0191 223 1454
Email: patient.relations@nuth.nhs.uk
Address: Patient Relations Department
The Newcastle upon Tyne Hospitals NHS Foundation Trust
The Freeman Hospital
Newcastle upon Tyne
NE7 7DN

We hope that you will agree to participate in this study. If you have any questions please ask.

Appendix G: Invitation to participate letter – group 2

THE BIOLOGICAL DETERMINANTS OF QUALITY OF LIFE IN HOME PARENTERAL NUTRITION
PARTICIPANT INFORMATION SHEET (Group 2)

INVITATION TO PARTICIPATE IN A RESEARCH PROJECT

We would like to invite you to take part in a research study which is a collaboration between Newcastle University, Newcastle Hospitals, Leeds Teaching Hospitals and Southampton General Hospital. Before you decide whether to volunteer or not it is important for you to understand why the research is being carried out and what it involves. Please take the time to read the enclosed information carefully and do not hesitate to contact us if there is anything you are not sure about, or if you would like more information.
The study is funded by the National Institute of Health Research (NIHR) and *has been approved by the XXXX Research Ethics Committee*

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Freeman Hospital

Dave Jones
Professor of Liver Immunology
Newcastle University

John Mathers
Professor of Human Nutrition
Newcastle University

Mark Pearce
Professor in Applied Epidemiology
Newcastle University

To contact the study team: **Tel:** 0191 2231231 **Email:** c.kirk3@newcastle.ac.uk

THANK YOU

What is the purpose of the study?

We would like to find out whether biological factors such as liver function/ weight/ dehydration etc. affect the quality of life of patients receiving home parenteral nutrition (HPN).

How will we use information about you?

We will need to use information from you and your medical records for this research project and entered into a research database.
This information will include your:

- NHS number
- Lifestyle data (smoking, alcohol, physical activity)
- Socioeconomic data (employment),

- Clinical data (diagnosis, reason for HPN, gastrointestinal anatomy, surgical history)
- Anthropometric measures (weight, height, body mass index, mid-arm circumference, tricep skinfold thickness, grip strength, bioelectrical impedance)
- Nutritional data (oral intake, number of infusions of HPN/week, composition of HPN)
- Medication history
- Blood test results

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

- You can find out more about how we use your information https://newcastlejro.com/research-in-newcastle/new-study/data-security/
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- by sending an email to nuth.genericqueries@nhs.net
- Or by ringing us on 0191 2231231.

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We are contacting patients who are currently receiving HPN from Newcastle Hospitals, Leeds Teaching Hospitals NHS Trust and Southampton General Hospital, to ask them to participate.

Do I have to take part?

The decision to take part is entirely up to you. If you decide to participate you will be free to withdraw at any time and without giving a reason. Your decision whether to take part will not affect any care or support you may be receiving at this time.

What will happen to the data collected?

The data will be examined at Newcastle University. We will look for links between the data collected from your routine clinic appointments, the stoma or stool samples and the information provided in the quality of life questionnaires.

What will happen to the samples collected in this study?

The stoma samples will be examined in laboratories in Newcastle University and the blood samples will be examined in laboratories at The Imperial College London. All samples will be stored securely and anonymously. We will perform tests to look at the profile of bacteria in your stoma sample and for patterns of nutrient metabolism in your blood. We will try to link these patterns with the information provided in the questionnaires.

Expenses and payments

No payment available however all postage will be free and freepost envelopes will be provided.

What are the possible disadvantages and risks of taking part?

There are no risks in taking part in the questionnaires and the blood samples will be taken during your routine blood tests. You do not have to answer any of the questions included in the survey if you do not want to.

What are the possible benefits of taking part?

We do not believe there will be any direct benefit to you as an individual. However, the study will help us to find out more about what factors affect quality of life in patients receiving HPN and, in the longer term, may help to improve the service offer to such patients. In particular, the findings will be used to design an intervention that will aim to improve the factors identified as affecting quality of life.

What will happen to the results of the study?

- All anonymised data will be analysed by the research team. The results will be:
- Shared amongst participants in the form of a patient information leaflet
- Shared through the charity PINNT
- Written up for publication in scientific and medical journals

Anonymous direct quotes from the questionnaires may be written up in an anonymised form as part of the results. However the identities of all participants will be kept confidential.

Will my taking part in this study be kept confidential?

Yes. All information about you will be handled in confidence and we will adhere to all relevant legal and ethical processes. Patients contacted will be logged anonymously by the clinical team at the corresponding hospital and assigned a unique ID number. This number will be written on the front of the questionnaires. The ID number will be used to track which patients have returned the questionnaires and then we can send out the follow up questionnaires. All information collected about you will be anonymous and will be kept strictly confidential.

What if there is a problem?

You are free to participate or not in the study and this will in no way affect your care at the hospital. If you have a minor complaint then please contact the research team in the first instance. If you prefer to raise your concerns with someone not involved in your care, you can contact the Patient Advise and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department through any of the details below:

Telephone: 0191 223 1382 or 0191 223 1454
Email: patient.relations@nuth.nhs.uk
Address: Patient Relations Department
The Newcastle upon Tyne Hospitals NHS Foundation Trust
The Freeman Hospital
Newcastle upon Tyne
NE7 7DN

We hope that you will agree to participate in this study. If you have any questions please ask.

Appendix H: Consent form – group 1

Project title: The biological determinants of quality of life in home parenteral nutrition
Principle investigator: Mrs Colette Kirk

CONSENT FORM (Group 1)

	Please initial
I freely consent to participate in the above study	☐
I confirm that I have read and understand the participant information sheet dated XXX (version 0.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	☐
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.	☐
I agree to complete questionnaires about my quality of life at the commencement of the study and 12 months later.	☐
I agree for my data to be used for future studies for which have been approved by the ethics committee.	☐
I agree to be contacted about future studies.	☐
I consent to representative from the sponsor and regulatory bodies accessing my data for the purpose of audit.	☐

I acknowledge that:

a. *this project is for the purpose of research and not for profit*
b. *any personal or health information about me which is gathered in the course of my participation will be retained and analysed solely for the purposes of the study*
c. *my anonymity will be preserved and I will not be identified in publications or otherwise without my express written consent*

Name of Participant:
Signature **Date**

Name of Investigator:
Signature **Date**

Appendix I: Consent form – group 2

Project title: The biological determinants of quality of life in home parenteral nutrition
Principle investigator: Mrs Colette Kirk

CONSENT FORM (Group 2)

	Please initial
I freely consent to participate in the above study	☐
I confirm that I have read and understand the participant information sheet dated XXX (version 0.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	☐
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.	☐
I agree to complete questionnaires about my quality of life at the commencement of the study and 12 months later.	☐
I agree that samples of my blood can be used to measure patterns of metabolism.	☐
I agree that samples of my stool can be examined to look for patterns of bacteria	☐
I agree to wear a wrist-based activity monitor, if required	☐
I agree for my data/samples to be used for future studies for which have been approved by the ethics committee.	☐
I agree to be contacted about future studies.	☐
I consent to representative from the sponsor and regulatory bodies accessing my data for the purpose of audit.	☐

I acknowledge that:

a. *this project is for the purpose of research and not for profit*

b. *any personal or health information about me which is gathered in the course of my participation will be retained and analysed solely for the purposes of the study*

c. *my anonymity will be preserved and I will not be identified in publications or otherwise without my express written consent*

Name of Participant:
Signature **Date**

Name of Investigator:
Signature **Date**

Appendix J: Euroqol five-dimension scale (EQ-5D-5L)

IRAS Project ID: 297366
21st May 2021

Health Questionnaire

English version for the UK

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

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

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

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

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

PAIN / DISCOMFORT

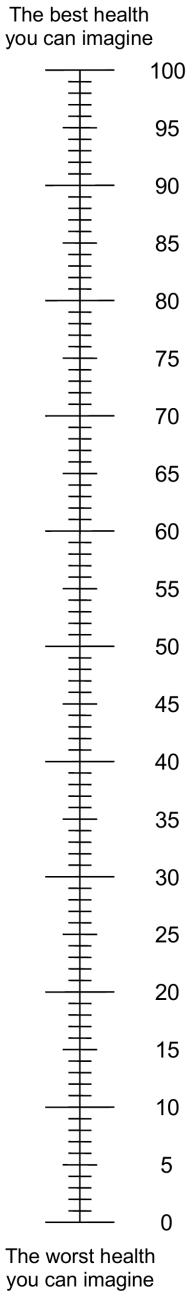
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

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

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

YOUR HEALTH TODAY = ☐



Appendix K: Short Form 36 (SF-36) questionnaire

RAND HEALTH

RAND > RAND Health > Surveys > RAND Medical Outcomes Study > 36-Item Short Form Survey (SF-36) >

36-Item Short Form Survey Instrument (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:

- 1 - Excellent
- 2 - Very good
- 3 - Good
- 4 - Fair
- 5 - Poor

---

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

- 1 - Much better now than one year ago
- 2 - Somewhat better now than one year ago
- 3 - About the same
- 4 - Somewhat worse now than one year ago
- 5 - Much worse now than one year ago

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

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○ 1	○ 2	○ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○ 1	○ 2	○ 3
5. Lifting or carrying groceries	○ 1	○ 2	○ 3
6. Climbing **several** flights of stairs	○ 1	○ 2	○ 3
7. Climbing **one** flight of stairs	○ 1	○ 2	○ 3
8. Bending, kneeling, or stooping	○ 1	○ 2	○ 3
9. Walking **more than a mile**	○ 1	○ 2	○ 3
10. Walking **several blocks**	○ 1	○ 2	○ 3
11. Walking **one block**	○ 1	○ 2	○ 3
12. Bathing or dressing yourself	○ 1	○ 2	○ 3

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

	Yes	No
13. Cut down the **amount of time** you spent on work or other activities	1	2
14. **Accomplished less** than you would like	1	2
15. Were limited in the **kind** of work or other activities	1	2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

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

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	1	2
18. **Accomplished less** than you would like	1	2
19. Didn't do work or other activities as **carefully** as usual	1	2

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

- 1 - Not at all
- 2 - Slightly
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

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

- 1 - None
- 2 - Very mild
- 3 - Mild
- 4 - Moderate
- 5 - Severe
- 6 - Very severe

---

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

- 1 - Not at all
- 2 - A little bit
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

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

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

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

- 1 - All of the time
- 2 - Most of the time
- 3 - Some of the time
- 4 - A little of the time
- 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5

ABOUT

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.

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Santa Monica, California 90401-3208

Appendix L: Home parenteral nutrition quality of life questionnaire (HPN-QoL)

IRAS Project ID: 297366
21st May 2021

HPN - QOL© (version 1.0)

Questionnaire to assess the quality of life of adult patients receiving home parenteral nutrition

Patient initials..... Date of birth (day, month, year).....

HPN centre ..... Today's date (day, month, year) .....

Please answer as many questions as possible by circling the number that reflects your experiences. **N/A = not applicable**

	During the past year (or since you started HPN)	**Much worse**	**Worse**	**No change**	**Better**	**Much better**
1	How has HPN made you feel?	1	2	3	4	5
2	How has HPN affected your ability to go on holiday?	1	2	3	4	5
3	How has HPN affected your ability to travel?	1	2	3	4	5
	During the past week	**Not at all**	**A little**	**Quite a bit**	**Very much**	
4	Has HPN felt a burden to you?	1	2	3	4	
5	Have you had concerns about your weight?	1	2	3	4	
6	Has the presence of your catheter affected your body image?	1	2	3	4	
7	Have you felt physically less attractive?	1	2	3	4	
8	Have you felt supported by your hospital nutrition team?	1	2	3	4	
9	Have you had access to a portable pump? Y / N If so, has it improved your ability to get around?	1	2	3	4	N/A
10	Have you had trouble doing strenuous activities, like carrying a heavy shopping bag or suitcase?	1	2	3	4	
11	Have you had trouble taking a long walk?	1	2	3	4	
12	Have you had trouble taking a short walk outside the house?	1	2	3	4	
13	Have you needed to stay in bed or a chair during the day?	1	2	3	4	
14	Have you needed help with eating, dressing, washing yourself or using the toilet?	1	2	3	4	
15	Have you felt tired?	1	2	3	4	
16	Have you felt lacking in energy?	1	2	3	4	
17	Has HPN disturbed your sleep pattern?	1	2	3	4	
18	Have you worried about your current health?	1	2	3	4	
19	Have you worried about the future?	1	2	3	4	
20	Were you able to socialise?	1	2	3	4	
21	Were you able to exercise?	1	2	3	4	

	During the past week	Not at all	A little	Quite a bit	Very much	
22	Were you able to do shopping?	1	2	3	4	
23	Were you able to take part in hobbies or leisure activities?	1	2	3	4	
24	Were you able to cope with daily life?	1	2	3	4	
25	Were you able to feel independent?	1	2	3	4	
26	Have you felt bloated?	1	2	3	4	
27	Were you able to eat food?	1	2	3	4	
28	Were you able to drink fluids?	1	2	3	4	
29	Have you had pain after eating or drinking?	1	2	3	4	N/A
30	Have you had nausea/vomiting?	1	2	3	4	
31	Have you had aches or pains in your muscles or joints?	1	2	3	4	
32	Have you had other pain?	1	2	3	4	
33	Have you felt depressed?	1	2	3	4	
34	Have you felt tense?	1	2	3	4	

	During the past YEAR (or since you started HPN)	Not at all	A little	Quite a bit	Very much
35	Have you felt you wanted to go out to work?	1	2	3	4
36	Were you able to go out to work?	1	2	3	4
37	Has HPN caused financial worries?	1	2	3	4

38 Do you have a stoma (ileostomy/colostomy/gastrostomy)? Please tick box Yes € No €

If you have a stoma please go to questions 39-40

If you do not have a stoma please go to questions 41-43

During the past week

For patients who have a stoma	Not at all	A little	Quite a bit	Very much
39 Have you had problems caring for your stoma?	1	2	3	4
40 Have you had problems with your stoma site?	1	2	3	4

For patients who do not have a stoma		Not at all	A little	Quite a bit	Very much
41	Have you had frequent bowel movements?	1	2	3	4
42	Have you had difficulty with moving your bowels?	1	2	3	4
43	Have you had painful bowel movements?	1	2	3	4

Please answer each of the following questions by circling the relevant number:

During the past week

44 How has your quality of life been?

0	1	2	3	4	5	6	7	8	9	10
Very bad										Very good

45 How has your quality of life been affected by your **HPN?**

-5	-4	-3	-2	-1	+1	+2	+3	+4	+5
Very much for the worse				0					Very much for the better

46 How has your quality of life been affected by your **underlying illness?**

-5	-4	-3	-2	-1	+1	+2	+3	+4	+5
Very much for the worse				0					Very much for the better

During the past FOUR WEEKS

		Not at all	A little	Quite a bit	Very much	
47	To what extent were you interested in sex?	1	2	3	4	
48	To what extent were you sexually active?	1	2	3	4	N/A

49 Are there any answers to the questionnaire that you would like to expand on? Please feel free to write in the space below:

……

……

……THANKYOU

Permission to use this questionnaire from:
Mrs Janet Baxter
Ninewells Hospital & Medical SchoolDUNDEE
DD1 9SY Telephone: + 44 1382 496558

This work is supported by:
TheScottish Home Parenteral Nutrition Managed Clinical Network

Appendix M: Stata do-file (descriptives & group comparisons)

```
sum underlying_disease if fudata==1
sum fuweight if fudata==1
sum fubmi if fudata==1
sum timeonhpn if fudata==1
tabulate gender_n if fudata==1
tabulate underlying_disease if fudata==1
tabulate hpn_reason if fudata==1
tabulate stoma_type if fudata==1
tabulate sb_length if fudata==1
tabulate colonincontinuity if fudata==1
sum underlying_disease if fudata==0
sum timeonhpn if fudata==0
tabulate gender_n if fudata==0
tabulate underlying_disease if fudata==0
tabulate hpn_reason if fudata==0
tabulate stoma_type if fudata==0
tabulate sb_length if fudata==0
tabulate colonincontinuity if fudata==0
sum new_und_disease if fudata==0
sum age if fudata==0
sum timeonhpn if fudata==0
tabulate gender_n if fudata==0
tabulate new_und_disease if fudata==0
tabulate reasonforhpn if fudata==0
tabulate typeofstoma if fudata==0
tabulate lengthofsb if fudata==0
tabulate colonincontinuity if fudata==0
tabulate marital_status if fudata==1
tabulate living_status if fudata==1
```

```
tabulate accommodation if fudata==1
tabulate education if fudata==1
tabulate employment if fudata==1
tabulate household_income if fudata==1
sum imd_rank if fudata==1
sum imddecile if fudata==1
sum imd_rank
tabulate marital_status if fudata==0
tabulate living_status if fudata==0
tabulate accommodation if fudata==0
tabulate education if fudata==0
tabulate employment if fudata==0
tabulate household_income if fudata==0
sum imd_rank if fudata==0
sum imddecile if fudata==0
sum imd_rank
sum imddecile

*EQ5D follow up data
tabulate fumob if fudata==1
tabulate fusc if fudata==1
tabulate fuua if fudata==1
tabulate fupd if fudata==1
tabulate fuad if fudata==1
sum fueq5dvas, detail
sum fuvs if fudata==1
sum blvalueset, detail
ttest bleq5dvas == fueq5dvas
ttest blvalueset == fuvs
```

```
* sf-36 descriptives
sum fusf36pf, detail
sum furlph, detail
sum fuenfat, detail
sum fuewb, detail
sum fusf36sf, detail
sum fusf36gh, detail
sum furlep, detail
sum fup, detail
sum blsf36pf, detail
sum blrolelimitationsph, detail
sum blrolelimitationsep, detail
sum blenergyfatigue, detail
sum blewb, detail
sum blsf, detail
sum blpain, detail
sum blsf36gh, detail

sort fudata
by fudata: summarize blsf36pf, detail
by fudata: summarize blrolelimitationsph, detail
by fudata: summarize blrolelimitationsep, detail
by fudata: sum blenergyfatigue, detail
by fudata: summarize blewb, detail
by fudata: summarize blsf, detail
by fudata: summarize blpain, detail
by fudata: summarize blsf36gh, detail
sort sitecode
by sitecode: summarize blsf36pf, detail
by sitecode: summarize blrolelimitationsph, detail
```

```
by sitecode: summarize blrolelimitationsep, detail
by sitecode: sum blenergyfatigue, detail
by sitecode: summarize blewb, detail
by sitecode: summarize blsf, detail
by sitecode: summarize blpain, detail
by sitecode: summarize blsf36gh, detail

* hpnqol descriptives
sum a_gh_hpnqol, detail
sum a_hol_hpnqol, detail
sum blphysicalfunctioning, detail
sum blcoping, detail
sum blabilityeatdrink, detail
sum a_employment_hpnqol, detail
sum a_sexfunction_hpnqol, detail
sum blemotionalfunctioning, detail
sum blnutritionteam, detail
sum a_pump_hpnqol, detail
sum blweight, detail
sum blimmobility, detail
sum blfatigue, detail
sum blsleeppattern, detail
sum blgisymptoms, detail
sum blotherpain, detail
sum blstoma, detail
sum blnostoma, detail
sum a_financial_hpnqol, detail
sum blqolnumericalratingscale, detail
sum blbodyimage, detail
```

```
sort fudata

by fudata: summarize a_gh_hpnqol, detail

by fudata: summarize  a_hol_hpnqol, detail

by fudata: summarize  blphysicalfunctioning, detail

by fudata: summarize  blcoping, detail

by fudata: summarize  blabilityeatdrink, detail

by fudata: summarize  a_employment_hpnqol, detail

by fudata: summarize  a_sexfunction_hpnqol, detail

by fudata: summarize  blemotionalfunctioning, detail

by fudata: summarize  blnutritionteam, detail

by fudata: summarize  a_pump_hpnqol, detail

by fudata: summarize blweight, detail

by fudata: summarize  blimmobility, detail

by fudata: summarize  blfatigue, detail

by fudata: summarize  blsleeppattern, detail

by fudata: summarize  blgisymptoms, detail

by fudata: summarize  blotherpain, detail

by fudata: summarize  blstoma, detail

by fudata: summarize  blnostoma, detail

by fudata: summarize  a_financial_hpnqol, detail

by fudata: summarize  blqolnumericalratingscale, detail

by fudata: summarize  blbodyimage, detail

tabulate newhpnpt

tabulate b_micro

*baseline blood results

sum blureammoll blcreatininemmoll blsodiummmoll blpotassiummmoll blcrpmgl blwcc
blmgmmoll blpo4mmoll bladcammoll blvitaumoll blvitb12pmoll blfolateugl blcopperumoll,
detail
```

sum blzincumoll blmanganeseumoll blseleniumumoll blironumoll blferritin bltransferrinsat bltransferringl blhbgl blcholesterolmmoll bltriglyceridesmmoll blhdlmmoll bltotalhdlratio blnonhdlmmoll blrandomglucosemmoll blvitdumoll, detail

sum blbilumoll blalpunitl blast blggtunitl blaltunitl, detail

sum blpo4mmoll blbilumoll blalpunitl blaltunitl blast blggtunitl

histogram blcrpmgl

sum blcholesterolmmoll bltriglyceridesmmoll blwcc

sum fuur fucr funa fuk fucrp fuwcc fumg fupo4 fuadca fuvita fuvite fuvitb12 fufolate fucu fuzn fumn fuse fufe fuferritin futrans fuhb futranssat fuchol futri fuhdl furatio funonhdl fugluc fuvitd fubil fualp fualt fuggt fuplate fuast, detail

tabstat blzincumoll blmanganeseumoll blseleniumumoll blironumoll blferritin ///

bltransferrinsat bltransferringl blhbgl blcholesterolmmoll bltriglyceridesmmoll ///

blhdlmmoll bltotalhdlratio blnonhdlmmoll blrandomglucosemmoll blvitdumoll ///

if fudata == 1, stats(p25 p50 p75) columns(statistics)

tabstat blureammoll blcreatininemmoll blsodiummmoll blpotassiummmoll blcrpmgl ///

blwcc blmgmmoll blpo4mmoll bladcammoll blvitaumoll blvitb12pmoll blfolateugl ///

blcopperumoll blbilumoll blalpunitl blast blggtunitl blaltunitl ///

if fudata == 1, stats(p25 p50 p75) columns(statistics)

sum bltransferrinsat blironumoll blferritin bltransferringl, detail

tabulate newhpnpt if fudata==1

sum fuur fucr funa fuk fucrp fuwcc fumg fupo4 fuadca fuvita fuvite fuvitb12 fufolate fucu fuzn fumn fuse fufe fuferritin futrans fuhb futranssat fuchol futri fuhdl furatio funonhdl fugluc fuvitd fubil fualp fualt fuggt fuplate fuast if fudata==1

*anthropometrics

sum blweightkg, detail

sum fuweight, detail

sum blbmikgm2, detail

sum fubmi, detail

sum blmaccm, detail

sum bltsfmm, detail

sum blmamccm, detail

```
sum blhgskg, detail
sum fumac, detail
sum fumamc, detail
sum futsf, detail
sum fuhgs, detail
summarize blweightkg if fudata == 1, detail
summarize blbmikgm2 if fudata == 1, detail
summarize blmaccm if fudata == 1, detail
summarize bltsfmm if fudata == 1, detail
summarize blmamccm if fudata == 1, detail
summarize blhgskg if fudata == 1, detail
sum visceralfatl, detail
sum blfatfreemasskg, detail
sum blfatfreemassindexkgm2, detail
sum blskeletalmusclemasskg, detail
sum tbw, detail
sum ecw, detail
sum phaseangledegree, detail
signrank blweightkg = fuweight if fudata==1
signrank blbmikgm2 = fubmi if fudata==1
signrank blmaccm = fumac if fudata==1
signrank bltsfmm = futsf if fudata==1
signrank blmamccm = fumamc if fudata==1
signrank blhgskg = fuhgs if fudata==1

* hpn prescription BL and FU
sum blhpnvol, detail
sum blinfusionswk, detail
sum blaveragelipiddg, detail
sum bllipidinfusionswk, detail
```

```
sum blglucoseinfusionswk, detail

sum blaveragekcald, detail

sum blaverageglucosedg, detail

sum blaveragenitrogendg, detail

tabulate a_hpntype if fudata == 1

tabstat blhpnvol blinfusionswk blaverageliпiddg bllipidinfusionswk ///

blglucoseinfusionswk blaverageliпiddg blaveragekcald blaverageglucosedg
blaveragenitrogendg ///

if fudata == 1, stats(min p25 median p75 max) columns(statistics)

sum fuhpnvol, detail

sum fuinfperwk, detail

sum fuavlipid, detail

sum fulipidinfwk, detail

sum fuglucinfwk, detail

sum fuavkcday, detail

sum fuavgluc, detail

sum fuavnday, detail


* difference between follow up and lost to follow up participants

signrank blinfusionswk = fuinfperwk if fudata==1

signrank blaverageliпiddg = fuavlipid if fudata==1

signrank blaveragekcald = fuavkcday if fudata==1

signrank blaverageglucosedg = fuavgluc if fudata==1

signrank blaveragenitrogendg = fuavnday if fudata==1

signrank bllipidinfusionswk = fulipidinfwk if fudata==1

signrank blglucoseinfusionswk = fuglucinfwk if fudata==1

signrank blhpnvol = fuhpnvol if fudata==1

signrank a_hpntype = b_hpntype if fudata==1
```

sum fuur fucr funa fuk fucrp fuwcc fumg fupo4 fuadca fuvita fuvite fuvitb12 fufolate fucu fuzn fumn fuse fufe fuferritin futrans fuhb futranssat fuchol futri fuhdl furatio funonhdl fugluc fuvitd fubil fualp fualt fuggt fuplate fuast if newhpnpt==1 & fudata==1

sum blzincumoll blmanganeseumoll blseleniumumoll blironumoll blferritin bltransferrinsat bltransferringl blhbgl blcholesterolmmoll bltriglyceridesmmoll blhdlmmoll bltotalhdlratio blnonhdlmmoll blrandomglucosemmoll blvitdumoll if newhpnpt==1

sum blsodiummmoll blpo4mmoll blpotassiummmoll blcreatininemmoll blureammoll bladcammoll blmgmmoll blvitaumoll blvitb12pmoll blfolateugl blcopperumoll blwcc blcrpmgl blbilumoll blalpunitl blaltunitl blggtunitl blast if newhpnpt==1

sum blvalueset if sitecode==3

sum fibroscanresultkpa

histogram fibroscanresultkpa

sum liverbiopsyresult

summarize fib4baseline

* cparing groups e.g. are there differences in employment between those that did and didnt send follow up data

xi: logistic fudata i.employment

xi: logistic fudata i.income

xi: logistic fudata i.marital_status

xi: logistic fudata i.household_income

xi: logistic fudata i.accommodation

xi: logistic fudata i.living_status

xi: logistic fudata i.education

*compares follow up data between centres e.g. did more newcastle patients respond than Leeds

xi: logistic fudata i.sitecode

* linear regression univariate, do this for every qol domain vs variable

* sf36

```
generate new_und_disease = ., after(underlying_disease)
regress blsf36pf timeonhpn
regress blrolelimitationsph timeonhpn
regress blrolelimitationsep timeonhpn
regress blenergyfatigue timeonhpn
regress blewb timeonhpn
regress blsf36gh timeonhpn
regress blpain timeonhpn
regress blsf36gh timeonhpn
regress a_gh_hpnqol timeonhpn
regress a_hol_hpnqol timeonhpn
regress blphysicalfunctioning timeonhpn
regress blcoping timeonhpn
regress blabilityeatdrink timeonhpn
regress a_employment_hpnqol timeonhpn
regress a_sexfunction_hpnqol timeonhpn
regress blemotionalfunctioning timeonhpn
regress blnutritionteam timeonhpn
regress a_pump_hpnqol timeonhpn
regress blbodyimage timeonhpn
regress blweight timeonhpn
regress blimmobility timeonhpn
regress blfatigue timeonhpn
regress blsleeppattern timeonhpn
regress blgisymptoms timeonhpn
regress blotherpain timeonhpn
regress blstoma timeonhpn
regress blnostoma timeonhpn
regress a_financial_hpnqol timeonhpn
regress blqolnumericalratingscale timeonhpn
```

```
regress blsf36pf i.new_und_disease
regress blrolelimitationsph i.new_und_disease
regress blrolelimitationsep i.new_und_disease
regress blenergyfatigue i.new_und_disease
regress blewb i.new_und_disease
regress blsf36gh i.new_und_disease
regress blpain i.new_und_disease
regress blsf i.new_und_disease
regress a_gh_hpnqol i.new_und_disease
regress a_hol_hpnqol i.new_und_disease
regress blphysicalfunctioning i.new_und_disease
regress blcoping i.new_und_disease
regress blabilityeatdrink i.new_und_disease
regress a_employment_hpnqol i.new_und_disease
regress a_sexfunction_hpnqol i.new_und_disease
regress blemotionalfunctioning i.new_und_disease
regress blnutritionteam i.new_und_disease
regress a_pump_hpnqol i.new_und_disease
regress blbodyimage i.new_und_disease
regress blweight i.new_und_disease
regress blimmobility i.new_und_disease
regress blfatigue i.new_und_disease
regress blsleeppattern i.new_und_disease
regress blgisymptoms i.new_und_disease
regress blotherpain i.new_und_disease
regress blstoma i.new_und_disease
regress blnostoma i.new_und_disease
regress a_financial_hpnqol i.new_und_disease
regress blqolnumericalratingscale i.new_und_disease
regress blsf36pf i.reasonforhpn
```

```
regress blrolelimitationsph i.reasonforhpn
regress blrolelimitationsep i.reasonforhpn
regress blenergyfatigue i.reasonforhpn
regress blewb i.reasonforhpn
regress blsf36gh i.reasonforhpn
regress blpain i.reasonforhpn
regress blsf i.reasonforhpn
regress a_gh_hpnqol i.reasonforhpn
regress a_hol_hpnqol i.reasonforhpn
regress blphysicalfunctioning i.reasonforhpn
regress blcoping i.reasonforhpn
regress blabilityeatdrink i.reasonforhpn
regress a_employment_hpnqol i.reasonforhpn
regress a_sexfunction_hpnqol i.reasonforhpn
regress blemotionalfunctioning i.reasonforhpn
regress blnutritionteam i.reasonforhpn
regress a_pump_hpnqol i.reasonforhpn
regress blbodyimage i.reasonforhpn
regress blweight i.reasonforhpn
regress blimmobility i.reasonforhpn
regress blfatigue i.reasonforhpn
regress blsleeppattern i.reasonforhpn
regress blgisymptoms i.reasonforhpn
regress blotherpain i.reasonforhpn
regress blstoma i.reasonforhpn
regress blnostoma i.reasonforhpn
regress a_financial_hpnqol i.reasonforhpn
regress blqolnumericalratingscale i.reasonforhpn
regress blsf36pf blhgskg
regress blrolelimitationsph blhgskg
```

```
regress blrolelimitationsep blhgskg
regress blenergyfatigue blhgskg
regress blewb blhgskg
regress blsf36gh blhgskg
regress blpain blhgskg
regress blsf blhgskg
regress a_gh_hpnqol blhgskg
regress a_hol_hpnqol blhgskg
regress blphysicalfunctioning blhgskg
regress blcoping blhgskg
regress blabilityeatdrink blhgskg
regress a_employment_hpnqol blhgskg
regress a_sexfunction_hpnqol blhgskg
regress blemotionalfunctioning blhgskg
regress blnutritionteam blhgskg
regress a_pump_hpnqol blhgskg
regress blbodyimage blhgskg
regress blweight blhgskg
regress blimmobility blhgskg
regress blfatigue blhgskg
regress blsleeppattern blhgskg
regress blgisymptoms blhgskg
regress blotherpain blhgskg
regress blstoma blhgskg
regress blnostoma blhgskg
regress a_financial_hpnqol blhgskg
regress blqolnumericalratingscale blhgskg
regress blsf36pf i.lengthofsb
regress blrolelimitationsph i.lengthofsb
regress blrolelimitationsep i.lengthofsb
```

regress blenergyfatigue i.lengthofsb

regress blewb i.lengthofsb

regress blsf36gh i.lengthofsb

regress blpain i.lengthofsb

regress blsf i.lengthofsb

regress a_gh_hpnqol i.lengthofsb

regress a_hol_hpnqol i.lengthofsb

regress blphysicalfunctioning i.lengthofsb

regress blcoping i.lengthofsb

regress blabilityeatdrink i.lengthofsb

regress a_employment_hpnqol i.lengthofsb

regress a_sexfunction_hpnqol i.lengthofsb

regress blemotionalfunctioning i.lengthofsb

regress blnutritionteam i.lengthofsb

regress a_pump_hpnqol i.lengthofsb

regress blbodyimage i.lengthofsb

regress blweight i.lengthofsb

regress blimmobility i.lengthofsb

regress blfatigue i.lengthofsb

regress blsleeppattern i.lengthofsb

regress blgisymptoms i.lengthofsb

regress blotherpain i.lengthofsb

regress blstoma i.lengthofsb

regress blnostoma i.lengthofsb

regress a_financial_hpnqol i.lengthofsb

regress blqolnumericalratingscale i.lengthofsb

regress blsf36pf phaseangledegree

regress blrolelimitationsph phaseangledegree

regress blrolelimitationsep phaseangledegree

regress blenergyfatigue phaseangledegree

regress blewb phaseangledegree

regress blsf36gh phaseangledegree

regress blpain phaseangledegree

regress blsf phaseangledegree

regress a_gh_hpnqol phaseangledegree

regress a_hol_hpnqol phaseangledegree

regress blphysicalfunctioning phaseangledegree

regress blcoping phaseangledegree

regress blabilityeatdrink phaseangledegree

regress a_employment_hpnqol phaseangledegree

regress a_sexfunction_hpnqol phaseangledegree

regress blemotionalfunctioning phaseangledegree

regress blnutritionteam phaseangledegree

regress a_pump_hpnqol phaseangledegree

regress blbodyimage phaseangledegree

regress blweight phaseangledegree

regress blimmobility phaseangledegree

regress blfatigue phaseangledegree

regress blsleeppattern phaseangledegree

regress blgisymptoms phaseangledegree

regress blotherpain phaseangledegree

regress blstoma phaseangledegree

regress blnostoma phaseangledegree

regress a_financial_hpnqol phaseangledegree

regress blqolnumericalratingscale phaseangledegree

regress blsf36pf blskeletalmusclemasskg

regress blrolelimitationsph blskeletalmusclemasskg

regress blrolelimitationsep blskeletalmusclemasskg

regress blenergyfatigue blskeletalmusclemasskg

regress blewb blskeletalmusclemasskg

regress blsf36gh blskeletalmusclemasskg

regress blpain blskeletalmusclemasskg

regress blsf blskeletalmusclemasskg

regress a_gh_hpnqol blskeletalmusclemasskg

regress a_hol_hpnqol blskeletalmusclemasskg

regress blphysicalfunctioning blskeletalmusclemasskg

regress blcoping blskeletalmusclemasskg

regress blabilityeatdrink blskeletalmusclemasskg

regress a_employment_hpnqol blskeletalmusclemasskg

regress a_sexfunction_hpnqol blskeletalmusclemasskg

regress blemotionalfunctioning blskeletalmusclemasskg

regress blnutritionteam blskeletalmusclemasskg

regress a_pump_hpnqol blskeletalmusclemasskg

regress blbodyimage blskeletalmusclemasskg

regress blweight blskeletalmusclemasskg

regress blimmobility blskeletalmusclemasskg

regress blfatigue blskeletalmusclemasskg

regress blsleeppattern blskeletalmusclemasskg

regress blgisymptoms blskeletalmusclemasskg

regress blotherpain blskeletalmusclemasskg

regress blstoma blskeletalmusclemasskg

regress blnostoma blskeletalmusclemasskg

regress a_financial_hpnqol blskeletalmusclemasskg

regress blqolnumericalratingscale blskeletalmusclemasskg

regress blsf36pf blinfusionswk

regress blrolelimitationsph blinfusionswk

regress blrolelimitationsep blinfusionswk

regress blenergyfatigue blinfusionswk

regress blewb blinfusionswk

regress blsf36gh blinfusionswk

regress blpain blinfusionswk

regress blsf blinfusionswk

regress a_gh_hpnqol blinfusionswk

regress a_hol_hpnqol blinfusionswk

regress blphysicalfunctioning blinfusionswk

regress blcoping blinfusionswk

regress blabilityeatdrink blinfusionswk

regress a_employment_hpnqol blinfusionswk

regress a_sexfunction_hpnqol blinfusionswk

regress blemotionalfunctioning blinfusionswk

regress blnutritionteam blinfusionswk

regress a_pump_hpnqol blinfusionswk

regress blbodyimage blinfusionswk

regress blweight blinfusionswk

regress blimmobility blinfusionswk

regress blfatigue blinfusionswk

regress blsleeppattern blinfusionswk

regress blgisymptoms blinfusionswk

regress blotherpain blinfusionswk

regress blstoma blinfusionswk

regress blnostoma blinfusionswk

regress a_financial_hpnqol blinfusionswk

regress blqolnumericalratingscale blinfusionswk

regress blsf36pf blaveragekcald

regress blrolelimitationsph blaveragekcald

regress blrolelimitationsep blaveragekcald

regress blenergyfatigue blaveragekcald

regress blewb blaveragekcald

regress blsf36gh blaveragekcald

regress blpain blaveragekcald

regress blsf blaveragekcald

regress a_gh_hpnqol blaveragekcald

regress a_hol_hpnqol blaveragekcald

regress blphysicalfunctioning blaveragekcald

regress blcoping blaveragekcald

regress blabilityeatdrink blaveragekcald

regress a_employment_hpnqol blaveragekcald

regress a_sexfunction_hpnqol blaveragekcald

regress blemotionalfunctioning blaveragekcald

regress blnutritionteam blaveragekcald

regress a_pump_hpnqol blaveragekcald

regress blbodyimage blaveragekcald

regress blweight blaveragekcald

regress blimmobility blaveragekcald

regress blfatigue blaveragekcald

regress blsleeppattern blaveragekcald

regress blgisymptoms blaveragekcald

regress blotherpain blaveragekcald

regress blstoma blaveragekcald

regress blnostoma blaveragekcald

regress a_financial_hpnqol blaveragekcald

regress blqolnumericalratingscale blaveragekcald

regress blsf36pf bldietint

regress blrolelimitationsph bldietint

regress blrolelimitationsep bldietint

regress blenergyfatigue bldietint

regress blewb bldietint

regress blsf36gh bldietint

regress blpain bldietint

```
regress blsf bldietint
regress a_gh_hpnqol bldietint
regress a_hol_hpnqol bldietint
regress blphysicalfunctioning bldietint
regress blcoping bldietint
regress blabilityeatdrink bldietint
regress a_employment_hpnqol bldietint
regress a_sexfunction_hpnqol bldietint
regress blemotionalfunctioning bldietint
regress blnutritionteam bldietint
regress a_pump_hpnqol bldietint
regress blbodyimage bldietint
regress blweight bldietint
regress blimmobility bldietint
regress blfatigue bldietint
regress blsleeppattern bldietint
regress blgisymptoms bldietint
regress blotherpain bldietint
regress blstoma bldietint
regress blnostoma bldietint
regress a_financial_hpnqol bldietint
regress blqolnumericalratingscale bldietint

*up to here for the regression results for HPN-QoL


regress blsf36pf i.education_level
regress blrolelimitationsph i.education_level
regress blrolelimitationsep i.education_level
regress blenergyfatigue i.education_level
```

```
regress blewb i.education_level
regress blsf36gh i.education_level
regress blpain i.education_level
regress blsf i.education_level
regress blsf36pf i.employment_status
regress blrolelimitationsph i.employment_status
regress blrolelimitationsep i.employment_status
regress blenergyfatigue i.employment_status
regress blewb i.employment_status
regress blsf36gh i.employment_status
regress blpain i.employment_status
regress blsf i.employment_status
regress blsf36pf imddecile
regress blrolelimitationsph imddecile
regress blrolelimitationsep imddecile
regress blenergyfatigue imddecile
regress blewb imddecile
regress blsf36gh imddecile
regress blpain imddecile
regress blsf imddecile

*if categorical always i:

*multivariable
*baseline
xi: regress blphysicalfunctioning i.marital_status

* multivariable using the signficant results

regress blrolelimitationsph bldietint gender
```

regress blewb bldietint gender

regress blsf bldietint gender

regress blewb blaveragenitrogendg

regress blewb blaveragenitrogendg age

regress blewb blaveragenitrogendg age i.gender

regress blsf blaveragenitrogendg

regress blsf blaveragenitrogendg age

regress blsf blaveragenitrogendg gender

regress blsf blinfusionswk

regress blsf blinfusionswk gender

regress blsf blinfusionswk age

regress blsf blaveragelipiddg

regress blsf blaveragelipiddg gender

regress blsf blaveragelipiddg age

regress blsf36pf phaseangledegree

regress blsf36pf phaseangledegree age

regress blsf36pf phaseangledegree i.gender

regress blrolelimitationsph phaseangledegree

regress blrolelimitationsph phaseangledegree age

regress blrolelimitationsph phaseangledegree i.gender

regress blrolelimitationsph blskeletalmusclemasskg

regress blrolelimitationsph blskeletalmusclemasskg age

regress blrolelimitationsph blskeletalmusclemasskg i.gender

regress blsf phaseangledegree

regress blsf phaseangledegree age

regress blsf phaseangledegree i.gender

regress blsf i.lengthofsb

regress blsf i.lengthofsb age

regress blsf i.lengthofsb i.gender

regress blenergyfatigue blskeletalmusclemasskg

regress blenergyfatigue blskeletalmusclemasskg age

regress blenergyfatigue blskeletalmusclemasskg i.gender

regress blpain blskeletalmusclemasskg

regress blpain blskeletalmusclemasskg age

regress blpain blskeletalmusclemasskg i.gender

regress a_employment_hpnqol blhgskg

regress a_employment_hpnqol blhgskg age

regress a_employment_hpnqol blhgskg age i.gender

regress blfatigue blhgskg

regress blfatigue blhgskg age

regress blfatigue blhgskg age i.gender

regress a_gh_hpnqol blhgskg

regress a_gh_hpnqol blhgskg age

regress a_gh_hpnqol blhgskg age i.gender

regress blphysicalfunctioning blhgskg

regress blphysicalfunctioning blhgskg age

regress blphysicalfunctioning blhgskg age i.gender

regress blphysicalfunctioning blskeletalmusclemasskg

regress blphysicalfunctioning blskeletalmusclemasskg age

regress blphysicalfunctioning blskeletalmusclemasskg age i.gender

regress a_sexfunction_hpnqol blhgskg

regress a_sexfunction_hpnqol blhgskg age

regress a_sexfunction_hpnqol blhgskg age i.gender

regress blsleeppattern blhgskg

regress blsleeppattern blhgskg age

regress blsleeppattern blhgskg age i.gender

regress blimmobility blhgskg

regress blimmobility blhgskg age

regress blimmobility blhgskg i.gender

*if significant then adjust for the following

xi: regress blphysicalfunctioning i.marital_status age

xi: regress blphysicalfunctioning i.marital_status gender

graph matrix blbmikgm2 blhgskg blsf36pf blsf36gh blinfusionswk

graph matrix blsf36gh blsf36pf blrolelimitationsep blrolelimitationsph blenergyfatigue blewb blsf blpain blbodyimage blweight blimmobility blfatigue blsleeppattern blgisymptoms blotherpain blstoma blnostoma a_financial_hpnqol a_employment_hpnqol a_gh_hpnqol a_hol_hpnqol

graph matrix blsf36gh blbilumoll blalpunitl blast blggtunitl

replace living_status (Withfamily=notalone)

signrank blsf36pf = fusf36pf

signrank blrolelimitationsph = furlph

signrank blrolelimitationsep = furlep

signrank blenergyfatigue = fuenfat

signrank blewb = fuewb

signrank blsf = fusf36sf

signrank blpain = fup

signrank blsf36gh = fusf36gh

signrank a_gh_hpnqol = fugh

signrank a_hol_hpnqol = fuhol

signrank blphysicalfunctioning = fupf

signrank blcoping = fuco

signrank blabilityeatdrink = fued

signrank a_employment_hpnqol = fuempl

signrank a_sexfunction_hpnqol = fusf

signrank blemotionalfunctioning = fuef

signrank blnutritionteam = funt

signrank a_pump_hpnqol = b_pump_hpnqol

signrank blweight = fuwt

signrank blbodyimage = fuim

signrank blimmobility = fuimm

signrank blfatigue = fufat

signrank blsleeppattern = fusp

signrank blgisymptoms = fugi

signrank blotherpain = fuop

signrank blstoma = fusto

signrank blnostoma = funosto

signrank a_financial_hpnqol = fufi

signrank blqolnumericalratingscale = fuqol

graph box blsf36pf blrolelimitationsph blrolelimitationsep blenergyfatigue blewb blsf blpain blsf36gh

graph box blsf36pf blrolelimitationsph blrolelimitationsep blenergyfatigue blewb blsf blpain blsf36gh, xlabel(, angle(45))

graph box a_gh_hpnqol a_hol_hpnqol blphysicalfunctioning blcoping blabilityeatdrink a_employment_hpnqol a_sexfunction_hpnqol blemotionalfunctioning, title("Functional scale items of the HPN QoL questionnaire") ytitle("Score")

graph bar (mean) blmobility blselfcare blusualactivities blpaindiscomfort blanxietydepression, over(sitecode) horizontal

swilk blcreatininemmoll blsodiummmoll blpotassiummmoll blcrpmgl blwcc blmgmmoll blpo4mmoll bladcammoll blvitaumoll blvitb12pmoll blfolateugl blcopperumoll

swilk blzincumoll blmanganeseumoll blseleniumumoll blironumoll blferritin bltransferrinsat bltransferringl blhbgl blcholesterolmmoll bltriglyceridesmmoll blhdlmmoll bltotalhdlratio blnonhdlmmoll blrandomglucosemmoll blvitdumoll

tabstat blcreatininemmoll blsodiummmoll blpotassiummmoll blcrpmgl blwcc blmgmmoll blpo4mmoll bladcammoll blvitaumoll blvitb12pmoll blfolateugl blcopperumoll, statistics(min median max)

tabstat blureammoll blzincumoll blmanganeseumoll blseleniumumoll blironumoll blferritin bltransferrinsat bltransferringl blhbgl blcholesterolmmoll bltriglyceridesmmoll blhdlmmoll

```
bltotalhdlratio blnonhdlmmoll blrandomglucosemmoll blvitdumoll, statistics(min median max)

signrank blmobility = fumob

signrank blselfcare = fusc

signrank blusualactivities = fuua

signrank blpaindiscomfort = fupd

signrank blanxietydepression = fuad


tabulate blmobility if fudata == 1

tabulate blselfcare if fudata == 1

tabulate blusualactivities if fudata == 1

tabulate blpaindiscomfort if fudata == 1

tabulate blanxietydepression if fudata == 1

tabstat blvalueset bleq5dvas if fudata == 1, stats(p25 p50 p75) columns(statistics)


graph bar (count) blpaindiscomfort fup, over(time, gap(0)) stack ///

   blabel(bar, size(small)) title("Pain Severity Distribution at Baseline and Follow-up")


        * Tabulate baseline data

tabulate blpaindiscomfort, generate(baseline_pdcount)


* Tabulate followup data

tabulate fupd, generate(followup_eqpdcount)

graph bar (sum) baseline_pdcount1 baseline_pdcount2 baseline_pdcount3 baseline_pdcount4 ///

   followup_eqpdcount1 followup_eqpdcount2 followup_eqpdcount3 followup_eqpdcount4, over(time, gap(0)) stack ///

   blabel(bar, size(small)) title("Distribution of Ordinal Data Between Baseline and Follow-up")


        reshape long baseline_pdcount followup_eqpdcount, i(id) j(time)
```

```
gen id = _n
graph bar (sum) baseline_pdcount followup_eqpdcount, over(time, gap(0)) stack ///
   blabel(bar, size(small)) title("Distribution of Ordinal Data Between Baseline and Follow-up")

*to understand differences in the eq5d across the different sites
kwallis blmobility, by(sitecode)
ranksum blmobility if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum blmobility if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blmobility if sitecode == 2 | sitecode == 3, by(sitecode)
kwallis blselfcare, by(sitecode)
ranksum blselfcare if sitecode == 1 | sitecode == 2, by(sitecode), exact
ranksum blselfcare if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blselfcare if sitecode == 2 | sitecode == 3, by(sitecode)
kwallis blusualactivities, by(sitecode)
ranksum blusualactivities if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum blusualactivities if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blusualactivities if sitecode == 2 | sitecode == 3, by(sitecode)

kwallis blpaindiscomfort, by(sitecode)

ranksum blpaindiscomfort if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum blpaindiscomfort if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blpaindiscomfort if sitecode == 2 | sitecode == 3, by(sitecode)

kwallis blanxietydepression, by(sitecode)
ranksum blanxietydepression if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum blanxietydepression if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blanxietydepression if sitecode == 2 | sitecode == 3, by(sitecode)
kwallis bleq5dvas, by(sitecode)
```

```
ranksum bleq5dvas if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum bleq5dvas if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum bleq5dvas if sitecode == 2 | sitecode == 3, by(sitecode)
kwallis blvalueset, by(sitecode)
ranksum blvalueset if sitecode == 1 | sitecode == 2, by(sitecode)
ranksum blvalueset if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blvalueset if sitecode == 2 | sitecode == 3, by(sitecode)

by sitecode: summarize bleq5dvas, detail
by newhpnpt: summarize blsf36pf, detail
reshape wide varname, i(id) j(time)

*new patient QoL sf36

sort newhpnpt
by newhpnpt: summarize blsf36pf, detail
by newhpnpt: summarize blrolelimitationsph, detail
by newhpnpt: summarize blrolelimitationsep, detail
by newhpnpt: summarize blenergyfatigue, detail
by newhpnpt: summarize blewb, detail
by newhpnpt: summarize blsf, detail
by newhpnpt: summarize blpain, detail
by newhpnpt: summarize blsf36gh, detail

by newhpnpt: summarize fusf36pf, detail
by newhpnpt: summarize furlph, detail
by newhpnpt: summarize furlep, detail
by newhpnpt: summarize fuenfat, detail
by newhpnpt: summarize fuewb, detail
by newhpnpt: summarize fusf36sf, detail
```

```
by newhpnpt: summarize fup, detail
by newhpnpt: summarize fusf36gh, detail

*difference in means new vs existing patients
ranksum blsf36pf if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blrolelimitationsph if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blrolelimitationsep if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blenergyfatigue if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blewb if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blsf if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blpain if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blsf36gh if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)


ranksum fusf36pf if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum furlph if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum furlep if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum fuenfat if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum fuewb if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum fusf36sf if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum fup if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum fusf36gh if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)

*EQ5D difference new vs existing
ranksum blmobility if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blselfcare if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blusualactivities if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blpaindiscomfort if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blanxietydepression if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum bleq5dvas if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
```

```
ranksum blvalueset if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)

*HPN-QoL difference new vs existing
ranksum a_gh_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum a_hol_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blphysicalfunctioning if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blcoping if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blabilityeatdrink if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum a_employment_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum a_sexfunction_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blemotionalfunctioning if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blnutritionteam if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum a_pump_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blbodyimage if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blweight if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blimmobility if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blfatigue if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blsleeppattern if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blgisymptoms if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blotherpain if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blstoma if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blnostoma if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum a_financial_hpnqol if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)
ranksum blqolnumericalratingscale if newhpnpt == 1 | newhpnpt == 0, by(newhpnpt)

sort newhpnpt
by newhpnpt: summarize blabilityeatdrink, detail
by newhpnpt: summarize a_pump_hpnqol, detail
by newhpnpt: summarize blqolnumericalratingscale, detail
sort fudata
```

```
by fudata: summarize bleq5dvas, detail
sum bleq5dvas, detail
sum blvalueset, detail
sum fuvs, detail
sort imd_rank
sum imd_rank, detail

sort imddecile
summarize imddecile, detail
sort fudata
by fudata: summarize age, detail
sum age, detail
sum timeonhpn, detail
sort fudata
by fudata: summarize timeonhpn, detail
by fudata: summarize b
sort newhpnpt
by newhpnpt: summarize blureammoll, detail
by newhpnpt: summarize blcreatininemmoll, detail
by newhpnpt: summarize blsodiummmoll, detail
by newhpnpt: summarize blpotassiummmoll, detail
by newhpnpt: summarize bladcammoll, detail
by newhpnpt: summarize blmgmmoll, detail
by newhpnpt: summarize blpo4mmoll, detail
by newhpnpt: summarize blcrpmgl, detail
by newhpnpt: summarize blwcc, detail
by newhpnpt: summarize blvitaumoll, detail
by newhpnpt: summarize blvitdumoll, detail
by newhpnpt: summarize blvitb12pmoll, detail
by newhpnpt: summarize blfolateugl, detail
```

by newhpnpt: summarize blcopperumoll, detail

by newhpnpt: summarize blzincumoll, detail

by newhpnpt: summarize blseleniumumoll, detail

by newhpnpt: summarize blmanganeseumoll, detail

by newhpnpt: summarize blcholesterolmmoll, detail

by newhpnpt: summarize blhdlmmoll, detail

by newhpnpt: summarize blnonhdlmmoll, detail

by newhpnpt: summarize bltriglyceridesmmoll, detail

by newhpnpt: summarize blironumoll, detail

by newhpnpt: summarize bltransferringl, detail

by newhpnpt: summarize bltransferrinsat, detail

by newhpnpt: summarize blferritin, detail

by newhpnpt: summarize blbilumoll, detail

by newhpnpt: summarize blalpunitl, detail

by newhpnpt: summarize blaltunitl, detail

by newhpnpt: summarize blggtunitl, detail

by newhpnpt: summarize blast, detail

by newhpnpt: summarize fibroscanresultkpa, detail

* follow up results new patients

by newhpnpt: summarize fuur, detail

by newhpnpt: summarize fucr, detail

by newhpnpt: summarize funa, detail

by newhpnpt: summarize fuk, detail

by newhpnpt: summarize fuadca, detail

by newhpnpt: summarize fumg, detail

by newhpnpt: summarize fupo4, detail

by newhpnpt: summarize fucrp, detail

by newhpnpt: summarize fuwcc, detail

by newhpnpt: summarize fuvita, detail

by newhpnpt: summarize fuvitd, detail

by newhpnpt: summarize fuvitb12, detail

by newhpnpt: summarize fufolate, detail

by newhpnpt: summarize fucu, detail

by newhpnpt: summarize fuzn, detail

by newhpnpt: summarize fuse, detail

by newhpnpt: summarize fumn, detail

by newhpnpt: summarize fuchol, detail

by newhpnpt: summarize fuhdl, detail

by newhpnpt: summarize funonhdl, detail

by newhpnpt: summarize futri, detail

by newhpnpt: summarize fufe, detail

by newhpnpt: summarize futrans, detail

by newhpnpt: summarize futranssat, detail

by newhpnpt: summarize fuferritin, detail

by newhpnpt: summarize fubil, detail

by newhpnpt: summarize fualp, detail

by newhpnpt: summarize fualt, detail

by newhpnpt: summarize fuggt, detail

by newhpnpt: summarize fuast, detail

* difference in bl and follow up blood results (new patients) wilcoxon signed rank test

by newhpnpt: signrank blcrpmgl = fucrp

*difference in bl and fu qol results (new patients)

by newhpnpt: signrank blsf36pf = fusf36pf

by newhpnpt: signrank blrolelimitationsph = furlph

by newhpnpt: signrank blrolelimitationsep = furlep

by newhpnpt: signrank blenergyfatigue = fuef

by newhpnpt: signrank blewb = fuewb

by newhpnpt: signrank blsf = fusf

by newhpnpt: signrank blpain = fup

by newhpnpt: signrank blsf36gh = fusf36gh

*difference in bl and fu HPN- qol results (new patients)

sort newhpnpt

by newhpnpt: signrank a_gh_hpnqol = fugh

by newhpnpt: signrank a_hol_hpnqol = fuhol

by newhpnpt: signrank blphysicalfunctioning = fupf

by newhpnpt: signrank blcoping = fuco

by newhpnpt: signrank blabilityeatdrink = fued

by newhpnpt: signrank a_employment_hpnqol = fuempl

by newhpnpt: signrank a_sexfunction_hpnqol = fusf

by newhpnpt: signrank blemotionalfunctioning = fuef

by newhpnpt: signrank blnutritionteam = funt

by newhpnpt: signrank a_pump_hpnqol = b_pump_hpnqol

by newhpnpt: signrank blbodyimage = fuim

by newhpnpt: signrank blweight = fuwt

by newhpnpt: signrank blimmobility = fuimm

by newhpnpt: signrank blfatigue = fufat

by newhpnpt: signrank blsleeppattern = fusp

by newhpnpt: signrank blgisymptoms = fugi

by newhpnpt: signrank blotherpain = fuop

by newhpnpt: signrank blstoma = fusto

by newhpnpt: signrank blnostoma = funosto

by newhpnpt: signrank a_financial_hpnqol = fufi

by newhpnpt: signrank blqolnumericalratingscale = fuqol

*eq-5d new patient longitudinal changes

by newhpnpt: signrank blmobility = fumob

by newhpnpt: signrank blselfcare = fusc

by newhpnpt: signrank blusualactivities = fuua

by newhpnpt: signrank blpaindiscomfort = fupd

by newhpnpt: signrank blanxietydepression = fuad

by newhpnpt: signrank blvalueset = fuvs

by newhpnpt: signrank bleq5dvas = fueq5dvas

* summary statistics non-normally distributed

by sitecode: summarize a_hol_hpnqol, detail

by sitecode: summarize blphysicalfunctioning, detail

by sitecode: summarize blcoping, detail

by sitecode: summarize blabilityeatdrink, detail

by sitecode: summarize a_employment_hpnqol, detail

by sitecode: summarize a_sexfunction_hpnqol, detail

by sitecode: summarize blemotionalfunctioning, detail

by sitecode: summarize blnutritionteam, detail

by sitecode: summarize a_pump_hpnqol, detail

by sitecode: summarize blweight, detail

by sitecode: summarize blbodyimage, detail

by sitecode: summarize blimmobility, detail

by sitecode: summarize blfatigue, detail

by sitecode: summarize blsleeppattern, detail

by sitecode: summarize blgisymptoms, detail

by sitecode: summarize blotherpain, detail

by sitecode: summarize blstoma, detail

by sitecode: summarize blnostoma, detail

by sitecode: summarize a_financial_hpnqol, detail

by sitecode: summarize blqolnumericalratingscale, detail

by sitecode: summarize a_gh_hpnqol, detail

*difference between centres hpnqol

sort sitecode

kwallis a_gh_hpnqol, by(sitecode)

kwallis a_hol_hpnqol, by(sitecode)

kwallis blphysicalfunctioning, by(sitecode)

kwallis blcoping, by(sitecode)

kwallis blabilityeatdrink, by(sitecode)

kwallis a_employment_hpnqol, by(sitecode)

kwallis a_sexfunction_hpnqol, by(sitecode)

kwallis blemotionalfunctioning, by(sitecode)

kwallis blnutritionteam, by(sitecode)

kwallis a_pump_hpnqol, by(sitecode)

kwallis blbodyimage, by(sitecode)

kwallis blweight, by(sitecode)

kwallis blimmobility, by(sitecode)

kwallis blfatigue, by(sitecode)

kwallis blsleeppattern, by(sitecode)

kwallis blgisymptoms, by(sitecode)

kwallis blotherpain, by(sitecode)

kwallis blstoma, by(sitecode)

kwallis blnostoma, by(sitecode)

kwallis a_financial_hpnqol, by(sitecode)

kwallis blqolnumericalratingscale, by(sitecode)

kwallis blsf36pf, by (sitecode)

kwallis blrolelimitationsph, by (sitecode)

kwallis blrolelimitationsep, by (sitecode)

kwallis blenergyfatigue, by (sitecode)

kwallis blewb, by (sitecode)

```
kwallis blsf, by (sitecode)

kwallis blpain, by (sitecode)

kwallis blsf36gh, by (sitecode)

*pairwaise comparisons

ranksum blphysicalfunctioning if sitecode == 1 | sitecode == 2, by(sitecode)

ranksum blphysicalfunctioning if sitecode == 1 | sitecode == 3, by(sitecode)

ranksum blphysicalfunctioning if sitecode == 2 | sitecode == 3, by(sitecode)

ranksum blemotionalfunctioning if sitecode == 1 | sitecode == 2, by(sitecode)

ranksum blemotionalfunctioning if sitecode == 1 | sitecode == 3, by(sitecode)

ranksum blemotionalfunctioning if sitecode == 2 | sitecode == 3, by(sitecode)

ranksum blqolnumericalratingscale if sitecode == 1 | sitecode == 2, by(sitecode)

ranksum blqolnumericalratingscale if sitecode == 1 | sitecode == 3, by(sitecode)

ranksum blqolnumericalratingscale if sitecode == 2 | sitecode == 3, by(sitecode)

 *boxplot symptom scales

graph box blbodyimage blweight blimmobility blfatigue blsleeppattern blgisymptoms
blotherpain blstoma blnostoma a_financial_hpnqol title("HPN-QoL - symptom scale items")

title("HPN-QoL - symptom scale items")

*combining leeds and NUH

gen newsitecode = .

replace newsitecode = 1 if sitecode == 1

replace newsitecode = 2 if sitecode == 2 | sitecode == 3

tabstat bleq5dvas blvalueset, stats(p25 p50 p75) by(newsitecode)
```

```
kwallis a_gh_hpnqol, by(newsitecode)

kwallis a_hol_hpnqol, by(newsitecode)

kwallis blphysicalfunctioning, by(newsitecode)

kwallis blcoping, by(sitecode)

kwallis blabilityeatdrink, by(newsitecode)

kwallis a_employment_hpnqol, by(newsitecode)

kwallis a_sexfunction_hpnqol, by(newsitecode)

kwallis blemotionalfunctioning, by(newsitecode)

kwallis blnutritionteam, by(newsitecode)

kwallis a_pump_hpnqol, by(newsitecode)

kwallis blbodyimage, by(newsitecode)

kwallis blweight, by(newsitecode)

kwallis blimmobility, by(newsitecode)

kwallis blfatigue, by(newsitecode)

kwallis blsleeppattern, by(newsitecode)

kwallis blgisymptoms, by(newsitecode)

kwallis blotherpain, by(newsitecode)

kwallis blstoma, by(newsitecode)

kwallis blnostoma, by(newsitecode)

kwallis a_financial_hpnqol, by(newsitecode)

kwallis blqolnumericalratingscale, by(newsitecode)

tabstat a_gh_hpnqol a_hol_hpnqol blphysicalfunctioning blcoping ///

blabilityeatdrink a_employment_hpnqol a_sexfunction_hpnqol ///

blemotionalfunctioning blnutritionteam a_pump_hpnqol blbodyimage ///

blweight blimmobility blfatigue blsleeppattern blotherpain ///

blstoma blnostoma a_financial_hpnqol blqolnumericalratingscale ///

if !missing(newsitecode), stats(p25 p50 p75) by(newsitecode) columns(statistics)-

tabstat blgisymptoms if !missing(newsitecode), stats(p25 p50 p75) by(newsitecode)
columns(statistics)
```

```
kwallis blsf36pf, by (newsitecode)
kwallis blrolelimitationsph, by (newsitecode)
kwallis blrolelimitationsep, by (newsitecode)
kwallis blenergyfatigue, by (newsitecode)
kwallis blewb, by (newsitecode)
kwallis blsf, by (newsitecode)
kwallis blpain, by (newsitecode)
kwallis blsf36gh, by (newsitecode)
tabstat blsf36pf blrolelimitationsph blrolelimitationsep blenergyfatigue ///
blewb blsf blpain blsf36gh, stats(p25 p50 p75) by(newsitecode) columns(statistics)
kwallis blmobility, by (newsitecode)
kwallis blselfcare, by (newsitecode)
kwallis blusualactivities, by (newsitecode)
kwallis blpaindiscomfort, by (newsitecode)
kwallis blanxietydepression, by (newsitecode)
kwallis bleq5dvas, by (newsitecode)
kwallis blvalueset, by (newsitecode)

* excluding participants over 67 years old
summarize a_employment_hpnqol if age <=67, detail
summarize fuempl if age <=67, detail
summarize a_sexfunction_hpnqol if age <=67, detail
summarize fusf if age <=67, detail

*comparing follow up and lost to follow up groups
sort (fudata)
tabulate new_und_disease fudata, exact
tabulate reasonforhpn fudata, exact
tabulate typeofstoma fudata, exact
tabulate lengthofsb fudata, exact
```

```
tabulate colonincontinuity fudata, exact
ranksum age, by(fudata)
ranksum timeonhpn, by (fudata)
tabulate gender fudata, exact
tabulate house_income fudata, exact
tabulate education_level fudata, exact
tabulate employment_status fudata, exact
tabulate maritalstatus fudata, exact
tabulate livingstatus fudata, exact
tabulate accomm fudata, exact
ranksum imddecile, by(fudata)
ranksum imd_rank, by (fudata)
summarize imd_rank, detail
summarize imddecile, detail
sort fudata
by fudata: summarize imd_rank, detail
by fudata: summarize imddecile, detail
tabulate maritalstatus fudata if maritalstatus == 1
tabulate maritalstatus if maritalstatus == 1 | maritalstatus == 2, exact
tabulate maritalstatus if maritalstatus == 1 | maritalstatus == 3, exact
tabulate maritalstatus if maritalstatus == 2 | maritalstatus == 3, exact
tabulate maritalstatus if maritalstatus == 1 | maritalstatus == 2, by (fudata)
ranksum blemotionalfunctioning if sitecode == 1 | sitecode == 3, by(sitecode)
ranksum blemotionalfunctioning if sitecode == 2 | sitecode == 3, by(sitecode)
* checking for collinearity
* SES
tab house_income education_level, chi2
spearman house_income education_level
spearman maritalstatus livingstatus
*body comp/ muscle function
```

pwcorr blmamccm blmaccm bltsfmm blhgskg blfatfreemassindexkgm blskeletalmusclemasskg phaseangledegree, sig

*kidney function

pwcorr blureammoll blcreatininemmoll blsodiummmoll blpotassiummmoll blmgmmoll bladcammoll blpo4mmoll, sig

*infection

pwcorr blwcc blcrpmgl, sig

*micronutrients

pwcorr blvitaumoll blvitb12pmoll blvitdumoll blfolateugl blcopperumoll blseleniumumoll blzincumoll blmanganeseumoll, sig

*liver function

pwcorr blbilumoll blalpunitl blast blggt blaltunitl, sig

Appendix N: Stat do-file (regression, correlation & PCA)

```
use "H:\V2 clean data 19.12.24.dta"

* cparing groups e.g. are there differences in employment between those that did and didnt
send follow up data

xi: logistic fudata i.employment
xi: logistic fudata i.income
xi: logistic fudata i.marital_status
xi: logistic fudata i.household_income
xi: logistic fudata i.accommodation
xi: logistic fudata i.living_status
xi: logistic fudata i.education

*compares follow up data between centres e.g. did more newcastle patients respond than
Leeds
xi: logistic fudata i.sitecode

* linear regression univariate, do this for every qol domain vs variable
* sf36

generate new_und_disease = ., after(underlying_disease)

** HPNQoL UNIVARIATE **

regress blqolnumericalratingscale timeonhpn
regress blqolnumericalratingscale i.livingstatus
regress blqolnumericalratingscale i.education_level
regress blqolnumericalratingscale i.employment_status
regress blqolnumericalratingscale i.lengthofsb
regress blqolnumericalratingscale i.new_und_disease
regress blqolnumericalratingscale blhgskg
regress blqolnumericalratingscale phaseangledegree
regress blqolnumericalratingscale blskeletalmusclemasskg
regress blqolnumericalratingscale blinfusionswk
regress blqolnumericalratingscale blaveragekcald
regress blqolnumericalratingscale bldietint

regress a_financial_hpnqol timeonhpn
regress a_financial_hpnqol i.livingstatus
regress a_financial_hpnqol i.education_level
regress a_financial_hpnqol i.employment_status
regress a_financial_hpnqol i.lengthofsb
regress a_financial_hpnqol i.new_und_disease
regress a_financial_hpnqol blhgskg
regress a_financial_hpnqol phaseangledegree
regress a_financial_hpnqol blskeletalmusclemasskg
```

```
regress a_financial_hpnqol blinfusionswk
regress a_financial_hpnqol blaveragekcald
regress a_financial_hpnqol bldietint

regress blnostoma timeonhpn
regress blnostoma i.livingstatus
regress blnostoma i.education_level
regress blnostoma i.employment_status
regress blnostoma i.lengthofsb
regress blnostoma i.new_und_disease
regress blnostoma blhgskg
regress blnostoma phaseangledegree
regress blnostoma blskeletalmusclemasskg
regress blnostoma blinfusionswk
regress blnostoma blaveragekcald
regress blnostoma bldietint

regress blstoma timeonhpn
regress blstoma i.livingstatus
regress blstoma i.education_level
regress blstoma i.employment_status
regress blstoma i.lengthofsb
regress blstoma i.new_und_disease
regress blstoma blhgskg
regress blstoma phaseangledegree
regress blstoma blskeletalmusclemasskg
regress blstoma blinfusionswk
regress blstoma blaveragekcald
regress blstoma bldietint

regress blotherpain timeonhpn
regress blotherpain i.livingstatus
regress blotherpain i.education_level
regress blotherpain i.employment_status
regress blotherpain i.lengthofsb
regress blotherpain i.new_und_disease
regress blotherpain blhgskg
regress blotherpain phaseangledegree
regress blotherpain blskeletalmusclemasskg
regress blotherpain blinfusionswk
regress blotherpain blaveragekcald
regress blotherpain bldietint

regress blgisymptoms timeonhpn
regress blgisymptoms i.livingstatus
regress blgisymptoms i.education_level
regress blgisymptoms i.employment_status
regress blgisymptoms i.lengthofsb
```

```
regress blgisymptoms i.new_und_disease
regress blgisymptoms blhgskg
regress blgisymptoms phaseangledegree
regress blgisymptoms blskeletalmusclemasskg
regress blgisymptoms blinfusionswk
regress blgisymptoms blaveragekcald
regress blgisymptoms bldietint

regress blsleeppattern timeonhpn
regress blsleeppattern i.livingstatus
regress blsleeppattern i.education_level
regress blsleeppattern i.employment_status
regress blsleeppattern i.lengthofsb
regress blsleeppattern i.new_und_disease
regress blsleeppattern blhgskg
regress blsleeppattern phaseangledegree
regress blsleeppattern blskeletalmusclemasskg
regress blsleeppattern blinfusionswk
regress blsleeppattern blaveragekcald
regress blsleeppattern bldietint

regress blfatigue timeonhpn
regress blfatigue i.livingstatus
regress blfatigue i.education_level
regress blfatigue i.employment_status
regress blfatigue i.lengthofsb
regress blfatigue i.new_und_disease
regress blfatigue blhgskg
regress blfatigue phaseangledegree
regress blfatigue blskeletalmusclemasskg
regress blfatigue blinfusionswk
regress blfatigue blaveragekcald
regress blfatigue bldietint

regress blimmobility timeonhpn
regress blimmobility i.livingstatus
regress blimmobility i.education_level
regress blimmobility i.employment_status
regress blimmobility i.lengthofsb
regress blimmobility i.new_und_disease
regress blimmobility blhgskg
regress blimmobility phaseangledegree
regress blimmobility blskeletalmusclemasskg
regress blimmobility blinfusionswk
regress blimmobility blaveragekcald
regress blimmobility bldietint

regress blweight timeonhpn
```

```
regress blweight i.livingstatus
regress blweight i.education_level
regress blweight i.employment_status
regress blweight i.lengthofsb
regress blweight i.new_und_disease
regress blweight blhgskg
regress blweight phaseangledegree
regress blweight blskeletalmusclemasskg
regress blweight blinfusionswk
regress blweight blaveragekcald
regress blweight bldietint

regress blbodyimage timeonhpn
regress blbodyimage i.livingstatus
regress blbodyimage i.education_level
regress blbodyimage i.employment_status
regress blbodyimage i.lengthofsb
regress blbodyimage i.new_und_disease
regress blbodyimage blhgskg
regress blbodyimage phaseangledegree
regress blbodyimage blskeletalmusclemasskg
regress blbodyimage blinfusionswk
regress blbodyimage blaveragekcald
regress blbodyimage bldietint

regress a_pump_hpnqol timeonhpn
regress a_pump_hpnqol i.livingstatus
regress a_pump_hpnqol i.education_level
regress a_pump_hpnqol i.employment_status
regress a_pump_hpnqol i.lengthofsb
regress a_pump_hpnqol i.new_und_disease
regress a_pump_hpnqol blhgskg
regress a_pump_hpnqol phaseangledegree
regress a_pump_hpnqol blskeletalmusclemasskg
regress a_pump_hpnqol blinfusionswk
regress a_pump_hpnqol blaveragekcald
regress a_pump_hpnqol bldietint

regress blnutritionteam timeonhpn
regress blnutritionteam i.livingstatus
regress blnutritionteam i.education_level
regress blnutritionteam i.employment_status
regress blnutritionteam i.lengthofsb
regress blnutritionteam i.new_und_disease
regress blnutritionteam blhgskg
regress blnutritionteam phaseangledegree
regress blnutritionteam blskeletalmusclemasskg
regress blnutritionteam blinfusionswk
```

```
regress blnutritionteam blaveragekcald
regress blnutritionteam bldietint

regress blemotionalfunctioning timeonhpn
regress blemotionalfunctioning i.livingstatus
regress blemotionalfunctioning i.education_level
regress blemotionalfunctioning i.employment_status
regress blemotionalfunctioning i.lengthofsb
regress blemotionalfunctioning i.new_und_disease
regress blemotionalfunctioning blhgskg
regress blemotionalfunctioning phaseangledegree
regress blemotionalfunctioning blskeletalmusclemasskg
regress blemotionalfunctioning blinfusionswk
regress blemotionalfunctioning blaveragekcald
regress blemotionalfunctioning bldietint

regress a_sexfunction_hpnqol timeonhpn
regress a_sexfunction_hpnqol i.livingstatus
regress a_sexfunction_hpnqol i.education_level
regress a_sexfunction_hpnqol i.employment_status
regress a_sexfunction_hpnqol i.lengthofsb
regress a_sexfunction_hpnqol i.new_und_disease
regress a_sexfunction_hpnqol blhgskg
regress a_sexfunction_hpnqol phaseangledegree
regress a_sexfunction_hpnqol blskeletalmusclemasskg
regress a_sexfunction_hpnqol blinfusionswk
regress a_sexfunction_hpnqol blaveragekcald
regress a_sexfunction_hpnqol bldietint

regress a_employment_hpnqol timeonhpn
regress a_employment_hpnqol i.livingstatus
regress a_employment_hpnqol i.education_level
regress a_employment_hpnqol i.employment_status
regress a_employment_hpnqol i.lengthofsb
regress a_employment_hpnqol i.new_und_disease
regress a_employment_hpnqol blhgskg
regress a_employment_hpnqol phaseangledegree
regress a_employment_hpnqol blskeletalmusclemasskg
regress a_employment_hpnqol blinfusionswk
regress a_employment_hpnqol blaveragekcald
regress a_employment_hpnqol bldietint

regress blabilityeatdrink timeonhpn
regress blabilityeatdrink i.livingstatus
regress blabilityeatdrink i.education_level
regress blabilityeatdrink i.employment_status
regress blabilityeatdrink i.lengthofsb
regress blabilityeatdrink i.new_und_disease
```

```
regress blabilityeatdrink blhgskg
regress blabilityeatdrink phaseangledegree
regress blabilityeatdrink blskeletalmusclemasskg
regress blabilityeatdrink blinfusionswk
regress blabilityeatdrink blaveragekcald
regress blabilityeatdrink bldietint

regress blcoping timeonhpn
regress blcoping i.livingstatus
regress blcoping i.education_level
regress blcoping i.employment_status
regress blcoping i.lengthofsb
regress blcoping i.new_und_disease
regress blcoping blhgskg
regress blcoping phaseangledegree
regress blcoping blskeletalmusclemasskg
regress blcoping blinfusionswk
regress blcoping blaveragekcald
regress blcoping bldietint

regress blphysicalfunctioning timeonhpn
regress blphysicalfunctioning i.livingstatus
regress blphysicalfunctioning i.education_level
regress blphysicalfunctioning i.employment_status
regress blphysicalfunctioning i.lengthofsb
regress blphysicalfunctioning i.new_und_disease
regress blphysicalfunctioning blhgskg
regress blphysicalfunctioning phaseangledegree
regress blphysicalfunctioning blskeletalmusclemasskg
regress blphysicalfunctioning blinfusionswk
regress blphysicalfunctioning blaveragekcald
regress blphysicalfunctioning bldietint

regress a_hol_hpnqol timeonhpn
regress a_hol_hpnqol i.livingstatus
regress a_hol_hpnqol i.education_level
regress a_hol_hpnqol i.employment_status
regress a_hol_hpnqol i.lengthofsb
regress a_hol_hpnqol i.new_und_disease
regress a_hol_hpnqol blhgskg
regress a_hol_hpnqol phaseangledegree
regress a_hol_hpnqol blskeletalmusclemasskg
regress a_hol_hpnqol blinfusionswk
regress a_hol_hpnqol blaveragekcald
regress a_hol_hpnqol bldietint


regress a_gh_hpnqol timeonhpn
```

```
regress a_gh_hpnqol i.lengthofsb
regress a_gh_hpnqol i.new_und_disease
regress a_gh_hpnqol blhgskg
regress a_gh_hpnqol phaseangledegree
regress a_gh_hpnqol blskeletalmusclemasskg
regress a_gh_hpnqol blinfusionswk
regress a_gh_hpnqol blaveragekcald
regress a_gh_hpnqol bldietint
regress a_gh_hpnqol i.livingstatus
regress a_gh_hpnqol i.education_level
regress a_gh_hpnqol i.employment_status



** gender interaction SF36 BL**

regress blsf36pf c.phaseangledegree##i.gender
regress blsf36pf c.blhgs##i.gender

regress blrolelimitationsph c.blhgs##i.gender
regress blrolelimitationsph i.employment_status##i.gender
regress blrolelimitationsph c.phaseangledegree##i.gender
regress blrolelimitationsph c.blskeletalmusclemasskg##i.gender
regress blrolelimitationsep i.employment_status##i.gender
regress blenergyfatigue c.blhgs##i.gender
regress blenergyfatigue c.blskeletalmusclemasskg##i.gender
regress blenergyfatigue i.employment_status##i.gender
regress blewb i.employment_status##i.gender
regress blewb c.phaseangledegree##i.gender
regress blsf i.employment_status##i.gender
regress blsf c.phaseangledegree##i.gender
regress blsf i.education_level##i.gender
regress blpain i.employment_status##i.gender
regress blpain c.blskeletalmusclemasskg##i.gender
regress blsf36gh i.employment_status##i.gender


**gender interactions** BL HPNQOL

regress a_gh_hpnqol c.blhgs##i.gender
regress blphysicalfunctioning c.blhgs##i.gender
regress blphysicalfunctioning c.blskeletalmusclemasskg##i.gender
regress blphysicalfunctioning i.education_level##i.gender
regress a_employment_hpnqol c.blhgs##i.gender
regress a_sexfunction_hpnqol c.blhgs##i.gender
regress a_sexfunction_hpnqol i.employment_status##i.gender
regress blimmobility i.education_level##i.gender
regress blimmobility i.employment_status##i.gender
```

```
regress blfatigue c.blhgs##i.gender
regress blsleeppattern c.blhgs##i.gender
regress blstoma i.employment_status##i.gender
regress blstoma c.phaseangledegree##i.gender
regress a_financial_hpnqol i.employment_status##i.gender
regress blqolnumericalratingscale i.employment_status##i.gender

** SIGNIFICANT**
regress blimmobility c.blhgs##i.gender
regress blfatigue c.blhgs##i.gender
regress blsleeppattern c.blhgs##i.gender
regress a_financial_hpnqol i.employment_status##i.gender
regress blqolnumericalratingscale i.employment_status##i.gender


** look at multivariable models separately for these!! **
regress blimmobility blhgs if gender == 0
regress blimmobility blhgs if gender == 1
regress blfatigue blhgs if gender == 0
regress blfatigue blhgs if gender == 1
regress blsleeppattern blhgs if gender == 0
regress blsleeppattern blhgs if gender == 1

regress blfatigue blhgs age if gender == 0
regress blfatigue blhgs age if gender == 1


* multivariable using the signficant results
** CONFOUNDERS **

regress blrolelimitationsph bldietint gender
regress blewb bldietint gender
regress blsf bldietint gender

regress blsf blinfusionswk
regress blsf blinfusionswk gender
regress blsf blinfusionswk age

regress blsf36pf phaseangledegree
regress blsf36pf phaseangledegree age
regress blsf36pf phaseangledegree i.gender

regress blsf36pf i.education_level
regress blsf36pf i.education_level age
regress blsf36pf i.education_level i.gender

regress blsf36pf i.employment_status
regress blsf36pf i.employment_status age
```

```
regress blsf36pf i.employment_status age i.gender

regress blsf36pf blhgskg
regress blsf36pf blhgskg age
regress blsf36pf blhgskg i.gender

regress blsf36pf blhgskg i.gender
regress blsf36pf blhgskg i.gender phaseangledegree

regress blrolelimitationsph phaseangledegree
regress blrolelimitationsph phaseangledegree age
regress blrolelimitationsph phaseangledegree i.gender

regress blrolelimitationsph blskeletalmusclemasskg
regress blrolelimitationsph blskeletalmusclemasskg age
regress blrolelimitationsph blskeletalmusclemasskg i.gender

regress blrolelimitationsph i.employment_status
regress blrolelimitationsph i.employment_status age
regress blrolelimitationsph i.employment_status age i.gender

regress blrolelimitationsph blhgskg
regress blrolelimitationsph blhgskg age
regress blrolelimitationsph blhgskg age i.gender

regress blrolelimitationsep i.employment_status
regress blrolelimitationsep i.employment_status age
regress blrolelimitationsep i.employment_status age i.gender

regress blenergyfatigue i.employment_status
regress blenergyfatigue i.employment_status age
regress blenergyfatigue i.employment_status age i.gender

regress blenergyfatigue blhgskg
regress blenergyfatigue blhgskg age
regress blenergyfatigue blaveragekcald blhgskg

regress blewb i.employment_status
regress blewb i.employment_status age
regress blewb i.employment_status age i.gender phaseangledegree

regress blewb phaseangledegree
regress blewb phaseangledegree age
regress blewb phaseangledegree i.gender

regress blsf phaseangledegree
regress blsf phaseangledegree age
regress blsf phaseangledegree i.gender
```

```
regress blsf i.employment_status
regress blsf i.employment_status age
regress blsf i.employment_status age i.gender

regress blsf i.education_level
regress blsf i.education_level age
regress blsf i.education_level age i.gender

regress blpain i.employment_status
regress blpain i.employment_status age
regress blpain i.employment_status age i.gender

regress blpain blskeletalmusclemasskg
regress blpain blskeletalmusclemasskg age
regress blpain blskeletalmusclemasskg i.gender

regress blenergyfatigue blskeletalmusclemasskg
regress blenergyfatigue blskeletalmusclemasskg age
regress blenergyfatigue blskeletalmusclemasskg i.gender

regress blsf36gh i.employment_status
regress blsf36gh i.employment_status age
regress blsf36gh i.employment_status age gender

regress blpain blskeletalmusclemasskg
regress blpain blskeletalmusclemasskg age
regress blpain blskeletalmusclemasskg i.gender

regress a_employment_hpnqol blhgskg
regress a_employment_hpnqol blhgskg age
regress a_employment_hpnqol blhgskg age i.gender

regress blfatigue blhgskg
regress blfatigue blhgskg age
regress blfatigue blhgskg age i.gender

regress a_gh_hpnqol blhgskg
regress a_gh_hpnqol blhgskg age
regress a_gh_hpnqol blhgskg age i.gender

regress a_gh_hpnqol bldietint
regress a_gh_hpnqol bldietint age
regress a_gh_hpnqol bldietint i.gender

regress blphysicalfunctioning blhgskg
regress blphysicalfunctioning blhgskg age
regress blphysicalfunctioning blhgskg i.gender
```

```
regress blphysicalfunctioning blskeletalmusclemasskg
regress blphysicalfunctioning blskeletalmusclemasskg age
regress blphysicalfunctioning blskeletalmusclemasskg i.gender

regress blphysicalfunctioning i.education_level
regress blphysicalfunctioning i.education_level age
regress blphysicalfunctioning i.education_level i.gender

regress a_sexfunction_hpnqol blhgskg
regress a_sexfunction_hpnqol blhgskg age
regress a_sexfunction_hpnqol blhgskg age i.gender

regress a_sexfunction_hpnqol i.employment_status
regress a_sexfunction_hpnqol i.employment_status age
regress a_sexfunction_hpnqol i.employment_status age i.gender

regress blsleeppattern blhgskg
regress blsleeppattern blhgskg age
regress blsleeppattern blhgskg age i.gender

regress blimmobility blhgskg
regress blimmobility blhgskg age
regress blimmobility blhgskg i.gender

regress blimmobility i.education_level
regress blimmobility i.education_level age
regress blimmobility i.education_level i.gender

regress blimmobility i.employment_status
regress blimmobility i.employment_status age
regress blimmobility i.employment_status i.gender

regress a_financial_hpnqol i.employment_status
regress a_financial_hpnqol i.employment_status age
regress a_financial_hpnqol i.employment_status age i.gender

regress blqolnumericalratingscale i.employment_status
regress blqolnumericalratingscale i.employment_status age
regress blqolnumericalratingscale i.employment_status age i.gender

regress blstoma i.employment_status
regress blstoma i.employment_status age
regress blstoma i.employment_status age i.gender_n

regress blnostoma i.employment_status
regress blnostoma i.employment_status age
regress blnostoma i.employment_status age i.gender_n
```

```
regress blstoma phaseangledegree
regress blstoma phaseangledegree age
regress blstoma phaseangledegree i.gender_n

regress a_employment_hpnqol
regress a_employment_hpnqol age
regress a_employment_hpnqol i.gender

regress a_sexfunction_hpnqol blhpnvol
regress a_sexfunction_hpnqol blhpnvol age
regress a_sexfunction_hpnqol blhpnvol i.gender

regress a_hol_hpnqol blhpnvol
regress a_hol_hpnqol blhpnvol age

*if significant then adjust for the following
xi: regress blphysicalfunctioning i.marital_status age
xi: regress blphysicalfunctioning i.marital_status gender

* checking for collinearity
* SES
tab house_income education_level, chi2
tab house_income livingstatus, chi2
spearman house_income education_level
spearman maritalstatus livingstatus

tab maritalstatus livingstatus, chi2

*body comp/ muscle function
pwcorr blmamccm blmaccm bltsfmm blhgskg blfatfreemassindexkgm
blskeletalmusclemasskg phaseangledegree, sig

*pn composition
pwcorr blaverageglucosedg blaveragekcald blaveragelipiddg blaveragenitrogendg
blinfusionswk bldietint, sig

pwcorr blaveragekcald bldietint blinfusionswk blhpnvol, sig

*kidney function
pwcorr blureammoll blcreatininemmoll blsodiummmoll blpotassiummmoll blmgmmoll
bladcammoll blpo4mmoll, sig

*infection
pwcorr blwcc blcrpmgl, sig

*micronutrients
```

```
pwcorr blvitaumoll blvitb12pmoll blvitdumoll blfolateugl blcopperumoll blseleniumumoll
blzincumoll blmanganeseumoll, sig

*liver function
pwcorr blbilumoll blalpunitl blast blggt blaltunitl, sig

*multivariable regression
*sf-36

regress blrolelimitationsph phaseangledegree if e(sample)
estimates store model1
regress blrolelimitationsph phaseangledegree bldietint
estimates store model2
lrtest model1 model2

regress blrolelimitationsph phaseangledegree if e(sample)
estimates store model1
regress blrolelimitationsph phaseangledegree blskeletalmusclemasskg
estimates store model2

regress blrolelimitationsph i.employment_status age gender if e(sample)
estimates store model1
regress blrolelimitationsph i.employment_status age gender phaseangledegree
estimates store model2
lrtest model1 model2

regress blrolelimitationsph i.employment_status age gender phaseangledegree if e(sample)
estimates store model2
regress blrolelimitationsph i.employment_status age gender phaseangledegree bldietint
estimates store model3
lrtest model2 model3

regress blrolelimitationsph i.employment_status age gender phaseangledegree if e(sample)
estimates store model2
regress blrolelimitationsph i.employment_status age gender phaseangledegree
blskeletalmusclemasskg
estimates store model3
lrtest model2 model3

regress blrolelimitationsph i.employment_status age gender phaseangledegree if e(sample)
estimates store model2
regress blrolelimitationsph i.employment_status age gender phaseangledegree i.lengthofsb
estimates store model3
lrtest model2 model3

regress blenergyfatigue bldietint if e(sample)
estimates store model1
regress blenergyfatigue bldietint blhgskg
```

```
estimates store model2
lrtest model1 model2

regress blenergyfatigue bldietint blhgskg if e(sample)
estimates store model2
regress blenergyfatigue bldietint blhgskg i.employment_status
estimates store model3
lrtest model2 model3

regress blenergyfatigue bldietint blhgskg if e(sample)
estimates store model2
regress blenergyfatigue bldietint blhgskg blskeletalmusclemasskg
estimates store model3
lrtest model2 model3

regress blenergyfatigue
regress blhgs

** interaction test
regress fuenfat i.gender
regress fuenfat fuhgs
regress fuenfat c.fuhgs##i.gender

regress fuenfat fuhgs i.gender

pwcorr phaseangledegree blskeletalmusclemasskg, sig

*** SF36 FINAL MVM ***

regress blenergyfatigue bldietint if e(sample)
estimates store model1
regress blenergyfatigue bldietint blhgskg
estimates store model2
lrtest model1 model2

regress blsf36pf blhgskg
estimates store model1
regress blsf36pf blhgskg i.gender
estimates store model2
lrtest model1 model2

regress blsf36pf blhgskg i.gender if e(sample)
estimates store model3
regress blsf36pf blhgskg i.gender phaseangledegree
estimates store model4
lrtest model3 model4

regress blsf blhgskg i.gender if e(sample)
```

```
estimates store model2
regress blsf blhgskg i.gender i.employment_status
estimates store model3
lrtest model2 model3

regress blsf blhgskg i.gender if e(sample)
estimates store model2
regress blsf blhgskg i.gender phaseangledegree
estimates store model3
lrtest model2 model3

regress blsf bldietint if e(sample)
estimates store model1
regress blsf bldietint i.employment_status
estimates store model2
lrtest model1 model2

regress blsf bldietint i.employment_status if e(sample)
estimates store model2
regress blsf bldietint i.employment_status i.lengthofsb
estimates store model3
lrtest model2 model3

regress blpain i.employment_status
estimates store model1
regress blpain i.employment_status age
estimates store model2
lrtest model1 model2

regress blpain i.employment_status age if e(sample)
estimates store model1
regress blpain i.employment_status age blskeletalmusclemasskg
estimates store model2
lrtest model1 model2

regress blpain i.employment_status age i.gender if e(sample)
estimates store model1
regress blpain i.employment_status age i.gender blskeletalmusclemasskg
estimates store model2
lrtest model1 model2

regress blrolelimitationsep i.employment_status i.gender

regress blewb i.employment_status
estimates store model1
regress blewb i.employment_status age
estimates store model2
lrtest model1 model2
```

```
regress blewb i.employment_status age if e(sample)
estimates store model2
regress blewb i.employment_status age i.gender
estimates store model3
lrtest model2 model3

regress blewb i.employment_status age i.gender if e(sample)
estimates store model1
regress blewb i.employment_status age i.gender phaseangledegree
estimates store model2
lrtest model1 model2

regress blrolelimitationsph i.employment_status
estimates store model1
regress blrolelimitationsph i.employment_status age
estimates store model2
lrtest model1 model2

regress blrolelimitationsph i.employment_status age if e(sample)
estimates store model1
regress blrolelimitationsph i.employment_status age i.gender
estimates store model2
lrtest model1 model2

regress blrolelimitationsph i.employment_status age i.gender if e(sample)
estimates store model2
regress blrolelimitationsph i.employment_status age i.gender phaseangledegree
estimates store model3
lrtest model2 model3

regress blsf36gh i.employment_status
estimates store model1
regress blsf36gh i.employment_status age
estimates store model2
lrtest model1 model2

** SF36 MVR DIAGNOSTICS ***
regress a_gh_hpnqol i.employment_status
estimates store model1
regress a_gh_hpnqol i.employment_status age
estimates store model2
lrtest model1 model2

regress a_gh_hpnqol i.employment_status age if e(sample)
estimates store model1
regress a_gh_hpnqol i.employment_status age i.gender
estimates store model2
```

```
lrtest model1 model2

** PF **
regress blsf36pf blhgskg i.gender phaseangledegree
rvfplot        // Residual vs Fitted plot
vif
predict r, resid
qnorm r
histogram r, normal
sktest r
predict cook, cooksd
predict h, hat

// Plot leverage vs squared residuals
lvr2plot

// List top 5 influential observations
sort cook
list cook h r if cook > 4/_N
estat hettest

*** RLPH ***
regress blrolelimitationsph i.employment_status age gender phaseangledegree

** Check for multicollinearity
vif
** Plot residuals vs fitted values
rvfplot
** Check normality of residuals
predict r, resid
qnorm r
histogram r, normal
sktest r
** Test for heteroskedasticity
estat hettest

** adjust the SE to be valid due to heteroskedasticity
regress blrolelimitationsph i.employment_status age gender phaseangledegree, vce(robust)

** Energy/ fatigue ***
regress blenergyfatigue bldietint blhgskg
vif
rvfplot
predict residuals_energy3, resid
qnorm residuals_energy3
histogram residuals_energy3, normal
sktest residuals_energy3
estat hettest
```

** EWB **
regress blewb i.employment_status age gender phaseangledegree
vif
rvfplot
predict residuals_energy5, resid
qnorm residuals_energy5
histogram residuals_energy5, normal
sktest residuals_energy5
estat hettest

** SF **
regress blsf bldietint i.employment_status i.lengthofsb
vif
rvfplot
predict residuals_energy3, resid
qnorm residuals_energy3
histogram residuals_energy3, normal
sktest residuals_energy3
lvr2plot
estat hettest

** PAIN **
regress blpain i.employment_status age gender blskeletalmusclemasskg
vif
rvfplot
predict residuals_energy, resid
qnorm residuals_energy
histogram residuals_energy, normal
sktest residuals_energy
lvr2plot
estat hettest

** GH **
regress blsf36gh i.employment_status age i.gender, vce(robust)

vif
rvfplot
predict residuals_energy2, resid
qnorm residuals_energy2
histogram residuals_energy2, normal
sktest residuals_energy2
lvr2plot
estat hettest

*** HPNQoL ***

** GH **

```
regress a_gh_hpnqol blhgskg
estimates store model1
regress a_gh_hpnqol blhgskg i.gender
estimates store model2
lrtest model1 model2

regress a_gh_hpnqol i.gender age
vif
rvfplot
predict residuals_energy3, resid
qnorm residuals_energy3
histogram residuals_energy3, normal
sktest residuals_energy3
lvr2plot
estat hettest

regress a_gh_hpnqol i.gender if e(sample)
estimates store model1
regress a_gh_hpnqol i.gender blhgskg
estimates store model2
lrtest model1 model2

regress blphysicalfunctioning i.employment_status if e(sample)
estimates store model1
regress blphysicalfunctioning i.employment_status i.gender
estimates store model2
lrtest model1 model2

regress blphysicalfunctioning i.employment_status i.gender if e(sample)
estimates store model3
regress blphysicalfunctioning i.employment_status i.gender i.education_level
estimates store model4
lrtest model3 model4

regress blphysicalfunctioning i.employment_status i.gender i.education_level
vif
rvfplot
predict residuals_energy4, resid
qnorm residuals_energy4
histogram residuals_energy4, normal
sktest residuals_energy4
lvr2plot
estat hettest

regress blphysicalfunctioning i.employment_status i.gender i.education_level if e(sample)
estimates store model3
regress blphysicalfunctioning i.employment_status i.gender i.education_level
blskeletalmusclemasskg
```

```
estimates store model4
lrtest model3 model4

regress blabilityeatdrink bldietint if e(sample)
estimates store model1
regress blabilityeatdrink bldietint blhgskg
estimates store model2
lrtest model1 model2

regress blabilityeatdrink bldietint blhgskg
vif
rvfplot
predict residuals_energy6, resid
qnorm residuals_energy6
histogram residuals_energy6, normal
sktest residuals_energy6
lvr2plot
estat hettest

regress blabilityeatdrink bldietint blhgskg if e(sample)
estimates store model1
regress blabilityeatdrink bldietint blhgskg blskeletalmusclemasskg
estimates store model2
lrtest model1 model2

regress a_employment_hpnqol i.education_level if e(sample)
estimates store model2
regress a_employment_hpnqol i.education_level blhgskg
estimates store model3
lrtest model2 model3

regress a_employment_hpnqol i.education_level blhgskg
estimates store model1
regress a_employment_hpnqol i.education_level blhgskg age
estimates store model2
lrtest model1 model2

regress a_employment_hpnqol i.education_level blhgskg age
estimates store model2
regress a_employment_hpnqol i.education_level blhgskg age i.gender
estimates store model3
lrtest model2 model3

regress a_employment_hpnqol blhgskg
estimates store model1
regress a_employment_hpnqol blhgskg age
estimates store model2
lrtest model1 model2
```

```
regress a_employment_hpnqol i.education_level blhgskg age, vce(robust)
vif
rvfplot
predict residuals_energy7, resid
qnorm residuals_energy7
histogram residuals_energy7, normal
sktest residuals_energy7
lvr2plot
estat hettest

regress a_sexfunction_hpnqol i.lengthofsb i.employment_status age i.gender, vce(robust)
vif
rvfplot
predict residuals_energy8, resid
qnorm residuals_energy8
histogram residuals_energy8, normal
sktest residuals_energy8
lvr2plot
estat hettest

regress a_sexfunction_hpnqol i.lengthofsb
estimates store model1
regress a_sexfunction_hpnqol i.lengthofsb i.employment_status
estimates store model2
lrtest model1 model2

regress a_sexfunction_hpnqol i.employment_status
estimates store model3
regress a_sexfunction_hpnqol i.employment_status age
estimates store model4
lrtest model3 model4

regress a_sexfunction_hpnqol i.employment_status age if e(sample)
estimates store model1
regress a_sexfunction_hpnqol i.employment_status age i.gender
estimates store model2
lrtest model1 model2

regress a_sexfunction_hpnqol i.lengthofsb i.employment_status age i.gender if e(sample)
estimates store model2
regress a_sexfunction_hpnqol i.lengthofsb i.employment_status age i.gender blhgskg
estimates store model3
lrtest model2 model3

regress blemotionalfunctioning blhgskg if e(sample)
estimates store model1
regress blemotionalfunctioning blhgskg age
```

```
estimates store model2
lrtest model1 model2

regress blemotionalfunctioning blhgskg age if e(sample)
estimates store model1
regress blemotionalfunctioning blhgskg age i.employment_status
estimates store model2
lrtest model1 model2

regress blemotionalfunctioning blhgskg age
vif
rvfplot
predict residuals_energy9, resid
qnorm residuals_energy9
histogram residuals_energy9, normal
sktest residuals_energy9
lvr2plot
estat hettest

** HPN ITEMS ***

regress blnutritionteam blhgskg blinfusionswk, vce(robust)
vif
rvfplot
predict residuals_energy0, resid
qnorm residuals_energy0
histogram residuals_energy0, normal
sktest residuals_energy0
lvr2plot
estat hettest

regress blnutritionteam blhgskg
estimates store model1
regress blnutritionteam blhgskg blinfusionswk
estimates store model2
lrtest model1 model2

regress blnutritionteam blhgskg blinfusionswk if e(sample)
estimates store model1
regress blnutritionteam blhgskg blinfusionswk phaseangledegree
estimates store model2
lrtest model1 model2

regress a_pump_hpnqol blhgskg if e(sample)
estimates store model1
regress a_pump_hpnqol blhgskg blskeletalmusclemasskg
estimates store model2
lrtest model1 model2
```

*** SYMPTOM SCALES ***

```
regress blfatigue blhgskg
estimates store model1
regress blfatigue blhgskg age
estimates store model2
lrtest model1 model2

regress blfatigue blhgskg age
vif
rvfplot
predict residuals_energy00, resid
qnorm residuals_energy00
histogram residuals_energy00, normal
sktest residuals_energy00
lvr2plot
estat hettest

regress blgisymptoms i.employment_status
estimates store model1
regress blgisymptoms i.employment_status i.lengthofsb
estimates store model2
lrtest model1 model2

regress blgisymptoms i.employment_status i.lengthofsb, vce(robust)
vif
rvfplot
predict residuals_energy01, resid
qnorm residuals_energy01
histogram residuals_energy01, normal
sktest residuals_energy01
lvr2plot
estat hettest

regress blotherpain i.employment_status
estimates store model1
regress blotherpain i.employment_status blhgskg
estimates store model2
lrtest model1 model2

regress blotherpain i.employment_status blhgskg
vif
rvfplot
predict residuals_energy02, resid
qnorm residuals_energy02
histogram residuals_energy02, normal
sktest residuals_energy02
```

```
lvr2plot
estat hettest

regress blstoma i.employment_status if e(sample)
estimates store model1
regress blstoma i.employment_status phaseangledegree
estimates store model2
lrtest model1 model2

regress blstoma phaseangledegree if e(sample)
estimates store model3
regress blstoma phaseangledegree i.lengthofsb
estimates store model4
lrtest model3 model4

regress blstoma i.employment_status phaseangledegree i.lengthofsb
vif
rvfplot
predict residuals_energy03, resid
qnorm residuals_energy03
histogram residuals_energy03, normal
sktest residuals_energy03
lvr2plot
estat hettest

regress blimmobility blhgskg if e(sample)
estimates store model1
regress blimmobility blhgskg i.education_level
estimates store model2
lrtest model1 model2

regress blfatigue blhgskg if e(sample)
estimates store model1
regress blfatigue blhgskg age
estimates store model2
lrtest model1 model2

regress blfatigue blhgskg age
estimates store model2
regress blfatigue blhgskg age i.gender
estimates store model3
lrtest model2 model3

regress blgisymptoms i.employment_status
estimates store model1
regress blgisymptoms i.employment_status i.lengthofsb
estimates store model2
lrtest model1 model2
```

```
regress blotherpain i.employment_status if e(sample)
estimates store model1
regress blotherpain i.employment_status blhgskg
estimates store model2
lrtest model1 model2

regress blotherpain i.employment_status blhgskg if e(sample)
estimates store model2
regress blotherpain i.employment_status blhgskg blskeletalmusclemasskg
estimates store model3
lrtest model2 model3

regress blsleeppattern blhgskg

regress blstoma i.employment_status if e(sample)
estimates store model1
regress blstoma i.employment_status phaseangledegree
estimates store model2
lrtest model1 model2

regress blstoma i.employment_status phaseangledegree if e(sample)
estimates store model1
regress blstoma i.employment_status phaseangledegree i.lengthofsb
estimates store model2
lrtest model1 model2

regress blnostoma i.lengthofsb if e(sample)
estimates store model1
regress blnostoma i.lengthofsb phaseangledegree
estimates store model2
lrtest model1 model2

*12m univariate regression
*****

regress fued timeonhpn
regress fued i.livingstatus
regress fued i.education_level
regress fued i.employment_status
regress fued i.lengthofsb
regress fued fuhgs
regress fued blskeletalmusclemasskg
regress fued phaseangledegree
regress fued bldietint
regress fued fuinfperwk

regress fugh timeonhpn
```

```
regress fugh i.livingstatus
regress fugh i.education_level
regress fugh i.employment_status
regress fugh i.lengthofsb
regress fugh fuhgs
regress fugh blskeletalmusclemasskg
regress fugh phaseangledegree
regress fugh bldietint
regress fugh fuinfperwk
regress fugh fuavkcday

regress fuhol timeonhpn
regress fuhol i.livingstatus
regress fuhol i.education_level
regress fuhol i.employment_status
regress fuhol i.lengthofsb
regress fuhol fuhgs
regress fuhol blskeletalmusclemasskg
regress fuhol phaseangledegree
regress fuhol bldietint
regress fuhol fuinfperwk
regress fuhol fuavgluc
regress fuhol fuavkcday

regress fusto timeonhpn
regress fusto i.livingstatus
regress fusto i.education_level
regress fusto i.employment_status
regress fusto i.lengthofsb
regress fusto fuhgs
regress fusto blskeletalmusclemasskg
regress fusto phaseangledegree
regress fusto bldietint
regress fusto fuinfperwk
regress fusto fuavkcday

regress fuenfat timeonhpn
regress fuenfat i.livingstatus
regress fuenfat i.education_level
regress fuenfat i.employment_status
regress fuenfat i.lengthofsb
regress fuenfat fuhgs
regress fuenfat blskeletalmusclemasskg
regress fuenfat phaseangledegree
regress fuenfat bldietint
regress fuenfat fuinfperwk
regress fuenfat fuavkcday
```

```
ologit blmobility i.house_income, or
ologit blmobility i.education_level, or
ologit blmobility i.employment_status, or

regress fuenfat fuhgs age
regress fuenfat fuhgs i.gender

regress fuenfat i.lengthofsb if e(sample)
estimates store model1
regress fuenfat i.lengthofsb fuhgs
estimates store model2
lrtest model1 model2

regress fuenfat i.lengthofsb fuhgs
estimates store model1
regress fuenfat i.lengthofsb fuhgs age
estimates store model2
lrtest model1 model2

regress fusto
estimates store model1
regress fusto i.education_level
estimates store model2
lrtest model1 model2

regress fusto i.education_level
estimates store model1
regress fusto i.education_level i.employment_status
estimates store model2
lrtest model1 model2

*12m multivariable regression

regress fued bldietint
estimates store model1
regress fued bldietint fuavkcday
estimates store model2
lrtest model1 model2

regress fued bldietint fuavkcday
estimates store model3
regress fued bldietint fuavkcday fuinfperwk
estimates store model4
lrtest model3 model4

regress fued bldietint fuavkcday
estimates store model1
regress fued bldietint fuavkcday i.lengthofsb
```

```
estimates store model2
lrtest model1 model2


*** COEFFICIENT PLOTS ***


clear
input byte id str20 domain float(coef lower_ci upper_ci pvalue)
1 "RLPH"      11.08   -5.44   39.11   0.416
2 "Energy"    0.01     0.01    0.02   0.001
3 "SF"        0.02     0.01    0.03   0.001
4 "GH"       20.26     2.31   30.06   0.000
end

label define domlbl 1 "RLPH" 2 "Energy/fatigue" 3 "Social Functioning" 4 "General Health"
label values id domlbl

twoway ///
(rcap id lower_ci upper_ci) ///
(scatter id coef, msymbol(circle)), ///
xlabel(1(1)4, valuelabel angle(0)) ///
ylabel(, grid) ///
yline(0, lpattern(dash)) ///
title("Multivariable Regression Coefficients for SF-36 Domains") ///
ytitle("Coefficient (with 95% CI)") ///
xtitle("") ///
legend(off)

** EQ5D univariate **

regress bleq5dvas timeonhpn
regress bleq5dvas i.lengthofsb
regress bleq5dvas blhgskg
regress bleq5dvas phaseangledegree
regress bleq5dvas blskeletalmusclemasskg
regress bleq5dvas blinfusionswk
regress bleq5dvas blaveragekcald
regress bleq5dvas bldietint
regress bleq5dvas i.livingstatus
regress bleq5dvas i.new_und_disease
regress bleq5dvas i.education_level
regress bleq5dvas i.employment_status

regress blvalueset timeonhpn
regress blvalueset i.new_und_disease
regress blvalueset i.lengthofsb
regress blvalueset blhgskg
```

```
regress blvalueset phaseangledegree
regress blvalueset blskeletalmusclemasskg
regress blvalueset blinfusionswk
regress blvalueset blaveragekcald
regress blvalueset bldietint
regress blvalueset i.livingstatus
regress blvalueset i.education_level
regress blvalueset i.employment_status

ologit blmobility timeonhpn, or
ologit blmobility i.new_und_disease, or
ologit blmobility i.reasonforhpn, or
ologit blmobility i.lengthofsb, or
ologit blmobility blhgskg, or
ologit blmobility phaseangledegree, or
ologit blmobility blskeletalmusclemasskg, or
ologit blmobility blinfusionswk, or
ologit blmobility blaveragekcald, or
ologit blmobility bldietint, or
ologit blmobility i.livingstatus, or
ologit blmobility i.education_level, or
ologit blmobility i.employment_status, or

ologit blselfcare timeonhpn, or
ologit blselfcare i.new_und_disease, or
ologit blselfcare i.lengthofsb, or
ologit blselfcare blhgskg, or
ologit blselfcare phaseangledegree, or
ologit blselfcare blskeletalmusclemasskg, or
ologit blselfcare blinfusionswk, or
ologit blselfcare blaveragekcald, or
ologit blselfcare bldietint, or
ologit blselfcare i.livingstatus, or
ologit blselfcare i.education_level, or
ologit blselfcare i.employment_status, or

ologit blusualactivities timeonhpn, or
ologit blusualactivities i.new_und_disease, or
ologit blusualactivities i.lengthofsb, or
ologit blusualactivities blhgskg, or
ologit blusualactivities phaseangledegree, or
ologit blusualactivities blskeletalmusclemasskg, or
ologit blusualactivities blinfusionswk, or
ologit blusualactivities blaveragekcald, or
ologit blusualactivities bldietint, or
ologit blusualactivities i.livingstatus, or
ologit blusualactivities i.education_level, or
ologit blusualactivities i.employment_status, or
```

```
ologit blpaindiscomfort timeonhpn, or
ologit blpaindiscomfort i.new_und_disease, or
ologit blpaindiscomfort i.lengthofsb, or
ologit blpaindiscomfort blhgskg, or
ologit blpaindiscomfort phaseangledegree, or
ologit blpaindiscomfort blskeletalmusclemasskg, or
ologit blpaindiscomfort blinfusionswk, or
ologit blpaindiscomfort blaveragekcald, or
ologit blpaindiscomfort bldietint, or
ologit blpaindiscomfort i.livingstatus, or
ologit blpaindiscomfort i.education_level, or
ologit blpaindiscomfort i.employment_status, or

ologit blanxietydepression timeonhpn, or
ologit blanxietydepression i.new_und_disease, or
ologit blanxietydepression i.lengthofsb, or
ologit blanxietydepression blhgskg, or
ologit blanxietydepression phaseangledegree, or
ologit blanxietydepression blskeletalmusclemasskg, or
ologit blanxietydepression blinfusionswk, or
ologit blanxietydepression blaveragekcald, or
ologit blanxietydepression bldietint, or
ologit blanxietydepression i.livingstatus, or
ologit blanxietydepression i.education_level, or
ologit blanxietydepression i.employment_status, or

regress bleq5dvas blhgskg
est store blhgskg
regress bleq5dvas blskeletalmusclemasskg
est store blskeletalmusclemasskg
regress bleq5dvas bldietint
est store bldietint
regress bleq5dvas blinfusionswk
est store blinfusionswk
coefplot blhgskg blskeletalmusclemasskg bldietint blinfusionswk, ///
   drop(_cons) xline(0) ///
   rename( ///
      blhgskg = "HGS (kg)" ///
      blskeletalmusclemasskg = "SMM (kg)" ///
      bldietint = "Dietary intake (kcal/d)" ///
      blinfusionswk = "Weekly PN infusions" ///
   ) ///
   title("Univariate Regressions: Predictors of EQ-5D VAS") ///
   legend(off)

         regress blmobility i.employment_status i.education_level i.gender
vif
```

```
rvfplot
predict residuals_energy3, resid
qnorm residuals_energy2
histogram residuals_energy3, normal
sktest residuals_energy3
lvr2plot
estat hettest

regress blusualactivities i.education_level i.employment_status i.gender
vif
rvfplot
predict residuals_energy4, resid
qnorm residuals_energy4
histogram residuals_energy4, normal
sktest residuals_energy4
lvr2plot
estat hettest

regress bleq5dvas i.employment_status blhgskg
vif
rvfplot
predict residuals_energy5, resid
qnorm residuals_energy5
histogram residuals_energy5, normal
sktest residuals_energy5
lvr2plot
estat hettest

regress blvalueset i.employment_status age i.gender blhgskg
vif
rvfplot
predict residuals_energy6, resid
qnorm residuals_energy6
histogram residuals_energy6, normal
sktest residuals_energy6
lvr2plot
estat hettest

** END EQ5D**

ssc install coefplot

regress blsf36pf blhgskg
est store blhgskg
regress blsf36pf phaseangledegree
est store phaseangledegree
regress blsf36pf blskeletalmusclemasskg
est store blskeletalmusclemasskg
```

```
coefplot blhgskg phaseangledegree blskeletalmusclemasskg,  drop(_cons) xline(0) ///
   title("Univariate Regressions: Predictors of SF-36") ///
   legend(off)

        ** SF-36 UNIVARIATE REGRESSION **

regress blsf36pf timeonhpn
regress blsf36pf i.lengthofsb
regress blsf36pf i.new_und_disease
regress blsf36pf blhgskg
regress blsf36pf blskeletalmusclemasskg
regress blsf36pf phaseangledegree
regress blsf36pf blinfusionswk
regress blsf36pf blaveragekcald
regress blsf36pf bldietint
regress blsf36pf i.livingstatus
regress blsf36pf i.education_level
regress blsf36pf i.employment_status

regress blrolelimitationsph timeonhpn
regress blrolelimitationsph i.lengthofsb
regress blrolelimitationsph i.new_und_disease
regress blrolelimitationsph blhgskg
regress blrolelimitationsph phaseangledegree
regress blrolelimitationsph blskeletalmusclemasskg
regress blrolelimitationsph blinfusionswk
regress blrolelimitationsph blaveragekcald
regress blrolelimitationsph bldietint
regress blrolelimitationsph i.livingstatus
regress blrolelimitationsph i.education_level
regress blrolelimitationsph i.employment_status

regress blrolelimitationsep timeonhpn
regress blrolelimitationsep i.lengthofsb
regress blrolelimitationsep i.new_und_disease
regress blrolelimitationsep blhgskg
regress blrolelimitationsep phaseangledegree
regress blrolelimitationsep blskeletalmusclemasskg
regress blrolelimitationsep blinfusionswk
regress blrolelimitationsep blaveragekcald
regress blrolelimitationsep bldietint
regress blrolelimitationsep i.livingstatus
regress blrolelimitationsep i.education_level
regress blrolelimitationsep i.employment_status

regress blenergyfatigue timeonhpn
regress blenergyfatigue i.lengthofsb
regress blenergyfatigue i.new_und_disease
```

```
regress blenergyfatigue blhgskg
regress blenergyfatigue phaseangledegree
regress blenergyfatigue blskeletalmusclemasskg
regress blenergyfatigue blinfusionswk
regress blenergyfatigue blaveragekcald
regress blenergyfatigue bldietint
regress blenergyfatigue i.livingstatus
regress blenergyfatigue i.education_level
regress blenergyfatigue i.employment_status

regress blewb timeonhpn
regress blewb i.lengthofsb
regress blewb i.new_und_disease
regress blewb blhgskg
regress blewb phaseangledegree
regress blewb blskeletalmusclemasskg
regress blewb blinfusionswk
regress blewb blaveragekcald
regress blewb bldietint
regress blewb i.livingstatus
regress blewb i.education_level
regress blewb i.employment_status

regress blsf timeonhpn
regress blsf i.lengthofsb
regress blsf i.new_und_disease
regress blsf blhgskg
regress blsf phaseangledegree
regress blsf blskeletalmusclemasskg
regress blsf blinfusionswk
regress blsf blaveragekcald
regress blsf bldietint
regress blsf i.livingstatus
regress blsf i.education_level
regress blsf i.employment_status

regress blpain timeonhpn
regress blpain i.lengthofsb
regress blpain i.new_und_disease
regress blpain blhgskg
regress blpain phaseangledegree
regress blpain blskeletalmusclemasskg
regress blpain blinfusionswk
regress blpain blaveragekcald
regress blpain bldietint
regress blpain i.livingstatus
regress blpain i.education_level
regress blpain i.employment_status
```

```
regress blsf36gh timeonhpn
regress blsf36gh i.lengthofsb
regress blsf36gh i.new_und_disease
regress blsf36gh blhgskg
regress blsf36gh phaseangledegree
regress blsf36gh blskeletalmusclemasskg
regress blsf36gh blinfusionswk
regress blsf36gh blaveragekcald
regress blsf36gh bldietint
regress blsf36gh i.livingstatus
regress blsf36gh i.education_level
regress blsf36gh i.employment_status

regress blrolelimitationsph blhgskg
est store blhgskg
regress blrolelimitationsph blskeletalmusclemasskg
est store blskeletalmusclemasskg
regress blrolelimitationsph phaseangledegree
est store phaseangledegree
regress blrolelimitationsph bldietint
est store bldietint
coefplot blhgskg phaseangledegree blskeletalmusclemasskg bldietint, ///
   drop(_cons) xline(0) ///
   rename( ///
      blhgskg = "HGS (kg)" ///
      blskeletalmusclemasskg = "SMM (kg)" ///
      phaseangledegree = "PA" ///
      bldietint = "Dietary intake (kcal/d)" ///
   ) ///
   title("Univariate Regression: Predictors of RLPH") ///
   legend(off)


*PCA
drop pc1 pc2
pca blsodiummmoll blpotassiummmoll blureammoll blcreatininemmoll bladcammoll
blmgmmoll blseleniumumoll, mineigen(1)
screeplot
predict pc1 pc2
regress bleq5dvas pc1 pc2
regress blvalueset pc1 pc2

drop pc1 pc2
pca blvitaumoll blvitb12pmoll blvitdumoll blcopperumoll blzincumoll blfolateugl
blmanganeseumoll blseleniumumoll
screeplot
predict pc1 pc2
```

```
regress bleq5dvas pc1 pc2
regress blvalueset pc1 pc2

drop pc1 pc2
pca blironumoll blferritin blhbgl bltransferringl bltransferrinsat, mineigen(1)
screeplot
predict pc1 pc2
regress bleq5dvas pc1 pc2
regress blvalueset pc1 pc2

drop pc1 pc2
pca blcholesterolmmoll bltriglyceridesmmoll bltotalhdlratio blnonhdlmmoll blhdlmmoll
screeplot
predict pc1 pc2 pc3 pc4
regress bleq5dvas pc1 pc2 pc3 pc4
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drop pc1 pc2
pca blbilumoll blalpunitl blaltunitl blggtunitl blplateletcount, mineigen(1)
screeplot
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pca blironumoll blferritin blhbgl bltransferringl bltransferrinsat, mineigen(1)
screeplot
predict pc1 pc2

pca blvitaumoll blvitb12pmoll blvitdumoll blcopperumoll blzincumoll blfolateugl
blmanganeseumoll blseleniumumoll, mineigen(1)
screeplot
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** SF36 PCA **

pca blsodiummmoll blpotassiummmoll blureammoll blcreatininemmoll bladcammoll
blmgmmoll blseleniumumoll, mineigen(1)
screeplot
predict pc1 pc2
regress blsf36pf pc1 pc2
regress blrolelimitationsph pc1 pc2
regress blrolelimitationsep pc1 pc2
regress blenergyfatigue pc1 pc2
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regress blsf36gh pc1 pc2
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pca blvitaumoll blvitb12pmoll blvitdumoll blcopperumoll blzincumoll blfolateugl
blmanganeseumoll blseleniumumoll, mineigen(1)
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mineigen(1)
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** HPNQoL PCA **
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blmgmmoll blseleniumumoll, mineigen(1)
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regress a_employment_hpnqol pc1 pc2
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pca blsodiummmoll blpotassiummmoll blureammoll blcreatininemmoll bladcammoll
blmgmmoll blseleniumumoll, mineigen(1)
screeplot
predict pc1 pc2 pc3
regress blnutritionteam pc1 pc2 pc3
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