

A Comprehensive Assessment of Nutritional Status and
Factors Impacting Nutrition Recovery in Hospitalized,
Critically Ill Patients Following Liberation from Mechanical
Ventilation

by

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STATEMENT OF CONTRIBUTIONS

Lesley Moisey is the sole author of all chapters in this thesis, which were written under the supervision of Dr. Marina Mourtzakis.

Research presented in Chapters 4, 5, and 6: This research was conducted at University Hospital (London Health Sciences Centre) which is an academic hospital affiliated with Western University in London, Ontario. It was funded by the Canadian Foundation for Dietetic Research (PI: Lesley Moisey, RD; Co-investigators: Dr. Marina Mourtzakis, PhD; Dr. Heather Keller, RD, PhD; Dr. Adam Rahman, MD; and Dr. Daren Heyland, MD). Lesley Moisey, under the guidance of Jill Pikul (RD), obtained input and approval from stakeholders at the hospital (outlined in Chapter 3) to facilitate completion of this research. Lesley Moisey, Dr. Marina Mourtzakis, Dr. Heather Keller, Dr. Adam Rahman, Dr. Daren Heyland, and Jill Pikul (RD) contributed to the study design for Chapters 4 and 5. Lesley Moisey, Dr. Marina Mourtzakis, Dr. Heather Keller, and Jill Pikul (RD) contributed to the study design for Chapter 6. Patient screening was completed by Tracey Bentall (ICU research coordinator), assisted by Jill Pikul; Lesley Moisey approached and obtained consent from eligible patients or their proxies. Data collection and entry were completed by Lesley Moisey and Emily Chi Yan Yeung (research assistant). Lesley Moisey performed data analysis with statistical consultation provided by Andrew Day. Lesley Moisey, Dr. Marina Mourtzakis, Dr. Heather Keller, and Jill Pikul were involved in data interpretation. Draft manuscripts from each of these chapters will be prepared by Lesley Moisey, with intellectual input provided by co-authors.

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ABSTRACT

Disease related malnutrition is a concern for the critically ill, however there is a paucity of research examining nutrition recovery in survivors of critical illness. Prior to the development of nutrition interventions to enhance recovery from critical illness, a more comprehensive understanding of the nutrition recovery trajectory and factors influencing the early stages of ward-based recovery is required. Thus, the overarching purpose of this thesis was to produce a comprehensive body of work that enhances our understanding of various facets of nutrition recovery in the hospitalized, critically ill patient following liberation from mechanical ventilation (LMV). To explore and characterize nutrition recovery, I first evaluated: 1) the feasibility of performing common measures of nutritional status during the first seven days following LMV, 2) nutrition intake following LMV, and 3) meal and food intake patterns of patients prescribed non-modified oral diets following LMV. The compilation of these findings illustrated some of the factors that contribute to compromised nutrition recovery in patients following LMV.

To better understand nutrition following LMV, feasibility of performing common measures to assess nutritional status was evaluated. Recruitment and retention into the study were also assessed to evaluate the capacity to investigate nutrition recovery. As part of this study, critically ill adults (>18 years) who received mechanical ventilation (MV) for at least 72 hours were recruited. Over a 6-month recruiting period, 538 patients were screened, and of the patients identified as meeting the study eligibility criteria (n=65), 35% consented to participate (n=23). Of the patients who participated (n=19, 42% male, aged 35-85 years), 32% were lost to follow-up prior to the seventh day following LMV. Common methods to

assess body composition (weight, mid-upper arm circumference, and bioelectrical impedance analysis to calculate phase angle) and physical function (hand-grip dynamometry) were obtained on greater than 70% of occasions they were to be measured, however, use of standardized and previously validated protocols to obtain these measures was not practical in this patient population. Protocol deviations occurred for 94%, 45%, and 44% of occasions that mid-arm circumference, bioelectrical impedance, and hand-grip strength were measured, respectively. Primarily, the disposition of recovering critically ill patients (decreased level of alertness, muscular weakness, discomfort and pain) precluded proper acquisition of these measurements.

Nutrition intake was measured using weighed food records during the first 7 days following LMV. Of the 227 meals served over 125 study days, energy and nutrient intake was successfully measured for 92% of meals. For all days patients were receiving enteral nutrition (EN), the volume of EN formula delivered could be extracted from the chart. Large variations in daily protein (range: 0-151 g/d) and energy (range: 0-2306 kcal/d) intake were observed across all study days. For patients receiving nutrition exclusively via EN (n=48 days), protein and calorie intake was >75% of prescribed on 77% and 88% of occasions, respectively. In contrast, for days that patients received an oral diet as their sole source of nutrition (n=54 days), protein intake was never >75% of prescribed and energy intake was >75% of prescribed on only 24% of occasions. Meal and food intake patterns were examined in a subgroup of 9 patients who had been prescribed a regular (non-texture or fluid modified) diet for at least one day over the study duration. Only 55% and 56% of the total amount of protein and calories provided, respectively were consumed. Although there were no

significant differences between the amounts of calories and protein consumed between main meals (195, 255, and 231 kcal and 9, 11, and 9 g protein for breakfast, lunch, and dinner, respectively) considerable individual variation in eating patterns between the patients was observed with respect to the amount of protein and calories consumed at meals and which meals (breakfast, lunch or dinner) the most was consumed.

To further characterize dietary prescription practices and use of EN following LMV, a retrospective chart review (n=134, 55% male, mean age 61 years) was conducted. We observed 16% of patients who received EN while ventilated had it discontinued concomitantly with LMV. However, considerable variation in the use of EN therapy and type of oral diet prescriptions in patients prior to hospital discharge was observed. Only 55% of patients who survived the hospital admission ever received a regular, non-modified diet without supplementary EN at the time of hospital discharge, and one in five patients were still receiving EN at the time of hospital discharge.

Collectively, these results advance our insight into nutrition recovery following critical illness from a Canadian perspective. Feasible and validated tools to properly assess nutritional status in this unique group of patients are required, as is the need for the development of interventions to enhance protein and energy intake in recovery. Due to the heterogeneity of the patients observed, nutrition interventions delivered by practicing clinicians should be as individualized as much as possible to achieve optimal outcomes.

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TABLE OF CONTENTS

Examining Committee Membership	ii
Author's Declaration	iii
Statement of Contributions.....	iv
Abstract.....	vi
Acknowledgements	ix
List of Figures.....	xviii
List of Tables	xix
List of Abbreviations	xxi
Chapter 1 Introduction	1
1.1 Rationale.....	1
1.2 Objectives.....	3
1.3 Hypotheses	4
1.4 Overview of the thesis.....	5
Chapter 2 Literature review	8
2.1 Critical illness in Canada.....	8
2.2 Critical illness and survivorship.....	8
2.3 Post-intensive care syndrome.....	9
2.3.1 Physical impairment and functional disability in ICU survivorship	10
2.3.1.1 Etiology of functional disability in survivors of critical illness.....	12
2.3.2 Cognitive impairment in ICU survivorship.....	13
2.3.3 Perturbations in mental health in ICU survivorship.....	14
2.3.4 Quality of life in ICU survivorship.....	15
2.4 Rehabilitation strategies to enhance recovery from critical illness.....	15
2.4.1 The role for nutrition rehabilitation in recovery from critical illness.....	16
2.5 The role of nutrition in the maintenance of functional, cognitive and psychological health.....	17
2.5.1 Nutrition and the maintenance of skeletal muscle and physical function	17

2.5.2 Nutrition and neurocognitive function	18
2.5.3 Nutrition and psychological health.....	19
2.6 The nutritional state of the critically ill over the trajectory of illness	20
2.6.1 Malnutrition	20
2.6.2 Malnutrition is prevalent in the critically ill at the time of ICU admission.....	23
2.6.3 Factors influencing changes in nutritional status of the critically ill patient while in ICU	24
2.6.4 Nutrition recovery following ICU discharge.....	26
2.6.4.1 Nutrition intake and adequacy following liberation from mechanical ventilation	26
2.6.4.2 Barriers to consuming adequate nutrition	30
2.7 Nutrition rehabilitation following critical illness	31
2.8 Conclusion.....	33
Chapter 3 Overview of methodology.....	41
3.1 Research design.....	41
3.2 Research site.....	41
3.2.1 Dietitian services at University Hospital	42
3.2.2 Stakeholder approval	43
3.3 Study population	43
3.4 Methods pertaining to the assessment of nutritional status.....	45
3.4.1 Assessing the nutritional status of the critically ill patient.....	47
3.4.2 Nutrient intake	48
3.4.2.1 Food services at University Hospital	48
3.4.2.2 Frequency of nutrient intake measurements	49
3.4.2.3 Dietary intake for patients consuming oral diets	50
3.4.2.4 Protein and energy intake from enteral and parenteral nutrition	54
3.4.2.5 Adequacy of protein and energy intake	54
3.4.2.6 Appetite and barriers to eating	55
3.4.3 Body composition measures.....	56

3.4.3.1 Weight and body mass index	57
3.4.3.2 Mid-upper arm circumference	58
3.4.3.3 Computed tomography.....	58
3.4.4 Bioelectrical impedance analysis: phase angle.....	59
3.4.5 Functional status	60
3.4.5.1 Hand-grip dynamometry	60
3.4.5.2 Other measures of functional status.....	61
3.4.6 Biochemical indices.....	61
Chapter 4 Nutrition recovery in critically ill patients following liberation from mechanical ventilation: a feasibility study assessing indices of nutritional status.....	62
4.1 Introduction	62
4.2 Methods.....	64
4.2.1 Study design	64
4.2.2 Study protocol.....	64
4.2.3 Patient demographics, admission characteristics, and outcomes	65
4.2.4 Measures of nutritional status.....	65
4.2.5 Assessment of dietary intake and appetite.....	66
4.2.6 Measurement of weight	67
4.2.7 Measurement of mid-upper arm circumference	68
4.2.8 Measurement of hand-grip strength.....	68
4.2.9 Measurement of phase angle	68
4.2.10 Statistical analysis.....	69
4.3 Results	69
4.3.1 Recruitment, retention and patient characteristics.....	69
4.3.2 Feasibility of measuring dietary intake and appetite	73
4.3.3 Feasibility of obtaining anthropometric, body composition, functional and biochemical measures.....	74
4.4 Discussion	81
4.5 Conclusions	86

4.6 Relevance to clinical practice.....	86
Chapter 5 Adequacy of protein and energy intake in critically ill adults following liberation from mechanical ventilation is dependent on route of nutrition delivery.....	87
5.1 Introduction	87
5.2 Methods.....	89
5.2.1 Study Population	89
5.2.2 Study protocol.....	90
5.2.3 Patient demographics, admission characteristics and outcomes	90
5.2.4 Measurement of protein and energy intake	91
5.2.5 Assessment of adequacy of protein and energy intake.....	92
5.2.6 Assessment of appetite and barriers to intake	93
5.2.7 Statistical analysis.....	93
5.3 Results	93
5.3.1 Dietary prescriptions following liberation from mechanical ventilation.....	95
5.3.2 Net protein and energy intake following liberation from mechanical ventilation..	96
5.3.3 Adequacy of protein and energy intake following liberation from mechanical ventilation	99
5.3.4 Barriers to eating and appetite	102
5.4 Discussion	104
5.5 Conclusions	109
5.6 Relevance to clinical practice.....	109
Chapter 6 Meal and food intake patterns in hospitalized, critically ill patients prescribed an oral diet following liberation from mechanical ventilation	111
6.1 Introduction	111
6.2 Methods.....	113
6.2.1 Study design	113
6.2.2 Patient characteristics	114
6.2.3 Measurement of food and liquid intake	115
6.2.4 Statistical analysis.....	116

6.3 Results	120
6.3.1 Patient characteristics and outcomes	120
6.3.2 Food and liquid consumption in relationship to amount provided	120
6.3.3 Distribution of calories and macronutrients consumed daily	122
6.3.4 Distribution of Calories and Macronutrients Consumed at Individual Meals	126
6.4 Discussion	130
6.5 Conclusions	133
6.6 Relevance to clinical practice	134
Chapter 7 Characterization of dietary prescribing practices in critically ill patients following liberation from mechanical ventilation	135
7.1 Introduction	135
7.2 Methods	137
7.2.1 Study design and population	137
7.2.2 Data collection	138
7.2.3 Statistical analysis	140
7.3 Results	140
7.3.1 Patient characteristics at ICU admission	140
7.3.2 Clinical outcomes	140
7.3.3 Use of dietitian and SLP services and prevalence of oropharyngeal dysphagia following liberation from mechanical ventilation	144
7.3.4 Use of enteral nutrition following liberation from mechanical ventilation	144
7.3.5 Characterization of diet prescriptions following liberation from mechanical ventilation and at hospital discharge	146
7.4 Discussion	149
7.5 Conclusions	152
7.6 Relevance to clinical practice	153
Chapter 8 General discussion	154
8.1 Summary of findings	154

8.2 Critically ill patients present with unique characteristics that challenge our capacity to evaluate in-hospital nutrition recovery between liberation from mechanical ventilation and hospital discharge.....	156
8.3 Protein and energy intake is inadequate following liberation from mechanical ventilation: delivery route, food intake patterns and barriers need careful consideration	159
8.4 Nutrition care approaches are inconsistent and may compromise continuity of care in survivors of critical illness	162
8.5 Strengths and limitations.....	164
8.6 Future directions.....	166
8.6.1 Development and validation of measurement tools for assessing nutritional status of recovering critically ill patients are required.....	166
8.6.2 What are the current knowledge, attitudes and practices of the health care team regarding the nutrition care of recovering critically ill patients?	167
8.6.3 Testing nutrition interventions: can delaying discontinuation of enteral nutrition therapy following liberation from mechanical ventilation improve nutrition recovery?	167
8.7 Implications for dietetic practice.....	169
8.8 Conclusions	170
References.....	171
Appendices.....	199
Appendix A Prospective study ethics approval forms	200
Appendix B Retrospective chart review ethics approval forms.....	203
Appendix C Sample menu selection form.....	205
Appendix D Weighed food record form	206
Appendix E Nutrition prescription and EN/PN intake log.....	208
Appendix F Body composition and hand-grip strength data collection form.....	211
Appendix G Barriers to intake and appetite rating form.....	212
Appendix H Individual measures of body composition and physical function in critically ill patients following LMV	213

Appendix I Individual daily protein and energy intake in critically ill patients following LMV	217
Appendix J Dietary prescriptions and transitions for individual patients over the duration of the study	218

LIST OF FIGURES

Figure 2.1 Significant phases along the trajectory of critical illness	22
Figure 2.2 Factors influencing the development of disease-related malnutrition following the onset of critical illness.	29
Figure 4.1 CONSORT diagram	71
Figure 5.1 Median daily protein intake and calorie intake across all study days stratified by route of nutrition delivery.....	97
Figure 5.2 Median daily protein intake and calorie intake on each study day stratified by route of nutrition delivery.....	98
Figure 5.3 Protein and calorie intake versus amounts prescribed.....	101
Figure 5.4 Patient reported barriers to eating.....	103
Figure 6.1 Amount of calories and protein provided and consumed daily relative to each patient's estimated usual body weight.....	125
Figure 6.2 Average amount of protein, carbohydrate, and fat calories consumed at each meal.	128
Figure 6.3 Average calories and protein consumed at each meal and snacks.	129
Figure 7.1 CONSORT diagram	142
Figure 7.2 First oral diets prescribed following liberation from mechanical ventilation	147

LIST OF TABLES

Table 2.1 Overview of studies examining nutrition in the recovery phase of critical illness.	35
Table 3.1 Dietitian staffing at University Hospital	42
Table 4.1 Patient characteristics at ICU admission	72
Table 4.2 Patient clinical outcomes	73
Table 4.3 Proportion of patients capable of rating appetite throughout the study protocol....	77
Table 4.4 Proportion of patients for which measures of nutritional status were obtained over the course of the study	78
Table 4.5 Summary of reasons measurements were not obtainable	79
Table 4.6 Summary of protocol violations for measurements that were obtained but deviated from the standard protocol.....	80
Table 5.1 Patient characteristics at ICU admission	94
Table 5.2 Patient clinical outcomes	95
Table 5.3 Adequacy of protein and energy intake in comparison to amounts prescribed across all study days and by route of nutrition delivery	100
Table 5.4 Proportion of days in which protein and energy intake was greater than 75% of prescribed across all study days and by route of nutrition delivery	100
Table 6.1 Food categories and the corresponding calorie and macronutrient content of items within each category	118
Table 6.2 Patient baseline characteristics at time of ICU admission	121
Table 6.3 Patient clinical outcomes, time to regular diet following liberation from mechanical ventilation, and prevalence of oropharyngeal dysphagia	122
Table 6.4 Total amount of food and liquid items wasted and consumed over 33 study days	123
Table 6.5 Total daily calories and macronutrients provided and consumed daily and calories and protein provided and consumed relative to body weight ¹	124
Table 6.6 Median daily calories and macronutrients consumed at each meal and for snacks	127

Table 7.1 Patient characteristics at ICU admission	143
Table 7.2 Patient clinical outcomes	144
Table 7.3 Timing of discontinuation of enteral nutrition in critically ill patients following liberation from mechanical ventilation.....	145
Table 7.4 Discharge diets and disposition of hospitalized critically ill patients.....	148

LIST OF ABBREVIATIONS

6MWT	6-minute walk test
ADLs	Activities of daily living
AND	Academy for Nutrition and Dietetics
APACHE	Acute Physiology and Chronic Health Evaluation
ARDS	Acute respiratory distress syndrome
ASPEN	American Society for Parenteral and Enteral Nutrition
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CIM	Critical illness myopathy
CIP	Critical illness polyneuropathy
CSA	Cross-sectional area
CT	Computed tomography
DRM	Disease-related malnutrition
DXA	Dual energy x-ray absorptiometry
EN	Enteral nutrition
ESPEN	European Society for Clinical Nutrition and Metabolism
ICU-AW	Intensive care unit acquired-weakness
ICU	Intensive care unit
IQR	Interquartile range
HGS	Hand-grip strength
LHSC	London Health Sciences Centre
LMV	Liberation from mechanical ventilation
LOA	Level of alertness
LOS	Length of stay
mNUTRIC	Modified Nutrition Risk in Critically Ill
MAC	Mid-upper arm circumference
MF-BIA	Multi-frequency bioelectrical impedance analysis

MMT	Manual muscle test
MPB	Muscle protein breakdown
MPS	Muscle protein synthesis
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MSICU	Medical-surgical intensive care unit
MV	Mechanical ventilation
PhA	Phase angle
PICS	Post-intensive care syndrome
PN	Parenteral nutrition
PTSD	Post-traumatic stress disorder
QOL	Quality of life
SCCM	Society of Critical Care Medicine
SGA	Subjective Global Assessment
SLP	Speech-language pathologist
SMI	Skeletal muscle index
SOFA	Sequential Organ Failure Assessment
TBI	Traumatic brain injury
TSF	Triceps skinfold
UH	University Hospital
VAD	Vascular access device
VAS	Visual analogue scale
WFR	Weighed food records

CHAPTER 1

INTRODUCTION

1.1 Rationale

Survivors of critical illness experience devastating functional, cognitive and psychological disabilities following discharge from the intensive care unit (ICU) (1-3). Ongoing identification of factors influencing ICU outcomes, identification of research gaps in post-ICU care, and the development of new interventions to minimize poor outcomes for survivors of critical illness are imperative (2). Disease-related malnutrition (DRM) is of significant concern in the critically ill, particularly for those with higher severity of illness who require invasive mechanical ventilation (MV). Many patients are nutritionally compromised at ICU admission and up to 54% of patients are malnourished at the onset of illness (4-7). The acute phase of critical illness is marked by an acute systemic inflammatory response (8). During this period, the production of inflammatory cytokines and immune mediators is upregulated and the sympathetic nervous system is stimulated, resulting in increased resting energy expenditure, hyperglycemia, muscle protein breakdown and lipolysis (9-11). Consequently, critically ill patients experience accelerated decreases in muscle mass and physical function (12), two indices of malnutrition (13-15). Furthermore, in-ICU nutrition delivery is largely inadequate with mechanically ventilated patients generally receiving only two-thirds of prescribed protein and calories (16-18). Thus, it is likely that patients who survive the acute phase of illness are malnourished by the time they are discharged from the ICU and begin the journey to recovery. Malnutrition is associated with reduced immunity, increased risk of infection and pressure ulcers, impaired wound healing, impaired mental health, cognitive decline, decreased respiratory and cardiac

function, gastrointestinal disorders, loss of muscle mass, and functional disability (19, 20). Thus, optimizing the nutritional state of survivors of critical illness to reduce the risk of developing the negative sequelae associated with malnutrition could theoretically enhance functional and psychological recovery and improve quality of life.

Currently, there is a paucity of research examining aspects of nutrition recovery in ICU survivors. Limited evidence suggests that survivors, in the early stages of ward-based recovery, consume inadequate nutrition in comparison to prescribed amounts (21-23), continue to accrue large protein and energy deficits (23), and experience a multitude of barriers that inhibit their ability to achieve adequate nutrition intake. These barriers are primarily related to: 1) the effects of illness such as loss of appetite, early satiety, nausea, vomiting, and taste changes (21, 22, 24, 25), and 2) poor transitional care, including failure to communicate nutrition care plans to ward staff when patients are transferred out of the ICU and lack of knowledge on the part of ward staff regarding the specialized needs of the recovering critically ill (24, 26). Currently, no guidelines exist for feeding critically ill patient following LMV, specifically with respect to route of administration (i.e. oral diets versus enteral or parenteral nutrition), when and how best to transition patients who received enteral nutrition (EN)[†] in ICU to an oral diet, and nutrient provision (i.e. energy and protein requirements). Thus, clinicians are challenged to deliver optimal and standardized nutritional care for patients who are discharged from the ICU. However, prior to the development of nutrition interventions to enhance recovery from critical illness, a more comprehensive understanding of the degree to which nutrition recovery is or is not occurring and factors influencing recovery in the early stages of ward-based recovery is required.

[†] For the purpose of this thesis, use of the term “enteral nutrition” (EN) will refer specifically to enteral tube feeding and will not include oral nutritional supplementation.

The purpose of this thesis was to produce a body of work that enhances our understanding of various facets of nutrition recovery in the hospitalized, critically ill patient following LMV. To achieve this goal, a prospective, observational feasibility study (Chapters 4, 5, and 6) and a retrospective chart review (Chapter 7) were undertaken. The studies presented in this thesis are the first in Canada to explore nutrition recovery in critically ill patients during the early stages of ward-based recovery.

1.2 Objectives

The study population of interest was hospitalized, critically ill patients who were recently liberated from MV. Specifically, aspects of nutrition were observed between the time of LMV and hospital discharge. The specific objectives of this thesis were to:

1. Assess the capacity to recruit and retain hospitalized, critically ill patients following LMV from a single-site that evaluated nutrition rehabilitation in the early, ward-based stages of recovery (Chapter 4). It is anticipated that these data will form the basis for a future, larger-scale study.
2. Determine the feasibility of obtaining measures commonly used to evaluate nutritional status (weight, mid-upper arm circumference, bioelectrical impedance analysis, and hand-grip strength) with previously validated protocols for this specific patient population (Chapter 4).
3. Precisely quantify nutrient (protein and energy) intake, adequacy of protein and energy intake in comparison to that prescribed (Chapter 5).
4. Characterize patient reported barriers to eating (Chapter 5).

5. Quantify the amount and types of foods and fluids that are consumed and wasted by patients prescribed non-modified oral diets following LMV (Chapter 6).
6. Determine whether differences in calorie and macronutrient intake exist between meals in patients prescribed non-modified oral diets following LMV (Chapter 6).
7. Characterize usual dietary prescribing practices within a single academic center specifically as it relates to route of nutrition delivery and the transition from EN to an oral diet in patients who received EN while mechanically ventilated (Chapter 7).
8. Characterize the types of diets (i.e. route, use of therapeutic and modified diets) patients are receiving at the time of hospital discharge (Chapter 7).

1.3 Hypotheses

The overall hypothesis of this thesis was that recovering critically ill patients would exhibit aspects of poor nutrition recovery during the early stages of ward based recovery. The specific hypotheses were:

1. In anticipation of completing a future larger-scale study, it was determined that the study would be considered feasible if one patient per week with a hospital length of stay (LOS) of at least 7-days following LMV is enrolled and measures commonly used to evaluate nutritional status could be obtained on greater than 90% of occasions as per previously established protocols (Chapter 4).
2. Common and practical anthropometric measures (weight, mid-upper arm circumference, bioelectrical impedance analysis, and hand-grip strength) used to assess nutritional status would not be feasible to obtain due to the unique disposition

- of this population (i.e. decreased conscious, functional impairment, alterations in cognition) that will preclude proper acquisition of measures (Chapter 4).
3. Protein and energy intake would be inadequate such that patients would consume less than 75% of prescribed protein and calories, but those receiving EN or PN would have superior intake in comparison to those prescribed oral diets (Chapter 5).
 4. The most common barriers to eating reported by patients would relate to the effects of illness (anorexia, nausea, vomiting, early satiety, and taste changes) (Chapter 5).
 5. Within patients prescribed non-modified oral diets post-LMV, only 60% of the total amount of all food and fluids provided would be consumed (Chapter 6).
 6. Patients consuming oral diets will consume a greater amount of protein and calories at lunch and dinner meals in comparison to breakfast (Chapter 6).
 7. Of patients who received EN while mechanically ventilated, 25% will have it discontinued at the time of LMV (Chapter 7).
 8. At the time of hospital discharge, only 55% of patients would be transitioned to a regular, non-modified diet, with the remainder of patients requiring a modified diet with or without enteral or parenteral nutrition (Chapter 7).

1.4 Overview of the thesis

This thesis comprises findings from a prospective, observational feasibility study and a retrospective chart review. The aims of the prospective study were to evaluate the feasibility of conducting nutrition research in hospitalized patients specifically following LMV and provide a comprehensive assessment of nutrition (specifically protein and calorie) intake and factors influencing adequacy of intake in this unique population. The findings

from the prospective study led to the conceptualization of the retrospective chart review in which the primary aim was to characterize dietary prescription practices after patients are liberated from MV, including measurement of the proportion of critically ill patients who continue to receive EN following LMV.

Chapter 2 presents a critical review of the literature, which comprises six sections. The first section provides an overview of the prevalence and economic impact of critical illness and survivorship in Canada. Following this overview, the trajectory of recovery in survivors of critical illness, with a specific focus on physical, cognitive and psychological disability is then explored. In section three, an overview of strategies currently being applied to enhance recovery and an introduction to the concept of nutrition rehabilitation is outlined. In the fourth section, the impact of nutrition on functional, cognitive and psychological health is critically reviewed. The fifth section will summarize the lack of prevalence data on malnutrition across the trajectory of care in the critically ill as well as factors influencing nutrition recovery during the early stages of ward-based recovery. In the final section, post-ICU nutrition rehabilitation programs will be discussed and potential target areas for the development of nutrition interventions to enhance nutrition recovery in this patient population will be highlighted.

Chapter 3 provides an overview of the study methodology, site where this research was conducted, and the targeted population that formed the basis for these studies.

Chapter 4 presents the feasibility of completing nutrition research in and assessing the nutritional status of the hospitalized, critically ill patient immediately following LVM. The ability to recruit and retain patients was measured and methods to assess nutritional status that were evaluated included: weighed food records, anthropometric measures (weight

and mid-upper arm circumference), hand-grip strength, and bioelectrical impedance analysis (used to determine phase angle).

Chapter 5 presents an evaluation of protein and energy intake in hospitalized, critically ill patients following LMV. Weighed food records and dietary recall were used to evaluate food intake and delivery of enteral nutrition solutions was abstracted from the charts. Daily protein and calorie intake was subsequently quantified and adequacy of protein and energy intake was determined by comparing intake to prescribed protein and calories.

Chapter 6 presents an evaluation of meal and food intake patterns in hospitalized, critically ill patients who were prescribed regular (non-modified) diets following LMV. Using data obtained from weighed food records, food and fluid waste was measured, types of foods and fluids commonly consumed and wasted were characterized, and differences in energy and macronutrient intake between meals was assessed.

Chapter 7 presents a retrospective chart review in which dietary prescribing practices between LMV and hospital discharge were observed. Specifically, the proportion of patients who continue to receive EN (tube feeding) after LMV was measured, the types of diets prescribed over the course of post-LMV hospital stay characterized, and diets patients were prescribed at the time of hospital discharge documented.

Chapter 8 provides an overall discussion of the key findings presented in these studies and the key themes arising from these findings. Future areas of research and implications to clinical practice are discussed.

CHAPTER 2

LITERATURE REVIEW

2.1 Critical illness in Canada

Critically ill patients present with life-threatening conditions that often require costly and sophisticated levels of care. In Canada, over 230,000 adults were admitted to an ICU in 2013-2014, representing a 12% increase in admissions since 2007-2008 (27). Of these admissions, 33% required invasive mechanical ventilation (MV), and of this subset of patients, 26% required long-term MV, defined as greater than 96 consecutive hours (27). Despite the high severity of illness, data from the Canadian Institute for Health Information indicate in-ICU mortality rates are less than 10% (27), which is in part due to advances in medical knowledge and technologies. Furthermore, a large retrospective cohort study following over 500,000 adults admitted to ICUs in Ontario between 2002 and 2012 found that 84% survived to hospital discharge (28). Following discharge from hospital, mortality rates of patients who require an ICU stay while hospitalized are greater than those who are not critically ill (28). Factors that have been associated with greater risk of mortality in ICU survivors include increased age, longer ICU and hospital lengths of stay (LOS), higher severity of illness, increased rates of preexisting comorbidities, poor functional status at hospital discharge, malnutrition, and discharge to a long-term care facility (28-35).

2.2 Critical illness and survivorship

For many critically ill patients, the period following discharge from the ICU marks the beginning of a long and arduous journey to recovery (36). Survivors of critical illness often face pronounced functional, cognitive and psychological disabilities that impact both short- and long-term recovery (2, 3), the ability to return to work (28, 37-39), and quality of

life (QOL) (40-42). Consequently, use of health care resources is high in survivors following hospital discharge. In a small, Canadian longitudinal cohort study in which 109 survivors of acute respiratory distress syndrome (ARDS) were followed, one-third attended inpatient rehabilitation following hospital discharge and half of all patients discharged home required home care services (43). In a similar study conducted in the United States in which 291 critically ill older adults (greater than 70 years of age) were followed, over 70% required enhanced care or rehabilitation following hospital discharge (44). During the first year following discharge from the ICU, survivors have a disproportionately high number of visits to primary care physicians and specialists (28, 39, 43) in comparison to non-critically ill patients, and higher rates of hospital readmission (43, 45). As the incidence of critical illness and patients requiring MV is projected to outpace population growth (46), the economic implications of a growing number of survivors experiencing multiple health-related morbidities and disability will be significant (45, 47, 48).

2.3 Post-intensive care syndrome

The term *post-intensive care syndrome* (PICS) has been coined to define a constellation of health-related morbidities and deficits experienced by survivors of critical illness across three broad domains encompassing physical, cognitive and psychological functioning (1-3). Patients with PICS may not experience symptoms or deficits related to all of these domains and the length of time and degree to which PICS-related symptoms manifest is variable amongst patients (1-3). Risk factors for developing PICS are numerous. Older patients, those with increased comorbidities, and those with impairments in baseline physical, cognitive and psychological function are at higher risk of developing features of PICS (1-3). Treatments, such as prolonged MV, heavy sedation, use of neuromuscular

blocking agents, and care delivered over the course of an ICU stay can also significantly impact health outcomes and recovery (1, 3). Finally, systemic factors including uncoordinated and compromised care for patients as they transition from the ICU to other care units, disjointed discharge planning, lack of community resources, and lack of family and other social support services can also negatively impact outcomes in ICU survivors (1-3, 49, 50). Ongoing identification of factors influencing ICU outcomes, identification of research gaps in post-ICU care, and development of new interventions to minimize poor outcomes for survivors of critical illness are essential components for improving ICU survivorship (2).

2.3.1 Physical impairment and functional disability in ICU survivorship

In the first week following ICU discharge, patients demonstrate severe impairments in function and ability to complete activities of daily living (ADLs). Seven days following ICU discharge, 60-73% of patients are unable to walk independently (35, 51), hand-grip strength is less than 50% of age- and sex-matched norms (51), and patients experience global muscular weakness (35, 51). Reduced walking capacity and low grip strength following ICU discharge have been identified as predictors for prolonged impairments in functional status (51).

Functional impairments in ICU survivors may persist for several years during recovery. In seminal work led by Dr. Margaret Herridge (37, 38), 109 survivors of ARDS were followed for up to 5-years after ICU discharge. While this cohort of patients had a high severity of illness (median Acute Physiology, Age, and Chronic Health Evaluation (APACHE) Score of 23 at ICU admission), they were young (median age of 45 years at enrolment) and healthy (78% had none or only one co-existing illness prior to ICU

admission), and 77% were working full-time before the onset of illness. Notably, 3-months following ICU discharge, 96% of the patients survived but only 16% had returned to work. Moreover, patients could only complete half the distance of predicted values during a 6-minute walk test (6MWT), a standardized measure of physical function. One-year following ICU discharge, 89% of the study population survived, but only half of survivors had returned to work, and while 6MWT performance improved, median distance walked was only 64% of predicted values (38). Most strikingly perhaps was that functional disability continued to persist 5-years following discharge from ICU. Only three-quarters of the remaining survivors had returned to work and median 6MWT distance was still only 76% of predicted norms (37).

Measures of functional status must be interpreted with caution given that the pre-critical illness functional capacity is typically unknown due to difficulty obtaining such measurements; thus, patients may have fully recovered or be at a substantially lower functional status if one was able to compare with pre-clinical functional capacity. Nonetheless, the findings from Dr. Herridge's group provide insight into the significant degree of long-term functional disability and prolonged rate of functional recovery experienced by survivors of critical illness. Since the publication of this landmark study, several other bodies of work including single (43, 52) and multi-center (35, 44, 53, 54) prospective cohort studies, and a large retrospective cohort study (34) have reported similar findings such that those surviving an ICU admission often experience persistent long-term functional disability.

2.3.1.1 Etiology of functional disability in survivors of critical illness

The etiology of functional disability in survivors of critical illness is largely attributable to muscle atrophy and dysfunction, which in turn results in severe muscular weakness. Many critically ill patients are affected by ICU-acquired weakness (ICUAW), a clinically detected weakness primarily manifesting in limb and respiratory muscles arising from critical illness polyneuropathy (CIP) and/or myopathy (CIM) (36, 55, 56), syndromes for which there is “no plausible etiology other than critical illness” (55). CIP is characterized by primary axonal degeneration of sensory and motor axons (55, 57, 58), whereas CIM refers to atrophy and necrosis of myofibers (55, 56, 59). Reports on the incidence of neuromuscular dysfunction range between 25% to 57% (60), with the strongest risk factors for the development of CIP noted to be prolonged MV (61), sepsis (60), and multiple organ failure (60).

Muscle atrophy occurs in the presence of an imbalance between muscle protein synthesis and muscle protein breakdown wherein the rate of proteolysis overwhelms that of muscle protein synthesis. During critical illness, several factors are known to increase muscle protein breakdown including inflammation (10, 62), immobilization (63), and corticosteroid use (64, 65). Critically ill patients also experience insulin resistance and anabolic resistance, a blunted anabolic response to amino acids characterized by failure to stimulate muscle protein synthesis and inhibit muscle protein breakdown (66-68). In contrast to CIP, muscle atrophy frequently occurs in the ICU with virtually all patients requiring MV experiencing some degree of muscle loss (69). Plank et al. (70) examined changes in total body weight and skeletal muscle mass (using dual energy X-ray absorptiometry) in septic patients over a 21-day period. At days 5, 10 and 21 post-admission to ICU, patients lost an average of 7, 13,

and 16%, respectively, of their total body weight (measured using a hoist weighing system) and 6, 17, and 15% of total body skeletal muscle mass, respectively. More recently, Puthuchery et al. (12) found that rectus femoris muscle cross-sectional area (CSA), measured using ultrasound, decreased by 3% and 16% in patients with single and multiple organ failure, respectively, over the first 7 days of ICU admission. Several other studies examining changes in body composition during the course of critical illness have similarly identified significant losses in muscle mass (4-7). These findings suggest that the rate of loss of total body weight and muscle mass is highest within the first two weeks of ICU admission, with sicker patients experiencing more substantial losses. In contrast, there is limited research evaluating longitudinal changes in body composition following critical illness. In the pivotal study by Herridge et al. (38), they found ARDS patients lost 18% of their baseline body weight over the course of ICU admission, however one-year following ICU discharge, 71% of surviving patients had returned to their preadmission weight. Weight represents a net sum of all tissues and cannot distinguish changes occurring in tissue compartments. While the return to pre-illness weight may be interpreted as a positive sign in recovery, three studies have reported weight gain following critical illness is secondary to increases in fat versus lean body mass (7, 71, 72). This may prove to have broader negative implications on functional recovery. From the patient perspective, ICU survivors frequently attribute their weight loss to the muscular weakness they experience in recovery (43).

2.3.2 Cognitive impairment in ICU survivorship

In addition to physical dysfunction, cognitive impairment is also characteristic of PICS. Features of cognitive impairment may include memory deficits, decreased attention span, slow mental processing, visuospatial deficits, and executive dysfunction (73). It is well

recognized that survivors of critical illness experience cognitive dysfunction that may persist for years following discharge from ICU (54, 74-77), which can result in significant economic burden due to loss of income (from both patients and caregivers), increased medical costs, and institutionalization (47). While older adults surviving critical illness have been found to be more susceptible to developing cognitive impairment (54), young and previously healthy individuals have also been found to develop impairments in survivorship (74). Critically ill patients often experience delirium and this usually occurs while in ICU or in the early days following ICU discharge (78). Patients with delirium may experience reduced orientation to their environment, a confused state and altered consciousness that tends to fluctuate in severity throughout the course of a day, hallucinations, abnormal sleep/wake cycles, and agitation (1, 73, 79, 80).

2.3.3 Perturbations in mental health in ICU survivorship

The third component of PICS relates to psychiatric and psychological morbidities, particularly anxiety, depression, and post-traumatic stress disorder (PTSD), that newly develop or worsen following critical illness (1-3). Several longitudinal studies have evaluated the prevalence of anxiety, depression and/or PTSD in critically ill patients during survivorship, and it is clear that psychological morbidities are prevalent amongst survivors and can persist for years following ICU discharge (35, 53, 76-78, 81, 82). Most recently, Huang and colleagues (81) completed a prospective, longitudinal study to evaluate mental health outcomes in a cohort of almost 700 young (mean age 49 years) survivors of ARDS and found the prevalence of depression, anxiety and PTSD was 36%, 42%, and 23%, respectively, one-year following illness. Similar findings have been reported from another recent multi-center trial led by Herridge et al. (35). In this study, 391 patients (mean age of

58 years) who survived an ICU admission were followed for up to one-year following ICU discharge. One-fifth of patients experienced depression and PTSD 3-months following ICU discharge, with no changes in the prevalence of depression occurring between the 3 and 12 month follow ups, and only a modest 5% reduction in the prevalence in PTSD (35).

2.3.4 Quality of life in ICU survivorship

Given the multiple physical and neuropsychological challenges that survivors of critical illness face, it does not come as a surprise that an admission to ICU can substantially impact QOL in survivorship. Measurements to assess QOL are ubiquitous in longitudinal, observational studies examining recovery in survivors of critical illness (76, 83-87).

Conclusions from a recent systematic review evaluating the burden of critical illness on long-term QOL indicate that critically ill patients report lower QOL in comparison to healthy reference group matched by age and sex (40). The 53 studies included in this review evaluated a variety of ICU populations allowing the authors to examine risk factors for worsened QOL, which were identified as high severity of illness at ICU admission (i.e. ARDS, sepsis and trauma) and prolonged MV (40). The functional and psychological disabilities experienced by survivors largely influence poor QOL ratings (42, 52, 85, 87); these results signify the need for effective interventions and rehabilitation strategies that enhance recovery in survivors of critical illness.

2.4 Rehabilitation strategies to enhance recovery from critical illness

The development of innovative strategies and interventions to mitigate PICS, aid in physical and neuropsychological recovery, and enhance quality of life in survivors of critically ill patients are needed (2, 3, 88, 89). To date, the summaries of two stakeholder meetings convened by the Society of Critical Care Medicine (SCCM) have been published

(2, 3). The aim of these meetings were to bring together stakeholders including health care workers from various professional organizations across North America, patients, and families, to inform on the issue of PICS, and develop strategies to improve long-term outcomes after critical illness (2, 3). Health care disciplines represented included medicine (including psychiatry, physical medicine, rehabilitation), physical therapy, occupational therapy and speech-language therapy, nursing, and pharmacy. Interestingly, no professionals representing the nutrition community were in attendance; given the effects of nutrition on physical, cognitive and mental health, nutrition may optimize ICU rehabilitation and it is essential to consider nutrition rehabilitation in ICU survivorship.

2.4.1 The role for nutrition rehabilitation in recovery from critical illness

The maintenance of nutritional health is essential for optimal physiological, physical and psychological functioning. While multiple reviews on ICU recovery, including the summary from the second SCCM Stakeholders meeting on PICS (2), acknowledge or at least hint at nutrition as an area for the prevention and treatment of PICS (9, 56, 89-94), surprisingly little research has actually focused on the role for nutrition in ICU recovery. Thus, several research gaps exist in this field of study, which may be a contributing factor for the underappreciation of the role of nutrition in optimizing recovery and improving QOL. The remainder of this literature review will discuss: 1) the theoretical basis underlying a supportive role for nutrition in the management or mitigation of PICS, specifically emphasizing the role of nutrition in functional and psychological health; 2) the current state of knowledge regarding aspects of nutrition care and malnutrition in critically ill patients along the trajectory of illness; 3) a review of existing studies that form the basis of our

current understanding of nutrition recovery in the critically ill, and; 4) research gaps in the field of nutritional rehabilitation for survivors of critical illness.

2.5 The role of nutrition in the maintenance of functional, cognitive and psychological health

2.5.1 Nutrition and the maintenance of skeletal muscle and physical function

Muscle mass is a determinant of strength and essential for physical functioning whether it be for completion of ADLs or for physical activity and exercise (95). In healthy individuals, skeletal muscle represents 30-45% of total body mass, with approximately 55% of total body muscle mass distributed in the lower limbs (96). Furthermore, skeletal muscle is highly important in regulating glucose disposal, protein turnover, and immune function (97-100). Therefore, any decreases in skeletal muscle mass, such as those occurring in critical illness, can be detrimental to overall health.

The primary determinants of the maintenance of skeletal muscle mass in healthy adults are nutrient availability and physical activity, as both amino acids and exercise are potential anabolic stimuli (101). After consumption of a meal, circulating amino acids and insulin concentrations increase and elicit a potent anabolic effect on muscle, which upregulates muscle protein synthesis. Conversely, in settings of poor nutrient availability, as might be seen in chronic starvation, muscle tissue is degraded to release amino acids which are used by other tissues to preserve their function. The onset of acute illness, triggered by an initial insult such as life-threatening injury or illness, sets in motion an acute inflammatory and immune response, with pronounced stress metabolism resulting in increased catabolism, insulin resistance, and anabolic resistance (9-11, 102). During this phase of illness, the provision of adequate nutrient substrate serves to support the host response to illness and

preserve organ function; muscle atrophy may still occur to support amino acid provision for these functions (10, 11). Thus, nutrient provision during critical illness does not completely inhibit muscle atrophy (103-105). However, in the early and later phases of recovery of critical illness, when factors driving the massive catabolic response to acute illness are abated (albeit not absent (106, 107)), it is likely that timely and adequate provision of nutrients could elicit beneficial effects to enhance recovery and replete lean tissue stores. However, aggressive dietary interventions alone are unlikely to improve functional outcomes and stimulate protein anabolism in a recovering patient with lingering inflammation (106-108), and persistent anabolic resistance (66, 107). It should be considered that nutrition interventions are more likely to produce positive outcomes when combined with physical rehabilitation interventions to maximize anabolic signaling and muscle protein synthesis to ultimately improve physical function.

2.5.2 Nutrition and neurocognitive function

Poor nutritional health has been linked with a decline in cognitive functioning, a comorbidity also observed in PICS. Evidence to date suggests malnutrition may be associated with cognitive decline as elderly hospitalized patients with mild cognitive impairment are more likely to be identified as at risk for malnutrition or malnourished (109-111). This relationship has not been investigated in younger adults, perhaps because cognitive decline is relatively atypical in this population. Nutritional status may be predictive of short-lived perturbations in cognition. Elderly patients identified as being at high risk for malnutrition or malnourished prior to undergoing orthopedic surgery have been shown to be more susceptible to developing post-operative delirium (112). However, the relationship

between nutritional status and the development of long-term cognitive impairment or post-ICU delirium has not been examined in critically ill patients.

In recent years, there has been a growing interest in delineating the relationship between acute nutrient ingestion on cognitive functioning and neuroplasticity. The *gut-brain axis* is a term to denote the crosstalk between the gastrointestinal tract and the emotional and cognitive centers of the brain (113). In brief, the ingestion of nutrients triggers the release of various gut hormones and peptides (i.e. ghrelin, leptin, glucagon-like peptide 1, insulin-like growth factor) which have been shown activate signal-transduction pathways that regulate neuronal synaptic plasticity, signaling and function which subsequently influence various domains of cognitive and emotional processing (Reviewed in: (114, 115)). Thus, given the relationship between nutrition and cognitive functioning, it is possible that targeted nutrition therapies could help to mitigate the cognitive disturbances experienced by some ICU survivors.

2.5.3 Nutrition and psychological health

As reviewed in Section 2.3.3, survivors of critical illness may experience significant and devastating psychiatric illnesses such as depression, anxiety, and PTSD (78, 81).

Nutrition is closely linked with human behavior and emotions. Perturbations in mood can impact food intake whereas nutritional state can also influence mood (Reviewed in: (116)).

For example, a large proportion of individuals with depression experience changes in appetite, however these changes are bidirectional such that some will experienced decreased appetite, while for others it is increased (117, 118). Appetite changes in depressed individuals are associated with altered nutrition intake patterns which have been shown to cause significant unintentional weight loss in individuals with blunted appetites and reduced intake,

or weight gain in individuals consuming increased amounts of foods due to increased appetite (119). Conversely, depression and anxiety frequently co-occur in patients with anorexia nervosa, a form of starvation-related malnutrition, however evidence to support a causal relationship is scarce (120). Attenuation of depressive and anxiety symptoms has been documented in patients with anorexia nervosa who gain weight during nutrition rehabilitation (121). Extrapolating from these findings, it is conceivable that optimizing the nutritional status of critically ill patients in recovery could help to improve psychological outcomes. The relationship between depressive symptoms and malnutrition has also been identified in residents living in long-term care facilities (122) as well as community dwelling older adults (123). While future research is required to better understand the relationship between nutrition and neuropsychological health, it is apparent that mental and cognitive health are important domains to consider when evaluating the nutritional health of compromised individuals, such as those recovering from critical illness.

2.6 The nutritional state of the critically ill over the trajectory of illness

Clearly, nutrition has a potentially important role in managing or mitigating features of PICS. Skeletal muscle atrophy is typically observed during the trajectory of critical illness and this may be related to reduced nutrient availability in the circulation. Understanding the nutritional status of ICU patients provides an important foundation for characterizing and developing nutrition therapies in survivorship.

2.6.1 Malnutrition

The optimal nutritional state occurs when dietary intake is sufficient to promote healthy body composition and normal physical function (124). Conversely, malnutrition is defined as “a state resulting from lack of intake or uptake of nutrition that leads to altered

body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease” (125). It is associated with reduced immunity, increased risk of infection and pressure ulcers, impaired wound healing, impaired mental health, cognitive decline, decreased respiratory and cardiac function, gastrointestinal disorders, loss of muscle mass, and functional disability (19, 20).

Classically, malnutrition has been associated with starvation (decreased intake of nutrients), invoking images of Kwashiorkor (protein deficiency) or Marasmus (protein-energy undernutrition). However, contemporary definitions of malnutrition have evolved such that inflammation is now also recognized as a significant underpinning to disease-related malnutrition, which is distinct from chronic starvation related malnutrition where inflammation is absent (13, 125-127). Inflammation is present to varying degrees in chronic (128, 129) and acute (8, 10) illness/disease states, and advanced aging (130-132). The inflammatory condition, characterized primarily by the upregulated production of pro-inflammatory cytokines and mediators, is associated with increased muscle catabolism resulting in a net loss of lean body mass, reduced functional capacity and immune function, and adverse health effects, all of which are cornerstone characteristics of malnutrition (13, 19, 133).

Malnutrition is a significant problem in the critically ill across all points in the trajectory of illness. Determining the nutritional status of an individual typically involves a comprehensive evaluation of clinical indices known to influence the nutritional state. Indices associated with malnutrition included decreased caloric intake, weight loss, loss of lean tissue, loss of subcutaneous fat mass, and decreased physical function (13, 15, 134, 135). A

more comprehensive discussion regarding the intricacies of nutrition assessment, particularly in the critically ill patient, is found in Chapter 3 of this thesis.

For the purposes of this review, I will be referring to various phases along this “trajectory”, which are defined as follows: the pre-critical illness phase (prior to and up to time of ICU admission), the acute phase of illness (patients are admitted to the ICU and may be receiving ventilatory support), chronic critical illness (patients requiring prolonged MV and ICU stay), the early (ward-based) stages of recovery (patients have been liberated from MV and transferred to a step-down unit or hospital ward for ongoing care), and the later stages of recovery (when patients are typically discharged from hospital) (Figure 2.1).

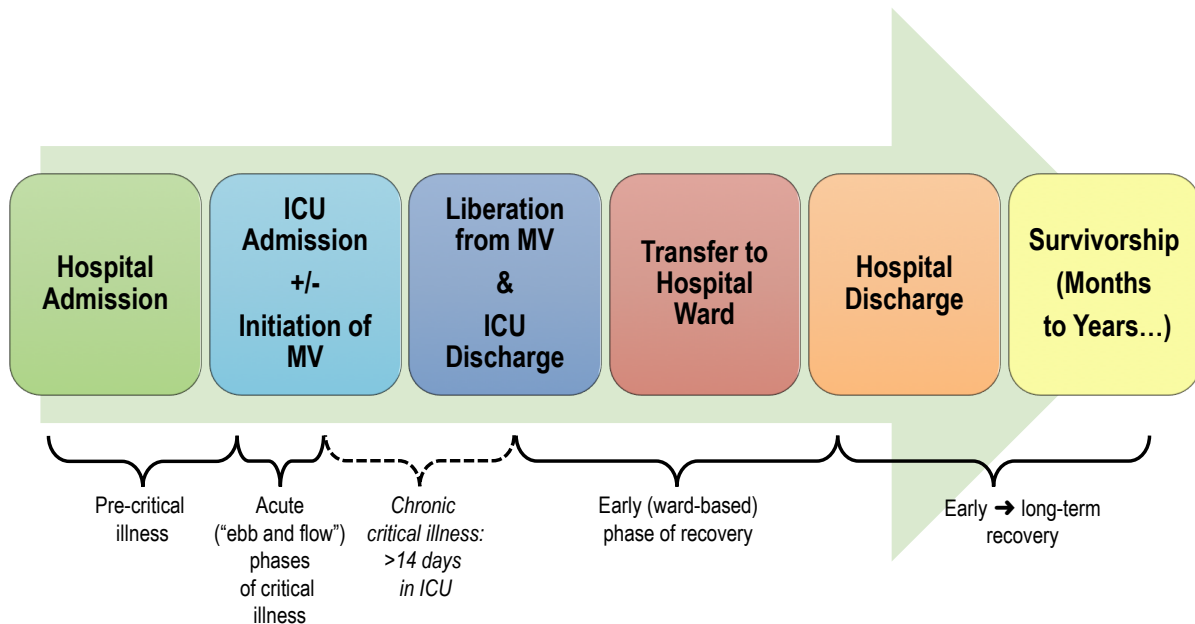


Figure 2.1 Significant phases along the trajectory of critical illness

2.6.2 Malnutrition is prevalent in the critically ill at the time of ICU admission

Critically ill patients are a heterogeneous population such that a variety of conditions may result in admission to an ICU. The most common admitting diagnoses in patients admitted to Canadian medical ICUs are of cardiac and respiratory origin (27) and many have chronic comorbid medical conditions such as cardiovascular disease, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, malignancies, liver disease and/or obesity (27, 136-138). A common pathology across multiple chronic disease states (i.e. obesity, diabetes, chronic kidney disease, cardiovascular disease) is chronic, low-grade inflammation (129, 139-141), which is associated with increased muscle protein breakdown and subsequent loss of muscle tissue (142-145). In Canada, half of adults admitted to ICU are greater than 65 years of age (27) and a common occurrence over the course of normal aging is loss of muscle mass and strength (146, 147), also termed sarcopenia (148). As loss of muscle mass is a hallmark feature of malnutrition (13, 127), it would not be surprising that many patients admitted to ICU are at high risk for becoming malnourished if not already so.

Subjective Global Assessment (SGA) is a tool widely used to assess nutritional status that is based on physical assessment of muscle and fat stores, history of nutrition intake, changes in weight, identification of physical symptoms that may impair intake or nutrient absorption, changes in functional capacity and the presence of illness that may alter metabolic demands (135). Based on SGA, it has been reported that 23-54% of patients admitted to ICU are moderately (SGA score of B) to severely (SGA score of C) malnourished at the time of ICU admission (134, 149-154), and malnutrition at this point in the trajectory of care has been associated with increased mortality (134, 153, 154), and increased rates of ICU readmission (154). Similarly, two studies (155, 156) have quantified

muscle cross-sectional area (CSA) at the level of the 3rd lumbar vertebra using computed tomography (CT) at ICU admission. Muscle CSA at this landmark is strongly correlated to whole-body muscle mass (157, 158), and while assessment of muscle mass is only one index of nutritional assessment and is not indicative of malnutrition in and of itself, it does provide insight into the baseline health of various patients admitted to ICU. The first of these studies, conducted by the author of this thesis, retrospectively measured skeletal muscle index (SMI) (skeletal muscle CSA standardized by height) in a group of elderly trauma patients (n=149, median age of 79 years) and found 71% had an SMI below previously established cut-points (157) for low muscle mass (156). Similarly, Weijs et al. (155) observed 63% of adult patients (n=240, mean age of 57 years) admitted to a medical ICU had low skeletal muscle CSA. Low muscularity was associated with negative outcomes including increased mortality (155, 156), decreased ventilator-free days (156), decreased ICU-free days (156) and a decreased propensity to be discharged home (156).

2.6.3 Factors influencing changes in nutritional status of the critically ill patient while in ICU

The assessment of nutritional status of critically ill patients at any given point during the acute phase of illness is challenging, as is determining the exact degree of change in nutritional status occurring during this time frame, or discerning the point along the trajectory of acute illness in which a patient becomes malnourished. The evaluation of changes in body composition and decreases in muscle strength are particularly difficult to assess in the critically ill due to their disposition. Mechanically ventilated patients often have decreased level of consciousness, fluid overload and edema (159) and we currently lack practical tools to accurately assess changes occurring in body composition throughout the course of illness (104, 125, 160). However, it is probable that the nutritional status of critically ill patients

worsens over the course of illness for several reasons. The acute phase of critical illness is characterized by an acute systemic inflammatory response (8) wherein pro-inflammatory cytokines and immune mediators are released and the sympathetic nervous system is stimulated, all of which result in increases in resting energy expenditure, hyperglycemia, muscle protein breakdown and lipolysis (9-11). Consequently, critically ill patients experience significant decreases in muscle mass and muscle function (12, 59, 161), two indices of malnutrition (13-15).

Nutrition therapy (i.e. enteral or parenteral nutrition) during critical illness is provided to attenuate the stress response and preserve lean body mass (162), and several clinical practice guidelines for feeding the mechanically ventilated patient have been published (162-165). However, in-ICU nutrition delivery is largely inadequate with mechanically ventilated patients receiving between 58-71% of the amount of protein and energy prescribed (16-18, 166). Furthermore, “permissive underfeeding”, a now discouraged practice in which critically ill patients are deliberately underfed both calories and protein (versus hypocaloric feeding in which protein delivery is not compromised) (167, 168), further contributes to inadequate nutrition delivery over the course of ICU stay. Consequently, over the course of ICU admission, patients accrue large protein and energy deficits (23, 169) which are associated with decreased ventilator-free days, increased ICU LOS, and increased hospital LOS (169). The protein and energy intakes of critically ill patients receiving non-invasive MV are similarly inadequate (170). Such chronic calorie and protein underfeeding over the course of ICU admission is likely to negatively influence the nutritional health of critically ill patients.

2.6.4 Nutrition recovery following ICU discharge

The prevalence of malnutrition at the time of LMV has not been measured and no consensus exists on how to objectively diagnose malnutrition in a critically ill patient at this specific point in the trajectory of illness (125). However, it is highly probable that critically ill patients with higher severity of illness who required invasive MV in ICU will be malnourished upon discharge from the ICU (refer to Figure 2.2).

The field of nutrition recovery following critical illness is understudied and our present understanding of the extent to which survivor's experience improvements in nutrition throughout recovery is limited. The current foundation of knowledge centering on nutrition recovery and rehabilitation after critical illness is based upon observations from eleven studies (21-26, 151, 171-173) that have reported on varying nutrition related indices (Table 2.1). Findings from these studies center on two main themes: nutrition (energy and protein) intake and adequacy of intake in relation to that prescribed, and barriers to achieving optimal nutrition during both the early stages of ward-based recovery and recovery following hospital discharge.

2.6.4.1 Nutrition intake and adequacy following liberation from mechanical ventilation

To date, measures of energy and protein intake in various critically ill patient populations following LMV have been quantified and reported in two studies (21, 23). Chapple et al. (23) utilized weighed food records, considered the gold standard method of evaluating dietary intake (174), to evaluate oral intake in 37 traumatic brain injury (TBI) patients. They found that patients on oral diets consumed 74% and 75% of their protein and energy requirements, respectively, whereas those receiving enteral nutrition received 89% of their estimated energy requirements and 76% of their estimated protein requirements. In

contrast, Peterson et al. (21) used a modified 24h recall method to measure dietary intake and found that a sample 50 patients from a medical/surgical ICU never consumed greater than 37% of their protein requirements and 55% of their energy requirements on any day during the first 7 days following extubation.

The discrepancy in energy and protein adequacies between these two studies may be related to the method used to determine adequacy of intake. Chapple et al. (23) compared intake to amounts prescribed by dietitians as part of routine care, whereas Peterson et al. (21) compared intake to requirements estimated for the purposes of the study using a set of standardized equations based on ICU admission weight versus prescriptions documented as part of the nutrition care plan (nutrition care plans are based on the nutrition assessment). It is also possible that the 24h recall method resulted in underestimation of foods consumed, particularly as this method is reliant on recall by patients, who are not always alert/oriented, or caregivers, who are not always present at all meals. The modified multiple-pass recall, delivered over the phone, has been shown to accurately assess nutrition intake in comparison to visual estimation (175), but it has not been validated for use in hospitalized patients, and in particular, ICU patients. More research is required to obtain a better understanding of dietary consumption in mixed medical/surgical populations, ideally using methods to assess intake that are not dependent on recall. Further exploration as to how route of nutrition administration (i.e. oral diet vs nutrition support therapies) can impact nutrient adequacy, and what factors determine choice of route used, is also warranted.

Given the lack of clearly characterized energy and protein intakes following LMV, no guidelines exist for feeding the critically ill patient following LMV, specifically with respect to: route of nutrition delivery (i.e. oral diets versus EN or PN), when and how best to

transition patients from nutrition support to oral diets, and nutrient provision (i.e. energy and protein requirements). Consideration must also be given to current in-ICU feeding practices and how they may influence feeding following LMV. For example, in the initial acute phases of critical illness, there is growing consensus that hypocaloric (i.e. 80-90% of estimated calorie requirement), high protein feeding should be initiated (168). As patients transition from the acute to the chronic or recovery phases of illness, the metabolic demands of patients should be reevaluated and energy prescriptions shifted to eucaloric feeding to ensure nutrition recovery is not compromised due to the accumulation of large calorie deficits (167, 168). However, further research is necessary to better understand current nutrition practices in the recovering critically ill patient and how they may influence nutrition delivery and adequacy of protein and calorie intake in recovery.

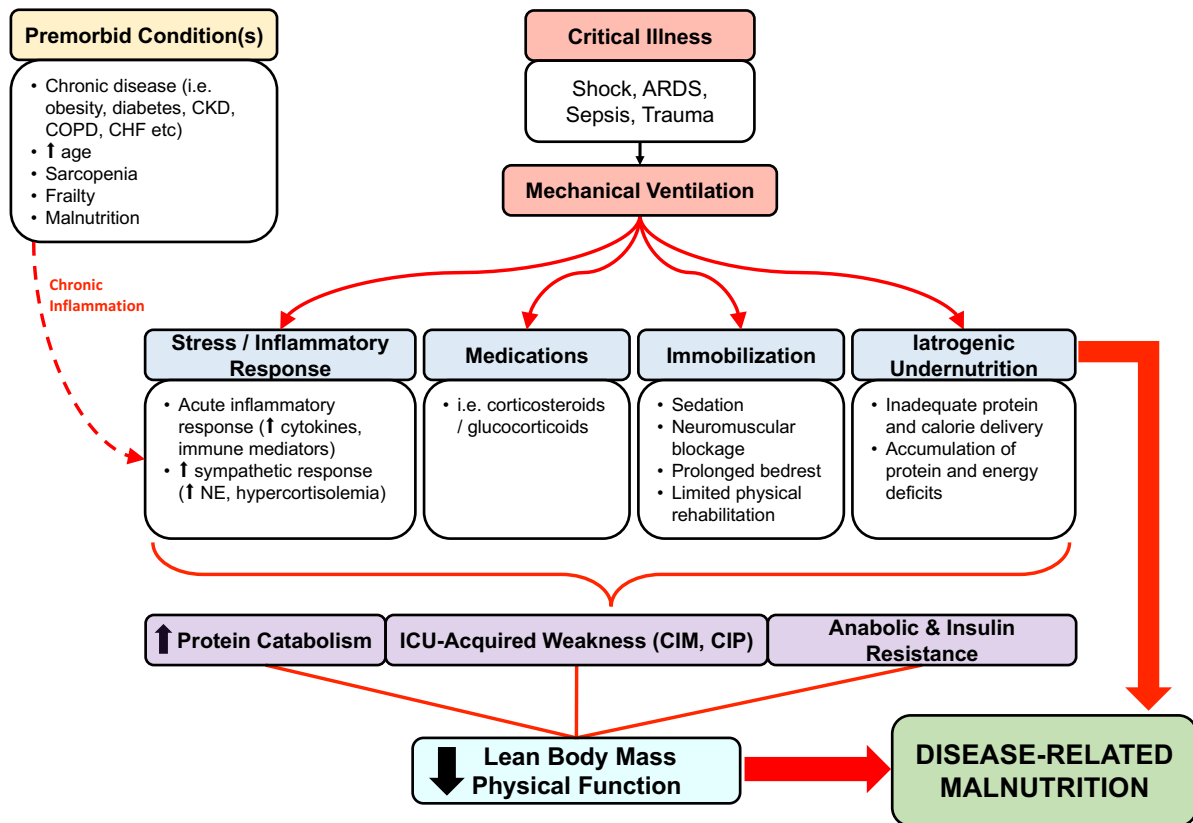


Figure 2.2 Factors influencing the development of disease-related malnutrition following the onset of critical illness

Patients admitted to ICU frequently have one or more premorbid chronic health conditions and consequent chronic, low-grade inflammation which is associated with increased muscle protein breakdown. Older adults, who make up greater than half of all ICU admissions, may be frail or sarcopenic. The onset of acute illness triggers an acute inflammatory response and pronounced stress metabolism which results in increased catabolism, insulin resistance, and anabolic resistance. Throughout the duration of mechanical ventilation, patients receive inadequate protein and energy and experience iatrogenic undernutrition. In the stressed state, tissues are less sensitive to anabolic stimuli such as protein/amino acids thus nutrient uptake is impaired. Throughout ICU admission, patients are frequently immobilized which is associated with muscle wasting and dysfunction. Patients may receive medications that increase muscle protein breakdown. Each of these factors independently contributes to a metabolic state that favors the loss of lean body mass and decreased functional capacity, which are established indicators of malnutrition. Thus, at the time of liberation from mechanical ventilation, patients are likely to have developed disease-related malnutrition, with the level of severity influenced by factors including premorbid health status, severity of illness, duration of mechanical ventilation, and length of ICU stay. ARDS, acute respiratory distress syndrome; CHF, congestive heart failure; CKD, chronic kidney disease; CIM, critical illness myopathy; CIP, critical illness polyneuropathy, COPD, chronic obstructive pulmonary disease; NE, norepinephrine.

2.6.4.2 Barriers to consuming adequate nutrition

Patients recovering from critical illness experience a multitude of barriers to consuming adequate calories and protein that may be distinct from other hospitalized populations. The most frequently reported barriers to eating relate to the physiological effects of illness, such as poor appetite (21, 22, 24, 25). Other illness-related barriers to eating that are frequently cited in this patient population include early satiety, nausea, vomiting, changes in taste, difficulties chewing and swallowing, pain and sleep disturbances, and neuromuscular weakness impacting ability to independently feed oneself (21, 22, 24, 25). In a recent qualitative study by Merriweather et al. (24), semi-structured interviews with patients who were recently discharged from ICU were performed to document nutrition-related challenges in the early phases of recovery. Many of the patients experienced low mood and anxiety, as is common in this population, but attributed this to poor food intake, predominantly because eating was viewed as low priority while patients struggled to cope with the drastic changes in their health (24).

The ability of any hospitalized patient to consume adequate nutrition can be negatively affected by organizational barriers including delivery of meals at inappropriate times, missed meals and snacks, and interrupted mealtimes (176-178). Hospital meal delivery times are frequently not suitable for the critically ill patient who is suffering from altered sleeping patterns/disturbances, as well as a poor appetite coupled with early satiety (24, 26). A common strategy to enhance nutrition intake in compromised individuals is the provision of small, nutrient dense meals and snacks frequently throughout the day (179-181), however hospitals are often not well suited to deliver this type of meal pattern. While snacks can be

prescribed or included in various therapeutic menus, failure to deliver snacks to the wards or have snacks delivered to the patient is a common problem in hospitals (24, 26, 177).

Transition of care may also influence nutrition recovery when patients are transferring from an ICU to the ward and this area of work has only recently been investigated. ICU transitional care refers to the “care provided before, during, and after the transfer of an ICU patient to another care unit to ensure minimal disruption and optimal continuity of care” (49). When a patient transfers out of the ICU, this often coincides with a transfer of care between health care providers and transfers to units where the staff-to-patient ratio is reduced and staff may lack specialized knowledge to provide the complex care required for a recovering, critically ill person (49, 182). Poor care transitions increase the risk of complications, ICU readmission, and mortality (49, 182). Unfortunately, nutrition care plans are poorly communicated between health care providers, ward staff do not have sufficient knowledge of the complex nutrition needs of a critically ill person, and nasogastric enteral feeding tubes are frequently removed prior to any assessment occurring by a dietitian (26). Each of these factors significantly hinders the nutritional rehabilitation of survivors of critical illness and could lead to increased complications or prolonged recovery.

2.7 Nutrition rehabilitation following critical illness

Although optimizing nutrition recovery in critically ill patients following LMV is important, recognition that nutrition care is an important component of rehabilitation is underappreciated as is evidenced by the limited number of studies found within the literature. With the emerging awareness of PICS in survivors of critical illness, much research has focused on physical rehabilitation interventions to improve functional outcomes. Post-ICU physical rehabilitation programs that have been developed (25, 183-185) have largely failed

to elicit extensive improvements in patient outcomes. Lack of response is felt to be secondary to implementation of rehabilitation programs to all patients (versus those with poorest functional or health status at ICU discharge who may see a greater benefit) and recognition that individually-tailored rehabilitation strategies may be more effective than broad, generic programs (186).

From a nutritional perspective, failure to assess and/or optimize the nutritional status of those who are enrolled in a physical rehabilitation program may limit the efficacy of the intervention. Studies conducted in clinical populations such as obese older adults (187) and patients with HIV (188) have found prescription of combined nutrition and exercise interventions result in greater increases in muscle mass and strength in comparison to nutrition or exercise only. To date, only one post-ICU rehabilitation study has evaluated a combined physical rehabilitation and nutrition intervention, which showed no effect on functional recovery or QOL (25), however the nutrition intervention was somewhat minimal. For this study, a generic rehabilitation assistant was employed to enhance nutritional care via monitoring enteral nutrition delivery, completing food records daily, ensuring meals, snacks and oral nutrition supplements were delivered, providing mealtime assistance, and communicating patient nutrition concerns to the unit dietitian. While patients in the intervention trial had increased frequency of dietitian visits, study outcomes did not include measurements of energy and protein intake or adequacy, thus it is difficult to discern whether the intervention applied was effective. Another limitation of this study is that no serial measures of nutritional status were taken throughout the duration of the study, thus any improvements that may have occurred in dietary intake and nutritional status were not documented. However, the authors did acknowledge in the protocol development phase (189)

that assessing the nutritional status of critically ill patients in recovery poses several challenges. This underscores the need for the identification of feasible and reliable measures to assess various indices of nutrition status that can be applied to patients recovering from critical illness.

Provision of enhanced and more aggressive multimodal nutrition care has proven to be successful in increasing nutrition intake and nutritional status in hospitalized patients as a whole (190) and inpatients with hip fractures (191, 192). However, as alluded to previously, two of the primary barriers to oral intake are poor appetite and early satiety (21, 22, 24, 25), thus strategies that aim to improve intake by improving food access or increasing the amount of food delivered will be futile. Strategies to enhance food intake in other high nutrition risk patient populations that face similar barriers to eating include, but are not limited to, fortifying or enhancing the nutrient content of foods (179, 193), serving nutrient dense foods and meals (194, 195), consuming small, frequent meals (196), and identifying population specific (i.e. cancer patients) food desires (197). Such strategies may be effective for survivors of critical illness however no research has characterized meal time feeding patterns and preferences in this patient population. The acquisition of knowledge regarding nutrition habits and behaviours in the critically ill may help guide the development of effective nutrition interventions.

2.8 Conclusion

Critically ill patients are a unique and vulnerable patient population who experience devastating health-related morbidities relating to physical, cognitive and psychological functioning in survivorship. Malnutrition is a significant concern for the critically ill and poor nutritional status can negatively impact physiological, functional and psychological health,

however very little research examining nutrition recovery and rehabilitation in the early stages of ward based recovery exists. The role of optimizing the nutritional state and care of critically ill patients following ICU discharge is underappreciated, however this is likely due to large gaps in our understanding to the degree of nutrition recovery that occurs with usual care, and even what “usual” nutrition rehabilitation care is. It is therefore clear that more research is required for us to determine the optimal tools to assess the nutritional status of the critically ill throughout the course of illness, to characterize how patients recover nutritionally both in hospital and post-hospital discharge, and to develop and test novel and integrative nutrition interventions aimed at improving nutrition and functional recovery in survivors of critical illness.

Table 2.1 Overview of studies examining nutrition in the recovery phase of critical illness

Citation, country of origin	Study design	Primary objective(s)	Study population and sample size	Nutrition indices assessed & methodologies used
Nematy et al, 2006 (22) (England)	Prospective, observational study	To investigate gut hormone concentrations in patients during ICU stay but following LMV and relate them to appetite and energy intake measures.	Critically ill adults requiring MV and anticipated ICU LOS >3 days n=16 ICU patients n=36 healthy controls Patients receiving EN, PN and/or oral diets included in study.	Energy intake: Oral diet: Food records completed daily by nursing staff EN/PN: calculated from flow sheets in the medical record. Healthy controls: 3-day food diary Estimation of requirements to assess adequacy: Compared energy intake of ICU patients to healthy control subjects. Factors affecting intake: Appetite VAS Body composition: ICU admission: weight, BMI, TSF, MAC ICU discharge: weight, BMI, TSF, MAC
Peterson et al, 2010 (21) (United States)	Prospective, observational study	To assess protein and energy adequacy and identify barriers to oral intake in ICU patients for the first 7 days following extubation.	Critically ill adults requiring MV for >24h n=50 Patients requiring EN/PN excluded	Energy and protein intake: Modified multiple-pass 24-hour recall conducted daily study duration. Estimation of requirements to assess adequacy: BMI<30: 25 kcal/kg admission weight, 1.2 g protein/kg admission weight BMI≥30: 11 kcal/kg admission weight, 2 g protein/kg ideal weight (calculated using Hawmi equation) Factors affecting intake: Patients asked open-ended questions to identify barriers to intake

				<p>Body composition: ICU admission: Weight, BMI, TSF, MAC</p> <p>Global nutritional status assessment: ICU admission: SGA</p>
Salisbury et al, 2010 (171) (Scotland)	Pilot feasibility study (this paper is a case description of one patient).	To describe the role and issues raised around the implementation of using a GRA to deliver enhanced physiotherapy and nutrition rehabilitation for up to 7-weeks after critical illness.	Critically ill adult requiring MV for >4 days (stroke, head injury and liver transplant patients excluded). n=1	<p>All measures taken 3-months following ICU discharge.</p> <p>Energy and protein intake: Food record charts (completion of food records was part of the enhanced nutrition care delivered by the GRA).</p> <p>Estimation of requirements to assess adequacy: Schofield and Elia equations</p> <p>Factors affecting intake: Appetite VAS</p> <p>Body composition: Weight, MAMC</p> <p>Global nutritional status assessment: Hand-grip strength</p> <p>Functional status assessment: River-mead mobility index, timed up and go, 10-meter walk test, hand-grip strength</p>

Salisbury et al, 2010 (189) (Scotland)	2 studies: 1) Service evaluation of care 2) Pilot feasibility RCT	1) Determine the ward-based physiotherapy and nutrition services patients current receive following ICU discharge. 2) Determine whether use of a GRA to provide enhanced physiotherapy and nutrition rehabilitation is feasible.	Critically ill adults requiring MV for >4 days (stroke, head injury and liver transplant patients excluded). Intervention group (assigned a GRA): n=8 Control group (standard care): n=8 Patients receiving EN, PN and/or oral diets included in study.	All measures taken 3-months following ICU discharge. Energy and protein intake: Food record charts (completion of food records was part of the enhanced nutrition care delivered by the GRA). Estimation of requirements to assess adequacy: Schofield and Elia equations Factors affecting intake: Appetite VAS Body composition: Weight, MAMC Global nutritional status assessment: Hand-grip strength Functional status assessment: River-mead mobility index, timed up and go, 10-meter walk test, hand-grip strength
Walsh et al, 2012 (172) (Scotland)	Protocol summary of multicentre, randomized parallel group intervention trial (the “RECOVER” study)	Evaluate the impact on physical, psychological and social functioning of a novel complex intervention strategy (i.e. use of GRA) to enhance delivery of physical and nutritional rehabilitation to patients during the 3-months following ICU discharge. <i>Various outcome variables will be assessed at ICU discharge and 3, 6, and 12 months post-ICU discharge.</i>	Critically ill adults requiring MV for >48h (TBI, intracerebral bleed, stroke, Guillain-Barre syndrome excluded). Patients receiving EN, PN and/or oral diets included in study.	Factors affecting intake: ICU discharge, 3, 6 and 12 month follow ups: Appetite VAS Body composition: 3-month follow up: Weight, BMI Global nutritional status assessment: 3-month follow up: SGA Weekly in hospital post-ICU discharge and 3-month follow up: hand-grip strength Functional status assessment: Weekly in hospital post-ICU discharge and

				3, 6 and 12-month follow up: River-mead mobility index 3-months follow up: timed up and go Weekly in hospital post-ICU discharge and 3-month follow up: hand-grip strength
Merriweather et al, 2014 (26) (Scotland)	Prospective observational study using qualitative research methodology	To examine organizational issues and barriers influencing nutrition care during the post-ICU hospital stay.	Critically ill adults requiring >48h MV n=17 Patients receiving EN, PN and/or oral diets included in study.	Organizational factors influencing nutrition care were acquired through researcher observation of usual care and semi-structured interviews.
Braunschweig et al, 2015 (151) (United States)	Prospective RCT	To evaluate the impact of intensive medical nutrition therapy in ALI patients from time of ICU admission to hospital discharge.	Critically ill adults with ALI Intervention group: n=40 Control group: n=38 Patients receiving EN, PN and/or oral diets included in study.	Energy and protein intake: EN/PN: calculated daily from flow sheets in the medical record. Oral diets: Modified multiple-pass 24-hour recall completed daily. Estimation of requirements to assess adequacy: BMI<30: 30 kcal/kg admission weight, 1.5 g protein/kg admission weight BMI≥30: 30 kcal/kg adjusted weight, 1.5 g protein/kg adjusted weight. Factors affecting intake: Appetite VAS Body composition: ICU admission: Weight, BMI Global nutritional status assessment: ICU admission: SGA

Walsh et al, 2015 (172) (Scotland)	Multicentre, randomized parallel group intervention trial (the “RECOVER” study)	To determine the effect of increased physical activity and nutrition rehabilitation delivered during the post-ICU acute hospital stay via use of a GRA on mobility, quality of life and disability.	Critically ill adults requiring MV for >48h (TBI, intracerebral bleed, stroke, Guillain-Barre syndrome excluded). Intervention group: n=120 Control group: n=120 Patients receiving EN, PN and/or oral diets included in study.	Factors affecting intake: ICU discharge, 3, 6 and 12 month follow ups: Appetite VAS Body composition: 3-month follow up: Weight, BMI Global nutritional status assessment: 3-month follow up: SGA Weekly in hospital post-ICU discharge and 3-month follow up: hand-grip strength Functional status assessment: Weekly in hospital post-ICU discharge and 3, 6 and 12-month follow up: River-mead mobility index 3-months follow up: timed up and go Weekly in hospital post-ICU discharge and 3-month follow up: hand-grip strength
Marshall et al, 2015 (173) (Australia)	Prospective cohort feasibility study (qualitative methodology)	To evaluate the feasibility and acceptability of a family-centered intervention designed to optimize nutrition during and following recovery from critical illness	Critically ill adults requiring MV for >48h n=49 Patients receiving EN, PN and/or oral diets included in study	No nutritional indices assessed however part of the intervention is daily completion of a nutrition diary based on the nutritionDay worldwide survey.
Chapple et al, 2016 (23) (Australia)	Prospective observational study	To quantify the amount of energy and protein prescribed and delivered throughout hospitalization in critically ill patients with TBI.	Critically ill adults with TBI requiring ICU stay \geq 48h n=37 Patients receiving EN, PN and/or oral diets included in study	Energy and protein intake: EN/PN: calculated daily from flow sheets in the medical record up to day 90 of hospitalization. Oral diets: weighed food records 3 days per week (2 weekdays, 1 weekend day) up to day 90 of hospitalization. Estimation of requirements to assess adequacy and cumulative deficit:

Energy and protein prescriptions assessed by the hospital dietitians as part of standard care were extrapolated from the charts.

Barriers to intake:

Interruptions to nutrient provision documented from patient medical records.

Merriweather et al, 2016 (24) (Scotland)	Prospective observational study using qualitative research methodology	To explore factors influencing nutrition care during hospitalization following ICU discharge and at 3 months following ICU discharge.	Critically ill adults requiring >48h MV n=17 Patients receiving EN, PN and/or oral diets included in study.	Factors influencing nutrition care were acquired through researcher observation of usual care (1h for 3 times weekly) and semi-structured interviews (weekly during patients stay on the ward and at 3 months post-ICU discharge).
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Abbreviations: ALI, acute lung injury; EN, enteral nutrition; GRA, generic rehabilitation assistant; ICU, intensive care unit; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; LMV, liberation from mechanical ventilation; MV, mechanical ventilation; PN, parenteral nutrition; RCT, randomized control trial; SGA, Subjective Global Assessment; TBI, traumatic brain injury; TSF, triceps skinfold; VAS, visual analogue scale.

CHAPTER 3

OVERVIEW OF METHODOLOGY

3.1 Research design

To better understand nutrition recovery in adult critically ill patients specifically following LMV, two studies, a prospective, observational feasibility study (presented in Chapters 4, 5, and 6) and a retrospective chart review (presented in Chapter 7) were undertaken. Both studies were approved by the Western University Health Sciences Research Ethics Board, the Lawson Health Research Institute, and the University of Waterloo Office of Research Ethics (Appendix A and Appendix B).

3.2 Research site

All research was completed at University Hospital (UH), an academic teaching hospital affiliated with Western University in London, Ontario. UH is part of London Health Sciences Centre (LHSC), which oversees three teaching hospitals (one of which is dedicated to pediatrics), two family medical centers, and two research institutes. Housed within UH is a 24-bed medical-surgical intensive care unit (MSICU) and includes an extended ICU, which consists of five beds allocated for patients with chronic ventilator dependency. The UH MSICU, where patients for this research were recruited, specializes in the care of a variety of populations including neurosurgery, transplantation, medical, and general surgery patients. It is a Level 3 ICU meaning it is “capable of providing the highest level of service to meet the needs of patients who require advanced or prolonged respiratory support, or basic respiratory support together with the support of more than one organ system” (198), and a major referral center for Southwestern Ontario. MSICU patients at UH are cared for by one of 10

intensivists who rotate on service weekly. As a teaching hospital, patients are followed by residents who complete 1-3 month rotations. When MSICU patients are ready for discharge from the ICU, they are typically transferred to one of the following wards at UH: general medicine, general surgery (includes gastroenterology, urology, plastics, and ENT), neurosciences (neurology and neurosurgery), cardiology, cardiovascular and thoracic surgery, orthopedic surgery, and hepatology/transplant. It is also possible for patients to be discharged directly from the ICU if no ward beds became available prior to discharge, or they may be repatriated back to a referring hospital directly from the ICU.

3.2.1 Dietitian services at University Hospital

Several dietitians are responsible for the nutrition care of patients at UH. Table 3.1 provides a summary of the dietitian staffing in 2015 for each of the units. The MSICU is staffed full-time by one RD on weekdays. Weekend RD coverage for the whole hospital is provided on an on-call basis.

Table 3.1 Dietitian staffing at University Hospital

Inpatient Units	Approximate number of beds	Approximate dietitian staffing full-time equivalents
Medical-surgical intensive care unit	19 + 5 EICU ¹	1.0
Cardiac surgery recovery unit	16	0.2
General medicine ²	108	1.8-2.0
Neurosciences ³	70	1.0
General surgery ⁴	60	1.3
Orthopedic surgery	45	0.3
Cardiovascular and thoracic surgery	41	0.4
Cardiology	32	0.4
Hepatology/transplant	12	0.5

¹Extended-stay ICU

²Includes nephrology

³Includes neurology and neurosurgery

⁴Includes gastroenterology, urology, plastics, otolaryngology

3.2.2 Stakeholder approval

To facilitate implementation of the research presented in this thesis, I obtained feedback and approval from a variety of stakeholders within LHSC and UH. The stakeholders included: the UH-ICU research committee, the UH MSICU Manager, the Manager of Clinical Nutrition Services, UH dietitians, the Manager of the Food Services Department, all managers and clinical nurse coordinators of wards where recruited patients were likely to be transferred to from the ICU, and the physical and occupational therapy clinical leaders.

3.3 Study population

In recovery, patients often experience features of PICS, which is characterized by significant functional, cognitive and psychological morbidities (2, 3). Patients with higher severity of illness at ICU admission, who require mechanical ventilation, and have longer ICU length of stay appear to be at highest risk of developing features of PICS (2, 3). They are also prone to losing greater amounts of protein and lean tissue mass (12, 199) and to develop swallowing disorders (200), and are thus at higher risk of being nutritionally compromised. Therefore, the general patient population that was included for the research presented in this thesis were adult (≥ 18 years of age) critically ill patients admitted to the UH MSICU who had received invasive MV for at least 72 consecutive hours. Data collection for the prospective, observational feasibility study occurred between February and October 2015. Data for the retrospective chart review was extracted from the medical records of all patients admitted to the MSICU in 2015 who met the inclusion criteria. A full year was chosen to minimize selection bias that could arise from seasonal variations and staffing turnover of the interprofessional team.

Exclusion criteria for the prospective, observational study were as follows:

- Patients for whom death was imminent or life sustaining therapies were withdrawn in the ICU.
- Patients who were pregnant. Pregnant women experience atypical changes in body composition that will continue throughout the duration of pregnancy. As our outcome measures include measures of body composition, including pregnant women in this study may have confounded our research findings.
- Patients with primary neuromuscular disease. Individuals with primary systemic neuromuscular disorders exhibit atypical changes in body composition secondary to altered health and disease state. Additionally, afflicted individuals may not be able to participate in study tests evaluating physical function.
- Patients with limb amputation(s) or spinal cord injury. Patients with limb amputation or spinal cord injury may not be able to participate in tests evaluating physical function such as hand-grip strength testing and they may also have experienced atypical changes or adaptations in body composition secondary to amputation or nerve injury.
- Patients with a traumatic brain injury (TBI). Patients with a TBI are anticipated to have altered level of consciousness or be unconscious over the course of their hospital stay and unlikely to be able to participate in this study.
- Patients who were admitted to hospital specifically for organ transplant. Organ transplant may significantly alter a patient's body composition and nutritional requirements and including measures from this unique population may confound our

research findings. LHSC has a program dedicated to organ transplant and it was also requested by our stakeholders that transplant patients be excluded from this study due to the high volume of studies transplant patients are recruited for.

- Patients who were enrolled into an intervention study affecting usual nutrition care. Patients enrolled into an intervention study may not be receiving standard care thus potentially confounding the results of our study. In addition, participation in multiple studies may add additional or unnecessary burden to the patient.
- Patients who were anticipated to be repatriated to an external hospital/institution prior to ICU discharge.
- Patients deemed inappropriate to approach for consent as per the discretion of the research investigator or at request of member(s) of the patient's health care team.

For the retrospective chart review (Chapter 7), patients were excluded if they:

- Expired or life sustaining therapies were withdrawn in ICU.
- Were receiving parenteral nutrition at the time of LMV.
- Were receiving long-term EN via gastrostomy or gastrojejunostomy feeding tube prior to ICU admission.
- Were transferred out of the ICU while still requiring ventilatory support.

3.4 Methods pertaining to the assessment of nutritional status

An overarching goal of the research completed as part of this thesis was to develop a better understanding of the nutritional state of adult survivors of critical illness following LMV. Currently, no consensus exists on how to diagnose malnutrition. The Academy for

Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) recommend that a minimum of two of the following six nutrition indices be present for a formal diagnosis of malnutrition: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, fluid accumulation/edema, and/or diminished functional status determined by hand-grip dynamometry (13). In contrast, the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends a diagnosis of malnutrition be based on a low body mass index (BMI; defined as $<18.5 \text{ kg/m}^2$) or the presence of unintentional weight loss ($>10\%$ over any period or time or $>5\%$ over 3 months) with either a reduced BMI ($<20 \text{ kg/m}^2$ if <70 years of age or $<22 \text{ kg/m}^2$ if ≥ 70 years of age) or low fat free mass index ($<15 \text{ kg/m}^2$ for females, $<17 \text{ kg/m}^2$ for males) that can be measured via bioelectrical impedance analysis (BIA), DXA, CT, or MRI (15). Interestingly, ESPEN's recommendations are only based on nutrition indicators related to objective measures of body composition, reasoning that the evaluation of food intake would not provide further value in assessing nutritional status when weight is evaluated and measures of physical function are not nutrition specific (15). In Canada, no consensus recommendations for the diagnosis of malnutrition exist, however the Canadian Malnutrition Task Force recommends SGA as the primary measure to diagnose malnutrition in hospitalized patients (201). This recommendation is based on the findings of a large prospective cohort study examining nutrition care in Canadian hospitals (201). SGA is based on assessment of dietary intake, symptoms influencing oral intake, weight changes, changes in muscle and subcutaneous fat mass and functional capacity, and metabolic requirement as it relates to the presence of illness (135). While the indicators used to diagnose malnutrition vary slightly between each of these groups, each recommends assessment of nutrition risk using a validated nutrition risk

screening tool prior to a diagnosis of malnutrition, and all apply the etiological-based approach to defining malnutrition as proposed by Jensen and colleagues (14, 127) as was previously discussed in Chapter 2 (section 2.6.1) of this thesis.

3.4.1 Assessing the nutritional status of the critically ill patient

Currently, there is no consensus on how to objectively diagnose malnutrition in the critically ill (104, 125). The clinical condition of a critically ill patient can preclude acquisition of accurate and reliable measures of nutritional status. Critically ill patients typically experience significant edema and fluid shifts secondary to resuscitative therapies and pre-existing conditions which impact the ability to accurately interpret some measures of body composition (159, 202). Medications, sedation, prolonged MV and prolonged immobilization can result in ICU-AW, functional limitations (36, 203, 204), and decreased level of alertness (LOA) or altered cognitive status (i.e. delirium, agitation) (185, 205). Consequently, obtaining nutrition assessment measures using procedures that are reliant on a patient's physical and/or cognitive disposition may not be practical or reliable (104, 149, 160, 206).

One objective of the prospective, observational study was to report on the feasibility of obtaining longitudinal measures (up to 14 days following LMV) used to evaluate nutritional status in the critically ill immediately following LMV (findings reported in Chapter 4). Measurements to assess some of the nutrition indices that are required to make a formal diagnosis of malnutrition set out by the AND and ASPEN were evaluated (13). Nutrition (protein and energy intake) was measured using weighed food records (WFR), dietary recall, and chart abstraction for patients receiving enteral (EN) or parenteral nutrition

(PN). Body composition was assessed by weight, BMI, mid-upper arm circumference (MAC), and phase angle (PhA) (obtained using BIA), and abdominal CT images if taken as part of usual care. Physical function was assessed with hand-grip dynamometry, and biochemical markers traditionally reported in nutrition research including albumin, prealbumin and C-reactive protein (CRP), were documented if taken as part of usual care. A summary of the measures utilized and rationale for their use is provided below.

3.4.2 Nutrient intake

3.4.2.1 Food services at University Hospital

All meals delivered to patients at UH are prepared, plated and loaded onto re-thermalization delivery carts at Victoria Hospital. This is the second adult acute care hospital that is part of LHSC and the distance between the hospitals is approximately 8 km. These carts are transported to UH on trucks three times per day prior to each meal. The hospital utilizes a Cook-Chill Meal Delivery System. Foods served to patients are imported by manufacturers; the hospital does not prepare its own food, with exception of some items such as sandwiches and salads. Individual food items are placed onto meal trays, which are then loaded onto re-thermalization carts. The Cook-Chill Retherm system works such that food items placed on one side of the meals tray are heated (“cooked”) and those on the other side of the cart are cooled (“chilled”) when the carts are plugged into a docking station. The UH Food Service Department receives the preloaded rethermalization carts from Victoria Hospital and cooks/chills the meals on site immediately prior to delivery to the patients.

The standard regular (non-modified texture/fluid) diets provided at UH provide an average 1500 kcal/d and 52 g protein/d. Capable patients are provided with the opportunity

to select their meals. Menus for the following day (Appendix C) are distributed every morning with breakfast and the completed menus (patients circle their selections) are collected shortly after lunch. If a menu selection sheet is not completed or a dietary prescription changes mid-day, a standard meal is provided. In general, the meals are structured to provide a source of protein (meat/meat alternative), and a serving of vegetables, grains/starch, milk, and fruit (and/or a dessert). Snacks are not provided as part of the regular diet unless requested. For patients who are unable to select their meals or miss the opportunity to complete the selection are provided with the standard diet being served that day. After menus are selected, a dietary assistant enters the selections into the hospital nutrition management software (CBORD) and meal tray tickets listing every item to be included on each individual meal tray are printed out. In 2015, the Food Services Department engaged in a project to update the standard portion size of the all food items served to patients. For each food item, a standard portion size was weighed three times and the mean weight used as the reference weight and inputted into CBORD. For food and fluid items that are packaged and come in pre-portioned containers (i.e. juices, milk, cookies/crackers etc.), the weight as reported by the manufacturer is what is listed in CBORD.

3.4.2.2 Frequency of nutrient intake measurements

As part of the prospective study, nutrition intake from all sources (i.e. oral diets including oral nutrition supplements, EN and PN) was documented daily for the first 7 days following LMV. Nutrition care plans can change frequently and sometimes multiple times per day in the critically ill following LMV. For example, patients are often transitioning from EN/PN to oral diets, the type/texture/consistency of the diet changes frequently due to the high incidence of dysphagia in patients following extubation (207), and protein and energy

prescriptions are reevaluated on an ongoing basis by dietitians as part of the nutrition care process. Given this fluctuation, it was important to capture daily measurements as this would help to identify trends (i.e. improvements or deterioration) in intake in the early phases of ward-based recovery. In a similar study that aimed to measure protein and energy intake in the recovery of critically ill patients, 66% of patients were lost to follow up by day 7 post-extubation (21). We anticipated similar rates of loss to follow up, thus we chose to capture dietary intake measurements at day 7 post-LMV. However, in the event our study population had an extended LOS following LMV, a day 14 measurement was added. This measurement could provide insight into the trajectory of nutrition recovery for patients who have longer hospital LOS and assist in planning future studies examining nutrition recovery.

3.4.2.3 Dietary intake for patients consuming oral diets

Another primary objective of the prospective study was to evaluate nutrient intake (calories, protein, carbohydrate and fat) as accurately as possible to gain insight into the adequacy of protein and energy intake in comparison to that prescribed (findings presented in Chapter 5), and meal and food intake patterns (findings presented in Chapter 6) of critically ill patients during the early phases of ward-based recovery. For this research, the chosen method to assess dietary intake was based on the following key considerations (174):

- The method would be feasible, reliable, accurate for estimations of macronutrient and energy intake, and be validated for use in hospitalized patients.
- Recall-based methods were avoided because critically ill patients following LMV often experience cognitive impairment, confusion or decreased level of consciousness

- (76, 205). Relying on family/caregivers (who may or may not be present) or healthcare staff to recall food/fluid items consumed was not ideal.
- The method had to be feasibly employed in multiple units within the hospital setting. It required the capacity to measure intake at each meal in an expedient manner. The method could not require substantial space or set up and had to be mobile such that the measurements could easily be obtained for multiple patients who were likely to be located on different hospital wards.
 - It had to be minimally disruptive to the patients and staff, and meet infection control standards as set out by the hospital.
 - The method chosen had to be acceptable to stakeholders (i.e. the Food Services Department, unit dietitians, dietary assistants, unit staff, infection control services, and so forth).
 - The method could not be dependent on the measurement of actual (versus estimated) serving sizes prior to patient delivery. The reason behind this is that food is not plated at UH, as described in Section 3.4.2.1. It was also not feasible, nor did it meet infection control standards, to weigh individual food items following re-thermalization but prior to patient delivery.

Several methods to assess food intake exist, however based on the above considerations, only two methods were identified as meeting the above criteria: weighed food records and visual estimation.

- *Weighed food records.* Food and fluid items are weighed prior to and after consumption. Described as the gold standard method for evaluating dietary intake, it

is highly precise and accurate in comparison to other methods (174, 208, 209).

Minimal training is required, it does not rely on recall, and can be used to evaluate all foods and fluids, regardless of packaging (210).

- *Visual estimation.* Using this indirect measure of plate waste, a trained observer estimates the portion of food/fluid items consumed (i.e. none, $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$, all). Valid estimates of protein and energy consumption (when compared to WFR) can be obtained when assessing intake in hospitalized patients admitted to a geriatric ward (211). In contrast, in a cardiothoracic hospital ward, visual estimation was shown to overestimate energy, but not protein intake, in comparison to weighed food records (212). Time consuming training to become familiarized with standard portion sizes of each item served is required (212, 213), and estimations of fluids not contained in clear containers such as oral nutritional supplements, milk, thickened fluids packaged in tetra-paks cannot be evaluated. In hospitalized patients, nutrient dense ONS are frequently prescribed (214) and could be a source of significant calories and protein consumed daily.

Other methods that have been used to assess intake in hospitalized or institutionalized patients include:

- *Dietary recall.* A modified multiple-pass 24h recall method was utilized by Peterson et al. (21) to evaluate nutrition intake in hospitalized patients following extubation. In community dwelling populations, this method provides an accurate assessment of food intake in comparison to direct observation (175), however it requires extensive training (175), has not been validated for use in hospitalized patients, is time

- consuming (21, 175), and is dependent on a patient/caregiver/staff to be able to recall all food consumed on a daily basis (174).
- *Digital imaging.* Photographs are taken of meal trays before and after consumption and waste is then estimated. Photographs taken in real time can be archived for analysis at an appropriate time when the rater is in a suitable, non-rushed environment (215). Photographs must be taken using a tripod and in standardized conditions (i.e. lighting, angle/height of camera) (215, 216) which is not feasible at the site this research was conducted. Findings are mixed with respect to interobserver reliability between raters without training (215, 216), but intraobserver reliability in trained raters is high (215). This method performs well with regular texture foods, but reliability of the measurement decreases when estimating waste of modified texture foods (i.e. puree, minced) and foods with sauces (215)
 - *Food diaries.* Providing patients (or their caregivers) with a food diary to record food intake has also been utilized as a method to evaluate intake in hospitalized patients (173, 217-219). Patients are asked to document what proportion of the meal was consumed (i.e. none, $\frac{1}{4}$, $\frac{1}{2}$, all), preferably at the time of consumption. This method is useful for large, cohort studies, however limited in its ability to accurately quantify amounts of calories and protein consumed.

All methods to evaluate food intake contain inherent error. For this research, we opted to use weighed food records to evaluate dietary intake. Only the waste (and not the pre-consumption weight) of each food and liquid item provided could be weighed and related to a reference portion size versus the actual amount serviced, thus additional measurement error was introduced. However, this method still provided an accurate and reliable measure of

nutrient intake in comparison to other methods, and at the time of study design, no other studies examining nutrition recovery in survivors of critical illness had utilized WFR to evaluate intake. While the limitations of dietary recall have been noted, patients, family members, and staff were asked, when food trays were retrieved, whether any foods/fluids had been consumed between meals either from the hospital or outside the hospital that were not recorded with the WFR. Patients and staff were asked to keep leftover food wrappers/containers from snacks, if possible, so they could be weighed.

3.4.2.4 Protein and energy intake from enteral and parenteral nutrition

The volume of EN formula and PN solution delivered on an hourly basis is consistently documented in nursing flow charts at UH. The brand of enteral formula, composition of PN solutions, and total volume delivered daily was documented and used to calculate total calories and protein delivered based on the nutrition composition of the EN formula or PN solution. This method is consistently used to evaluate EN and PN intake in studies of critically ill patients.

3.4.2.5 Adequacy of protein and energy intake

At UH, a patient's energy and protein prescriptions are determined by the dietitian. Over 200 predictive equations exist for estimating energy requirements. While predictive equations are inaccurate (162), they are the only tools available to clinicians working with patients who are not receiving MV. To determine adequacy of protein and energy intake, measured intake was compared to prescribed protein and calories as documented in the medical record by the dietitian. This is the method used to evaluate adequacy of intake in large, multicenter ICU studies evaluating adequacy of protein and energy delivery (16-18).

All patients in ICU are seen by the ICU dietitian, however if a patient was not subsequently followed by a ward RD following ICU discharge, or the ward RD did not reevaluate protein and calorie prescriptions, the last documented prescription was used as the reference for determining adequacy of intake.

3.4.2.6 Appetite and barriers to eating

Previous studies examining nutrition recovery in the critically ill during the early stages of ward-based recovery have also reported on barriers to eating (21, 22, 24, 26). Peterson et al. (21) asked patients open-ended questions at the end of each study day (i.e. “Can you tell me why you did not eat more”) to identify barriers to eating. Responses were documented and grouped into categories (i.e. No appetite, nausea/vomiting etc.). In contrast, Merriweather et al. (24, 26) used a qualitative approach (semi-structured interviews) to identify barriers to eating, as well as observed ward-based practices that influenced nutrition care. This qualitative approach allowed for an in-depth and comprehensive exploration of the patient experience as well as identification of barriers that were not patient-centred. Taken together, the predominant barriers to eating in this population were related to the effects of illness, and organizational issues relating to poor transitional care (21, 24, 26).

In the prospective study presented in this thesis, a quantitative approach was taken to identify barriers to eating experienced by the patient, with the aim of identifying barriers experienced by patients in a Canadian hospital. Naithani et al. (176) have developed and validated a 27-item questionnaire to evaluate barriers to eating in hospitalized patients. For this study, level of alertness and ability to complete a written form due to fatigue or weakness was a concern, thus patients were asked, similar to the method used by Peterson et al. (21), to

identify up to three barriers to eating they experienced that day. Patients were also asked to rate their appetite using a numerical scale between 0 and 10, with 0 being no appetite at all and 10 being the best appetite possible. Visual analogue scales (VAS) are commonly used to rate appetite (220), however Nematy et al. (22) observed many critically ill patients to be too unwell to complete a VAS. In this research, patients were asked to report barriers to eating and rate their appetite after dinner when the study investigators were collecting the dinner meal tray. When appetite is rated could influence or alter a patient's response in comparison to if appetite was rated before eating or another time of day (220). However, to maintain consistency, appetite and barriers to eating were evaluated at the same time of day over the course of the study. Patients who were exclusively receiving EN/PN were asked to rate their appetite but were not asked to identify barriers to eating.

3.4.3 Body composition measures

Anthropometric and body composition measures were taken on the first, fourth, seventh and fourteenth day following LMV if the patient remained in hospital. Daily measurements were likely to be burdensome and this concern was raised by stakeholders prior to the initiation of the study. As the primary goal was to determine the feasibility of obtaining these measures in the critically ill in the immediate days following LMV, it was decided to obtain measures every 3 days starting with the first day following LMV to see if baseline measures were feasible to obtain. As the average hospital length of stay following LMV was unknown, having relatively frequent measures would facilitate acquisition of longitudinal measurements for patients with a shorter length of stay.

3.4.3.1 Weight and body mass index

One of the most commonly used indicators of malnutrition is unintentional weight loss (13, 14, 221). Several types of weigh scales exist to obtain weight measurements including standing scales/stadiometers, chair scales, wheelchair scales, lift/hoist scales and bed scales. The accuracy of each varies based on the quality of the equipment, proper care, and regular calibration (222). For hospitalized patients, access to scales is dependent on availability and will differ between institutions and even between wards in the same institution. In the critically ill, and to a lesser extent, hospitalized patients, reliably obtaining weight is a challenging task (171, 223-225) due to decreased level of alertness, mobility limitations, and body habitus (i.e. obesity). Subsequently, weight is often estimated (226) and inaccurate (223, 227, 228). For the purposes of this research, weight was measured using the scales available to the health care team and feasibility of obtaining the measurement was evaluated.

BMI is a measure derived from weight and height, and has traditionally been used as an index to classify underweight, overweight and obesity in adults (229). Within critical care research, it is one of the most common indices used to assess nutritional status (160, 225, 230). The presence of edema secondary to fluid shifts and resuscitative therapies in the critically ill significantly increases weight and subsequently BMI (160). Despite this known limitation of assessing weight in the ICU, it and BMI are widely used, and protein and calorie prescriptions are frequently based on these variables (162).

3.4.3.2 Mid-upper arm circumference

Estimation of muscle and subcutaneous fat stores can be derived from MAC and triceps skinfold (TSF) measures, respectively. Changes in MAC typically reflect changes in muscle, and to a lesser extent, subcutaneous fat mass (231, 232). TSF thickness allows for the estimation of subcutaneous fat stores and several equations have been developed in which TSF thickness is used to predict total body fat stores (233), although none exist for the critically ill. In hospitalized patients, MAC and TSF measures, in conjunction with weight and BMI, can be used to classify a patient's nutritional status (overweight, normal, malnourished or severely malnourished) (234). In the critically ill, MAC has some clinical utility such that patients with a MAC under the 15th percentile of normative values (231) are likely to be chronically malnourished and benefit from early nutrition support (160). MAC has been reported as feasible to perform in critically ill patients at the time of ICU admission (160) and throughout the duration of ICU stay (4), and it is inexpensive, requires only a measuring tape, and is an expedient measurement that is simple to perform. It, as well as TSF, are influenced by edema in the upper extremities (160). In contrast, TSF has limited value in critically ill for assessing nutritional status and has been found to poorly correlate with nutritional status (134). It requires skinfold calipers, is time consuming, and is more difficult to perform in ICU patients (160). For these reasons, TSF measurements were not obtained in this research.

3.4.3.3 Computed tomography

CT imaging is a precise and reliable method of evaluating skeletal muscle mass (235). The CSA of skeletal muscle in a single transverse CT image at the level of the third lumbar

vertebra is highly correlated with whole body skeletal muscle mass (157, 158). Sex-specific muscle CSA cut-points have been derived to identify patients with low muscle area in critically ill patients requiring MV (155). Interest in the use of CT to evaluate body composition in the critically ill as a means of identifying patients who may benefit from targeted nutrition interventions has grown in the past few years (5), however its use is limited as it is dependent on abdominal CT scans acquired as part of usual care. For our research, CT scans taken as part of usual care were sought and the proportion of patients for whom scans were available was reported.

3.4.4 Bioelectrical impedance analysis: phase angle

Traditionally, BIA has been used as a method to assess body composition (236). Impedance data generated from the device can be used to estimate tissue compartments such as fat-free mass through application of regression equations derived from reference populations (236). To date, no equations have been generated for critically ill patients. However, the raw BIA parameter, phase angle (PhA), has been implicated as a potential marker of nutritional status (237-239). Bioelectrical PhA may also be a good prognostic indicator. It has been shown to relate to numerous indices such as muscle strength and function, QOL, disease severity, and survival in various clinical patient populations such as cancer (240), COPD (241), HIV (242), and the critically ill (243, 244). Longitudinal measures of PhA have not been evaluated in survivors of critical illness, nor has the prognostic value of PhA at time of ICU discharge. The feasibility of performing longitudinal BIA measures in the recovering critically ill using a standardized protocol (245) were evaluated.

3.4.5 Functional status

3.4.5.1 Hand-grip dynamometry

Hand-grip strength (HGS) is the recommended tool to assess functional status as per the AND and ASPEN criteria for diagnosing malnutrition (13), however it is not recommended for use in the critically ill (246). HGS is an independent predictor of nutritional status in hospitalized patients (247, 248), and is predictive of decreased functional status (248), increased hospital length of stay (LOS) (201, 248), and hospital readmission rates (201, 248). In contrast, in surgical ICU patients, Lee et al. (249) found HGS was not predictive of mortality, ICU and hospital LOS, or duration of MV. Interestingly, while 88% of the patients tested were able to perform the HGS test within 3 days of ICU admission, 55% had a HGS of 0, which was attributed to ICU-AW (249). In contrast, an experienced strength examiner was able to perform manual muscle testing (MMT) and derive a Medical Research Council (MRC) sum-score, in 89% of the study population, and total MRC scores were predictive of mortality, ICU and hospital LOS, or duration of MV (249). In recovering critically ill patients, HGS has not been validated as a tool to predict nutritional status and the feasibility of obtaining this measurement in critically ill patients from a mixed medical/surgical population at the time of LMV has not been evaluated. As critically ill patients are prone to ICU acquired paresis (36), HGS in the early stages of recovery may not be predictive of nutritional status *per se*, but sex-specific cut-points have been derived from a critically ill patient to aide in the diagnosis of neuromuscular weakness (250). Regardless, observing a patient's ability to perform the HGS test is useful for nutrition clinicians as it may provide additional insights such as whether a patient can independently feed him/herself or potentially have difficulty using utensils.

3.4.5.2 Other measures of functional status

Several other measures of physical function may be used in critically ill patients in the later phases of recovery, including: MMT with MRC sum-score, 6MWT, 4 minute timed walk, timed up and go, and the functional independence measure (91). In the studies reported in this thesis, none of these measures were taken due to concerns that patients could not be mobilized by the assessor safely, lack of trained individuals to perform these tests, and concerns that in the days immediately following LMV most patients would not be able to mobilize independently. Recently, however, it has been shown that after extensive training, RD's can feasibly perform MMT in patients with cardiac failure (251), thus it may be a useful technique to apply in future studies.

3.4.6 Biochemical indices

Traditionally, serum albumin and prealbumin have been used as indicators of nutritional status, however these are also acute phase reactant proteins more indicative of an inflammatory response (13). Use of these markers, as well as CRP, for nutrition assessment in the critically ill is recommended, however, to facilitate identification of the etiological basis for diagnosing nutrition (13, 104). In our research, albumin, prealbumin, and CRP measures were documented for descriptive purposes if they were taken as part of usual care.

CHAPTER 4

NUTRITION RECOVERY IN CRITICALLY ILL PATIENTS FOLLOWING LIBERATION FROM MECHANICAL VENTILATION: A FEASIBILITY STUDY ASSESSING INDICES OF NUTRITIONAL STATUS

4.1 Introduction

Survivors of critical illness frequently experience a constellation of health-related morbidities including significant functional, cognitive and psychological impairments (1) that are associated with reduced quality of life and long-term disabilities (37, 38, 53). To date, the role of optimizing nutritional status to enhance recovery from critical illness has remained largely unexplored. Between 35-68% of critically ill patients are malnourished at the time of ICU admission (134, 149, 150, 153, 154, 252), and over the course of ICU admission, nutrition delivery to patients is often below prescribed resulting in underfeeding (16, 166). Thus, it is probable that malnutrition will also be highly prevalent in survivorship; however, studies reporting on the prevalence of malnutrition following ICU discharge are scarce. As nutrition plays an essential role in maintaining optimal physiological and physical functioning, poor nutrition in survivorship is likely to hinder recovery as well as reduce the effectiveness of rehabilitative interventions (9, 91). It is plausible that the limited research reporting on the nutritional status of ICU survivors is secondary to the unique challenges related to the clinical condition of this population that may prohibit the acquisition of reliable and accurate measurements of nutritional status (253-255).

Evaluation of nutritional status is commonly based on indicators falling within three main categories: dietary (caloric) intake, body composition, and functional status (13).

Critically ill patients typically experience significant edema and fluid shifts secondary to resuscitative therapies and pre-existing conditions which impact the ability to accurately interpret some measures of body composition (159, 202). Medications, sedation, prolonged mechanical ventilation and prolonged immobilization can result in ICU-acquired weakness, functional limitations (36, 203, 204), and decreased level of alertness (LOA) or altered cognitive status (i.e. delirium, agitation) (76, 205). Consequently, obtaining nutrition assessment measures using procedures that are reliant on a patient's physical and/or cognitive disposition may not be practical or reliable (104, 160, 206).

The feasibility of performing common measures of nutrition assessment using standardized and validated protocols in hospitalized critically ill patients after they have been liberated from MV has not been evaluated. The primary objective of this study was to assess the capacity to recruit and retain hospitalized, critically ill patients following LMV from a single-site in anticipation of completing a larger study to evaluate nutrition rehabilitation in the early, ward-based stages of recovery. Secondary objectives were two-fold: 1) to determine the feasibility of obtaining measures commonly used to evaluate nutritional status using previously validated protocols; and, 2) to provide a summary of any barriers experienced in obtaining these measures. This study will be considered feasible if one patient per week with a hospital length of stay (LOS) of at least 7-days following LMV is enrolled and measures commonly used to evaluate nutritional status are obtained on greater than 90% of occasions as per previously established protocols.

4.2 Methods

4.2.1 Study design

This prospective, observational feasibility study was conducted at a university-affiliated teaching hospital in southwestern Ontario, Canada. Adult critically ill patients requiring MV for at least 72 consecutive hours were recruited from a 24-bed MSICU over a 6-month recruiting period between February and October 2015. Patients were screened for eligibility daily. Patients for whom death was imminent or were not expected to survive ICU admission, were pregnant, had primary neuromuscular disease, spinal cord injury, limb amputations, traumatic brain injury, admitted to hospital for organ transplant, or enrolled into an intervention study affecting usual nutrition care were excluded. Written informed consent was obtained by patients prior to enrolment into the study and consent was obtained from a patient's legal substitute decision maker (SDM) if the patient was incapable of consenting him/herself at the time of enrolment. Any patient enrolled by his/her SDM who became capable of making an informed decision throughout the study period was required to provide written informed consent at that time. This protocol was approved by the Western University Health Sciences Research Ethics Board and the University of Waterloo Office of Research Ethics (Appendix A).

4.2.2 Study protocol

The study comprised a 14-day protocol with study day 0 defined as the day a patient was successfully liberated from MV and study day 1 designated as the first day following LMV. Nutrition intake and appetite were assessed on study days 1-7 and 14. Weight, mid-upper arm circumference (MAC), bioelectrical impedance analysis (BIA) to assess phase angle (PhA), and hand-grip strength (HGS) were measured on study days 1, 4, 7 and 14.

Cross-sectional computed tomography (CT) images taken at the level of the 3rd lumbar vertebra to evaluate skeletal muscle index, and biochemical indices (albumin, prealbumin and C-reactive protein) were obtained from the patient medical record if taken as part of usual care on study days 1, 4, 7 and 14. The study terminated on day 14 post-LMV or on the date of hospital discharge if the patient was discharged prior to day 14. Patients for whom the study was terminated due to reinstatement of ventilator support >24 hours after the initial extubation were not eligible to participate in the study a second time.

4.2.3 Patient demographics, admission characteristics, and outcomes

Patient age, sex, ICU admission and diagnostic categories, and place of residence prior to admission were documented to facilitate description of the study population recruited. Acute Physiology and Chronic Health Evaluation II (APACHE II) score (256) and Sequential Organ Failure Assessment (SOFA) score (257) were calculated to evaluate severity of illness, and the Charlson Comorbidity Index (CCI) (258) and Functional Comorbidity Index (FCI) (259) were calculated to assess health status upon admission to ICU. The modified Nutrition Risk in Critically Ill (mNUTRIC) score (260), which determines patients most likely to benefit from aggressive nutrition therapy at time of ICU admission, was also calculated. Clinical outcomes including hospital and ICU length of stay (LOS), number of days requiring MV, in-hospital mortality and discharge destination were documented.

4.2.4 Measures of nutritional status

To assess nutritional status, dietary intake was evaluated by weighed food records (WFR) (Appendix D) or chart abstraction for patients receiving enteral (EN) or parenteral nutrition (PN) (Appendix E). Tests conducted to evaluate body composition included weight,

mid-upper arm (MAC) circumference, multi-frequency bioelectrical impedance analysis (MF-BIA) (Appendix F), and CT (if taken as part of usual care). All tests were completed by the same investigator. Hand-grip dynamometry was used to assess functional status, and biochemical indices commonly associated with nutritional status were obtained if taken as part of usual care. For each measurement, the frequency that it was conducted, barriers preventing the test to be completed, and deviations from the standardized/validated measurement protocols that occurred while performing the measurement were documented.

4.2.5 Assessment of dietary intake and appetite

For all study days, diet orders and nutrition prescriptions documented by the unit dietitian were obtained from each patient's medical record. Daily protein and energy intake were assessed using a multiple methods approach that included the use of weighed food records, dietary recall and chart review (230, 261). For patients receiving EN or PN, the volume of the EN supplement or PN solution delivered was obtained from nursing flow sheets in the medical record and used to calculate protein (grams) and energy (calories) delivered or infused. It is standard nursing practice to document volume delivered on an hourly basis. For patients consuming food by mouth, after each meal (breakfast, lunch, dinner) patient meal trays were collected and the remaining waste of each food and fluid item that was served was weighed (i1200 scale, MyWeigh, Phoenix, AZ) to the nearest 0.1 gram. Meal tickets were collected to verify each item served. In the event a meal ticket was missing from the patient's tray, the items served were verified through the hospital nutrition management software. When meal trays were collected, patients (and/or their family members or members of the health care team in the event patients were not capable) were asked to recall any foods consumed between meals (i.e. snacks, oral nutrition supplements)

or foods brought from outside sources (i.e. home, commercially prepared). If leftover snacks or foods brought from outside the hospital remained, they were weighed. In the event a meal tray could not be collected to weigh food waste, alternative methods of assessing intake were utilized, if possible, including calorie counts and dietary recall by the patient, family, and/or health care professional. The number of times weighed food records were utilized for each meal served and number of days the total daily volume of EN/PN administered was documented in the chart for patients receiving EN/PN was recorded for the feasibility analysis.

After dinner (for patients receiving oral diets) or at the end of the day (for patients receiving EN or PN), patients were asked to rate their appetite using a numerical score (between 0-10, with 0 being no appetite at all and 10 being best appetite possible) (Appendix G). The proportion of patients able to complete this task over the duration of the study was documented.

4.2.6 Measurement of weight

The patient's usual (before ICU admission) weight was obtained from the patient or his/her SDM. Weight on study days 1, 4, 7, and 14 was obtained using devices available to clinicians in the hospital including bed, standing, chair, or wheelchair scales. The choice of scale was determined by the ability of a patient to mobilize and availability of scales on each ward. Patients were not weighed if they were unsafe to mobilize or if a health care provider capable of safely mobilizing/transferring patients were not available to assist. Measurements were taken to the nearest 0.1 kg.

4.2.7 Measurement of mid-upper arm circumference

MAC measurements were taken in either the erect or supine positions (232). In the standing position, the patient was asked to bend their elbow at 90° and the tip of the olecranon and acromion process were palpated. A non-stretch tape measure was positioned along the posterior aspect of the arm and the midpoint between the two palpated sites was marked. With the patient's arm relaxed, a measuring tape was placed around the arm and positioned perpendicular to the long axes of the arm at the marked midpoint. With the measuring tape snug to the skin but not compressing soft tissues, the circumference was recorded to the nearest 0.1 cm. For patients unable to stand, the measurement was taken in the supine position, in which the patient was instructed to bend the arm at a 90° at the elbow and lift it so the acromion process and olecranon could be palpated and the point of the mid-upper arm located and circumference subsequently measured (232).

4.2.8 Measurement of hand-grip strength

Maximal grip strength was measured using a calibrated Jamar analogue hand-grip dynamometer (Patterson Medical, Warrenville, IL). The patient was asked to position his/her elbow at 90° and press his/her upper arm against his/her trunk while sitting upright. With the dynamometer, adjusted for hand size, in hand, the patient was asked to squeeze it with as much force as possible. Three measurements on each hand were taken with a pause between each trial. Results were recorded to the nearest kilogram and the highest of the 3 measures was used (262).

4.2.9 Measurement of phase angle

MF-BIA was performed using a QuadScan 4000 (Bodystat LTD, Isle of Man, UK) to acquire phase angle (PhA), a raw variable generated by the device (245). PhA is an indicator

of body cell mass and cellular membrane integrity (263) and low PhA values have been associated with decreased fat free mass (264, 265) and malnutrition (238, 266). To perform the test, patients were placed in the supine position with limbs separated from the trunk, using rolled blankets if necessary, and electrodes were placed on the right hand and foot in the standard tetrapolar position (253). MF-BIA was not performed on patients with a pacemaker or electronic implantable device.

4.2.10 Statistical analysis

Statistical analysis was carried out using SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA). Continuous data are presented as median and interquartile range (IQR: Q1, Q3) [minimum, maximum] and categorical data as counts (percentages). For all measures, the proportion of times the measurement was obtained out of the total number of times it was supposed to be measured as per the study protocol was reported. Reasons measurements were not obtainable and a summary of protocol violations for measurements that were obtained but deviated from the standardized protocol are summarized. For measurements taken bilaterally (MAC and HGS), differences between left and right side measures were assessed using the Wilcoxon signed-rank test. A *P*-value of <0.05 was considered statistically significant.

4.3 Results

4.3.1 Recruitment, retention and patient characteristics

Over the 26-week recruiting period, all patients admitted to the MSICU at the study site (n=538) were screened for eligibility. Of these, 65 (12%) were eligible, 34 were approached for consent, and 23 were enrolled (35% consent rate for those eligible) (Figure 4.1). Three patients for whom consent was obtained to participate in the study (either by the

patient or his/her proxy) while still receiving ventilatory support died prior to LMV, and one patient was excluded because of discharge to a ward in which the study had not yet been approved. An average of 0.9 patients per week were enrolled, and 0.5 patients per week completed 7 days of the study. Of the 23 for whom consent was obtained, 7 (30%) could consent him/herself, whereas 16 (70%) were consented via proxy. Patients were enrolled into the study 8 (IQR: 6, 11) [3, 38] days after ICU admission and 1 (IQR: 0, 4) [0, 11] days prior to study day 1. Baseline characteristics of all patients enrolled in the study are presented in Table 4.1. The median age was 63 years, 48% of patients enrolled were male, and the most common ICU admission diagnosis was respiratory. Patient clinical outcomes are presented in Table 4.2. Median post-LMV length of hospital stay was 12 days. Of the 19 patients who participated in the study, all completed study day 1, 89% completed study day 4, and 68% and 37% completed study days 7 and 14, respectively (Figure 4.1).

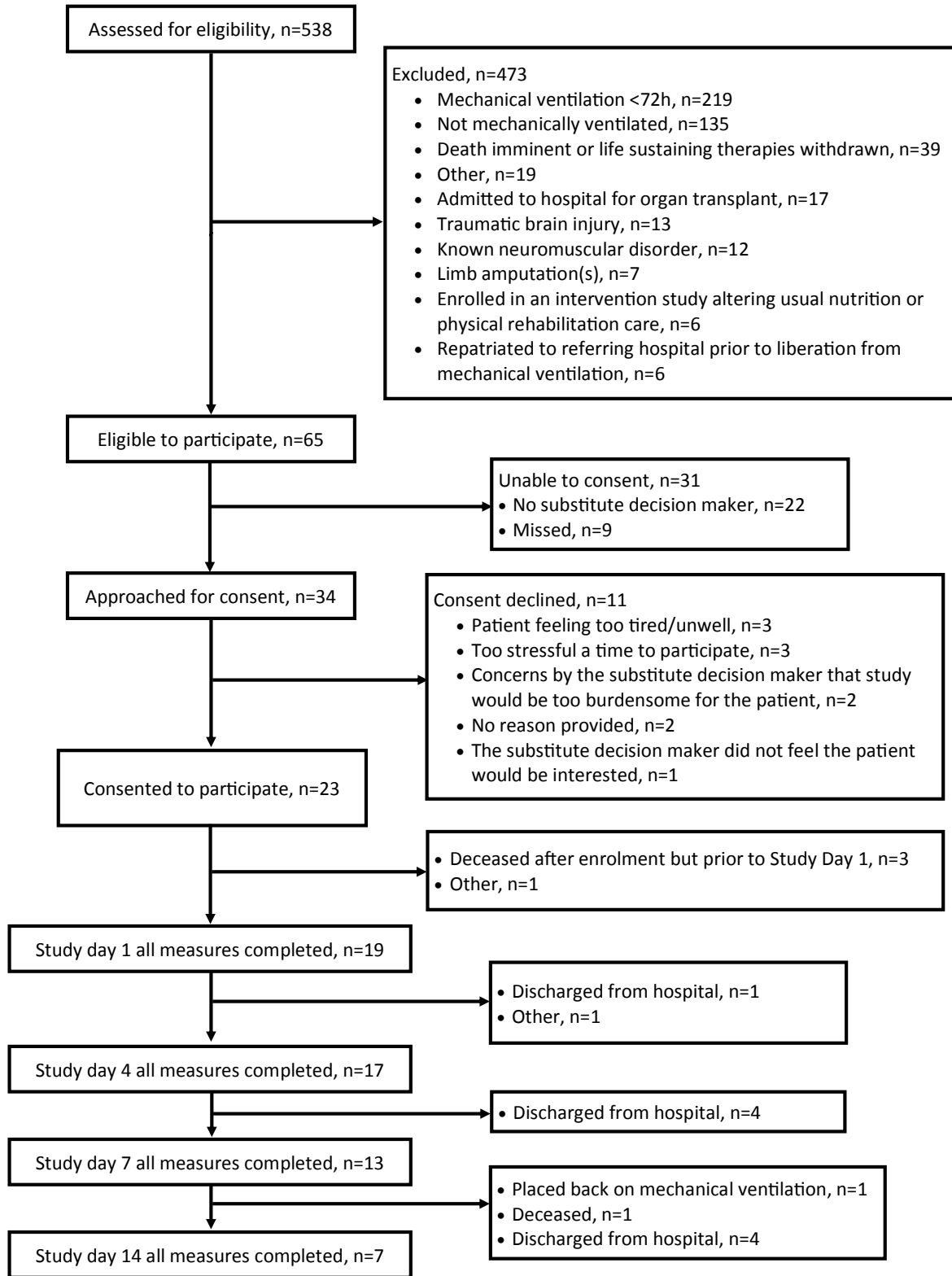


Figure 4.1 CONSORT diagram

Table 4.1 Patient characteristics at ICU admission

Characteristic (n) ¹	Value ²
Sex	Male, 11 (48), Female, 12 (52)
Age (y)	63 (54, 67) [35, 85]
Residence prior to admission	
Home, living independent	22 (96)
Home, with PSW	1 (4)
ICU admission type	
Medical	20 (87)
Surgical	3 (13)
ICU admission category	
Respiratory	10 (44)
Cardiovascular	7 (30)
Sepsis	3 (13)
Gastrointestinal	2 (9)
Neurological	1 (4)
APACHE II score (n=22)	25 (21, 30) [13, 40]
SOFA score (n=18)	12 (8, 14) [3, 18]
mNUTRIC risk category (n=18)	
Low risk (score 0-4)	4 (22)
High risk (score 5-9)	14 (78)
Charlson Comorbidity Index	2 (1, 3) [0, 9]
Functional Comorbidity Index	4 (2, 5) [0,7]

¹Data are for n=23 unless otherwise specified.

²Continuous data are presented as median and interquartile range (Q1, Q3) [minimum, maximum] and categorical data are presented as counts (percentages). APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICU, intensive care unit; mNUTRIC, modified Nutrition Risk in Critically Ill; PSW, personal support worker; SOFA, Sequential Organ Failure Assessment.

Table 4.2 Patient clinical outcomes

Clinical Outcomes ¹	Value ²
Duration of MV (d)	11 (6.6, 16) [3.0, 41]
ICU LOS (d)	15 (9.4, 21) [4.2, 101]
Total hospital LOS (d)	22 (16, 29) [9.2, 113]
Post-LMV length of stay (d) (n=20)	12 (7.4, 17) [3.0, 61]
In hospital mortality	5 (23)
In hospital mortality post-LMV (n=20)	2 (10)
Discharge destination of survivors (n=18)	
Home, living independent	7 (39)
Home, with PSW/home care	4 (22)
Moved in with family	2 (11)
Inpatient rehabilitation	1 (5.6)
Outpatient rehabilitation	2 (11)
Retirement home	1 (5.6)
Repatriated to referring hospital (lost to follow-up)	1 (5.6)

¹Data are for n=23 unless otherwise specified.

²Continuous data are presented as median and interquartile range (Q1, Q3) [minimum, maximum] and categorical data are presented as counts (percentages). ICU, intensive care unit; LMV, liberation from mechanical ventilation; LOS, length of stay; MV, mechanical ventilation.

4.3.2 Feasibility of measuring dietary intake and appetite

Over 125 study days, 227 meal trays for which protein and energy consumption could be evaluated were delivered. Intake was assessed via weighed food records for 208/227 (92%) of the meals delivered. The primary reason dietary intake could not be evaluated using WFR was that the meal tray had been accidentally collected and disposed of by staff (n=14 occasions). On these occasions, intake was estimated by dietary recall obtained from the patients or their caregivers. For 5 meals, no research staff were available, however detailed calorie counts were completed by nursing staff. Patients received EN either exclusively or

with an oral diet on 71/125 study days and the amount of enteral formula delivered was retrieved from the patient's medical record on 100% of these occasions. No patients in this study received PN during the study period. The proportion of patients able to rate their appetite is presented in Table 4.3. The primary reasons patients could not report appetite were LOA and altered cognition.

4.3.3 Feasibility of obtaining anthropometric, body composition, functional and biochemical measures

Over the course of the study, there were a total of 58 occasions for which each measurement (weight, MAC, HGS, PhA, CT and biochemical measures) was to be taken as per the study protocol. The number of times each measurement was obtained is found in Table 4.4. The reasons measurements were not obtainable and a summary of deviations from the standard measurement protocol that occurred during the acquisition of the measurements, if applicable, are found in Table 4.5 and Table 4.6, respectively. All patients were right-hand dominant.

Weight was obtained on 72% of occasions (Table 4.4), using a bed scale (n=19), standing bathroom scale (n=10), chair scale (n=6), standing scale with rails (n=6), and wheelchair scale (n=1). Weight was not obtainable when patients could not be mobilized due to muscular weakness, decreased LOA, or exhibited violent behaviour (Table 4.5). In each of these instances the patient was not positioned on a bed with a scale, and on 3 occasions when weight was obtained via bed scale, the scale could not be zeroed prior to weighing (Table 4.6). Fourteen patients had longitudinal weight measurements taken, and of these, only 8/14 (57%) had the measurements taken using the same scale. At time of ICU admission, weight

ranged between 43 and 186 kg (Appendix H, Figure H-1), no patients were underweight, defined as a body mass index (BMI) $<18.5 \text{ kg/m}^2$, whereas 42% were obese (BMI $>30 \text{ kg/m}^2$), and 26% morbidly obese (BMI $>40 \text{ kg/m}^2$) (data not shown).

MAC was obtained on 86% and 83% of total occasions for the left and right arm, respectively (Table 4.4). The most common reason for not obtaining the measurement was due to an obstructed measurement site (i.e. by vascular access devices (VADs), equipment or clothing that could not easily be removed). When MAC could be measured, it was not obtained using a validated protocol on 94% of occasions due to the inability to appropriately position the patient in a standing or fully supine position (Table 4.6). For bed bound patients with morbid obesity, who made up one-quarter of the study participants, separating the arm from the trunk to wrap the tape measure around the arm was also a significant challenge identified by the researchers in acquiring this measurement. There were no significant differences between MAC measurements on the left and right sides (Appendix H, Figure H-2).

Hand-grip strength was obtained on 76% occasions (Table 4.4), with missed measurements predominantly occurring secondary to altered cognition (Table 4.5). The standard protocol to test HGS was not followed for 44% of occasions the measure was obtained (Table 4.4) because many patients were bed bound when performing the test and could not be positioned in an upright (90°) position or could not perform the test with the dynamometer unsupported. There were no significant differences between left and right hand measurements within patients at any time during the study (Appendix H, Figure H-3).

BIA was successfully obtained on 98% of all possible occasions, however the measurement was only obtained without deviations from the standardized protocol for 55% of the measures (Table 4.4). Violations to the standard protocol are summarized in Table 4.6 and PhA measurements are presented in Appendix H, Figure H-4.

No abdominal CT scans were taken as part of usual care during the study for any of the patients and albumin, prealbumin and CRP were only taken as part of usual care on 33%, 9% and 2% of occasions (Table 4.4).

Table 4.3 Proportion of patients capable of rating appetite throughout the study protocol

	Study Day (n) ^{1,2}							
	1 (n=19)	2 (n=19)	3 (n=18)	4 (n=17)	5 (n=16)	6 (n=16)	7 (n=13)	14 (n=7)
Missed data collection	0 (0)	3 (16)	0 (0)	0 (0)	1 (6)	1 (6)	1 (8)	0 (0)
Proportion of patients evaluated able to rate their appetite	14 (74)	12 (75)	13 (72)	13 (77)	11 (73)	10 (67)	10 (83)	6 (86)
Reason patient unable to rate his/her appetite								
Decreased LOA or altered cognition	3 (21)	2 (17)	2 (11)	2 (15)	2 (1.8)	2 (20)	1 (10)	0 (0)
Developmental delay	1 (7.1)	1 (8.3)	1 (7.7)	1 (7.7)	1 (0.1)	1 (10)	1 (10)	0 (0)
Agitation/violent/delirium	1 (7.1)	1 (8.3)	1 (7.7)	1 (7.7)	1 (0.1)	1 (10)	1 (10)	1 (17)
Sleeping	0 (0)	0 (0)	1 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

¹Number of patients actively enrolled in the study.

²Data are presented as counts (percentages). LOA, level of alertness.

Table 4.4 Proportion of patients for which measures of nutritional status were obtained over the course of the study

Measurement	Study protocol day (n) ^{1,2}				Total (n=58)	Protocol violated during measurement
	1 (n=19)	4 (n=17)	7 (n=15)	14 (n=7)		
Weight (kg)	10 (53)	15 (88)	11 (73)	6 (86)	42 (72)	3/42 (7)
MAC (cm) (left arm, right arm)	15, 13 (79, 68)	16, 16 (94, 94)	13, 13 (87, 87)	6, 6 (86, 86)	50, 48 (86, 83)	93/98 (94)
HGS (kg) (left hand, right hand)	14, 14 (74, 74)	13, 13 (77, 77)	11, 11 (73, 73)	6, 6 (86, 86)	44, 44 (76, 76)	36/82 ³ (44)
BIA	19 (100)	17 (100)	14 (93)	7 (100)	57 (98)	25/55 ⁴ (45)
Transverse CT at level of L3	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Albumin	9 (47)	4 (24)	5 (33)	1 (14)	19 (33)	N/A
Prealbumin	1 (5)	1 (6)	3 (20)	0 (0)	5 (9)	N/A
CRP	0 (0)	1 (6)	0 (0)	0 (0)	1 (2)	N/A

¹Number of patients for whom measures of nutritional status were obtained on each study day.

²Data are presented as counts (percentages).

³On 3 occasions, the protocol used to obtain hand-grip strength for both the left and right hand measures was not documented.

⁴On 2 occasions, the protocol used for the BIA measure was not documented. BIA, bioelectrical impedance analysis; CRP, C-reactive protein; HGS, hand-grip strength; L3, third lumbar vertebra; MAC, mid-arm circumference; N/A, not applicable.

Table 4.5 Summary of reasons measurements were not obtainable

Measurement (n) ¹	Reason measure was not obtainable
Weight (n=16)	Patient could not be mobilized (n=8) Patient not alert/oriented (n=4) Patient refused/agitated/in soft restraints (n=4)
MAC (n=18) ²	Blood pressure cuff on (n=7) IV lines taped directly over measurement site/obstructing measure (n=5) Patient refused/agitated/in soft restraints (n=3) Clothing impeded measurement (n=2) Missed measurement (n=1)
HGS (n=28) ²	Patient refused/agitated/in soft restraints (n=10) Patient not alert/oriented (n=8) Equipment failure; hand-grip dynamometer not available (n=8) Patient unable to follow commands (n=2)
BIA	Patient refused/agitated/in soft restraints (n=1)

¹Number of times a study measurement was not obtained.

²Number of missed measurements are the sum of missed measurements for both left and right sides. BIA, bioelectrical impedance analysis; HGS, hand-grip strength; MAC, mid-arm circumference.

Table 4.6 Summary of protocol violations for measurements that were obtained but deviated from the standard protocol

Measurement	Type of violation of standardized protocol when measurement obtained (n) ¹
Weight	Unable to zero scale prior to weighing (n=3)
MAC ²	Patient unable to stand upright or lie supine (n=46) Measurement taken over thick bandages (n=4)
HGS ²	Patient unable to sit in chair with elbow unsupported (i.e. was lying in bed or a recliner chair with elbow supported by the mattress or sitting at the side of the bed with back unsupported) (n=14) Less than 3 attempts secondary to fatigue (n=9) Neurological injury affecting the patient's ability to properly perform the test (n=1)
BIA	Patient not lying supine (i.e. HOB was at a 15-60° angle) (n=19) Patient only able to lie on side (n=2) Due to morbid obesity, patient's body parts touching bed rails and/or limbs dangling over side of bed (n=4) Unable to landmark lateral malleolus at ankle due to severe edema (n=4) Measurement taken on the left side due to IV lines taped over measurement site on the right side (n=2) Patient unable to remain still for the measurement due to agitation (n=1)

¹Number of times each violation occurred. For some measurements, more than one violation was reported.

²For bilateral measurements, protocol violations were the generally the same for each side, therefore the number of violations only for the right side are presented here. BIA, bioelectrical impedance analysis; HGS, hand-grip strength; HOB, head of bed; MAC, mid-arm circumference

4.4 Discussion

Prior to the implementation of a larger study examining changes in nutritional status of critically ill patients following LMV, it is essential to demonstrate the feasibility of both executing such a study and utilizing standardized methods to assess nutritional status throughout this recovery trajectory. Utilization of standard methods is necessary to compile comprehensive and comparable data across studies to better understand nutritional status and a cohesive approach to therapies in this population.

Within a single-academic centre, we recruited one patient every two weeks with a hospital LOS of a least 7-days following LMV, thus falling short of our goal to recruit one patient per week. However, this feasibility study highlighted the challenges that exist in conducting comprehensive nutrition-focused, observational research that commences specifically at the time of LMV. Despite the utilization of strategies to enhance consent rates (267), of all patients identified as eligible, 35% consented to participate while 48% were missed due to difficulties contacting SDMs or the absence of an SDM altogether. These findings are consistent with consent rates and recruitment challenges documented in Canadian intensive care units (268). In contrast, 32% of patients who participated in the study were lost to follow-up by study day 7 because they were either discharged from the hospital or repatriated to a referring hospital. These findings highlight the importance of evaluating strategies for improving recruitment.

Analogous to previous nutrition (230, 269, 270) and non-nutrition (271, 272) oriented studies in the critically ill, we recruited patients who received MV for at least 72 consecutive hours. Of all patients screened for eligibility, 41% were mechanically ventilated for less than

72 hours. Thus, one strategy to increase recruitment could be to decrease the minimum length of mechanical ventilation to 48 hours. However, our aim was to study critically ill patients who were at higher risk for developing the functional morbidities associated with critical illness and may have experienced greater benefit from targeted nutrition interventions in recovery. Those experiencing an ICU LOS greater than 72 hours are more prone to losing greater amounts of protein and lean tissue mass (12, 199) and to develop swallowing disorders (200), hence the decision to include patients requiring MV for a longer duration. In the only previous study to quantify protein and energy intake in hospitalized, MSICU patients following extubation, only patients prescribed oral diets were included (21). In the present study, we chose to include patients receiving nutrition via any route (i.e. oral, EN, PN) to comprehensively evaluate nutrition intake of all patients regardless of dietary prescription following LMV. In doing so, we also maximized recruitment as all patients in this study received EN while ventilated and 74% continued to receive EN either exclusively or with an oral diet on study day 1.

Assessing calorie and nutrient intake is a cornerstone of nutrition assessment (13) and understanding nutritional status. In hospitalized patients, reduced food intake is associated with nutritional decline (273). Dietary intake was measured using weighed food records for 92% of meals served and thus determined to be a feasible method to quantify protein and energy intake in the research setting. These findings are in agreement with recent work by Chapple et al. (23) in which protein and calorie intake in critically ill patients following traumatic brain injury was recorded using weighed food records for 98% of meals served over the duration of their measurement period. In the present study, 70% of patients recruited were not capable of providing informed consent, thus reliance on recall or self-reporting

based methods would have significantly reduced our capacity to accurately quantify daily energy and macronutrient intake. This emphasizes the necessity of using comprehensive dietary assessment methods that are not reliant on recall or self-reporting to evaluate dietary intake in the recovering critically ill.

Nutrition status can also be assessed by evaluation body composition and functional status (13, 15). In this study, the feasibility of obtaining weight and MAC, two measures of body composition, and HGS, a measure of physical function, was evaluated. Weight is a frequently reported measure to describe nutritional status and is also required to derive energy and protein prescriptions in the hospitalized patients (162, 165). On the day following LMV, weight was only obtained for half of the study population as patients could not be mobilized to a scale or were bound to a bed with a scale that had not been zeroed following the initial ICU admission. Weight provides an assessment of net whole body size and does not provide insight into changes in tissue compartments such as adipose or muscular tissue or total body water (233). This is an important point for consideration as the loss of lean tissue mass is a hallmark feature of malnutrition (104). While weight loss may be indicative of malnutrition via the assumption that it is correlated with loss of muscle mass, in the recovering, critically ill patient who regains hemodynamic stability, weight loss closely parallels fluid losses (6, 274, 275). In contrast, weight gain should be interpreted with caution as there is growing evidence to suggest that it is secondary to increases in fat mass rather than repletion of lean tissue (7, 71, 72). Given the limitations of weight changes as a marker of nutritional status in the critically ill, it is recommended that future studies aimed at assessing nutrition recovery in the critically ill consider use of emerging tools such as

bedside ultrasound (276) to more specifically and accurately characterize changes in body composition.

Measures of MAC and HGS were obtained for greater than 75% of the occasions they were scheduled for, however, standardized protocols were violated for almost half of occasions HGS was measured, and MAC was rarely measured as per protocol. The primary barriers inhibiting measurements to be performed using standardized protocols were related to the clinical condition of the patients which has been previously observed (92, 254, 255). Muscular weakness, altered level of alertness, discomfort and pain were identified as major barriers to positioning patients as protocols dictated. Proper positioning for measurements is crucial as failure to do so may impact outcomes. For example, when performing hand-grip dynamometry, HGS measures taken when a patient is sitting in a chair with the elbow unsupported, in comparison to having the elbow supported on a bed or armrest, will falsely generate a larger value (262). It is also plausible that non-modifiable factors such as the presence of a VAD, common in hospitalized patients, may result in swelling or peripheral weakness which could influence measures such as MAC and HGS, however this has not been tested. HGS has garnered significant interest within the nutrition community as a surrogate marker of nutritional status and prognostic indicator for outcomes such as hospital length of stay, readmission rates and mortality (201, 247, 248, 277, 278). Rarely is compliance to validated HGS protocols reported when acquiring these measures in hospitalized patients. As 44% of HGS measurements in our severely ill patients could not be obtained as per dictated protocols, critical examination is essential to the interpretation of studies reporting on HGS.

Traditionally, BIA has been used as a method to assess body composition (236). Impedance data generated from the device can be used to estimate tissue compartments such as fat-free mass through application of regression equations derived from reference populations (236). The precision of BIA measurements is reliant on numerous conditions being satisfied (reviewed in (236)). To date, no equations have been generated for critically ill patients (236). In contrast, PhA is a raw marker produced by a BIA instrument. A low PhA is associated with decreased fat-free mass (264), malnutrition in hospitalized patients (238) and may also be a prognostic indicator for hospital LOS and survival in critically ill patients (243, 244, 264). However, precision of any BIA measurement is reliant on numerous conditions being satisfied (reviewed in (236)). In almost half of the occasions where BIA was measured in the present study, one or more of these conditions were violated. The degree to which PhA measurements are altered by body positioning and habitus, presence of VADs and urinary catheters, continuous fluid and nutritive infusions, and requirement for continuous renal replacement therapy, specifically in the recovering critically ill patient is unclear, and warrants further investigation.

A strength of this study is that we successfully recruited a heterogeneous population with higher severity of illness at the time of ICU admission, despite the small sample size. Our findings are limited in that we chose not to interpret the anthropometric data as failure to obtain measures using validated protocols and high attrition rates over the course of the study decreased confidence in these data. However, exploration of the raw data reveals large variation, perhaps the most notable being the 143kg difference in admission body weight between the lightest and heaviest patient. This emphasizes the importance of using assessment measures that are valid and reliable across all body types.

4.5 Conclusions

The clinical condition of the recovering critically ill largely precludes acquisition of reliable serial measures of body composition and strength. The multiple barriers inhibiting acquisition of various nutrition assessment measures using standardized protocols that have been identified may serve as a foundation for the development of new protocols specific to the critically ill. The design of future studies examining nutrition recovery from critical illness should include assessment tools that are not reliant on a patient's cognitive or physical capacity, and can be feasibly obtained at the time LMV to ensure baseline measurements are established. To fully understand the role that nutrition plays in the recovery trajectory, long-term studies that comprehensively evaluate various aspects of nutrition health that extend beyond hospital discharge are vital.

4.6 Relevance to clinical practice

Feasible and valid measurements to objectively assess nutritional status and diagnose malnutrition in the recovering critically ill following LMV are lacking. Due to the nature of critical illness and iatrogenic undernutrition in ICU, survivors are likely malnourished or at high risk for malnutrition at the time of ICU discharge. It is therefore of the utmost importance that dietitians recognize this risk and continue to monitor dietary intake of patients as they transition out of the ICU and enter into the early stages of ward-based recovery.

CHAPTER 5

ADEQUACY OF PROTEIN AND ENERGY INTAKE IN CRITICALLY ILL ADULTS FOLLOWING LIBERATION FROM MECHANICAL VENTILATION IS DEPENDENT ON ROUTE OF NUTRITION DELIVERY

5.1 Introduction

Malnutrition is a significant problem affecting critically ill patients throughout the trajectory of illness. Between 23-54% of adult patients are malnourished as per Subjective Global Assessment (SGA) (21, 134, 149-151, 153), and greater than two-thirds have significant muscle atrophy (155, 156), a defining diagnostic criteria for malnutrition (13, 15), at the time of admission to an ICU. Throughout the duration of an ICU admission, nutrient intake is inadequate in patients requiring MV as they only receive approximately two-thirds of prescribed energy and protein (16, 17, 166). Subsequently, large protein and energy deficits are accrued, which are associated with increased ICU length of stay (LOS), hospital LOS, and increased mortality (169). Given the high prevalence of malnutrition at ICU admission, inadequate nutrition delivery throughout ICU stay, and the heightened catabolic processes during critical illness that promote lean tissue loss (10-12, 279), critically ill patients are likely to be malnourished at the time of LMV and ICU discharge. Malnutrition is associated with increased risk of infection, impaired wound healing, mental health disturbances, decreased respiratory and cardiac function, loss of muscle mass, and functional disability (19, 20). Therefore, it is imperative that nutrition therapies are augmented in

survivors of critical illness to facilitate recovery, reduce the risk of the negative sequelae associated with malnutrition, and improve quality of life.

Insufficient calorie intake is also a diagnostic criteria for malnutrition (13). Currently, no guidelines exist for feeding the critically ill patient following LMV and studies examining nutrition intake in ICU survivors during the early phases of ward-based recovery are scarce. To date, only one study has quantified protein and energy intake in a cohort of critically ill patients admitted to a mixed medical-surgical ICU (MSICU) and who were receiving oral diets as their sole source of nutrition following extubation (21). Adequacy of protein and energy intake never exceeded 37% and 55% of estimated requirements, respectively, in the first 7 days following extubation (21). Dietary intake was assessed using dietary recall, which relies on well-trained interviewers and patients that are capable of recalling daily food consumption (174). In the early days following ICU discharge, patients frequently experience decreased level of alertness or delirium (78), thus to effectively evaluate dietary intake in this patient population, methods that do not rely on cognitive capacity are ideal. One such method, considered the gold standard of evaluating dietary intake due to its high precision and accuracy in comparison to other methods, is weighed food records (174, 210).

Dietary intake is influenced by numerous factors. Survivors of critical illness frequently report poor appetite, nausea, vomiting, early satiety and difficulty swallowing as primary barriers to eating (21, 22, 26, 200). Given the paucity of research examining aspects of nutrition recovery in the critically ill, further research is required to comprehensively evaluate nutrition intake and barriers affecting intake. Thus, the primary objective of this study was to precisely quantify protein and energy intake and adequacy of intake in

relationship to that prescribed in hospitalized, critically ill patients admitted to a mixed medical-surgical ICU following LMV. It was hypothesized that patients would have inadequate (<75% of prescribed) protein and energy intake in relationship amounts prescribed, but those receiving enteral (EN) or parenteral nutrition (PN) would have greater intake in comparison to those consuming oral diets. A secondary objective was to characterize patient-reported barriers to eating and self-perceived appetite, and it was hypothesized that the most frequently reported barriers to eating would relate to the effects of illness, specifically poor appetite, early satiety, and nausea/vomiting.

5.2 Methods

5.2.1 Study Population

This prospective, observational study was conducted at a university-affiliated teaching hospital in southwestern Ontario, Canada. Adult critically ill patients requiring MV for at least 72 consecutive hours were recruited from a 24-bed MSICU between February and September 2015. Patients for whom death was imminent or were not expected to survive ICU admission, were pregnant, had primary neuromuscular disease, spinal cord injury, limb amputations, traumatic brain injury, admitted to hospital for organ transplant, or enrolled into an intervention study affecting usual nutrition care were excluded. Written informed consent was obtained from patients prior to enrolment into the study. Consent was obtained from the patient's legal substitute decision maker (SDM) if the patient was incapable of providing consent to participate at the time of enrolment. Deferred consent was obtained from patients initially enrolled by an SDM who became capable thereafter. Patient refusal resulted in withdrawal from the study. This protocol was approved by the Western University Health

Sciences Research Ethics Board and the University of Waterloo Office of Research Ethics (Appendix A).

5.2.2 Study protocol

The study comprised a 14-day protocol with study day 0 defined as the day a patient was liberated from MV and study day 1 designated as the first day following LMV. Protein and calorie intake and patient-identified barriers to eating were assessed on study days 1 through 7 and 14. The study terminated on the 14th day following LMV. If a patient was discharged from hospital prior to day 14, the study was terminated on the date of discharge. Patients for whom the study was terminated due to reinstatement of invasive ventilatory support greater than 48 hours after the initial extubation were not eligible to participate in the study a second time.

Following ICU discharge, recruited patients could be transferred to several different wards including general medicine, general surgery (includes gastroenterology, urology, plastics, and ENT services), neurosciences (neurology and neurosurgery), cardiology, cardiovascular and thoracic surgery, and orthopedic surgery. Patients could also be discharged from hospital (i.e. to home, another institution, rehabilitation) directly from the ICU if no ward beds became available prior to discharge. Dietitian services were available on all units.

5.2.3 Patient demographics, admission characteristics and outcomes

Patient age, sex, and ICU admission and diagnostic categories were documented to facilitate description of the study population recruited. Acute Physiology and Chronic Health Evaluation II (APACHE II) score (256) and Sequential Organ Failure Assessment (SOFA)

score (257) were calculated to evaluate severity of illness, and the Charlson Comorbidity Index (CCI) (258) and Functional Comorbidity Index (FCI) (259) were calculated to assess health status upon admission to ICU. Clinical outcomes including ICU, total hospital, and post-LMV LOS, number of days requiring MV, and in-hospital mortality.

5.2.4 Measurement of protein and energy intake

For all study days, diet orders and protein and calorie prescriptions as determined by the dietitian(s) caring for each patient were obtained from the patient's medical record. Daily protein and energy intake was assessed using a mixed methods approach that included the use of weighed food records, dietary recall and chart reviews. For patients receiving EN or PN, the volume of the EN supplement, amount of modular protein, and PN solution delivered on an hourly basis was obtained from the nursing flow sheets in the patient's medical record and used to calculate protein (grams) and energy (kcal) delivered or infused.

For patients consuming an oral diet, after each meal (breakfast, lunch, dinner) patient meal trays were collected and the remaining waste of each food and fluid item that was served was weighed (i1200 scale, MyWeigh, Phoenix, AZ) to the nearest 0.1 gram (Appendix D). Meal tickets generated by the Food Services Department were collected to verify each item served. In the event a meal ticket was missing from the patient's tray, the items served were verified through the hospital nutrition management software. When meal trays were collected, patients (and/or their family members or members of the health care) were asked to recall any foods and beverages consumed between meals (i.e. snacks, oral nutrition supplements) or foods brought from outside sources (i.e. home, commercially prepared). If leftover snacks or foods remained at the bedside, they were weighed. In the

event meal tray collection was missed, intake was estimated using a dietary recall approach with the patient, his/her family member, or a member of the patient's health care team (21). The amount of each food and fluid item consumed was calculated by subtracting the measured waste from a reference portion weight. At per the hospital procedures where these data were collected, all patient meals were plated at a separate facility, placed into re-thermalization carts and delivered by truck to the hospital 3 times daily for breakfast, lunch and dinner. Upon arrival, carts were immediately delivered to each ward and plugged into a docking station to commence the re-thermalization process. This food delivery system precluded weighing individual portions prior to delivery to the patient. Thus, for each food item offered on the hospital menu, three standard portions were weighed and the average weight was used as the reference standard portion size. Protein (grams) and energy (kcal) content of each item was determined by referring to the nutritional content reported on labels by the food manufacturers or by referring to the Canadian Nutrient File.

5.2.5 Assessment of adequacy of protein and energy intake

Adequacy of protein and energy intake was determined by comparing daily protein and energy intake to the amount of protein and energy prescribed by the dietitian as part of usual care. The dietitian prescriptions, assessed as part of usual care, were specific to the needs of each patient and calculated using equations based on guidelines and practice recommendations (164, 165, 280), 24h urinary nitrogen losses and clinical judgment. Patient charts were reviewed daily to identify when dietary prescriptions changed as part of routine monitoring (Appendix E).

5.2.6 Assessment of appetite and barriers to intake

On days that food intake was measured, capable patients were asked after their last meal (dinner) to rate their appetite using a numerical score (between 0-10, with 0 being no appetite at all and 10 being best appetite possible). They were also asked to identify up to 3 barriers to eating they may have experienced that day by completing a written survey (Appendix G) that contained checklist of barriers to eating commonly experienced by hospitalized patients. Patients who were exclusively receiving EN or PN were asked to rate their appetite but were not asked to identify barriers to eating.

5.2.7 Statistical analysis

Descriptive statistics are presented as median and interquartile range (IQR: Q1, Q3) [minimum, maximum] or mean \pm standard deviation, as appropriate. Categorical data as presented as counts (percentages). Descriptive statistics were used to summarize daily protein and calorie intake and adequacy of intake in relation to prescribed amounts across all and specific study days and by route of delivery, barriers to eating, daily appetite scores. Statistical analysis was carried out using SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA).

5.3 Results

Between February and September 2015, 33 of the 538 patients that were screened were eligible to participate, consent was obtained from 23, and 19 participated (Chapter 4, Figure 4.1). In total, data were collected over 125 study days. Patients were 60 ± 12 years of age and 42% were male. Baseline patient characteristics are shown in Table 5.1. Patients

required MV for a median of 11 (IQR: 6.6, 14) [3.0, 41] days and median post-LMV hospital LOS was 11 (IQR: 7.1, 17) [3.0, 61] days. Patient outcomes are summarized in Table 5.2.

Table 5.1 Patient characteristics at ICU admission

Characteristic ¹	Value ²
Sex, male	8 (42)
Age (y)	60 ± 12
ICU admission type	
Medical	16 (84)
Surgical	3 (16)
APACHE II score (n=18)	25 ± 6
SOFA score (n=15)	11 ± 4
mNUTRIC risk category (n=15)	
Low risk (score 0-4)	4 (27)
High risk (score 5-9)	11 (73)
Charlson Comorbidity Index	2 (1, 3) [0, 6]
Functional Comorbidity Index	4 (2, 5) [0,7]
Body Mass Index (kg/m ²)	28 (23, 43) [20, 61]
Underweight (<18.5 kg/m ²)	0 (0)
Normal (18.5 – 24.9 kg/m ²)	7 (37)
Overweight (25 – 29.9 kg/m ²)	4 (21)
Obese, all classes (>30 kg/m ²)	8 (42)
Class I (30 – 34.9 kg/m ²)	3 (16)
Class II (35 – 39.9 kg/m ²)	0 (0)
Class III (>40 kg/m ²)	5 (26)

¹Data are for n=19 unless otherwise specified.

²Continuous data are presented as mean ± standard deviation or median and interquartile range (Q1, Q3) [minimum, maximum] as appropriate; categorical data are presented as counts (percentages). APACHE, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICU, intensive care unit; mNUTRIC, modified Nutrition Risk in Critically Ill; SOFA, Sequential Organ Failure Assessment

Table 5.2 Patient clinical outcomes

Clinical Outcomes ¹	Value ²
Duration of MV (d)	11 (6.6, 14) [3.0, 41]
Patients with a tracheostomy at time of LMV	1 (5.3)
ICU LOS (d)	15 (9.4, 23) [4.2, 101]
Total hospital LOS (d)	24 (19, 30) [9.2, 113]
Post-LMV hospital LOS (d)	11 (7.1, 17) [3.0, 61]
In-hospital mortality	2 (11)

¹Data are for n=19 unless otherwise specified.

²Continuous data are presented median and interquartile range (Q1, Q3) [minimum, maximum] and categorical data are presented as counts (percentages). LMV, liberation from mechanical ventilation; LOS, length of stay; MV, mechanical ventilation

5.3.1 Dietary prescriptions following liberation from mechanical ventilation

Within the 125 total study days, patients received EN (tube feeding) as sole source nutrition (EN+NPO) for 48 days, EN supplemented with any type of oral diet (EN+PO) for 23 days, and an oral diet exclusively (PO only) for 54 study days. No patients in this study received PN following LMV. Of the 19 patients, 2 received EN as sole source of nutrition for the entire duration of the study, 5 consumed only oral diets and did not receive any EN following LMV, and the remaining 12 received nutrition from both EN and oral diets. Specifically, in the first 7 days following LMV, 16/19 patients were transitioned to an oral diet (the remaining 3 continued to receive EN exclusively), 5/16 (31%) of whom had EN discontinued at the time of LMV (Appendix I). Oral diet prescriptions varied widely and included clear and full fluid diets of both normal and thickened consistencies, modified texture (i.e. puree or minced) diets, and regular (non-modified) diets (Appendix I). A speech-language pathologist (SLP) was referred to assess swallowing in 12/19 patients following LMV, and of these, 10/12 were diagnosed with oropharyngeal dysphagia (OPD). Of the

patients with OPD, 6 were deemed unsafe to consume anything by mouth after the initial SLP assessment and continued to receive EN as sole source nutrition. The remaining 4 were prescribed modified diets.

5.3.2 Net protein and energy intake following liberation from mechanical ventilation

Across all 125 study days, median protein intake was 56 (IQR: 29, 107) [0, 151] g protein/day and median energy intake was 1260 (IQR: 729, 1757) [0, 2306] kcal/d. When patients received nutrition via EN+NPO (n=48 study days) or EN+PO (n=23 study days), protein intake was higher than the PO only days (n=54 study days) (106 (IQR: 87,119) [0, 137] vs 75 (IQR: 23, 130) [5, 151] vs 32 (IQR: 17, 46) [0, 77] g/d, respectively) (Figure 5.1A). When mode of nutrition delivery was EN+NPO or EN+PO, calorie consumption was 1628 (IQR: 1396, 1920) [0, 2016] kcal/d and 1586 (IQR: 619, 1954) [147, 2306] kcal/d, respectively, which was about 2 times that of the PO only diets (870 (IQR: 455, 1173) [100, 1856] kcal/d) (Figure 5.1B). Patients consuming oral diets consistently consumed fewer grams of protein (Figure 5.2A) and calories (Figure 5.2B) per day, regardless of the day following LMV. Across all PO only days, when protein and energy intake were related to admission body weight, protein intake was equivalent to 0.4 (IQR: 0.2, 0.5) [0, 1.1] g/kg and 9 (IQR: 6, 14) [1, 34] kcal/kg/d, respectively. In contrast, across all EN+NPO days, median protein intake was equivalent to 1.2 (IQR: 0.8, 1.7) [0, 2.0] g/kg/d and median calorie intake was 19 (IQR: 11, 27) [0, 32] kcal/kg/d. Daily protein and calorie intake of individual patients are presented in Appendix J.

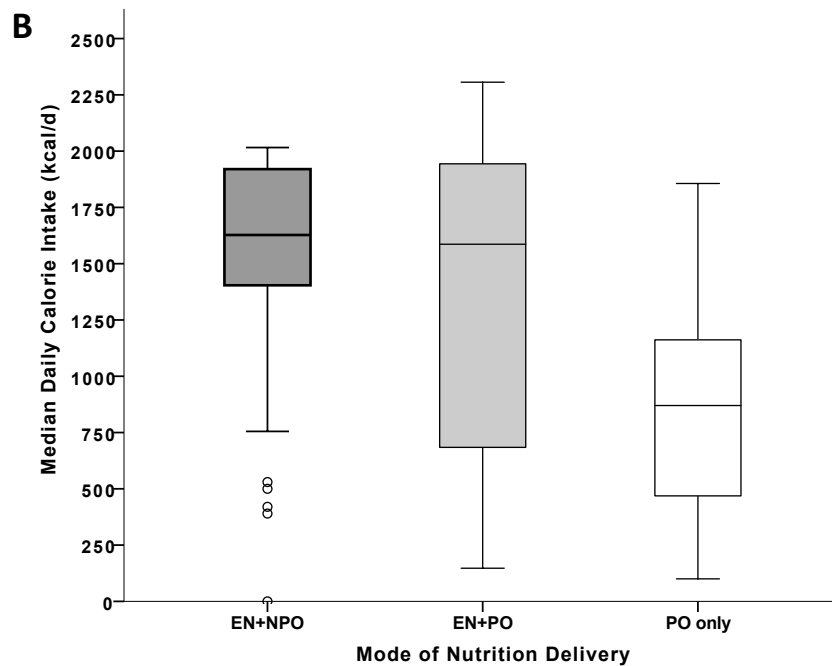
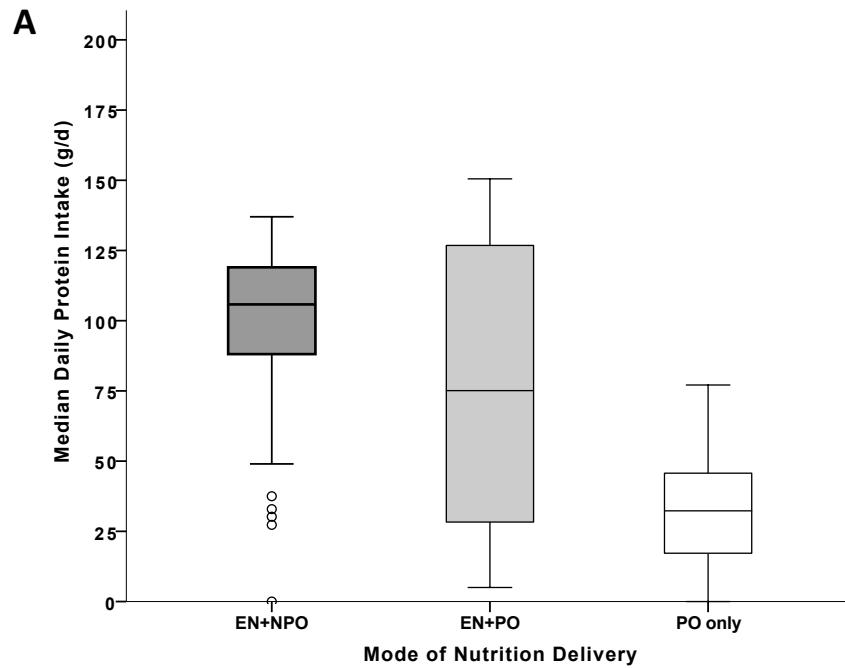


Figure 5.1 Median daily protein intake (A) and calorie intake (B) across all study days (n=125) stratified by route of nutrition delivery

EN+NPO (n=48 days), EN+PO (n=23 days), and PO Only (n=54 days). Boxplots represent the median and interquartile range, whereas the tails indicate the minimum and maximum. Circles represent outliers.

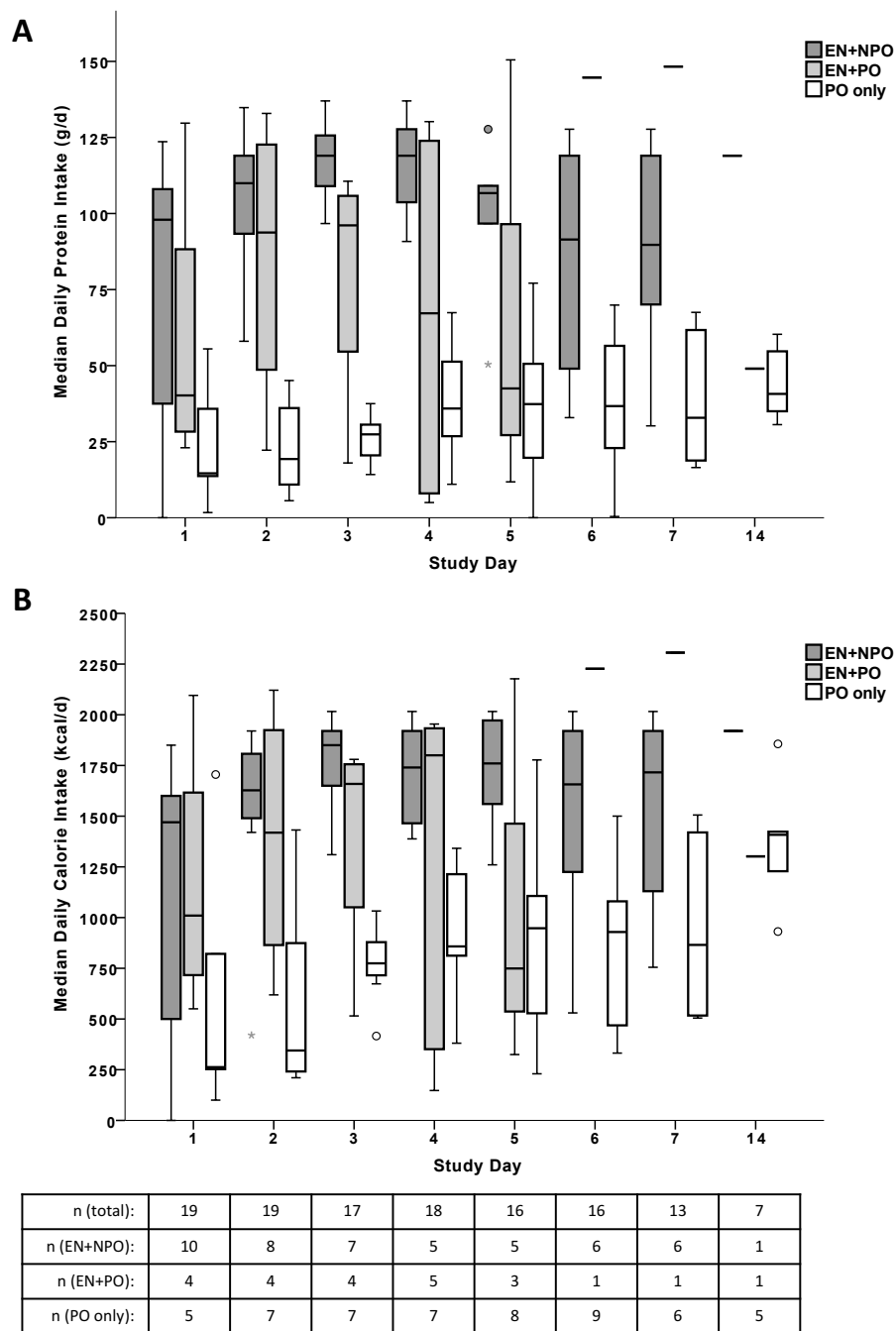


Figure 5.2 Median daily protein intake (A) and calorie intake (B) on each study day stratified by route of nutrition delivery

Boxplots represent the median and interquartile range, tails indicate minimum and maximum values, circles represent outliers, stars represent extreme outliers, and solid dashes represent data for n=1.

5.3.3 Adequacy of protein and energy intake following liberation from mechanical ventilation

Across all study days, median adequacy of protein and energy intake when related to prescribed amounts, was 46 (IQR: 26, 100) [0, 129] % and 71 (IQR: 38, 100) [0, 125] %, respectively. Adequacy of intake across study groups is presented in Table 5.3. Patients consumed less than 50% of their estimated protein requirements on 64/125 (51%) of the study days, and less than 50% of their estimated energy requirements on 44/125 (35%) occasions (Table 5.4). Adequacy was examined based on mode of nutrition delivery, adequacy of protein intake for patients receiving EN+NPO was greater than 75% on 37/48 (77%) of occasions, whereas patients exclusively consuming oral diets consumed greater than 75% of prescribed protein on only 3/54 (6%) of occasions (Table 5.4). A similar pattern was seen when examining adequacy of energy intake such that patients prescribed oral diets had worse adequacy of intake in comparison to those receiving EN (Table 5.3).

Protein and energy intake versus prescribed amounts are examined in Figure 5.3. In the EN+NPO and EN+PO, the absolute proportions of energy and protein consumed in relation to that prescribed were similar. Conversely, in the PO only group, the absolute proportions of adequacy energy and protein intake were dissimilar such that adequacy of protein intake was always lower than adequacy of caloric intake (Figure 5.3). For example, patients on PO only diets consuming ~75% of prescribed calories were only consuming ~30% of prescribed protein.

Table 5.3 Adequacy of protein and energy intake in comparison to amounts prescribed across all study days and by route of nutrition delivery

	All study days (n=125 days)	Route of nutrition delivery ¹		
		EN+NPO (n=48 days)	EN+PO (n=23 days)	PO Only (n=54 days)
Protein (%)	46 (26, 100) [0, 129]	100 (81, 100) [0, 129]	75 (25, 102) [4.2, 122]	27 (15, 41) [0, 61]
Energy (%)	71 (38, 100) [0, 125]	100 (77, 100) [0, 105]	75 (39, 104) [7.7, 125]	47 (29, 66) [4.9, 119]

¹Data are presented as median and interquartile range (Q1, Q3) [minimum, maximum]

Table 5.4 Proportion of days in which protein and energy intake was greater than 75% of prescribed across all study days and by route of nutrition delivery

Adequacy of intake	Prescription	All study days (n=125 days)	Route of nutrition delivery ¹		
			EN+NPO (n=48 days)	EN+PO (n=23 days)	PO Only (n=54 days)
Intake <50% of prescribed	Protein	64 (51)	6 (13)	9 (39)	49 (77)
	Energy	44 (35)	6 (13)	7 (30)	31 (57)
Intake 50-75% of prescribed	Protein	13 (10)	5 (10)	3 (13)	5 (9.3)
	Energy	27 (22)	6 (13)	5 (22)	16 (30)
Intake >75% of prescribed	Protein	48 (38)	37 (77)	11 (48)	0 (0)
	Energy	69 (55)	42 (88)	14 (61)	13 (24)

¹Data are presented as counts (percentages).

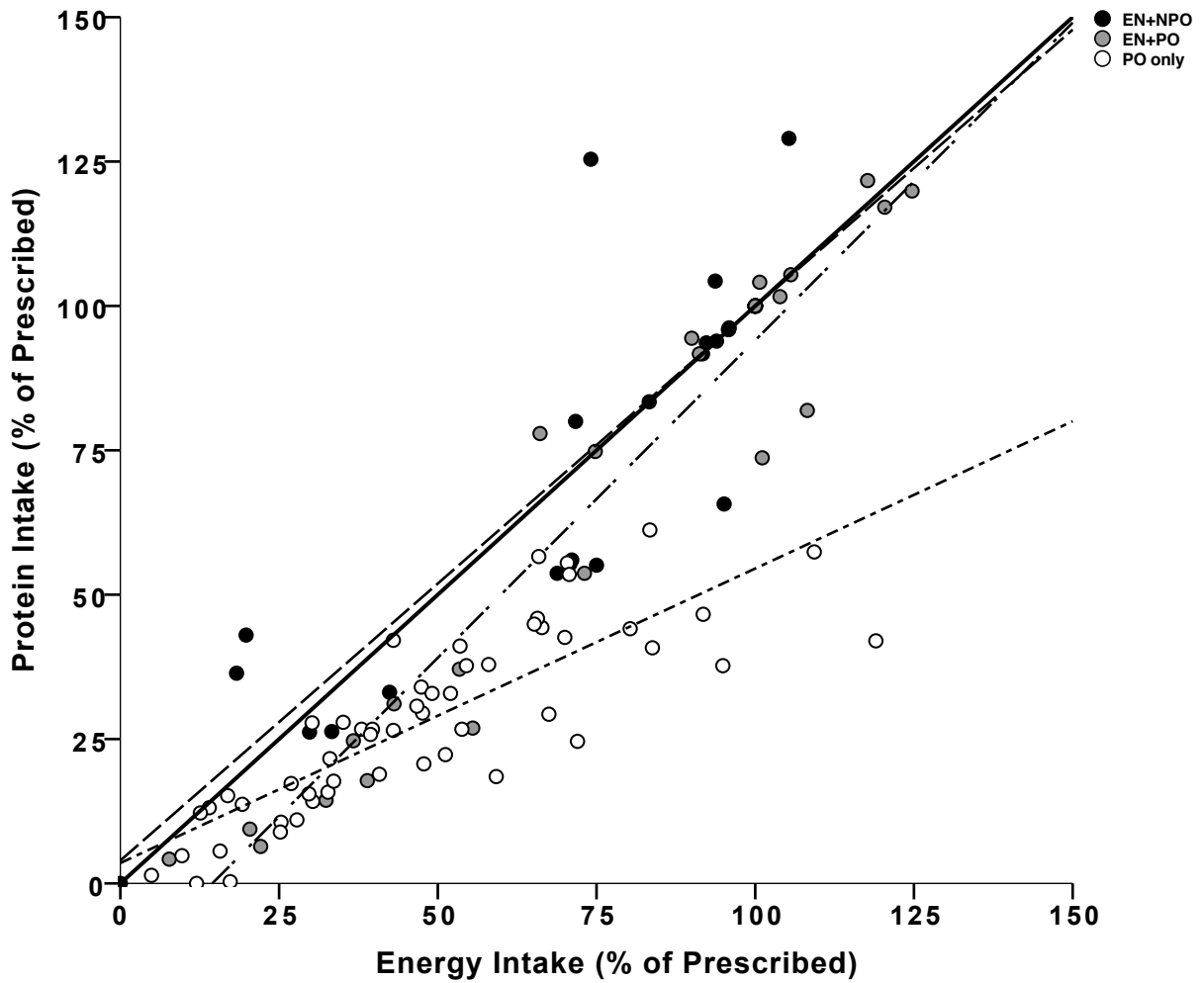


Figure 5.3 Protein and calorie intake versus amounts prescribed

Lines represent the line of best fit for the EN+NPO group (n=48, ---), EN+PO group (n=23, -.-.), and PO only group (n=54, - - -). The line of identity (x=y) is denoted by (—).

5.3.4 Barriers to eating and appetite

Patients in the EN+NPO group were not asked to report barriers they experience to eating. Of the total days patients received an oral diet (n=77), patients were capable of reporting self-perceived barriers to eating on 61 (79%) days. On 16 (26%) of these days, patients reported no barriers to eating. For the remaining days, a total of 102 barriers were reported. The most frequent barriers reported were poor appetite (24%), early satiety (15%), taste changes (11%), nausea/vomiting (9.8%), and disliking the food (9.8%) (Figure 5.4). Other barriers to eating identified by patients are shown in Figure 5.4. Median appetite scores for days 1, 2, 3, 4, 5, 6, 7, and 14 of the study were 5 (2, 6), 3 (1, 7), 4 (2, 6), 5 (4, 6), 5 (2, 8), 5 (2, 7), 5 (0, 7), and 5 (5, 9), respectively.

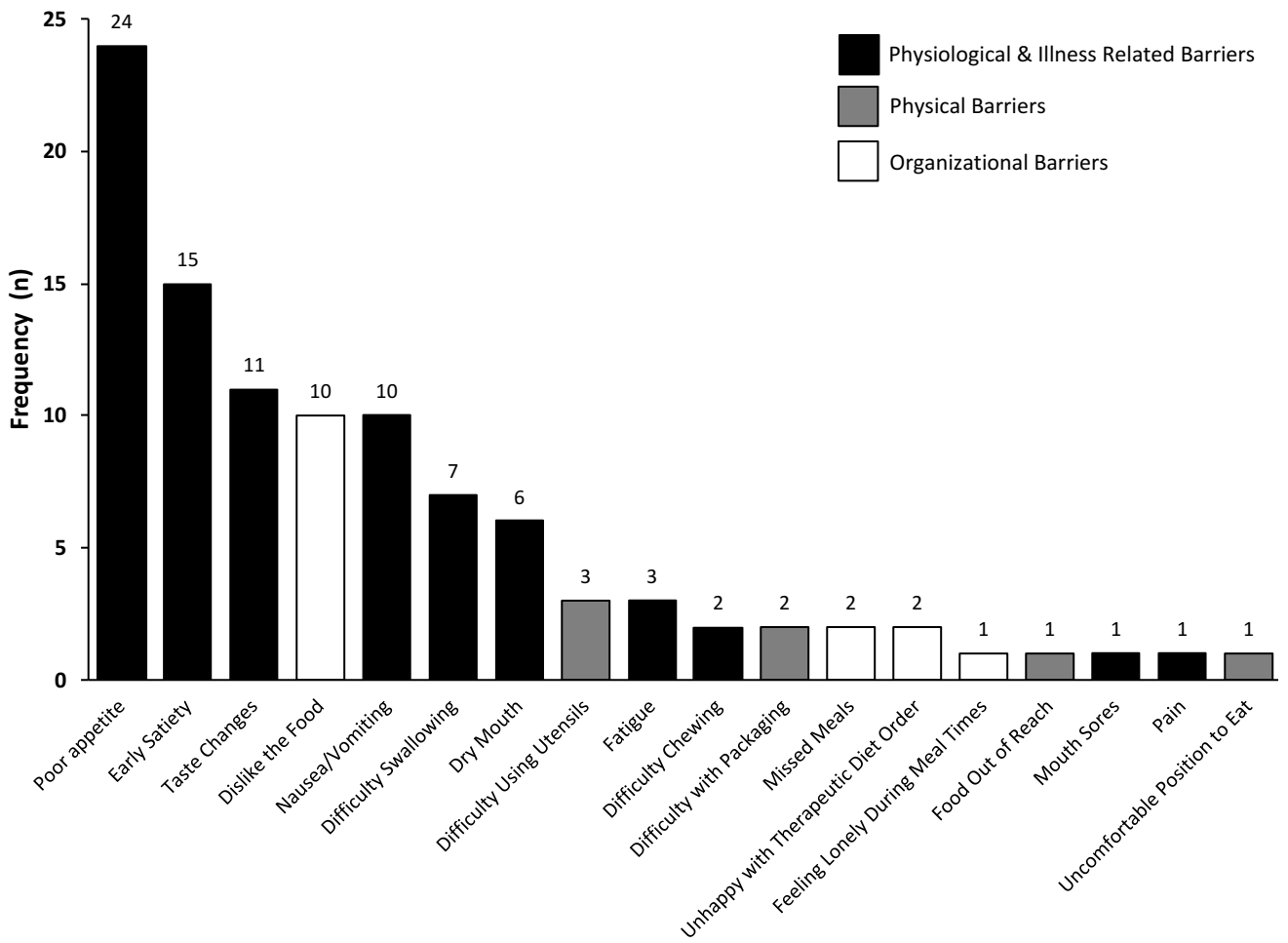


Figure 5.4 Patient reported barriers to eating

5.4 Discussion

This study is the first to examine protein and energy intake in MSICU patients prescribed oral diets versus and those who continued to receive EN following LMV. The primary finding showed that patients exclusively consuming nutrition orally had grossly low protein and calorie intakes relative to prescribed amounts; whereas, those on EN with or without an oral diet had greater net intakes of protein and calories and greater adequacy of intake in relation to prescribed amounts. These findings suggest that route of nutrition delivery could heavily influence the degree to which nutrition recovery occurs in ICU survivors prior to hospital discharge.

Patients consuming oral diets exclusively demonstrated median daily protein and energy consumption of 32 g/d and 870 kcal/d, respectively, which was similar to the only other study to report on protein and energy intake in a heterogeneous group of MSICU patients (6). Peterson et al. (21) only examined those who received oral diets as sole source nutrition and found that patients never consumed greater 767 kcal/d (equivalent to 55% of estimated caloric requirement) and 34 g protein/d (equivalent to 37% of estimated protein requirement) in the first 7 days following LMV (21). Kondrup (281) defines inadequate oral intake as less than 75% of estimated calorie requirements based on the premise that consuming less than this threshold results in significant weight loss in hospitalized patients. In the present study, calorie intake was greater than this threshold on only 24% of occasions patients were consuming oral diets. More alarming was that this threshold was never met for protein when patients received oral diets. Combined, these data indicate most patients receiving oral diets as sole source nutrition following LMV are incapable of consuming adequate nutrition. Given that protein and energy deficits are accumulating during the ICU

stay (166, 169) and patients continue to accrue high protein and energy deficits (23), patients experience further decline in nutritional status (273). Our work, combined with our knowledge on malnutrition that evolves in the ICU, emphasizes the critical importance of identifying effective nutrition rehabilitation interventions for this highly unique subset of patients.

The preferred method of feeding a mechanically ventilated critically ill patient is via EN (162, 163), which is also indicated for patients at high nutrition risk who are unable to maintain volitional intake (282). Following LMV, critically ill patients may continue to receive EN if EN access devices remain *in situ* (23, 26); however, post-LMV prescription practices have not been well characterized in the literature and the degree to which route of nutrition delivery influences intake in mixed MSICU patients has not been studied. Here we report that 14 (74%) of recruited patients continued to receive EN for at least one day following LMV. Our hypothesis was confirmed such that the delivery of EN with or without an oral diet resulted in higher daily protein and energy intakes and a larger proportion of patients consumed greater than 75% of prescribed amounts. Our data suggest that delaying discontinuation of EN until a patient can demonstrate the ability to consume adequate nutrition orally could be an effective intervention to enhance nutrition intake and adequacy in this population.

Successful LMV and transition from the ICU to ward marks a significant point in the trajectory of critical illness (90) and the beginning of the journey to recovery (36). While no formal guidelines for transitioning patients from EN to an oral diet exist specifically for the recovering critically ill, Massanet et al. (283) propose permanent discontinuation of EN only

when a patient has demonstrated the ability to consume >75% of daily caloric needs. Reasons why EN was discontinued were not documented during data collection for this study, however it is probable a formal assessment to evaluate adequacy of oral intake did not occur. Half of the patients transitioned from EN to an oral diet in the first 7 days following LMV had EN discontinued prior to initiation of any oral diet, and thus, eliminating any opportunity for assessment of oral intake. Ward cultures that promote removal of tubes (including feeding tubes), the misperception that removal of a feeding tube will promote oral intake, and lack of knowledge regarding the specialized nutrition care needs of the recovering critically ill are all factors that have been associated with early feeding tube removal (24, 26).

The most common barriers to eating reported by patients in this study related to the physiological effects of illness, including poor appetite, early satiety, taste changes, nausea/vomiting and disliking food served. In this study, patients consuming oral diets were asked to identify up to three barriers to eating they experienced each day. For reference, they were provided with a non-validated list of the most common barriers to eating identified in previous research (24, 176). However, this approach may have biased patient responses and failed to capture barriers experienced by patients with altered LOA or impairments in executive functioning. Regardless, our findings are highly congruent with previous reports (21, 22, 26, 200) and underscore the challenges faced in adequately feeding sick patients experiencing such barriers that are not easily modified. These findings lend support to more aggressively promoting the use of EN as a therapeutic strategy to adequately feed patients experiencing these barriers.

The effectiveness of promoting EN use on improving nutritional status, reducing the risk of negative health outcomes, and reducing costs of care warrants further investigation. The unintended consequences of oral feeding with a nasogastric feeding tube *in situ* such as impaired swallowing (284) and potentially poor acceptability by patients must also be evaluated. Identification of food-focused strategies to enhance nutrition intake is equally crucial. In the setting of multiple barriers to eating, simply increasing the amount of food provided to patients would be ineffective and can be unpleasant for patients with poor appetite (24, 285). Promising strategies shown to enhance oral intake in hospitalized patients including serving protein fortified (179, 193) and nutrient dense foods (195), identifying foods that are more commonly desired for specific patient populations (197), and enhancing the presentation of food (286) warrant future testing in the recovering critically ill.

Protein plays an essential role in wound healing, immune function, the maintenance of lean body mass and is required to maintain optimal nutritional status (20). In determining whether nutrition intake is adequate, emphasis is often placed on calorie, and not protein intake (13, 281). ASPEN and the AND consider insufficient calorie intake as one of the diagnostic criteria for malnutrition without mention of protein intake (13). In a group of hospitalized cardiac patients, Van Bokhorst-de van der Schueren et al. (287) reported a strong linear relationship between adequacy calorie and protein consumption, such that the percent of required calories consumed matched the percent of required protein. In contrast, in patients consuming an oral diet only, we showed a disproportionate relationship such that the percent of prescribed calories consumed was higher than the percent of prescribed protein consumed on a given day. This has broader implications if calorie consumption is used as a surrogate marker of nutrition adequacy as the nutrition risk or nutritional status of patients

who are consuming adequate calories may be misperceived if protein intake remains insufficient. It is possible this discrepancy is noted in our study cohort because recovering critically ill patients are likely to have a greater protein requirement (107, 288) and be prescribed a higher protein dose in comparison to the non-critically ill. However, when patients received EN we found this relationship to be more proportionate, which was not surprising as adequacy of energy intake is typically proportional to adequacy of protein intake in patients receiving EN (17). Furthermore, the volume of EN delivered can easily be matched to that prescribed, whereas matching food delivery to prescriptions in a hospital environment where standard menus are not designed to meet the needs of all patients is challenging.

A primary strength of this study was use of weighed food records, a highly precise and accurate method of assessing intake (174), to quantify protein and energy intake. The only study to previously quantify intake in MSICU patients did so using dietary recall, a less accurate method to assess intake (174). Recall methods rely on the cognitive capacity of the patient and many recovering critically ill patients, including 70% the patients enrolled in this study, are not capable of self-reporting due to decreased consciousness, delirium and cognitive dysfunction (76, 205). Thus we were successfully able to quantify intake in even the most compromised patients.

There are several methodological limitations in this study. Statistical comparisons of nutrition intake between study groups (route of nutrition delivery) and by study day were not possible as several patients received nutrition by different routes over the course of the study and thus observations were not independent. Interpretation of adequacy of nutrient intake

was based on dietitian prescriptions. For the recovering critically ill, no guidelines or equations exist to estimate nutrient requirements, likely leading to inaccuracies in the true adequacy of protein and energy intake reported. However, we chose to compare intake to requirements estimated by the RD responsible for each patient's care, all of whom have extensive-experience and use the most up-to-date evidence and clinical judgement to inform their practice. Lastly, this is a single-site study, limiting external validity, with a small sample size. This is, however, the first Canadian study of its kind to evaluate nutrition intake in hospitalized survivors of critical illness.

5.5 Conclusions

In conclusion, patients recovering from critical illness have inadequate protein and energy intake following LMV, however adequacy appears to be largely influenced by route of feeding. Delaying discontinuation of EN after LMV may be a promising strategy to enhance protein and calorie intake hospitalized survivors of critical illness, the impact of doing so on improving overall nutritional status is unknown. These findings underscore the need for future studies that evaluate nutrition recovery in survivors of critical illness. The development of effective interventions that enhance adequacy of nutrition intake and improve the overall health of this unique patient population are required.

5.6 Relevance to clinical practice

Patients prescribed oral diets as sole source nutrition following LMV consume inadequate protein and calories, which may be attributable to the multiple barriers to eating experienced that relate to the physiological effects of illness. As most patients receive EN while intubated and ventilated, at the time of LMV, EN access devices should remain *in situ*

and EN continued until a patient can demonstrate the ability to consume sufficient nutrition. For patients who are consuming oral diets, calorie intake is a poor surrogate for assessing adequacy of protein intake, such that patients consuming adequate calories may not be consuming adequate protein. Thus, when adequacy of dietary intake is assessed, consumption of both protein and calories must be evaluated.

CHAPTER 6

MEAL AND FOOD INTAKE PATTERNS IN HOSPITALIZED, CRITICALLY ILL PATIENTS PRESCRIBED AN ORAL DIET FOLLOWING LIBERATION FROM MECHANICAL VENTILATION

6.1 Introduction

Liberation from mechanical ventilation (LMV) marks the beginning of recovery from critical illness (102). The acute phase of critical illness is dominated by catabolic and pro-inflammatory processes that are associated with significant depletion of lean tissue stores and muscle wasting (10-12, 279). In contrast, the recovery phase is characterized by a shift toward physiological homeostasis in which the catabolic response to illness is dampened and there is a gradual transition toward an anabolic environment (102). Restoration of lean tissue mass and physical function, a primary goal of critical illness rehabilitation (59, 92), is reliant on adequate nutrient, and more specifically, amino acid availability (95, 289). In the early phases of in-hospital recovery, critically ill patients prescribed oral diets following LMV have substantially poor dietary intake (21, 22) (Chapter 5), consuming as little as one-quarter and one-half of their estimated protein and energy requirements, respectively (21) (Chapter 5). Furthermore, the amount of protein and calories consumed in relationship to that prescribed is disproportionate such that patients may consume adequate calories but not adequate protein (Chapter 5). This misalignment may be secondary to the failure of standard hospital diets to provide sufficient protein to meet the increased needs of a recovering, critically ill patient. In the absence of adequate protein and calorie consumption, it is

plausible that the effectiveness of rehabilitative interventions is dampened and recovery prolonged. Likewise, suboptimal food intake in hospitalized patients with lower illness acuity is independently associated with poor outcomes including malnutrition, functional decline, prolonged recovery and increased mortality (20, 219, 273, 290, 291).

Poor dietary intake in non-critically ill hospitalized patients is not attributable to insufficient provision of energy and protein as only 60% of food that is provided is consumed (287, 292). The amount and types of foods and liquids that are consumed in relationship to what is delivered has not been examined in the recovering critically ill who are prescribed oral diets. However, it is probable that consumption patterns are similarly low given the multitude of barriers to eating that have been identified in this subset of patients. The predominant barriers reported relate to the physiological effects of acute illness and include poor appetite, early satiety, taste changes, nausea, vomiting, and difficulties chewing and swallowing (21, 22, 26) (Chapter 5). Over-prescription of restrictive therapeutic diets and nutrition care delivery failures such as unacceptable mealtime delivery, failure to deliver or provide sufficient snacks, and disliking food served are also significant barriers that negatively impact food intake in this patient population (21, 24, 26) (Chapter 5). To overcome these barriers, multifaceted interventions are necessary to address inadequate intake in seriously ill patients (293, 294).

Food-based strategies to enhance food intake in other high nutrition risk patient populations that face similar barriers to eating include, but are not limited to, prescription of oral nutrition supplements (ONS) (295, 296), fortifying or enhancing the protein and energy content of foods or meals served (179-181, 193-195, 297), increasing the number of eating

episodes (i.e. providing snacks in between meals) (179, 180), and identifying and serving foods that are more widely accepted or desired (197, 298). Such strategies may be effective for survivors of critical illness, however no research to date has examined meal and food intake patterns specifically in the recovering critically ill patient. Such research is a necessary preliminary step to help identify efficacious food-specific strategies that could increase protein and energy intake in this population. Thus, in the present study, we sought to: (i) quantify the amount and types of foods and fluids that are consumed and wasted by hospitalized, critically ill patients prescribed non-modified oral diets following LMV; (ii) determine whether differences in calorie and macronutrient intake exist between meals; and (iii) characterize the distribution of calories consumed at meals coming from protein, carbohydrates and fat. It was hypothesized that only 60% of combined foods and liquids provided would be consumed and that differences would exist in calorie and macronutrient intake between meals with patients consuming the least amount of protein and calories at breakfast in comparison to lunch or dinner meals.

6.2 Methods

6.2.1 Study design

The present study was a pre-planned sub-analysis using data obtained from a 6-month prospective observational study aimed at evaluating the feasibility of assessing nutritional status in hospitalized patients following LMV. The protocol has been described in Chapter 2. Briefly, adult critically ill patients requiring mechanical ventilation for at least 72 consecutive hours were recruited from a 24-bed medical/surgical intensive care unit between February and September 2015. Patients for whom death was imminent or were not expected

to survive ICU admission, were pregnant, had primary neuromuscular disease, spinal cord injury, limb amputations, traumatic brain injury, admitted to hospital for organ transplant, or enrolled into an intervention study affecting usual nutrition care were excluded. Written informed consent was obtained by patients or their legal substitute decision maker prior to enrolment into the study. The protocol was approved by the Western University Health Sciences Research Ethics Board and the University of Waterloo Office of Research Ethics (Appendix A).

The study comprised a 14-day protocol with study day 0 defined as the day a patient was liberated from MV and study day 1 designated as the first day following LMV. The study terminated on the 14th day following LMV. Macronutrient and calorie intake was measured on study days 1-7 and 14. If a patient was discharged from hospital prior to day 14, the study was terminated. For the present analysis, only patients who were prescribed an oral diet exclusively without modification to textures or fluids for at least one day during the study protocol were included.

6.2.2 Patient characteristics

Patient age, sex, ICU admitting diagnosis, Acute Physiology and Chronic Health Evaluation II (APACHE II) score (256) at ICU admission, and the modified Nutrition Risk in Critically Ill (mNUTRIC) score (260) were documented to facilitate description of the study population recruited. Clinical outcomes including number of days requiring MV, ICU length of stay (LOS), hospital LOS and prevalence of OPD following LMV, and in-hospital mortality were recorded.

6.2.3 Measurement of food and liquid intake

The standard menu for non-modified diets at the hospital this research was performed is set to provide approximately 1500 kcal/d and 50 g protein/d. Patients are provided with the opportunity to select their meals. Menus for the following day (Appendix C) are distributed every morning with breakfast and the completed menus (patients circle their selections) are collected shortly after lunch. If a menu selection sheet is not completed or a dietary prescription changes mid-day, a standard meal is provided. In general, the meals are structured to provide a source of protein (meat/meat alternative), and a serving of vegetables, grains/starch, milk, and fruit (and/or a dessert). Snacks are not provided as part of the regular diet unless requested. For patients who are unable to select their meals or miss the opportunity to complete the selection are provided with the standard diet being served that day.

After each meal (breakfast, lunch, dinner) patient meal trays were collected and the remaining waste of each food and fluid item that was served was weighed (i1200 scale, MyWeigh, Phoenix, AZ) to the nearest 0.1 gram. Meal tickets were collected to verify each item served. In the event a meal ticket was missing from the patient's tray, items served were verified through the hospital nutrition management software. When meal trays were collected, patients (and/or their family members or members of the health care team in the event patients were not capable) were asked to recall any foods consumed between meals (i.e. snacks, oral nutrition supplements) or foods brought from outside sources (i.e. home, commercially prepared). If leftover snacks or foods remained at the bedside, they were weighed. In the event a meal tray could not be collected to weigh food waste, alternative methods of assessing intake, including calorie counts or dietary recall by the

patient/family/health care professional, were utilized. The amount of each food and fluid item consumed was calculated by subtracting the measured waste from the standard portion size. For each food item offered by the hospital's Patient Food Services Department, a standard portion was weighed three times and the mean weight used as the reference weight. Protein, carbohydrate, fat, and energy content of each item was determined by referring to the nutritional content reported on labels by the food manufacturers or to the Canadian Nutrient File and used to calculate the total amount of energy and macronutrients provided and consumed daily and at each meal. The amount of calories and protein provided and consumed daily was related to each patient's usual body weight to allow for comparison to standard energy (25 kcal per kg body weight) and protein (1.2 g protein per kg body weight) prescriptions (162).

To facilitate description of the types of foods and fluids frequently wasted or consumed, all food and fluid items offered on the hospital menu for non-modified dietary prescriptions were classified into 22 categories on the basis of similarities in calorie and macronutrient profile and cuisine type (197, 299) (Table 6.1). A twenty-third category ("non-hospital foods") for items consumed by patients that were not provided by the hospital was included. For each category, the frequency items were served, and the total combined weight of foods and fluids provided, wasted and consumed over the course of the study were documented.

6.2.4 Statistical analysis

Descriptive statistics are presented as median and interquartile range (Q1, Q3) [minimum, maximum] or mean \pm standard deviation and categorical data as presented as

counts (percentages). Comparisons between nutrients consumed and provided were evaluated using the Wilcoxon Signed Ranks test, and the Kruskal-Wallis test was used to examine differences in nutrient consumption between meals. Statistical analysis was carried out using SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA).

Table 6.1 Food categories and the corresponding calorie and macronutrient content of items within each category¹

Food category	Items in each food category	Mean Portion Size (g)	Mean calorie and macronutrient content			
			Calorie (kcal)	Protein (g)	CHO (g)	Fat (g)
Added fats	Butter, margarine, peanut butter	12 ± 5.7	76 ± 29	1.2 ± 2.1	1.6 ± 2.8	7.8 ± 1.8
Bread	White, brown, whole wheat bread	30 ± 0	74 ± 0	2.7 ± 0.5	13 ± 0.3	0.7 ± 0
Cereal	Cooked cereals, cold cereals	59 ± 54	74 ± 29	1.9 ± 1.1	16 ± 8.1	0.6 ± 0.6
Cheese	Hard and soft cheeses	67 ± 53	95 ± 17	9.0 ± 4.7	5.5 ± 7.1	3.8 ± 3.2
Desserts	Brownies, cookies, custards, tarts, dessert squares	44 ± 32	164 ± 100	2.5 ± 2.1	23 ± 13	7.6 ± 5.8
Eggs	Hard boiled eggs, omelettes	78 ± 29	104 ± 67	9.0 ± 3.2	2.0 ± 1.3	6.3 ± 6.1
Fruit	Fresh fruit, canned/packaged fruit, fruit/applesauce	110 ± 33	57 ± 20	0.5 ± 0.5	14 ± 5.2	0.1 ± 0.1
Juice	All fruit and vegetable juices	114 ± 22	52 ± 16	0.4 ± 0.4	12 ± 4.1	0 ± 0
Milk	1% and 2%-fat milk	125 ± 0	58 ± 7	4.2 ± 0.1	6.0 ± 0.3	1.8 ± 0.9
Muffins & pastries	Muffins, loafs, croissants, Danish pastries, cereal bars	68 ± 32	214 ± 108	3.5 ± 1.1	33 ± 16	7.9 ± 5.0
Pasta	Hot pasta entrées, i.e. spaghetti, macaroni and cheese	223 ± 62	255 ± 51	14 ± 3.1	35 ± 12	6.3 ± 2.3
Protein (from main entrées)	Standard hot entrées (beef, pork, poultry, fish, vegetarian) prepared and served by the hospital. Side vegetables and starches not included unless pre-mixed with the entrée	177 ± 93	196 ± 97	15 ± 5.2	22 ± 20	5.5 ± 4.2
Pudding & ice cream	Puddings, ice creams, sorbets	110 ± 7	104 ± 17	1.9 ± 1.4	15 ± 4.2	2.5 ± 1.8
Sandwiches	Any type of sandwich	154 ± 35	280 ± 74	18 ± 5.7	35 ± 10	9.0 ± 4.1

Soup	All soups except broths/consommés	146 ± 22	54 ± 12	2.4 ± 1.5	8.6 ± 2.1	1.1 ± 0.5
Starch	Potatoes, turnips, sweet potatoes, rice, corn, bean salad	99 ± 20	117 ± 39	2.9 ± 1.7	21 ± 6.9	2.6 ± 1.6
Tea & coffee	Tea, coffee (caffeinated and decaffeinated)	180 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Vegetables (cooked)	Broccoli, carrots, green beans, carrots, peas, zucchini, vegetable blends	70 ± 11	29 ± 12	1.5 ± 0.9	5.3 ± 2.3	0.1 ± 0.1
Vegetables (raw) & salads	Lettuce/salad mixes, carrots, cucumber, tomatoes	68 ± 32	23 ± 19	0.7 ± 0.4	4.6 ± 4.2	0.5 ± 0.8
Yogurt	Plain and fruit-flavoured yogurt, Greek yogurt	144 ± 56	116 ± 39	5.8 ± 1.5	19 ± 7.8	1.8 ± 0.8
Other	Condiments (i.e. mustard, mayonnaise, ketchup), sugar, milkettes, jam, salad dressing, soda, popsicles, gel snacks, crackers, melba toast	52 ± 87	43 ± 40	0.2 ± 0.3	6.6 ± 7.7	1.7 ± 3.7
Oral nutritional supplements	Commercial meal replacement beverages	237 ± 0	201 ± 38	12 ± 3.2	31 ± 9.8	3.7 ± 3.4
Non-hospital foods	Any food items received by the patient that were not served by the hospital (i.e. food from home or retail outlets)	187 ± 195	267 ± 141	7.1 ± 8.5	33 ± 19	11 ± 5.9

¹Data are presented as mean ± standard deviation. CHO, carbohydrate

6.3 Results

6.3.1 Patient characteristics and outcomes

Between February and September 2015, 538 patients were screened for eligibility into this feasibility study and 19 were recruited to participate (Figure 4.1). Of the patients who participated, only 9 (47%) were prescribed an oral diet exclusively without modification to textures or fluids for at least one day during the study protocol (Appendix H). The remaining patients in the study population were excluded because they were receiving enteral nutrition (EN) and/or prescribed oral diets with modified textures (i.e. pureed, minced) or fluids (i.e. thickened fluids). Patient baseline characteristics at the time of ICU admission are shown in Table 6.2. The mean age was 57 years, 44% of the patients were male, and mean weight and BMI at time of ICU admission were 79 kg and 28.6 kg/m², respectively. Patients had high severity of illness (mean APACHE II score of 25) and 5/7 (71%) had a high (≥ 5) mNUTRIC score. All patients in this cohort received EN while in ICU and all survived the hospital admission. Patient outcomes are presented in Table 6.3. Across all patients, the total number of days for which dietary intake was evaluated as part of the study protocol and patients received a regular (i.e. without modification to textures or thickening of fluids) oral diet as the sole source of nutrition was 33. The average time between LMV and prescription of a regular diet was 3.7 days and of the 7 patients who were referred to an SLP for a swallowing assessment, 86% were diagnosed with OPD.

6.3.2 Food and liquid consumption in relationship to amount provided

Of the total amount (by weight) of foods and fluids served over 33 meal days (66,659 g), only 57% was consumed (Table 6.4). The total amount of calories and protein provided

was 50,787 kcal and 1925 g, respectively, and similarly, only 55% and 56% of all calories and protein provided, respectively, were consumed. Excluding non-hospital foods, 46% of the total weight of items provided came from liquids (tea, coffee, juice, milk and soups) and 54% from solids, with 55% and 56% of liquids and solids consumed, respectively. No ONS were prescribed to any patients in this cohort and foods/liquids brought from outside sources comprised 5% (by weight) of all items provided. Within the individual food/liquid categories, the category in which the greatest proportion of that provided was consumed was the non-hospital foods. In contrast, added fats were most commonly wasted. The protein sources that accompanied standard hot entrees made up 10% of the total amount (by weight) of food/liquids provided, but only half of that amount consumed which contributed to 17% and 36% of all the calories and protein wasted, respectively.

Table 6.2 Patient baseline characteristics at time of ICU admission

No. (n=9)	Age (y)	Sex	Weight (kg)	BMI (kg/m ²)	Admission diagnosis	APACHE II score	mNUTRIC score
1	67	F	50	20.0	Respiratory	N/A	N/A
2	53	M	71	21.4	Cardiovascular	21	N/A
3	68	M	77	27.5	Sepsis	30	8
4	60	M	91	27.1	Respiratory	31	7
5	55	M	105	30.4	Cardiovascular	32	6
6	43	F	73	23.7	Cardiovascular	22	3
7	60	F	143	57.7	Respiratory	30	6
8	47	F	43	19.9	Gastrointestinal	21	4
9	63	F	59	29.2	Respiratory	13	5

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; F, female; M, male; MV, mechanical ventilation; mNUTRIC, modified Nutrition Risk in Critically Ill; N/A, data not available

Table 6.3 Patient clinical outcomes, time to regular diet following liberation from mechanical ventilation, and prevalence of oropharyngeal dysphagia

No. (n=9)	Duration of MV (d)	ICU LOS (d)	Hospital LOS post-LMV (d)	Time to regular diet post-LMV (d)	No. of study days on a regular diet (n=33)	Assessed by SLP ¹	Diagnosed with OPD
1	3.1	11	3.0	1	2	No	-
2	4.3	7.4	4.8	3	2	No	-
3	8.0	11	14	2	2	Yes	Yes
4	3.8	9.5	15	1	8	Yes	Yes
5	14	21	17	14	1	Yes	Yes
6	8.5	9.0	6.3	2	5	Yes	Yes
7	17	20	7.0	6	1	Yes	No
8	14	15	7.1	2	5	Yes	Yes
9	3.0	4.2	16	2	7	Yes	Yes

¹ SLP referred to patient specifically to assess swallowing function. LMV, liberation from mechanical ventilation; LOS, length of stay; OPD, oropharyngeal dysphagia; SLP, speech-language pathologist.

6.3.3 Distribution of calories and macronutrients consumed daily

On average, the amount of total daily calories provided to patients was 15% protein, 59% carbohydrate and 26% fat. Similarly, the proportion of calories consumed was 15% protein, 63% carbohydrate and 22% fat. The net amounts of calories and macronutrients consumed daily are shown in Table 6.5. Patients consumed significantly less calories (608 kcal, $P<0.0001$), protein (25 g, $P<0.0001$), carbohydrate (87 g, $P<0.0001$), and fat (18 g, $P<0.0001$) daily in comparison to that provided (Table 6.5). Of the 9 patients, 5 were provided with greater than 25 kcal/kg, whereas 8 consumed less than 25 kcal/kg (Figure 6.1A). Only 1 patient was provided greater than 1.2 g protein/kg, but this patient did not consume sufficient amounts to meet this threshold (Figure 6.1B).

Table 6.4 Total amount of food and liquid items wasted and consumed over 33 study days

Food Category	Frequency items provided ¹	Total amount delivered (g)	Total consumed (g)	% Consumed	Total wasted (g)	% Wasted	Calories consumed (kcal)	Protein consumed (g)
Non-hospital foods	22	3532	3045	86%	488	14%	3279	73.3
Fruit	57	6632	4843	73%	1789	27%	2802	22.7
Pasta	5	1058	757	71%	302	29%	675	27.3
Milk	50	6239	4403	71%	1836	29%	1415	8.8
Bread	13	390	274	70%	116	30%	2149	151.1
Other	91	2390	1651	69%	740	31%	1015	60.6
Cereal	31	1442	978	68%	464	32%	2595	11.8
Juice	68	7961	5342	67%	2619	33%	1594	37.4
Pudding & ice cream	13	1396	912	65%	484	35%	1005	23.7
Cheese	14	662	396	60%	266	40%	828	63.9
Main courses (protein)	40	6948	3554	51%	3395	49%	3488	348.3
Yogurt	13	2025	989	49%	1036	51%	822	40.5
Eggs	7	465	225	48%	240	52%	349	26.9
Sandwiches	12	1798	843	47%	954	53%	1651	95.9
Vegetables (raw) & salads	22	1565	733	47%	832	53%	270	6.4
Muffins & pastries	23	2011	919	46%	1092	54%	0	0
Tea & coffee	78	13860	5895	43%	7965	57%	154	7.1
Soup	7	1078	448	42%	630	58%	1154	29
Starch	29	2937	1078	37%	1858	63%	1468	28.8
Vegetables (cooked)	22	1541	561	36%	980	64%	221	10.3
Desserts	12	482	161	33%	321	67%	765	7.8
Added fats	30	247	64	26%	183	74%	417	7.2
Oral nutrition supplements	0	-	-	-	-	-	-	-
TOTAL		66659	38070	57%	28589	43%	28116	1089

¹Refers to the total number of times an item from each food category was delivered over the 33 study days

Table 6.5 Total daily calories and macronutrients provided and consumed daily and calories and protein provided and consumed relative to body weight¹

	Calories (kcal)	Protein (g)	Carbohydrate (g)	Fat (g)	Calories per kg body weight (kcal/kg) ²	Protein per kg body weight (g/kg) ²
Provided	1456 (1270, 1862) [842, 3560]	58 (51, 65) [32, 93]	222 (190, 259) [111, 423]	36 (29, 57) [19, 173]	26 (16, 30) [10, 49]	0.86 (0.70, 1.00) [0.40, 1.50]
Consumed ³	848 (530, 1147) [214, 1475]	33 (16, 45) [4.0, 67]	135 (12, 18) [1.5, 24]	18 (11, 32) [1.4, 58]	11 (8.5, 15) [2.4, 28]	0.45 (0.30, 0.60) [0.10, 1.00]

¹Data are presented as median and interquartile range (Q1, Q3) [minimum, maximum]

²Based on patient's estimated usual weight reported at ICU admission

³Using the Wilcoxon Signed Ranks test, the amount consumed was found to be significantly less ($P < 0.0001$) than that provided within each category

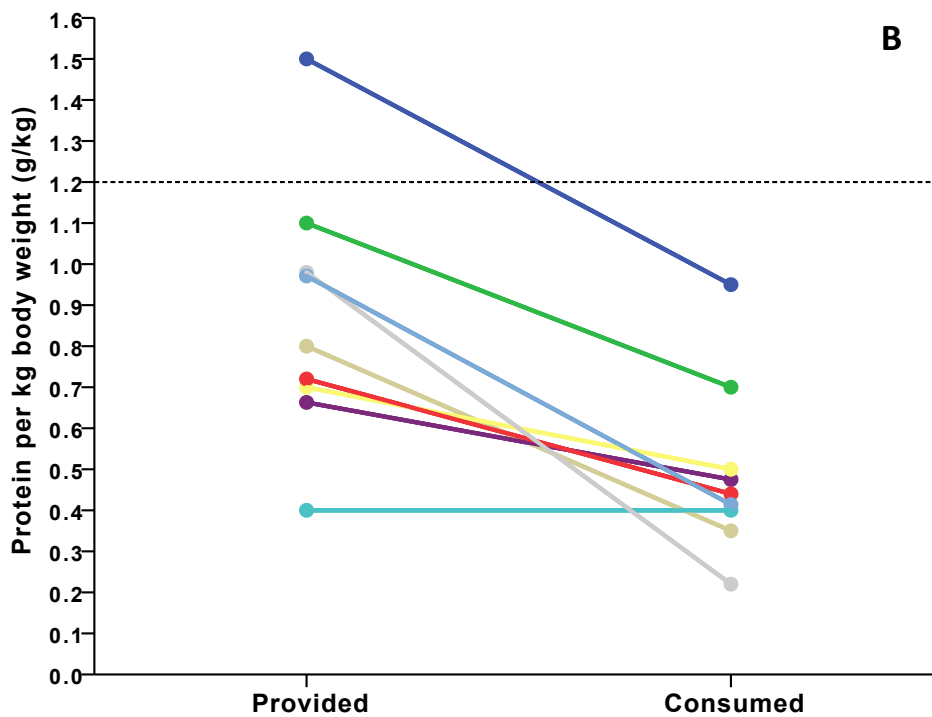
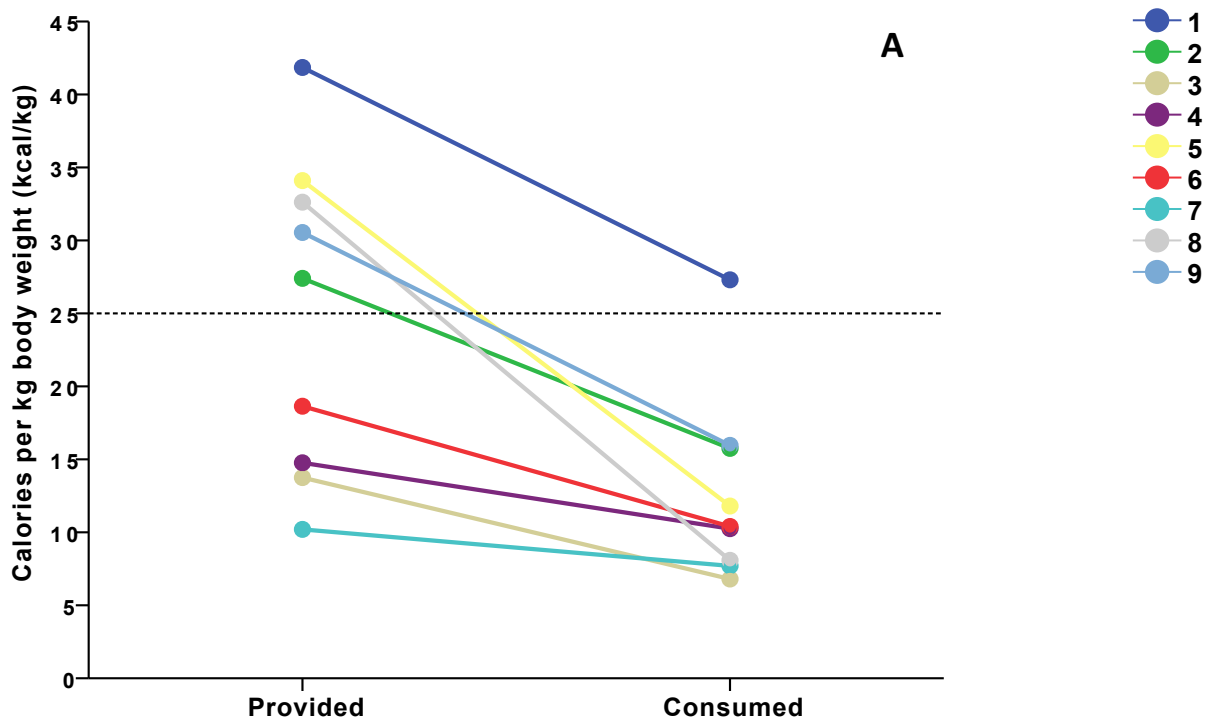


Figure 6.1 Amount of calories (A) and protein (B) provided and consumed daily relative to each patient's estimated usual body weight

Each colored line represents a patient (n=9), and the dotted lines represent 25 kcal/kg (A) and 1.2 g protein/kg (B).

In this subpopulation, snacks were requested by and provided to patients on 16 of the 33 study days, and 7/9 patients were provided with a snack for at least one study day. For 3 of these patients, the snacks consumed were solely non-hospital foods, for 2, the snacks consumed were provided by the hospital, and 2 more consumed snacks provided both by the hospital and from outside the hospital. Snacks provided by the hospital specifically in this patient group included cookies, cheese, crackers, milk, juice and ice cream. Snacks that were not provided by the hospital that patients consumed included chocolate, muffins, pastries, juice, chips, and frozen coffee beverages.

6.3.4 Distribution of Calories and Macronutrients Consumed at Individual Meals

There was not a significant difference between the median amount of calories or fat consumed at breakfast, lunch, dinner and snacks (195, 255, 231 and 97 kcal, respectively, $P=0.063$, and 3.3, 4.3, 4.4, and 5.2 g fat, $P=0.682$, respectively Table 6.6). Patients did consume significantly less protein ($P<0.0001$) and carbohydrate ($P<0.05$) at snacks than at breakfast, lunch, or dinner, however there were no differences in intake of either of these nutrients between the three main meals (Table 6.6). The proportion of calories coming from protein, carbohydrate and fats at each meal are shown in Figure 6.2. Individual variations in total calories and protein consumed at each meal and snacks are illustrated in Figure 6.3 (A and B). One patient consumed the highest amount of protein at his/her breakfast, whereas four consumed the highest amount at lunch, and four at dinner. With respect to calorie consumption at meals, two patients consumed the greatest at breakfast, four at lunch, two at dinner, and one patient consumed similar amounts of calories at each meal and snacks.

Table 6.6 Median daily calories and macronutrients consumed at each meal and for snacks^{1,2}

	Calories (kcal)	Protein (g)	Carbohydrate (g)	Fat (g)
Breakfast (n=33)	195 (124, 348) [0, 595]	8.9 ^a (4.0, 13) [0, 17]	36 ^a (16, 59) [0, 110]	3.3 (1.7, 8.4) [0, 21]
Lunch (n=33)	255 (159, 464) [5.0, 661]	11 ^a (4.9, 17) [0.1, 29]	40 ^a (29, 62) [1.2, 99]	4.3 (2.2, 12) [0. 34]
Dinner (n=33)	231 (165, 309) [36, 418]	9.1 ^a (4.9, 16) [0.2, 30]	36 ^a (26, 45) [5.0, 65]	4.4 (2.2, 6.6) [0, 15]
Snacks (n=16)	97 (38, 311) [0, 503]	1.0 ^b (0.6, 3.1) [0, 11]	14 ^b (5.5, 33) [0, 63]	5.2 (2.1, 15) [0, 23]
Significance ³	0.063	<0.0001	<0.05	0.682

¹Data are presented as median and interquartile range (Q1, Q3) [minimum, maximum]

²Across 33 meal days, snacks were provided to patients on only 16 of those days.

³Differences in calories and macronutrients consumed between meals (including snacks) was determined using the Kruskal-Wallis test and a *P*-value <0.05 was considered significant. Post-hoc pairwise comparisons were performed when appropriate; different subscripted letters indicate the amounts of calories or macronutrients consumed between meals/snacks are significantly different.

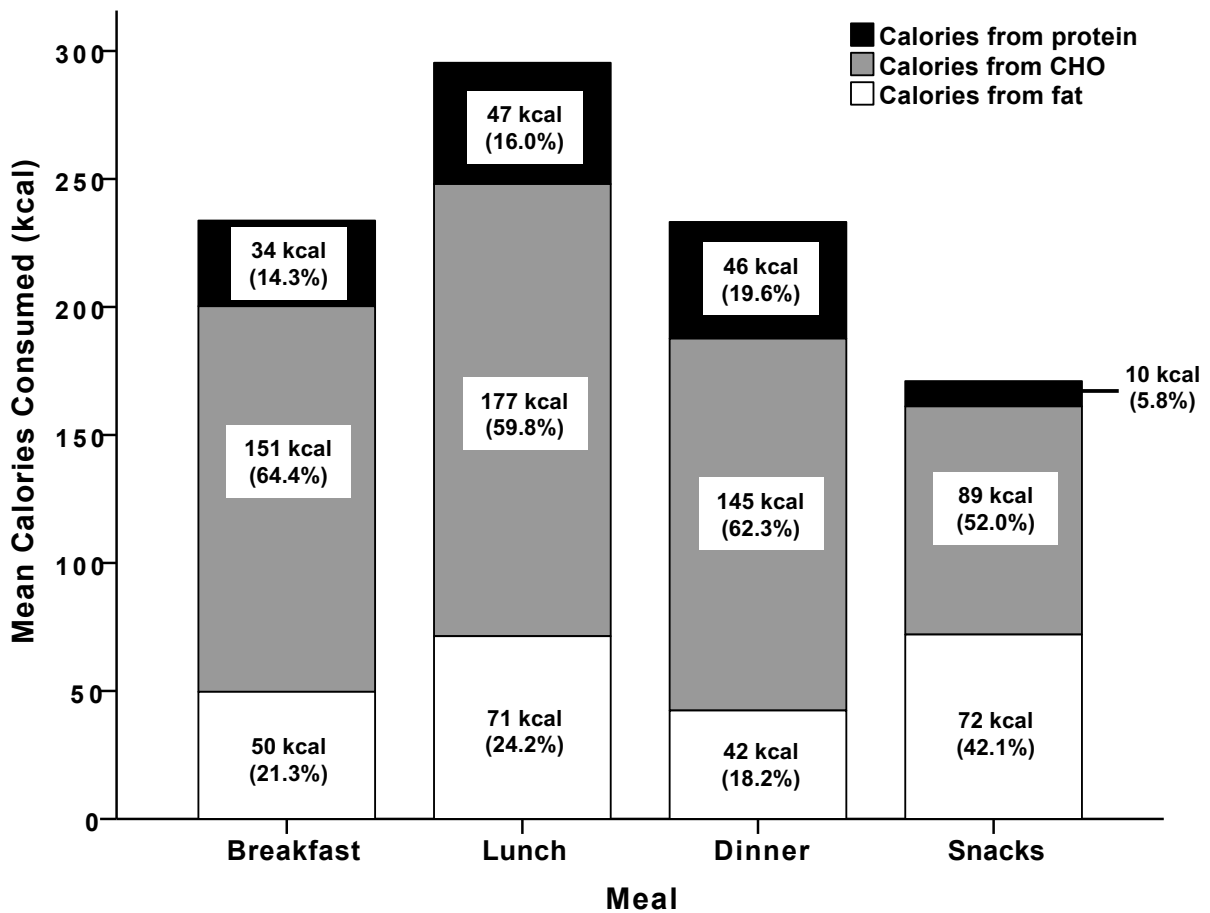


Figure 6.2 Average amount of protein, carbohydrate, and fat calories consumed at each meal

Percentages represent the proportion of total calories consumed per meal or snack. CHO, carbohydrates.

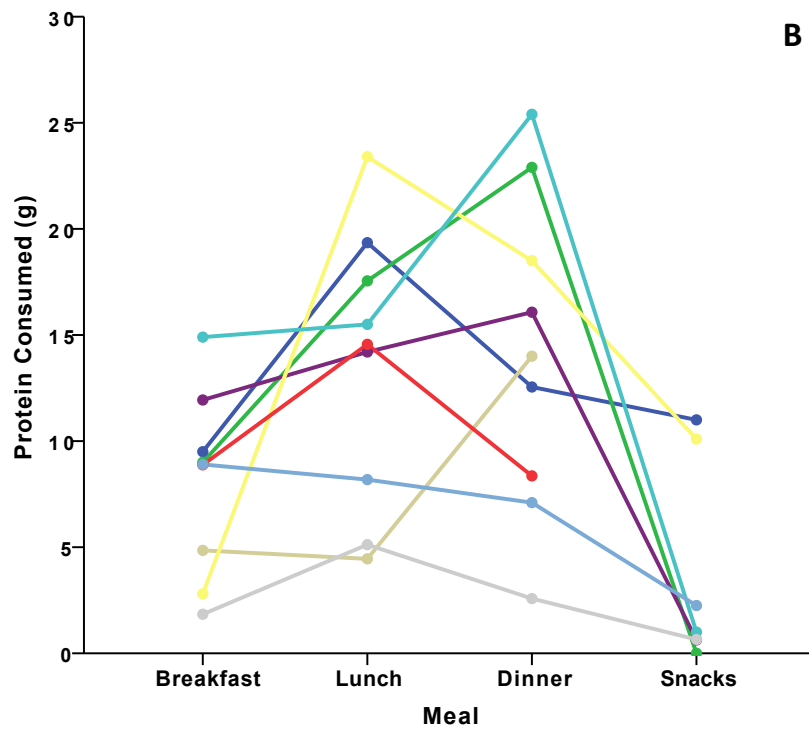
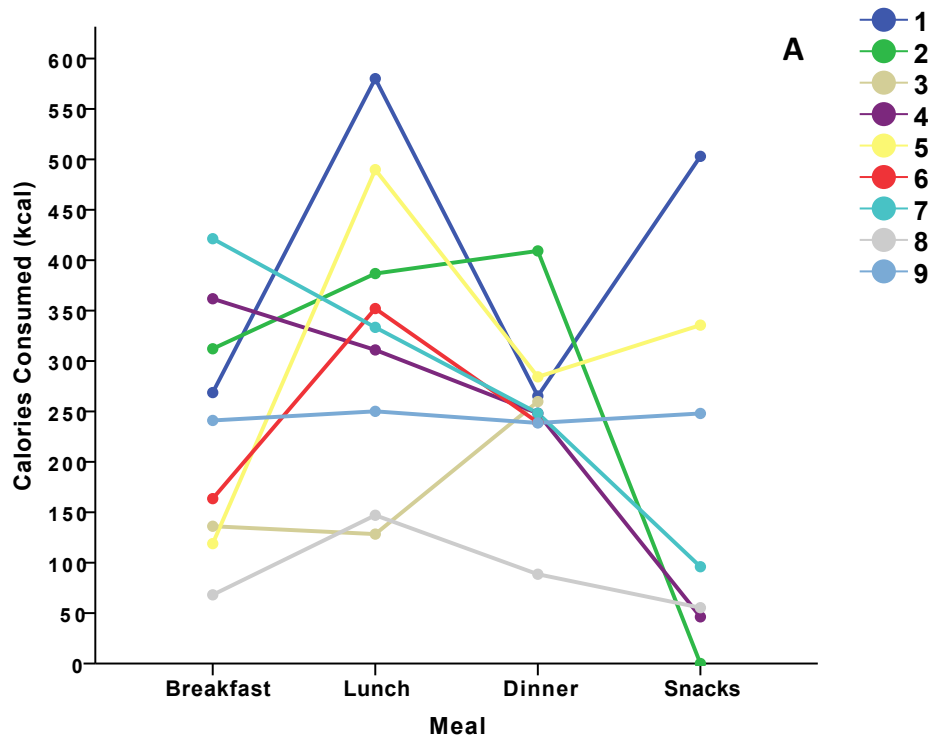


Figure 6.3 Average calories (A) and protein (B) consumed at each meal and snacks

Each colored line represents a single patient (n=9).

6.4 Discussion

To our knowledge, the present study is the first to examine food and meal intake patterns specifically in critically ill patients prescribed non-modified oral diets following LMV. We found that over 40% of all calories, protein, and foods/fluids (by weight) provided to patients was wasted, with patients consuming significantly less than that provided. Non-hospital foods, i.e. those brought to patients by family or purchased from commercial sources, were the least wasted category of food. Contrary to our hypothesis, there were no significant differences in calorie or macronutrient intake between the breakfast, lunch and dinner meals.

Previous studies examining food waste in hospitalized patients have found that 30-42% of food provided is wasted (181, 287), and our results are highly congruent with these observations. Similarly, in a large prospective study evaluating food intake in more than 1200 non-critically ill patients, Thibault et al. (300) reported 25% and 27% of protein and calories provided were wasted. It is therefore not surprising that a large proportion of the patients consuming below recommended energy and protein intakes despite providing meals that provided sufficient nutrition (287, 292, 300). In this study, patients consumed grossly inadequate protein and calories. No patients consumed greater than 1.2 g protein/kg body weight and 78% of patients consumed less than 0.6 g/kg body weight, well below even the minimum recommendations of 0.8-1.2 g/kg for healthy adults (301, 302). Contrary to previous research, we found that the meals delivered to this small patient population provided insufficient calories and protein when related to weight based prescriptions. As primary barriers to eating faced by the recovering critically ill include anorexia, early satiety, taste changes, nausea, and vomiting (21, 22, 26), in the setting of high waste, food-based

interventions should not increase the amount/volume of food provided and be as patient-centered as possible (181, 293).

Food fortification refers to the addition of energy and/or nutrients to a food product as a means to enhance its caloric or nutrient density (125). Enhancing the caloric and protein content of hospital foods via fortification has been effective in increasing energy, but not always protein intake in patients (179, 181). Increasing protein intake is essential for recovery and enhancing the protein content of regular foods that are less likely to go unconsumed by this population may be an effective strategy to do so. In a recent randomized control trial in hospitalized patients (>55 years of age), Stelten et al. (193) examined the effect of substituting protein-fortified bread and yogurt (versus the non-fortified versions served on the standard hospital diet) on protein intake. The fortified bread and yogurt contained 6.9 g and 20 g of protein, respectively, while the standard versions contained 3.8 g and 7.5 g protein, respectively. They found that patients receiving the protein-fortified foods had significantly greater protein intake (1.1 g/kg/d) versus those receiving the regular bread and yogurt served (0.9 g/kg/d) (193). Enriching a variety of hospital menu items with protein powder to enhance protein content has also been shown to be an effective strategy for increasing protein intake in hospitalized patients (297). In our study, we found that greater than 70% of food served was consumed for only 5 of the 23 food/fluid categories: bread, milk, pasta, fruit and non-hospital foods. While we did not assess food desirability or preferences, food/fluid items from any of these 5 categories may be suitable candidates for fortification.

We sought to determine whether patients consumed increased calories and protein at certain meals but found no significant differences in intake between breakfast, lunch and

dinner. However, upon examination of individual trends, it becomes apparent that there is significant individual variation with some patients showing evidence of increased intake at specific meals whereas others have relatively similar intake across meals. These findings underscore the importance of individualized nutrition assessment and treatment, and patients should be provided with preferred energy and/or nutrient dense foods at the meals where they tend to consume more food. In contrast, the provision of smaller meal portions and snacks served at more frequent intervals throughout the day has also been shown to increase energy intake in hospitalized patients (179-181), however broadly implementing this strategy and placing high emphasis on increasing calorie versus protein content could result in undesirable effects including weight gain that is predominantly fat mass and consumption of a poor quality diet (196). In the present study, the snacks that were provided either by the hospital or brought by family or caregivers tended to be poor quality items higher in refined sugars and fat. Not surprisingly though, of all food categories evaluated in this study, non-hospital foods yielded the least waste with 86% of the total amount served going consumed. Engaging families and caregivers in the nutrition care process is a vital component to improving dietary intake in the recovering critically ill (173), and our data provides support to the recommendation that families should be encouraged to bring preferred foods into the hospital. However, families and caregivers should be counseled about the role proper nutrition plays in promoting recovery and encouraged to bring foods that are of higher nutrition quality.

This study is not without its limitations. We have characterized the food intake patterns of a small subgroup of recovering critically ill patients from a single institution, which limits the interpretation and generalizability of our findings. However, the study met

our objectives to explore food and meal intake patterns to better understand how to deliver interventions in the future. Food and meal intake patterns were only characterized for patients receiving regular diets, however the recovering critically ill have a high prevalence of oropharyngeal dysphagia (207, 303) necessitating the prescription of modified texture and/or thickened fluid diets which are associated with even lower caloric and protein intakes (304). Future research should investigate the meal patterns of patients receiving all types of oral diets. Despite this small sample size, the amount of waste we reported was similar to previous reports from large studies. While there was large variability in the net amounts of calories and protein provided and consumed both daily and at meals between patients, every patient in this small sample had poor caloric intake and grossly inadequate protein intake when related to body weight. These findings echo previous work examining oral intake in the recovering critically ill following extubation (21, 22) and underscores the importance of identifying new strategies to enhance intake in this vulnerable population. The findings of this study are strengthened by our methodology in evaluating intake. Use of weighed food records allows for accurate assessment of both food and fluid consumption (174) and we also performed recalls every morning after each meal to capture intake of any items consumed in between meals or brought in from outside sources.

6.5 Conclusions

Our clinical observations suggest that the caloric, and more so, protein intake of patients recovering from critical illness who are prescribed regular diets is not sufficient to meet minimum recommendations. While the foods/fluids provided were also not sufficient to meet requirements, greater than 40% was wasted, underscoring the challenge of sufficiently feeding patients who experience multiple illness-related and somewhat non-modifiable

barriers to eating. Intervention studies in the recovering critically ill that examine the acceptability and impact of various food based strategies on increasing protein and energy intake are vital. Future studies should also examine the impact of increasing dietary adequacy in this population on broader outcomes including changes in body composition, functional status, and quality of life.

6.6 Relevance to clinical practice

Patients recovering from critical illness who are prescribed non-modified oral diets consume inadequate protein and calories. Several strategies to enhance oral intake have been identified. These include: ensuring dietitians are involved in the patient's care, prescribing ONS as appropriate, engaging families and caregivers in nutrition care, and providing individualized nutrition care plans that take into consideration the patient's food and meal intake patterns. The economic impact of a high volume of food wastage that is secondary to insufficient intake is likely significant. These findings emphasize the importance of engaging with food service departments to implement strategies (i.e. related to food delivery methods, patient menu selection, inclusion of protein fortified foods on the menu) to improve nutrition intake in hospitalized patients with high acuity of illness.

CHAPTER 7

CHARACTERIZATION OF DIETARY PRESCRIBING PRACTICES IN CRITICALLY ILL PATIENTS FOLLOWING LIBERATION FROM MECHANICAL VENTILATION

7.1 Introduction

Nutrition therapy in mechanically ventilated critically ill patients has been extensively studied over the last few decades, however the predominant focus has centered on the delivery of nutrition care during a patient's stay in the intensive care unit (ICU) and its impact on broad clinical outcomes (305). In contrast, fewer than 20 studies (Chapter 2, Table 2.1) have been published that examine aspects of nutrition in the recovery phases of critical illness (i.e. following ICU discharge) suggesting a considerable knowledge gap.

By the time patients are discharged from ICU it is probable they are malnourished secondary to several factors. A large proportion of critically ill patients are already malnourished at the time of ICU admission (306). With the severe stress and pro-inflammatory cascades induced at the onset of illness (9, 10), combined with largely inadequate nutrition delivery in ICU (17, 18), significant losses of lean tissue and fat mass, as well as muscular dysfunction result by the time a patient is liberated from the ventilator. These losses in tissues and function are key indices of malnutrition (13, 15) and stem from large protein and energy deficits that accumulate from these catabolic and insufficient nutritional processes (23, 169). As the sequelae of malnutrition include reduced immunity, impaired wound healing, impaired mental health, cognitive decline, impaired organ function, loss of muscle mass, and functional disability (19, 20), a vicious cycle is generated toward greater physical and clinical impairment. Thus, it is imperative that further research be

undertaken to broaden our understanding of nutrition recovery in the critically ill following liberation from mechanical ventilation (LMV) and subsequent ICU discharge.

In Chapter 5, we examined protein and energy intake in hospitalized patients following LMV and found that when patients received an oral diet as the sole source of nutrition, consumption of $\geq 75\%$ of prescribed protein and energy was achieved on only 0% and 24% of days, respectively. In contrast, when patients continued to receive enteral nutrition (EN) as the sole source nutrition beyond LMV, protein and energy intake was $\geq 75\%$ of prescribed on 77% and 88% of occasions, respectively (Chapter 5). As the preferred method for feeding the mechanically ventilated patient is EN (162, 163, 165), it was postulated that delaying the removal of enteral access devices (i.e. feeding tubes) and continuing to provide EN until a patient can demonstrate sufficient oral intake (283) could optimize their nutritional health during the early phases of ward-based recovery.

Further justification for prolonging the use of EN relates to the high prevalence of swallowing disorders following endotracheal intubation. Post-LMV, up to 84% of patients are diagnosed with post-extubation oropharyngeal dysphagia (OPD) (200, 207), a condition associated with malnutrition (307, 308), prolonged hospital length of stay (303, 309), and increased mortality (309). Treatment of OPD includes dietary modification (i.e. prescription of modified texture solids or thickened fluids) (310, 311), however patients prescribed modified diets tend to consume less protein and energy in comparison to patients receiving non-modified diets (304). Patients with severe OPD may be deemed unsafe to swallow by mouth thus requiring artificial nutrition (312), and are more likely to have long-term feeding tubes (i.e. gastrostomy tube) placed (200, 303). Post-extubation OPD has been associated with greater time elapsed between LMV and prescription of oral diets compared with patients

who do not have OPD (303), however little else is known about feeding practices in the critically ill including prevalence in the use of EN and modified diets following LMV.

Prior to the development of interventions to enhance nutrition recovery following critical illness, it is crucial to first garner a better understanding of usual dietary prescription practices following ICU discharge. Thus, the primary objectives of this study were two-fold: 1) characterize dietary prescribing practices within a single academic center specifically as it relates to route of nutrition delivery and the transition from EN (tube feeding) to an oral diet in patients who received EN while mechanically ventilated, and 2) characterize the types of diets (i.e. route, use of modified and therapeutic diets) patients are receiving at the time of hospital discharge. Based on findings from Chapter 5, we hypothesized that: 1) 25% patients who received EN while ventilated would have it discontinued on the same day as LMV, and 2) at the time of hospital discharge only 55% of patients would have transitioned to a regular non-modified diet, with the remainder of patients requiring a modified diet with or without enteral nutrition.

7.2 Methods

7.2.1 Study design and population

A retrospective chart review was performed on all adult (≥ 18 years of age) patients admitted to a 24-bed medical-surgical ICU (MSICU) at a teaching hospital in southwestern Ontario in 2015 who required MV for ≥ 72 consecutive hours and received EN while ventilated. Patients were excluded if they expired or care was withdrawn in ICU, were on parenteral nutrition at the time of LMV, were receiving long-term EN via gastrostomy/gastrojejunostomy feeding tube prior to ICU admission, or were transferred out of the ICU while still requiring ventilatory support. This study was approved by the Western

University Health Sciences Research Ethics Board and the University of Waterloo Office of Research Ethics (Appendix B).

7.2.2 Data collection

Patients admitted to the MSICU in 2015 who received MV for at least 72 consecutive hours and survived ICU admission were identified from a critical care statistical database maintained by the hospital informatics department. The charts of patients identified as meeting the inclusion criteria were subsequently screened for exclusion criteria. Data were extracted from both paper (including ICU flow sheets and ventilation records) and electronic medical records by one trained data abstractor.

Patient age, sex, ICU admission and diagnostic categories, ICU admission height and weight (to calculate BMI), and place of residence prior to hospital admission were extracted from the chart to facilitate description of the study population recruited. To evaluate severity of illness at the time of ICU admission, all variables required to compute Acute Physiology and Chronic Health Evaluation II (APACHE II) (256) and Sequential Organ Failure Assessment (SOFA) scores (257) were abstracted from the charts. Variables to calculate Charlson Comorbidity Index (CCI) (258) and Functional Comorbidity Index (FCI) (259), indices used to assess health status upon admission to ICU, were also extracted. The modified Nutrition Risk in Critically Ill (mNUTRIC) score was calculated. This score quantifies the risk of critically ill patients developing adverse events (i.e. mortality, days requiring MV) that may be modified by nutrition therapy in ICU (260). Patients with a low mNUTRIC score (between 0-4) are considered to have low malnutrition risk and patients with a high score (between 5-9) are more likely to benefit from aggressive nutrition therapy in the ICU (260).

Data required to compute the following clinical outcomes were abstracted: ICU LOS, duration of MV, total hospital length of stay, post-LMV time to discharge alive and time to death, rate of ICU re-admissions requiring reinstatement of ventilatory support, 30-day hospital readmission, in-hospital mortality, and discharge destination.

Various indices related to nutrition care were documented. At the study site, there are several wards where a surviving MSICU patient can be transferred to following LMV. It is also possible for patients to be discharged home (or to rehabilitation, long-term care etc.) directly from the ICU if no ward beds are available. The wards, the number of beds per ward, and dietitian staffing on each ward is listed in (Chapter 3, Table 3.1). The MSICU is staffed full-time by one full-time dietitian on weekdays. Weekend dietitian coverage for the whole hospital is provided on an on-call basis unless otherwise stated. Full-time equivalent for speech-language pathology (SLP) services for the entire hospital ranges from 5.0-6.0. The use of ICU and ward dietitian, and SLP services were determined by the presence of documentation of an assessment or follow-up in the medical record. The date of documentation was noted to determine time between ICU discharge and ward RD assessment. Prevalence of OPD was determined by the number of patients who were formally diagnosed by an SLP with OPD at any time following LMV. The date and type of first oral diet prescribed and the date a regular diet was first prescribed were documented to assess time to first oral diet and time to regular diet. In this study, a regular diet refers to a diet without modification to texture or fluids. Non-modified diets with therapeutic attachments such as diabetic, cardiac, renal, and so forth were included in the regular diet category. Lastly, the proportion of patients who had tracheostomy and gastrostomy/gastrojejunostomy tubes inserted was also documented.

7.2.3 Statistical analysis

The distribution of all continuous data was examined using graphical methods (histograms, boxplots, and stem-and-leaf plots) and data are presented as mean \pm standard deviation or median and interquartile range (IQR: Q1, Q3), as appropriate. Categorical data are presented as counts (percentages).

7.3 Results

In 2015, 1073 patients were admitted to the MSICU and 939 were excluded for reasons summarized in Figure 7.1. In total, 134 patients were identified as eligible for inclusion in the analysis (Figure 7.1).

7.3.1 Patient characteristics at ICU admission

Patient characteristics at ICU admission are presented in Table 7.1. Patients were an average of 61 ± 14 years of age, 55% of whom were male. The most common ICU admitting diagnoses were neurological (30%) and respiratory (27%). Median BMI at time of ICU admission was 26.0 kg/m^2 ; 28% of the population was obese ($\text{BMI} > 30 \text{ kg/m}^2$), whereas only 3.1% of the population was underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$). Most patients lived at home (with or without any type of in-home supportive care) prior to hospital admission ($n=128$, 96%), 2 (1.5%) were admitted from a retirement home, 2 (1.5%) from long-term care, 1 (0.8%) from a group home, and 1 (0.8%) had no fixed address.

7.3.2 Clinical outcomes

Patients required MV for a median of 8.0 (IQR: 4.8, 14) days, median ICU length of stay was 12 (IQR: 7.8, 19) days, and 20 (15%) of patients had tracheostomy tubes inserted prior to LMV. Under 10% of patients were readmitted to ICU for reinstatement of ventilatory support, 13% of patients died in hospital, and 8.5% were readmitted to the study hospital

within 30 days of hospital discharge. Data regarding readmissions to hospitals other than the study site could not be obtained. Median hospital LOS was 30 (IQR: 21, 48) days, and median post-LMV time to discharge was 18 days (Table 7.2). Within survivors (n=117), 21 (18%) were repatriated to another hospital with an unknown final discharge destination, 56 (48%) were discharged back home, 24 (21%) went to inpatient rehabilitation, 5 (4.2%) to outpatient rehabilitation, 8 (6.8%) to long-term or complex care, 1 (0.9%) to a retirement home, 1 (0.9%) to transitional care, and 1 (0.9%) to hospice care. Of the survivors who were admitted from home, only 45% were discharged back home.

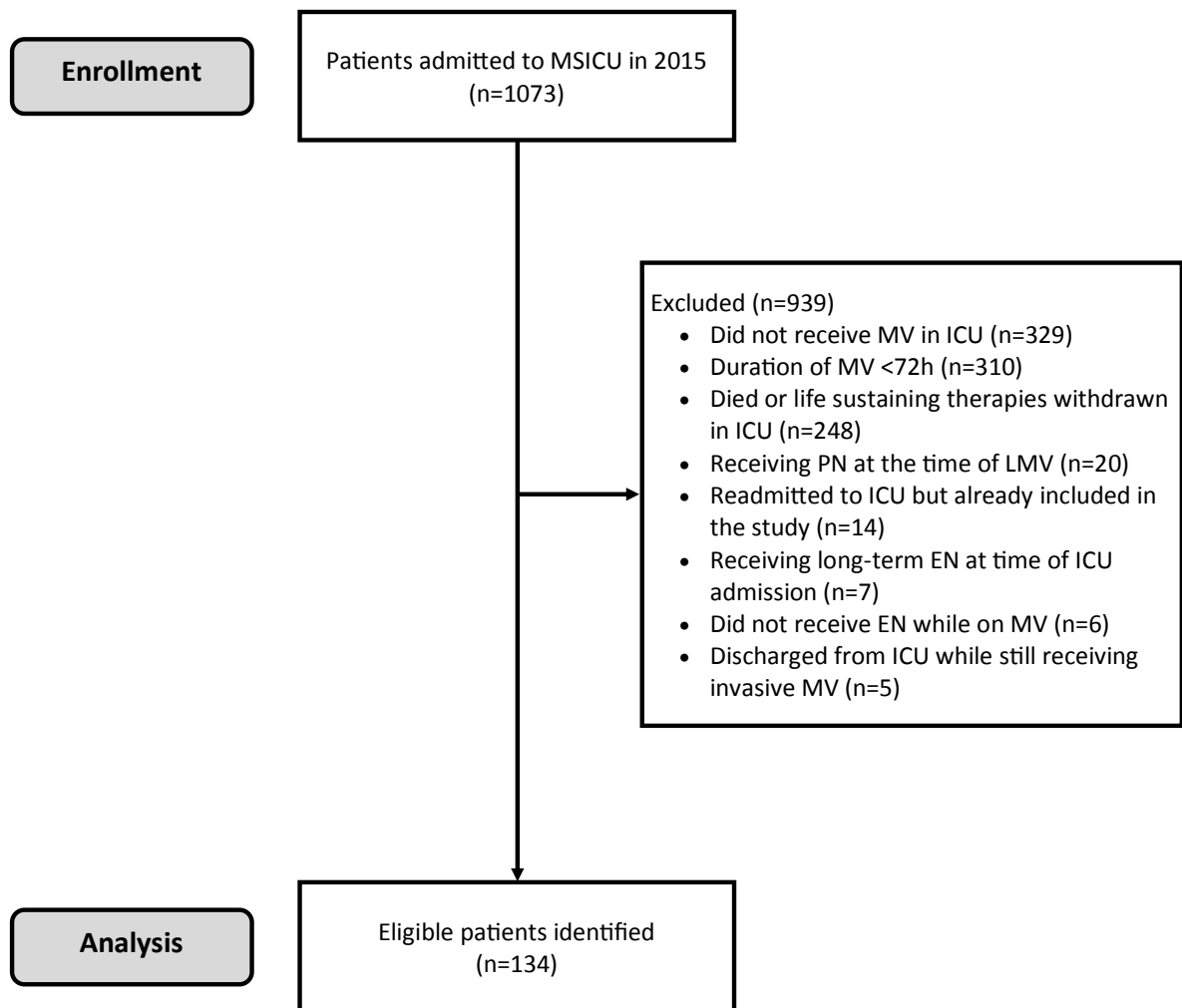


Figure 7.1 CONSORT diagram

EN, enteral nutrition; LMV, liberation from mechanical ventilation; MSICU, medical-surgical intensive care unit; MV, mechanical ventilation; PN, parenteral nutrition.

Table 7.1 Patient characteristics at ICU admission

Characteristic ¹	Value ²
Sex, male	73 (55)
Age (y)	61 ± 14
ICU admission type	
Medical	112 (84)
Surgical	20 (15)
Trauma	2 (1.5)
ICU admission diagnosis	
Neurological	40 (30)
Respiratory	36 (27)
Cardiovascular	22 (16)
Gastrointestinal	17 (13)
Sepsis	11 (8.2)
Other	5 (3.7)
Metabolic	2 (1.5)
Malignancy	1 (0.7)
APACHE II score (n=115)	28 ± 7
SOFA score (n=82)	10 ± 3
Charlson Comorbidity Index	1 (0, 3)
Functional Comorbidity Index	2 (1, 3)
mNUTRIC risk category (n=77)	
Low risk (score 0-4)	8 (10)
High risk (score 5-9)	69 (90)
Weight (kg) (n=133)	77 (67, 91)
BMI (kg/m ²) (n=131)	26.0 (23.0, 30.3)
BMI Classification (n=131)	
Underweight (<18.5 kg/m ²)	4 (3.1)
Normal (18.5 – 24.9 kg/m ²)	51 (39)
Overweight (25 – 29.9 kg/m ²)	40 (31)
Obese, all classes (>30 kg/m ²)	36 (28)
Class I (30 – 34.9 kg/m ²)	15 (12)
Class I (35 – 39.9 kg/m ²)	7 (5.3)
Class III (>40 kg/m ²)	14 (11)

¹Data are for n=134 unless otherwise specified.

²Continuous data are presented as mean ± SD or median and interquartile range (Q1, Q3) as appropriate, and categorical data presented as counts (percentages).
APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICU, intensive care unit; mNUTRIC, modified Nutrition Risk in Critically Ill; SOFA, Sequential Organ Failure Assessment.

Table 7.2 Patient clinical outcomes

Characteristic ¹	Value ²
Duration of MV (d)	8.0 (4.8, 14)
ICU LOS (d)	12 (7.8, 19)
Readmitted to ICU for reinstatement of ventilator support	12 (9.0)
Died in hospital	17 (13)
Hospital LOS (n=117, survivors only) (d)	30 (21, 48)
Post-LMV time to discharge alive (n=117) (d)	18 (11, 29)
Post-LMV time to death (n=17) (d)	18 (9, 29)
30-day hospital readmission (n=117, survivors only) (d) ³	10 (8.5)

¹Data are for n=134 unless otherwise specified.

²Continuous data are presented as mean \pm SD or median and interquartile range (Q1, Q3) as appropriate, and categorical data are presented as counts (percentages).

³Hospital readmission rates reflect patients readmitted to the study site; data regarding 30-day readmissions to other hospitals unable to be obtained. ICU, intensive care unit; LMV, liberation from mechanical ventilation; LOS, length of stay; MV, mechanical ventilation.

7.3.3 Use of dietitian and SLP services and prevalence of oropharyngeal dysphagia following liberation from mechanical ventilation

Almost all patients (97%) were assessed by an RD in the intensive care unit, whereas only 65% received RD consultations following transfer to the ward. Median time between ICU discharge and ward RD assessment was 2 (IQR: 1, 4) days. Following LMV, referrals to SLP services were ordered for 92 (69%) patients and 88 were formally assessed with a bedside swallowing assessment, modified barium swallow assessment, and/or a fiberoptic endoscopic evaluation of swallowing test, as deemed appropriate by the SLP. Of those assessed, 66 (75%) were diagnosed with OPD.

7.3.4 Use of enteral nutrition following liberation from mechanical ventilation

Enteral nutrition was discontinued on the same day as LMV for 21 (16%) of patients with the remainder (84%) continuing to receive EN for at least one day post-LMV. Timing of discontinuation of EN in relation to day of LMV for all patients is found in Table 7.3.

Reasons for discontinuation of EN could not be reliably abstracted from the chart. Twenty-five (19%) of patients never had EN discontinued during the remainder of their hospital stay and 18 (13%) had nasogastric feeding tubes replaced with gastrostomy tubes for long-term EN. Within the 109 patients who did have EN discontinued prior to hospital discharge, median time between LVM and permanent discontinuation of EN was 4 (IQR: 1, 11) days.

Table 7.3 Timing of discontinuation of enteral nutrition in critically ill patients following liberation from mechanical ventilation

Timing of EN discontinuation	Number of patients (n=134) ¹	Cumulative percent of patients with EN permanently discontinued (%)
On day of LMV	21 (15.7)	15.7
Post-LMV day 1	16 (11.9)	27.6
Post-LMV day 2	10 (7.5)	35.1
Post-LMV day 3	6 (4.5)	39.6
Post-LMV day 4	7 (5.2)	44.8
Post-LMV day 5	3 (2.2)	47.0
Post-LMV day 6	3 (2.2)	49.3
Post-LMV day 7	7 (5.2)	54.5
Post-LMV day 8	2 (1.5)	56.0
Post-LMV day 9	6 (4.5)	60.4
Post-LMV day 10	0 (0)	60.4
Post-LMV day 11	4 (3.0)	63.4
Post-LMV day 12	3 (2.2)	65.7
Post-LMV day 13	2 (1.5)	67.2
Post-LMV day 14	3 (2.2)	69.4
Post-LMV day 15+	16 (11.9)	81.3
EN never discontinued	25 (18.7)	-

¹Data are presented as counts (percentages). EN, enteral nutrition; LMV, liberation from mechanical ventilation.

7.3.5 Characterization of diet prescriptions following liberation from mechanical ventilation and at hospital discharge

Following LMV, 119 (89%) patients were prescribed any type of oral diet prior to hospital discharge and median time to first oral diet was 2 (IQR: 1, 7) days. Patients with tracheostomies *in situ* were not included in this calculation as oral diets can be initiated prior to fully weaning from the ventilator. The type of first oral diets prescribed varied considerably with respect to texture and consistency of fluids and 45% of patients continued to receive EN when the first oral diet was initiated (Figure 7.2). Only 15% of first diets prescribed were a regular (non-modified) texture; 26% were first prescribed a modified texture (diced, minced or pureed), 32% were prescribed full fluids, and 27% were prescribed clear fluids (Figure 7.2). Furthermore, of all first diets ordered, 33% were with thickened (nectar, honey or pudding consistency) fluids. Only 64 (55%) patients who survived the hospital admission ever received a regular, non-modified diet without supplementary EN at the time of hospital discharge, thus confirming our hypothesis. Median time to regular diet post-LMV was 4 (IQR: 1, 13) days. Discharge diets stratified by patient discharge disposition are outlined in Table 7.4. Notably, of the patients admitted from home who were discharged back home, only 36% were discharged on a regular, non-therapeutic diet; 21% were discharged on a modified texture or fluid diet, 3.6% were discharged on EN, and 39% were discharged home on a regular texture but therapeutic diet (i.e. cardiac, diabetic, low sodium or renal) (Table 7.4). Within all survivors, 22% were discharged from hospital while still receiving EN (Table 7.4).

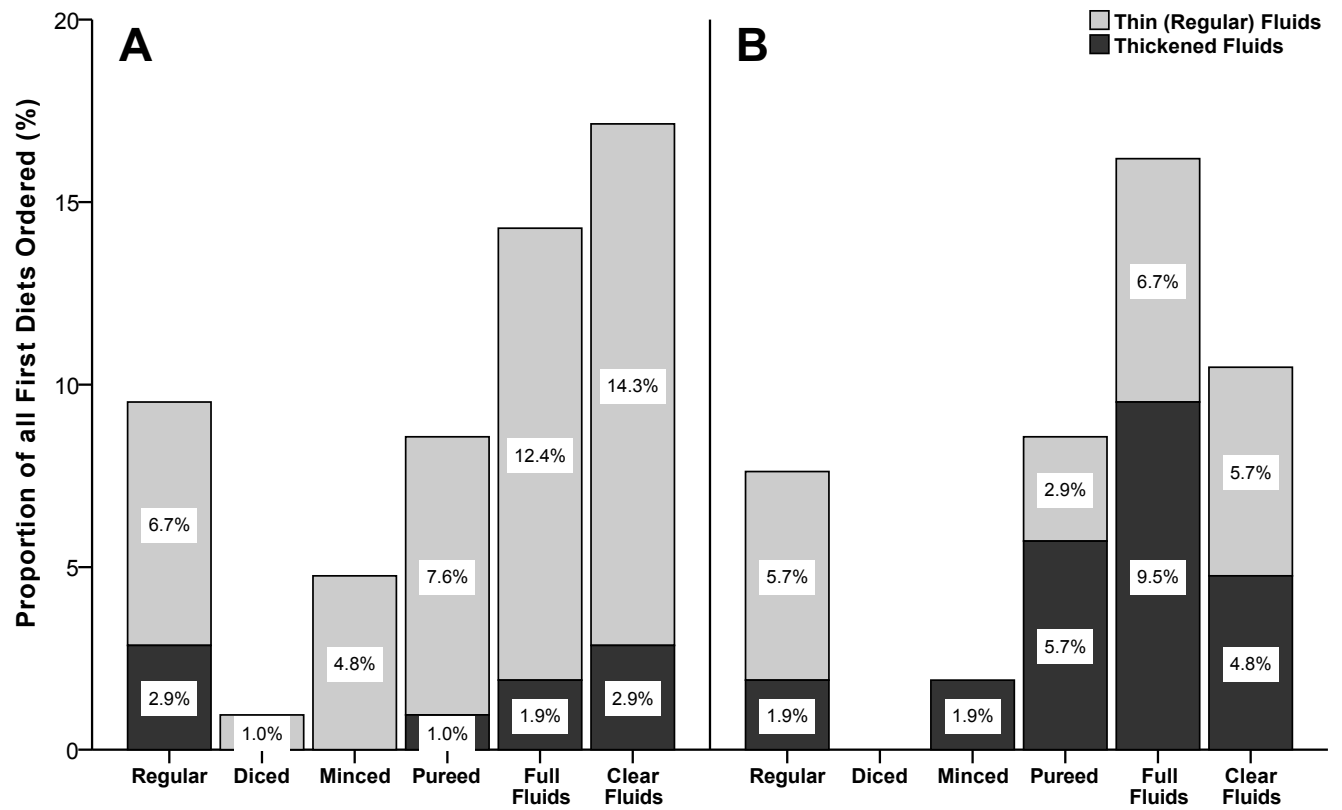


Figure 7.2 First oral diets prescribed following liberation from mechanical ventilation

Figure A represents the type of first diets ordered in patients who had EN discontinued prior to commencement of the first diet and Figure B represents the type of first diets ordered in patients who continued to receive EN when first oral diets commenced.

Table 7.4 Discharge diets and disposition of hospitalized critically ill patients

Type of diet	Discharge disposition (n=117) ^{1,2}							
	Home (n=56)	Retirement home (n=1)	LTC/CCC (n=8)	Transitional care (n=1)	Inpatient rehabilitation (n=24)	Outpatient rehabilitation (n=5)	Hospice (n=1)	Repatriated to another hospital (n=21)
Regular								
Regular	20 (36)	1 (100)	-	-	9 (38)	3 (60)	-	3 (14)
Cardiac	9 (16)	-	-	-	-	1 (20)	-	-
Diabetic	12 (21)	-	2 (25)	-	-	-	-	2 (9.5)
Low sodium	1 (1.8)	-	-	-	-	-	-	-
Renal	-	-	-	-	-	-	-	1 (4.8)
Diced								
Thin fluids	2 (3.6)	-	-	1 (100)	4 (17)	-	-	1 (4.8)
Thick fluids	-	-	-	-	-	-	-	-
Minced								
Thin fluids	4 (7.1)	-	-	-	2 (8.3)	-	-	-
Thick fluids	1 (1.8)	-	-	-	-	-	-	-
Pureed								
Thin fluids	1 (1.8)	-	-	-	1 (4.2)	-	-	1 (4.8)
Thick fluids	4 (7.1)	-	-	-	-	-	-	-
Full fluids	-	-	1 (13)	-	-	-	-	1 (4.8)
EN + oral diet								
Thin fluids	1 (1.8)	-	1 (13)	-	1 (4.2)	-	-	3 (14.3)
Thick fluids	-	-	1 (13)	-	2 (8.3)	-	-	2 (9.5)
EN+NPO	1 (1.8)	-	3 (75)	-	3 (13)	1 (20)	1 (100)	6 (29)
TPN	-	-	-	-	-	-	-	1 (4.8)

¹Data are presented as counts (percentages).

²Data shown only for survivors. CCC, complex continuing care; LTC, long-term care; NPO, *nil per os* (no food by mouth); TPN, total parenteral nutrition.

7.4 Discussion

The present study is the first to provide a comprehensive examination of dietary prescription practices, including the use of EN therapy, in a heterogeneous group of critically ill patients following LMV. We report 16% of patients who received EN while ventilated had it discontinued on the same day as LMV which was lower than hypothesized, although by day 3 post-LMV, 40% of patients had EN discontinued. However, our second hypothesis was confirmed in that 55% of patients were transitioned back to a regular, non-modified diets by the time of hospital discharge. These data provide significant insight into the use of EN therapy and diversity of dietary prescriptions in critically ill patients throughout the duration of hospitalization following LMV.

Prescription of oral diets as the sole source of nutrition following LMV is associated with low and inadequate protein and calorie intakes in both mixed MSICU patients (21) (Chapter 5) and the critically ill with traumatic brain injury (23). In contrast, those who continue to receive EN have higher intakes and adequacy of intake in relation to prescribed amounts (23) (Chapter 5). While evidence-based guidelines do not exist for feeding a critically ill patient following LMV, for patients who receive EN while mechanically ventilated, it should only be discontinued once they can demonstrate sufficient oral intake (i.e. >75% of estimated caloric requirements) (283, 313, 314). In this study, it was observed that only 45% of patients continued to receive EN at the time of first oral diet prescription, suggesting that proposed weaning algorithms (283, 313) are not commonly followed in the recovering critically ill. Given poor adequacy of protein and energy intake observed in patients prescribed oral diets following LMV (21) (Chapter 5), failure to ensure patients are

able to consume sufficient nutrition prior to discontinuation of EN is likely to hinder nutrition recovery.

We observed 75% of the patients who were formally assessed by an SLP were confirmed to have OPD, which is similar to previous reports (200, 207). As 34% of patients did not receive a formal swallowing assessment, the true incidence of OPD is unknown. However, patients with OPD are at increased risk of malnutrition (307, 308), which is partially related to the prescription of modified texture/fluid diets, a primary treatment for patients with post-extubation OPD (310, 311). Patients consuming modified diets consume fewer grams of protein and calories in comparison to those on regular diets (304), and modified diets tend to have lower nutrient density (315). Furthermore, transitioning from regular foods, which many patients may have been consuming prior to admission, to texture-modified foods can be a source of distress for the patient, and thus, may negatively impact dietary intake (316). Clearly, we are evaluating a nutritionally vulnerable group of patients because a large proportion of them continue to receive EN therapy, are prescribed modified diets in hospital (and these may continue following hospital discharge), experience post-extubation dysphagia, and likely have greater nutrition needs secondary to catabolic illness. Collectively, these characteristics underscore the need for routine nutrition assessment and monitoring by the health care team following LMV to ensure their nutritional health is not further compromised (317).

At the time of hospital discharge, only 55% of patients were transitioned back to a regular, non-modified diet and almost 20% remained on EN therapy. Ensuring optimal continuity of care is essential to maintaining a unified approach to assessing and monitoring

nutritional recovery of patients as they transition through critical junctures in the recovery stages of critical illness (24, 49). Continuity of care is also essential when these patients are discharged into the community. Patients not only require monitoring but also strong nutrition educational support for managing their nutrition recovery independently. Interventions such as the provision of nutrition counselling in the community has been noted to improve indices of nutritional status (318, 319). This is specifically critical given that many of these patients are leaving on a therapeutic or modified diets that they are not accustomed to, which may lead to weight loss following discharge (320).

The present study had several strengths. Data were collected over a one-year period to minimize selection bias that could arise from seasonal variations and staffing turnover of health care professionals and trainees involved in nutrition care. Only patients who received MV for greater than 72 consecutive hours were recruited as these patients typically have higher severity of illness and are more prone to losing greater amounts of lean body mass (12) and developing swallowing disorders (200) in comparison to patients with a short ICU stay. Thus, they are likely at higher nutrition risk and may potentially benefit from more aggressive nutrition intervention and monitoring (260). Additionally, at this study site, no formal frameworks or pathways guiding the nutrition care of the critically ill as they transition from ICU to the wards exist, thus providing an opportunity to explore usual practices.

Any retrospective chart review comes with inherent limitations (321). The data abstractor was not blinded to the objectives and hypotheses of the study thus increasing the risk of reviewer bias (321), however an electronic data abstraction tool was created to ensure

data collection was consistent. Furthermore, the tool was designed to limit or restrict responses for variables, thus minimizing error and coder interpretation. A primary limitation was that we could only identify diets prescribed, but were unable to evaluate protein and calorie intake associated with these prescriptions. Thus, we are left to infer how prescribing practices continuing the use of EN or prescribing modified texture diets could positively or negatively impact intake. Likewise, we were unable to determine oral nutrition supplement (ONS) use due to the nature of the dietary order entry system. Use of ONS have been shown to be an effective strategy in increasing calorie and nutrient intake in hospitalized patients (295, 322) and it cannot be discounted that patients consuming modified diets were prescribed ONS to enhance intake. Furthermore, the primary decision makers and rationale behind implementation of nutrition care plans as it related to dietary prescription practices could not be elucidated which will be important to consider in future research. Lastly, as this was a single-site study, the application of these findings to other institutions where staffing ratios, types of patients treated, and nutrition care processes differ may be limited.

7.5 Conclusions

There is tremendous variation in the use of EN and dietary prescription practices in the recovering critically ill. Many patients are likely to be discharged on a modified diet and 1 in 5 continued to require EN therapy at the time of hospital discharge. These findings emphasize the importance of ensuring seamless continuity of care as patients transition through critical points along the trajectory of recovery. These data highlight the need to increase our understanding of the knowledge, values and beliefs of all health care providers regarding the nutrition care of patients recovering from critical illness, particularly as relates

to decision making. Perhaps more importantly, to provide patient-centered and effective care, more work must be done to characterize the attitudes and experiences of patients and their caregivers regarding nutrition in the context of rehabilitation from critical illness.

7.6 Relevance to clinical practice

Patients recovering from critical illness transition through several different types of diets and receive nutrition via multiple routes following LMV. It is essential that nutrition care is provided before, during, and after the patient is discharged from ICU. Given the high nutrition risk of the recovering critically ill, these patients should be consulted and monitored by ward dietitians upon transfer from the ICU to ensure nutrition care is not compromised. As many patients were observed to be discharged from hospital on therapeutic or modified diets or EN, proper discharge planning must occur and nutrition care plans be developed and communicated to patients or those responsible for their nutritional care following discharge. This should include a formal re-assessment of the patient's nutritional status (i.e. using Subjective Global Assessment) at the time of discharge to determine whether further dietary intervention is required and to monitor the response to interventions implemented as part of the nutrition care plan.

CHAPTER 8

GENERAL DISCUSSION

At the time of liberation from mechanical ventilation (LMV) and subsequent discharge from an intensive care unit (ICU), critically ill patients are likely to have developed disease-related malnutrition. There is a paucity of research examining nutrition recovery in ICU survivorship. Thus, the purpose of this thesis was to produce a body of literature examining nutrition recovery in the hospitalized, critically ill patient following LMV. While in-depth discussions have been included in each of the previous chapters summarizing the overall implications of the findings in each individual study, the purpose of this chapter is to provide a more general discussion summarizing key overarching themes identified from across the research studies presented in this thesis. Strengths and limitations to the work are discussed and recommendations for future research outlined. Lastly, implications of the collective findings of this research to clinical practice are discussed.

8.1 Summary of findings

A series of studies were performed to advance our knowledge on the nutritional characteristics of patients and processes that need to be considered for improving nutrition recovery in ICU patients following LMV. The studies examined feasibility to assess nutritional status and recovery, characterized nutrition intake in terms of nutrition delivery and meal intake patterns the first 7 days following LMV, and characterized dietary prescription practices occurring between LMV and hospital discharge. In their entirety, they illustrate key challenges and features of nutrition recovery that warrant consideration and further exploration.

The feasibility study (Chapter 4) examined the ability to properly assess nutritional status in patients following LMV. Here, standardized protocols used for measures of body composition (weight, mid-upper arm circumference, and phase angle) and physical function (hand-grip strength) were frequently violated or not obtained primarily due to the clinical disposition of the patients under investigation (Chapter 4). Predominantly, patients could not be mobilized or properly positioned due to muscular weakness, pain, agitation, or decreased consciousness thus precluding proper acquisition of these measurements. In contrast, weighed food records (WFR) were a feasible research tool to quantify daily protein and energy intake in patients prescribed oral diets (Chapter 4).

When protein and energy intakes were measured (Chapter 5), route of nutrition delivery (enteral nutrition versus oral) heavily influenced intake and adequacy of intake in relation to prescribed amounts (Chapter 5). The primary barriers to eating reported by patients largely related to the physiological effects of illness (Chapter 5). Further examination of meal and food intake patterns of patients prescribed non-modified diets (Chapter 6) demonstrated that patients consumed significantly less protein and energy than the amount provided to them. While no differences were observed in macronutrient and calorie intake between meals, examination of individual data revealed substantial variations in the amount of protein and calories consumed at individual meals and which meal times patients tended to consume greater calories and macronutrients (Chapter 6).

Lastly, dietary prescription practices in patients between LMV and hospital discharge were characterized in a retrospective chart review (Chapter 7). The findings from this study revealed that continued provision of enteral nutrition (EN) after patients were liberated from

mechanical ventilation (MV) is highly prevalent. The types of oral diets prescribed to patients following LMV varied considerably with respect to modifications to textures, fluids and therapeutic prescriptions, which may have diverse implications on nutrition recovery. At hospital discharge, just under half of patients were consuming diets requiring modifications to textures or fluids and one in five patients continued to receive EN therapy at the time of discharge (Chapter 7).

8.2 Critically ill patients present with unique characteristics that challenge our capacity to evaluate in-hospital nutrition recovery between liberation from mechanical ventilation and hospital discharge

There are several challenges that are highlighted in this thesis in assessing nutrition recovery in ICU patients following LMV: retention of patients in follow-up assessments is poor, performing measures to assess nutrition status are difficult because of illness-related effects, mixed routes and types of nutrition delivery, and the vast majority of survivors are discharged to another facility rather than home which presents challenges in long-term follow-up. In the prospective, feasibility study (Chapter 4), 32% of recruited patients were lost to follow-up by day 7. This short time to hospital discharge and high loss to follow-up highlights a primary challenge faced to prospectively studying in-hospital nutrition recovery. To grasp a better understanding of true nutrition recovery and facilitate acquisition of sensitive longitudinal measures of nutrition status in survivorship, we need more robust research before hospital discharge and we also need to extend research beyond hospital discharge. To improve recruitment and retention, we need to thoroughly examine the reasons for inability to recruit and retain patients in future studies.

The ability to perform hands-on assessments on ICU patients post-LMV is challenging. Understanding nutritional status prior to discharge is limited but highly important in this cohort of patients. Widely used tools to assess nutritional status in non-critically ill, hospitalized patients include weight, mid-upper arm circumference (MAC), and hand-grip strength (HGS) (13, 323). We have shown that these measures are not easily obtained or feasible to perform using validated protocols in critically ill patients after LMV (Chapter 4). This may in part explain why few studies have measured nutritional status in the recovering critically ill. These limitations in measures may also explain the basis for exclusion from large-scale studies assessing malnutrition in hospitalized patients (217, 324). Therefore, little is known about the nutritional status of this unique patient cohort that is no longer under the auspices of ICU care, and this may be due in part to inadequate measures. New approaches or modified existing protocols need to be developed to provide more consistent and interpretable methods for assessing nutritional status in this group of patients.

The critically ill patient who is post-LMV is distinct from the non-critically ill patient due in part to the significant functional, cognitive and psychological morbidities that develop secondary to an ICU admission (1, 2). In our feasibility study (Chapter 4), some of the most prominent barriers to acquiring measures of nutritional status related to significant muscular weakness preventing proper positioning required for the tests performed and decreased level of consciousness preventing participation to complete the tests (Chapter 4). To better understand nutrition recovery, acquisition of baseline measurements taken at the time of or shortly after LMV is essential so comparisons can be made along the recovery trajectory. These findings emphasize the need to develop and validate sensitive measurement tools for assessing indices of nutritional status that are feasible to perform in these patients.

Assessment of dietary intake has distinct complexities in critically ill patients following LMV. For patients consuming oral diets, intake at each meal was measured using WFR (Chapter 4, Chapter 5, Chapter 6), a method characterized as the gold standard of quantitative dietary assessment due to its high degree of precision and accuracy (174, 208, 209, 261). In previous studies examining intake in the critically ill following LMV, intake was assessed using dietary recall by a trained investigator (21) or dietary records completed by nursing staff (22), both of which are less precise and more prone to reporting error (174, 208, 210). Assessment of dietary intake using WFR minimized missed or incomplete intake measurements as many of the patients recruited were not capable of recall due to decreased consciousness or altered cognition (i.e. delirium and agitation) (Chapter 4), and caregivers were not present at every meal each day for proxy reporting. We therefore obtained a comprehensive assessment of macronutrient and calorie intake (discussed in Chapter 3, Section 3.4.2.3), which has not previously been done and advances our knowledge of nutrition recovery in the critically ill.

In the retrospective chart review (Chapter 7), half of the patients who survived their hospital admission were discharged to locations other than home, including repatriation to referring hospitals, rehabilitation programs, and long-term or complex care, which is consistent with previous work that has reported on discharge destinations of critically ill patients (43, 325). In contrast, a recent Canadian study examining changes in weight in non-critically ill patients following hospital discharge reported 94% of patients, for whom discharge data was available, were discharged home (320). Our data together with others who have examined discharged destinations in ICU patients, emphasize a unique challenge in studying nutrition recovery in critically ill versus non-critically ill following a hospital stay.

Completing hands-on follow-up measurements (i.e. measures of body composition) in patients who are discharged to other facilities may not always be practical or feasible, and the trajectory of nutrition recovery is likely to differ in patients who continue to receive nutrition care at facilities versus those who are discharged home.

8.3 Protein and energy intake is inadequate following liberation from mechanical ventilation: delivery route, food intake patterns and barriers need careful consideration

For the first time in a group of MSICU patients, we have quantified protein and energy intake in patients receiving nutrition via any route (EN and oral; no patients recruited were receiving parenteral nutrition) (Chapter 5). In the two previous studies examining post-LMV intake in MSICU patients, one (152) only examined intake in patients consuming oral diets while the other (22) measured intake in patients receiving nutrition by any route, but did not examine differences in intake between route. Furthermore, Nematy et al. (22) only measured calorie (and not protein) intake. Following LMV, up to 84% of patients continued to receive EN for at least one day following LMV (Chapter 5, Chapter 7) and this proportion varied thereafter. Impressively, those that continued with EN (in combination with NPO or PO) had better intakes compared with PO only. Thus, this inclusive data set provided a more thorough understanding of nutrition recovery in all versus only a small and selective group of critically ill patients through the early trajectory of LMV.

We showed that MSICU patients who continue to receive EN following LMV have higher absolute daily protein and energy intake compared to patients consuming oral diets (Chapter 5). Dietary requirements are influenced by factors such as sex, age, and weight and protein and energy recommendations for critically ill and hospitalized patients are typically

based on these variables (107, 162, 326). The patients studied were between 20 and 90 years of age and ICU admission weight ranged from 43 to 186 kg (Chapter 5 and Chapter 7), which attests to the heterogeneity of the patients studied. Thus, examination of average absolute daily intakes across all patients prevents interpretation of whether intake is “sufficient” or “insufficient” to meet the needs of individual patients. In contrast, examining intake in relation to amounts prescribed by dietitians during usual care (“adequacy of intake”) and in relation to weight (i.e. grams of protein and total calories per kilogram body weight per day), as we have done, provided the opportunity to evaluate adequacy of intake and differences between routes of delivery as well as make comparisons to previous studies. Regardless of the approach used to assess adequacy, it is important to consider the influence that these approaches have on interpreting data and clinical results in terms of over- or under-estimating adequacy.

In spite of this suboptimal ability to measure energy and protein requirements, median adequacy of protein and energy intake was 100% for patients who continued to receive EN exclusively post-LMV, meaning they were meeting their estimated dietary requirements. In contrast, adequacy was only 27% and 47% for protein and energy, respectively, when patients were consuming oral diets (Chapter 5). Thus, patients consuming oral diets are at high risk of experiencing a decline in nutritional status as they are not consuming sufficient nutrients to maintain health and promote recovery.

While there are no guidelines for feeding a critically ill patient in recovery, minimum recommendations for mechanically ventilated patients are 1.2 g protein/kg body weight and 25 kcal/kg body weight (162, 163, 165). In recovery, patients receiving EN were closer to

meeting these thresholds (median intake: 1.2 g protein/kg/d and 19 kcal/kg/d) (Chapter 5) than patients consuming oral diets (0.40-0.45 g protein/kg/d and 9-11 kcal/kg/d) (Chapter 5 and Chapter 6), who consumed well below these thresholds. This has considerable implications as decreased protein and energy intake is a risk factor for malnutrition (13, 273), thus patients consuming oral diets in the early phases of recovery could be at high risk for developing health complications associated with malnutrition (19) and experience prolonged recovery. In contrast, our evidence suggests that this risk may be mitigated if patients do not have EN access devices hastily removed following LMV and thus continue to receive EN to ensure adequate protein and calories are consumed. However, to fully understand the influence of protein and energy intake on changes in nutritional status and physical recovery, feasible and validated tools to assess nutritional status must be developed.

Among patients consuming oral diets, we identified several barriers to eating that reflected common physiological effects of illness including poor appetite, early satiety, taste changes, nausea and vomiting, and difficulty swallowing (Chapter 5). These factors have consistently been identified as barriers to eating in the recovering critically ill (21, 22, 24, 26), and are not easily resolved. Furthermore, a high proportion of patients were diagnosed with oropharyngeal dysphagia (OPD) (Chapter 5 and Chapter 7), a condition that affects up to 84% of patients who required endotracheal tube intubation (200, 303). OPD is commonly treated by prescription modified texture and/or fluid diets (310-312), which were widely prescribed to patients during their post-LMV hospital stay (Chapter 5 and Chapter 7). In fact, characterization of prescribing practices led to the observation that 12 different types of texture/fluid modified diets were prescribed with or without one of four different therapeutic types (i.e. cardiac, diabetic, renal, low sodium) (Chapter 5 and Chapter 7). Prescription of

modified diets have are associated with poor intake in the recovering critically ill (21, 24), and as a large proportion of patients will be prescribed a modified diet in the recovery trajectory (Chapter 7), it is clear this cohort of patients is nutritionally vulnerable.

It should be noted, however, that a novel finding from this research is that we observed the regular, non-modified diets provided to patients to be insufficient in protein and calories (Chapter 6), which is incongruent with previous observations in non-critically ill patients (287). However, patients only consumed 60% of what was provided. Interestingly, when meal patterns were examined, it became apparent that the “best meal of the day” (in terms of when the most calories and energy were consumed) was quite variable between patients (Chapter 6). This, along with the numerous barriers faced to consuming adequate nutrition (Chapter 5) and with the variability in food preferences, highlights the need for individualized nutrition therapies to best meet the needs of patients.

8.4 Nutrition care approaches are inconsistent and may compromise continuity of care in survivors of critical illness

Multiple evidence-based clinical guidelines exist for feeding the critically ill, mechanically ventilated patients (162, 163, 165). These guidelines provide several recommendations including how to feed patients (i.e. EN and/or parenteral nutrition), timing of initiation of feeding following admission to ICU, and amount of protein and calories to feed (162, 163, 165). In contrast, no guidelines exist for how and what to feed patients following LMV and findings from this thesis shed light on current nutrition practices.

In this thesis, nutrition care, primarily as it relates to dietary prescription practices, was observed in two critical junctures in the trajectory of critical illness: transition from the

ICU to the ward following LMV, and at time of hospital discharge (49, 90). Following LMV, we demonstrated considerable variability in the continued use of EN, timing of initiation of oral diets, and types of oral diets prescribed (Chapters 5 and 7). At the hospital where this research was conducted, no formal pathways, protocols or checklists (beyond verbal transfer of nutrition care between dietitians) to guide nutrition care as patients enter the early stages of ward-based recovery exist. Almost all patients followed were assessed and monitored by a dietitian while in ICU, but only 65% continued to be followed by a ward RD after transfer from the ICU (Chapter 7). This is not to say that all patients discharged from the ICU require further monitoring by a dietitian, and for this to occur would not be feasible due to workload and staffing ratios. However, these findings emphasize the importance of shifting the institutional culture to one that both recognizes the importance of continuity of nutrition care, educates and empowers patients and caregivers, and understands the unique nutrition care needs of the recovering critically ill patient (24, 317).

To create a culture that values continuity of nutrition care, awareness that this type of care of hospitalized patients is not just the responsibility of dietitians, but of the entire care team is critical (317). Notably, speech-language pathologists (SLPs) are integral members of the health care response to supporting patients during these transitions given their knowledge and skills related to swallowing assessment and treatment of OPD. In our studies, SLPs were frequently involved in the care of patients (Chapters 5 and 7) due to the high prevalence of OPD that occurs in the recovering critically ill (200, 303). For patients diagnosed with OPD, the SLP will make a determination as to whether a patient is safe to consume food by mouth and whether a modified texture diet is required (310, 327). Recommendations from an SLP thus directly influence the nutritional care of the patient and highlight the importance of

coordinated care between the SLPs and dietitians in managing patients with post-extubation dysphagia to ensure their nutrition is not compromised (328, 329).

Nutrition care for ICU survivors beyond hospital discharge has not been investigated with exception of one study conducted in the UK (26). In this qualitative study, survivors of critical illness often did not receive ongoing nutrition care in the community, yet they expressed concerns about their nutritional health and desired strategies to improve it (26). Interestingly, at the time of hospital discharge, the dietitian frequently provided patients with a supply of oral nutrition supplements (ONS) to continue consuming at home, but often they were not consumed (26). In Ontario, Canada, public funds to subsidize the cost of ONS for community-dwelling individuals are only available for individuals on disability (enrolled into the Ontario Disability Support Program) who meet strict criteria (330). Thus, for most patients, the cost of ONS is their responsibility, which could also discourage use.

Recovering critically ill patients are likely to be malnourished at discharge due to chronic undernutrition during the post-LMV hospital stay (Chapter 5 and Chapter 6) and two-thirds of whom would be receiving modified and/or therapeutic diets at the time of discharge which is associated with post-discharge weight loss (320) and poor nutrition recovery. To ensure continuity of care, patient-centered discharge planning that incorporates nutrition care, education, and referrals to community supports and resources will be vital to enhancing the nutrition recovery of patients (317, 331).

8.5 Strengths and limitations

Throughout the thesis, various strengths and limitations have been outlined. Here, I would like to highlight key areas that form the foundation for future directions. As iterated in

Chapters 4-6, a major strength of the prospective, observational feasibility study related to the robust nature of dietary assessment that facilitated a comprehensive analysis of nutrient intake, adequacy of intake, and food and meal intake patterns. As many of the patients studied had decreased consciousness or cognitive impairment, dietary intake as measured by WFR versus recall methods ensured a complete set of measurements was obtained. In the retrospective chart review (Chapter 7), all patients admitted to ICU within a one-year period that were eligible for inclusion were evaluated. This strategy minimized selection bias that can arise from seasonal variations and rotating staffing schedules. The data abstraction tool developed for this study was pilot tested prior to formal data collection was started. The tool was also designed such that only specific responses for code variables could be inputted, thus minimizing data entry error and interpretation bias.

The major limitations of the prospective study (Chapters 4-6) related to small sample size, however as this was a feasibility study, a rich set of data was obtained that will help guide the development of future studies. Our ability to perform statistical analyses were limited due to small sample sizes, missing data (for measures of body composition and HGS that were not obtainable), variable lengths of stay and high loss to follow-up. However, small sample sizes provided an opportunity to look at individual data which revealed substantial variability, particularly with respect to intake and meal patterns, that was not apparent when all data were collapsed together. In Chapter 5, comparisons in intake between patients consuming EN versus oral diets could not be made as many patients received both types of nutrition over the recovery trajectory and thus observations were not independent.

Importantly, all studies were conducted at a single-site and thus the findings may not have external validity. There are distinct features that vary from site to site that can influence our findings. For example, the capacity for extensive assessments and follow-up by registered dietitians and SLP's are specific to an institution and can influence the type and route of nutrition delivery for this group of patients. Moreover, the culture of the institution in integrating and collaborating expertise from different disciplines will also mold the prescription practices for this patient population. And finally, the type of patients and etiology for patient ICU admission will vary amongst sites, which may ultimately have implications on nutrition practices and outcomes. Clearly, there will be differences in rural versus urban communities as well as community versus academic facilities; exploring these diversities may be helpful prior to embarking on multi-center studies.

8.6 Future directions

8.6.1 Development and validation of measurement tools for assessing nutritional status of recovering critically ill patients are required

This thesis has demonstrated that tools to evaluate body composition and physical function, key indices of nutritional status (13, 15, 201), are not easily obtained or feasible to perform in critically ill patients during the initial recovery stages of illness. To effectively determine whether optimization of nutritional status can improve outcomes in survivors of critical illness, it is essential that new protocols for measurement tools that were not deemed feasible be tested and validated specifically in the recovery critically ill. Furthermore, we must look to new and emerging technologies that may facilitate assessment of nutritional status. For example, use of ultrasound to measure muscle mass is a technique that is applied

at the bedside and shows promise as a reliable and objective method of body composition in the critically ill (332-334).

8.6.2 What are the current knowledge, attitudes and practices of the health care team regarding the nutrition care of recovering critically ill patients?

The research presented in this thesis was observational in nature: nutrition intake was measured and dietary prescription practices observed. However, we were not able to obtain a comprehensive assessment as to why intake was poor, why specific diets were prescribed, why (or why not) and how were patients transitioned from EN to an oral diet, what factors influence whether a patient receives dietitian consultations, and which members of the interprofessional team are involved in providing nutrition care. Addressing these questions is a fundamental step to better understanding nutrition care in the recovering critically ill patient. However, this step is also elemental to building an institutional culture that fosters collaboration in improving transition of care and nutrition practices for ICU patients post-LMV. Thus, it is essential to garner an understanding of the knowledge, attitudes and practices of all health care providers (i.e. physicians, nurses, dietitians, SLPs, occupational and physical therapists, respiratory therapists, discharge planners) who provide nutrition care to the critically ill in and out of the ICU.

8.6.3 Testing nutrition interventions: can delaying discontinuation of enteral nutrition therapy following liberation from mechanical ventilation improve nutrition recovery?

One of the primary findings of this thesis was that patients who continue to receive EN following LMV consume sufficient protein and energy to meet their estimated requirements. As reported in Chapter 7, many patients receive EN while ventilated and thus

have enteral access devices *in situ* at the time of LMV. Given our understanding of how little patients consume when oral diets are prescribed following LMV, it would make intuitive sense to continue providing patients with EN until they demonstrate the ability to consume sufficient protein and energy. However, there are several factors that must be evaluated before such a broad recommendation can be implemented. These include:

- First and foremost, would provision of adequate protein and energy to meet a patient's estimated requirements via EN impact changes to clinical meaningful outcomes such as repletion of lean tissue stores, return of physical functioning?
- Are there certain types of critically ill patients who would benefit from continued aggressive nutrition therapy following LMV? For example, would patients who had longer ICU length of stay, longer duration of MV, higher severity of illness or increased comorbidities at ICU admission be at higher nutrition risk specifically at the time of LMV?
- If EN continues to be provided several days following LMV, what is the optimal delivery schedule (i.e. bolus, intermittent, nocturnal feeding), how and when should a patient be transitioned back to an oral diet, and when should gastrostomy tubes be inserted for longer-term EN therapy?
- What risks are associated with continued provision of EN? Will swallowing function be negatively affected by presence of nasogastric feeding tubes?
- What are the costs and resources associated with continued use of EN?
- What is the acceptability of such an intervention to the patient?

Clearly, continuation of EN following LMV may present as an approach that may improve nutrition intake in patients early following LMV. However, there are important questions that should be addressed to evaluate the implications of this approach in terms of optimal outcomes for patients and feasibility in practice.

8.7 Implications for dietetic practice

There is a plethora of literature examining aspects of nutrition care in critically ill patients, however only recently has an awareness begun to emerge regarding the unique care needs of the recovering critically ill patient. This group of patients emerges from the ICU with physical, cognitive, and psychological dysfunction that have developed over the course of ICU stay. Physical dysfunction may be secondary to ICU-acquired weakness (ICU-AW), which manifests as myopathies and polyneuropathies that occur specifically during critical illness. This constellation of health-related morbidities has been termed *post-intensive care syndrome* (PICS), and from a dietetics perspective, it is essential for dietitians to be aware that these syndromes exist. Knowledge of the factors driving disease-related malnutrition over the course of critical illness, combined with an understanding of ICU-AW and PICS should be considered when prioritizing patient care and determining the need for dietitian services, particularly for ward dietitians receiving patients from ICU. Most importantly, the need for an interprofessional approach is crucial to enhance recovery of the critically ill patient. The data from this research were observational and exploratory in nature, and no interventions were tested, thus specific and targeted recommendations for improving the nutritional care of the critically ill cannot be made. However, this research will hopefully

serve to heighten awareness of the nutritional vulnerability of this very unique group of patients, as well as highlight the importance of interprofessional and patient-centered care.

8.8 Conclusions

The body of work summarized in this thesis is the first in Canada to explore aspects of nutrition recovery in critically ill patients during the early stages on ward-based recovery. Feasible and validated tools to properly assess nutritional status in this unique group of patients are required, as is the need for the development of interventions to enhance protein and energy intake in recovery. Due to the heterogeneity of the patients observed, nutrition interventions delivered by practicing clinicians should be as individualized as possible to achieve optimal outcomes. Collectively, the findings from this work emphasize the need for future research that aims to better understand factors influencing nutrition recovery in the critically ill as they transition into the recovery phase of the trajectory of illness. Development of feasible and validated tools to assess nutritional status and determine the extent to which nutrition recovery is occurring are essential, as are the development of targeted and multidisciplinary nutrition interventions to augment recovery.

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APPENDICES

APPENDIX A

PROSPECTIVE STUDY ETHICS APPROVAL FORMS



Research Ethics

Western University Health Science Research Ethics Board HSREB Full Board Initial Approval Notice

Principal Investigator: Dr. Adam Rahman
Department & Institution: Schulich School of Medicine and Dentistry/Gastroenterology, St. Joseph's Health Care London

HSREB File Number: 105268
Study Title: A comprehensive evaluation of nutritional status and physical function in critically ill patients after extubation.
Sponsor: Canadian Foundation for Dietetic Research

HSREB Initial Approval Date: October 17, 2014
HSREB Expiry Date: May 31, 2016

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Sponsor Protocol	Study Protocol (received for information only)	2014/04/17
Western University Protocol	Revised Western University (ROMEO) Protocol - clean version (PDF)	2014/08/12
Data Collection Form/Case Report Form	Dietary Intake Assessment: Weighed Food Intake Form (APPENDIX C1)	2014/08/12
Data Collection Form/Case Report Form	Factors Affecting Dietary Intake Assessment Form (APPENDIX C2)	2014/08/12
Data Collection Form/Case Report Form	Modified Patient-Generated Subjective Global Assessment Form (Appendix A)	2014/08/12
Other	Revised and Amended Study Protocol - clean version (PDF) (received for information only)	2014/08/12
Letter of Information & Consent		2014/10/15
Caregiver Letter of Information & Consent		2014/10/15
Instruments	APPENDIX D: Confusion Assessment Method for the ICU Worksheet	2014/04/17
Instruments	APPENDIX B: Barthel Activities of Daily Living Index Form	2014/03/11

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review. If an Updated Approval Notice is required prior to the HSREB Expiry Date, the Principal Investigator is responsible for completing and submitting an HSREB Updated Approval Form in a timely fashion.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.


Ethics Officer, on behalf of Dr. Joseph Gilbert, HSREB Chair

Ethics Officer to Contact for Further Information

Erika Basile ebasile@uwo.ca	Grace Kelly grace.kelly@uwo.ca	Mina Mekhal mmekhal@uwo.ca	Mikki Tran mikki.tran@uwo.ca
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This is an official document. Please retain the original in your files.

UNIVERSITY OF WATERLOO
OFFICE OF RESEARCH ETHICS

Notification of Ethics Clearance of Application to Conduct Research with Human Participants

Principal/Co-Investigator: Marina Mourtzakis	Department: Kinesiology
Principal/Co-Investigator: Heather Keller	Department: Kinesiology
Student Investigator: Lesley Moisey	Department: Kinesiology
Collaborator: Adam Rahman	Department: Department of Medicine, University of Western Ontario
Collaborator: Daren Heyland	Department: Clinical Evaluation Research Unit, Kingston General Hospital

ORE File #: 19766

Project Title: A comprehensive evaluation of nutritional status and physical function in critically ill patients after extubation.

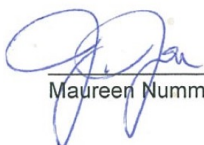
This certificate provides confirmation the above project has been reviewed in accordance with the University of Waterloo's Guidelines for Research with Human Participants and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. This project has received ethics clearance through a University of Waterloo Research Ethics Committee.

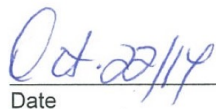
Note 1: *This ethics clearance is valid for one year from the date shown on the certificate and is renewable annually. Renewal is through completion and ethics clearance of the Annual Progress Report for Continuing Research (ORE Form 105).*

Note 2: *This project must be conducted according to the application description and revised materials for which ethics clearance has been granted. All subsequent modifications to the project also must receive prior ethics clearance (i.e., Request for Ethics Clearance of a Modification, ORE Form 104) through a University of Waterloo Research Ethics Committee and must not begin until notification has been received by the investigators.*

Note 3: *Researchers must submit a Progress Report on Continuing Human Research Projects (ORE Form 105) annually for all ongoing research projects or on the completion of the project. The Office of Research Ethics sends the ORE Form 105 for a project to the Principal Investigator or Faculty Supervisor for completion. If ethics clearance of an ongoing project is not renewed and consequently expires, the Office of Research Ethics may be obliged to notify Research Finance for their action in accordance with university and funding agency regulations.*

Note 4: *Any unanticipated event involving a participant that adversely affected the participant(s) must be reported immediately (i.e., within 1 business day of becoming aware of the event) to the ORE using ORE Form 106. Any unanticipated or unintentional changes which may impact the research protocol must be reported within seven days of the deviation to the ORE using ORE form 107.*


Maureen Nummelin, PhD


Date



LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-14-409

PROJECT TITLE: A comprehensive evaluation of nutritional status and physical function in critically ill patients after extubation.

PRINCIPAL INVESTIGATOR: Dr. Adam Rahman

LAWSON APPROVAL DATE: February 9, 2015

Health Sciences REB#: 105268

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and Lawson Administration and the project:

Was Approved

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill
V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Lawson Approval Number and should be directed to Sherry Paiva, Research Approval Officer, Lawson Health Research Institute, 750 Baseline Road, East, Suite 300.

cc: Administration

APPENDIX B

RETROSPECTIVE CHART REVIEW ETHICS APPROVAL FORMS



**Western University's Health Sciences Research Ethics Board (HSREB) and the University of Waterloo Clinical Research Ethics Committee (CREC)
Delegated Initial Approval Notice ****Revised******

Principal Investigator: Dr. Michael Sharpe
Department & Institution: Schulich School of Medicine and Dentistry\Anaesthesia, London Health Sciences Centre

Review Type: Delegated
HSREB File Number: 108319
University of Waterloo File Number: 21670
Study Title: Incidence and impact of early discontinuation of enteral nutrition in hospitalized, critically ill patients following endotracheal tube liberation from mechanical ventilation: a retrospective chart review.

Initial Approval Date: August 26, 2016
Expiry Date: August 26, 2017

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Revised Western University Protocol	Received August 22, 2016	
Data Collection Form/Case Report Form		2016/08/11
Other	Site Study Protocol	2016/07/04

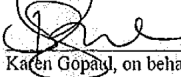
Western University's HSREB and the University of Waterloo's CREC has reviewed and approved the above named study, as of the Initial Approval Date noted above.

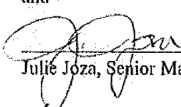
Approval for this study remains valid until the Expiry Date noted above, conditional to timely submission and acceptance of the Continuing Ethics Review.

Western University's HSREB and the University of Waterloo CREC operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of both institutions REB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940. The University of Waterloo CREC is registered under IRB 00007409.


Karen Gopal, on behalf of Western Universities HSREB Chair/Vice Chair

and

Julie Joza, Senior Manager, on behalf the University of Waterloo CREC.



LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-16-450

PROJECT TITLE: Incidence and impact of early discontinuation of enteral nutrition in hospitalized, critically ill patients following endotracheal tube liberation from mechanical ventilation: a retrospective chart review.

PRINCIPAL INVESTIGATOR: Dr. Michael Sharpe

LAWSON APPROVAL DATE: October 26, 2016

Health Sciences REB#: 108319

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and Lawson Administration and the project:

Was Approved

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill
V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Lawson Approval Number and should be directed to Sherry Paiva, Research Approval Officer, Lawson Health Research Institute, 750 Baseline Road, East, Suite 300.

cc: Administration

APPENDIX C

SAMPLE MENU SELECTION FORM

Monday REG		Monday REG		Monday REG		Monday REG	
Breakfast		Lunch		Dinner		Dinner	
7/03/13		3		3		3	
2282293		10139441		10139441		10139441	
Cereal		Appetizers		Appetizer			
027 Cheerios	029 Gluten Free Rice Chex	172 Marinated Bean Salad	174 Vegetable Soup	283 Cranberry Spring Mix Salad			
036 Fibre One	031 Rice Krispies			275 Raspberry Poppyseed Drsg			
038 Cream of Wheat				281 Ranch Salad Dressing			
043 Oatmeal							
Breakfast Fare		Entrees		Entrees			
012 Lemon Cranberry Muffin/ Cheddar Cheese	083 Chicken Strips & Potato Wedge & Plum Sce	196 Roasted Pork Loin with Mushroom Sauce	198 Tomato Beef Macaroni Casserole				
014 Creamy Peach Yogurt	095 Deli Salmon Sandwich on Brown						
016 Chilled Hard Cooked Egg	097 Vegetarian Stew						
047 Fresh Diced Fruit Salad							
049 Pumpkin Muffin							
051 Cream Cheese Mini Bagels							
Spreads		Desserts		Desserts			
045 Margarine	056 Strawberry Jam	179 Butterscotch Pudding	180 Fresh Apple	310 Mashed Potato			
	058 Peanut Butter	185 Pineapple Tidbits		321 Peas & Carrots			
Beverages		Breads and Spreads		Breads and Spreads			
071 Coffee	082 2% Milk	107 Whole Wheat Bread		287 Banana Cake			
076 Tea	084 1% Milk	109 White Bread		290 Diced Honeydew			
078 Decaf Coffee	018 Apple Juice	120 Crackers		326 Chocolate Chip Cookie			
023 Orange Juice		105 Margarine					
025 Prune Juice							
062 Sugar	089 Milkette						
064 Sweetener	091 Lemon Juice						
069 Brown Sugar							
U-9	A9-106-A	U-9	A9-106-A	U-9	A9-106-A	U-9	A9-106-A
	10139441		10139441		10139441		10139441

APPENDIX D

WEIGHED FOOD RECORD FORM

Dietary Intake Assessment: Weighed Food Intake & Dietary Recall

RESEARCH ASSISTANT: _____ MEAL: Breakfast/Lunch/Dinner _____ DATE: _____ (DD / MM / YYYY) TIME: _____ PATIENT ID: _____ STUDY DAY: _____

DIET ORDER: _____

	Food Item	Source <small>(i.e. hospital, home, vendor etc.)</small>	Portion Size* <small>(g or mL)</small>	Measured Waste** <small>(g or mL)</small>	Comments <small>(i.e. portion consumed, time snacks or foods from home consumed etc.)</small>
	<i>i.e. plain chicken breast, 1 whole, minced texture</i>	Hospital		36.5 g	
	<i>i.e. Coffee with 1 tsp sugar</i>	Tim Horton's	Medium	all	<i>Pt reporting consuming all of it at ~10:00 am</i>
Main entrée / Protein:					
Starch:					
Vegetable:					
Fruit:					
Dessert:					
Beverage:					
Beverage:					
Beverage:					
Condiments:					

* If known. Portion sizes of hospital prepared foods will be obtained from the Food Services Department.
 ** If waste cannot be measured (i.e. food containers thrown out etc), please ask patient to estimate amount consumed (i.e. none, 1/4, 1/2, 3/4, all). Document in the comments section.
 *** If the meal is a mixed meal/entrée, i.e. lasagna, please record amount consumed. If a mixed meal from home, document ingredients/recipe if able to. *See over for more space.*

	Food Item	Source <i>(i.e. hospital, home, vendor etc.)</i>	Portion Size* <i>(g or mL)</i>	Measured Waste** <i>(g or mL)</i>	Comments <i>(i.e. proportion consumed, time snacks or foods from home consumed etc.)</i>
Supplements:					
Other(s):					

COMMENTS:

APPENDIX E

NUTRITION PRESCRIPTION AND EN/PN INTAKE LOG

NUTRITION PRESCRIPTION, ENTERAL / PARENTERAL INTAKE LOG & SLP ASSESSMENT HISTORY	PT ID: _____
---	---------------------

Date (dd/mm/yyyy)	Study Day	Nutrition Rx (EN/PN & PO Diet)	EN/PN/Propofol Received	Vitamin / Mineral Supplements
	1	Date of Nutr Rx: _____, by _____ Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx:	kcal received: ____ g protein rcv'd: ____	
	2	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	
	3	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	
	4	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	
	5	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	
	6	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	
	7	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: <p style="text-align: right;"><i>Same as Above</i></p>	kcal received: ____ g protein rcv'd: ____	

**NUTRITION PRESCRIPTION,
ENTERAL / PARENTERAL INTAKE LOG &
SLP ASSESSMENT HISTORY**

PT ID: _____

DATE (dd/mm/yyyy)	STUDY DAY	PO DIET Rx and/or NUTRITION SUPPORT Rx	NUTRITION SUPPORT RECEIVED	VITAMIN/ MINERAL SUPPLEMENTS
	8	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	9	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	10	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	11	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	12	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	13	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above		
	14	Rx (EN/PN): Provides: _____ kcal, _____ g protein PO Diet Rx: Same as Above	kcal received: ____ g protein rcv'd: ____	

**NUTRITION PRESCRIPTION,
ENTERAL / PARENTERAL INTAKE LOG &
SLP ASSESSMENT HISTORY**

PT ID: _____

SLP Consults

DATE (dd/mm/yyyy)	STUDY DAY	Seen by SLP? (Y/N)	SLP Recommendation
	1		
	2		
	3		
	4		
	5		
	6		
	7		
	8		
	9		
	10		
	11		
	12		
	13		
	14		

APPENDIX F

BODY COMPOSITION AND HAND-GRIP STRENGTH DATA COLLECTION FORM

BODY COMPOSITION & HGS DATA COLLECTION FORM

PATIENT ID:

Study Day (circle): 1 4 7 14

Date & Time of Assessments: 20 Y Y M M D D H H : M M 24 hour clock

Height (cm): _____

Weight (kg): _____

Knee Height (cm): _____

How was weight obtained? (i.e. chart, scale, lift, reported/estimated)

Hand-Grip Strength

Patient's dominant hand (circle): left right

Measurements (Left hand / Right hand):

Has the patient experienced recent injury to hand/arm or have any conditions that contraindicate testing? Yes No
If Yes, please state: _____

1) _____ / _____ kg
2) _____ / _____ kg
3) _____ / _____ kg

Circumferences

Circumference	Left Side	Right Side	Sitting / Supine
Mid-Upper Arm (cm)			
Calf (cm)			

Notes: *i.e. reasons test cannot be completed, edema, IV lines etc.*

Bioelectrical Impedance Analysis (BIA)

Does the pt have a pacemaker or any implantable electronic device? **YES NO**

If YES, do NOT perform this test

Quadscan Test Number: _____

Comments: _____

Impedance: 5kHz: _____ 50kHz: _____

100kHz: _____ 200kHz: _____

Prediction Marker: _____

Resistance: _____ Reactance: _____

Phase Angle: _____

APPENDIX G

BARRIERS TO INTAKE AND APPETITE RATING FORM

Assessment of Factors Affecting Nutrition Intake

RESEARCH ASSISTANT: _____ PT ID: _____

STUDY DAY: _____ DATE: ____/____/____ TIME: _____
(DD / MM / YYYY)

How would you rate your appetite today? _____ (numerical score)



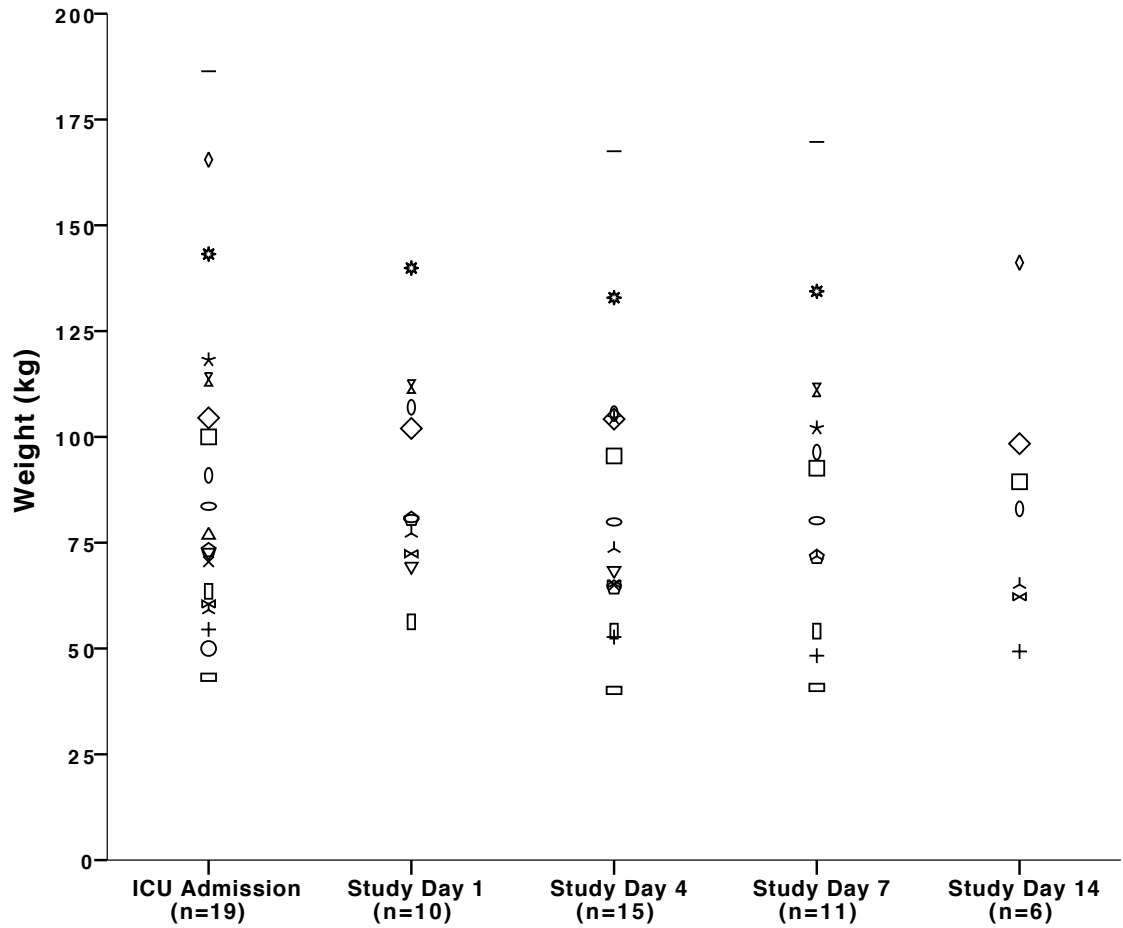
Primary Barriers to Eating Today

Rank the top 3 barriers you experienced by putting the numbers 1, 2 and 3 in the respective boxes. If you did not experience any barriers to eating, place a checkmark in the “No barriers to eating” box.

- | | |
|--|--|
| <input type="checkbox"/> Poor appetite
<input type="checkbox"/> Nausea / Vomiting
<input type="checkbox"/> Difficulty chewing
<input type="checkbox"/> Difficulty swallowing
<input type="checkbox"/> Constipation
<input type="checkbox"/> Physical fatigue
<input type="checkbox"/> Dry mouth
<input type="checkbox"/> Mouth sores
<input type="checkbox"/> Pain. (Where? _____)
<input type="checkbox"/> Feeling depressed
<input type="checkbox"/> No barriers to eating | <input type="checkbox"/> Missed meal (i.e. due to tests)
<input type="checkbox"/> Meal interruptions
<input type="checkbox"/> Unsuitable serving times
<input type="checkbox"/> Food out of reach
<input type="checkbox"/> Not in a comfortable position to eat
<input type="checkbox"/> Difficulty using utensils
<input type="checkbox"/> Difficulty with food packaging
<input type="checkbox"/> Feel full quickly
<input type="checkbox"/> Things taste funny or have no taste
<input type="checkbox"/> Dislike the food
<input type="checkbox"/> Other (please state):

<hr style="width: 100%; border: 0; border-top: 1px solid black; margin-bottom: 5px;"/> <hr style="width: 100%; border: 0; border-top: 1px solid black;"/> |
|--|--|

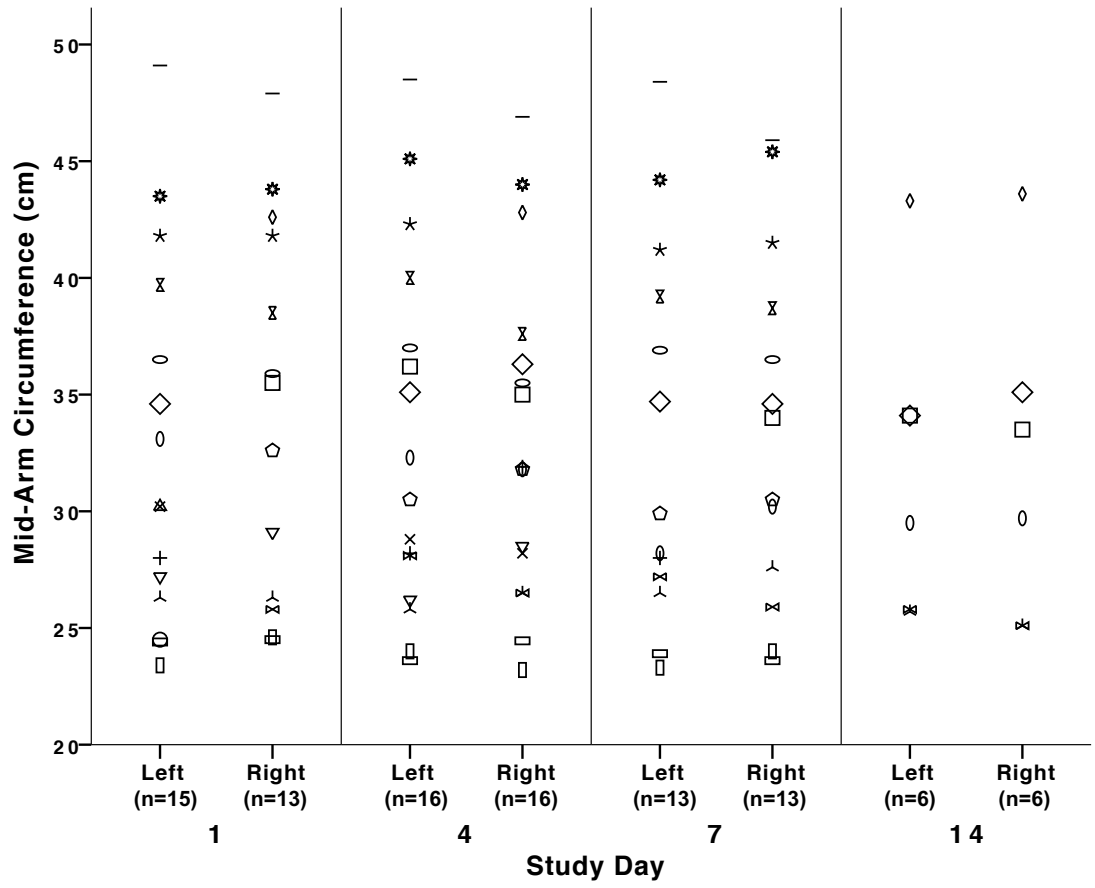
APPENDIX H
INDIVIDUAL MEASURES OF BODY COMPOSITION AND PHYSICAL
FUNCTION IN CRITICALLY ILL PATIENTS FOLLOWING LMV



Median (kg)	77	81	74	86	83
IQR (kg)	61, 114	72, 108	64, 105	58, 109	62, 98
Min, Max (kg)	43, 186	56, 140	40, 168	41, 170	49, 141

Figure H - 1 Weight (kg) over the duration of the study

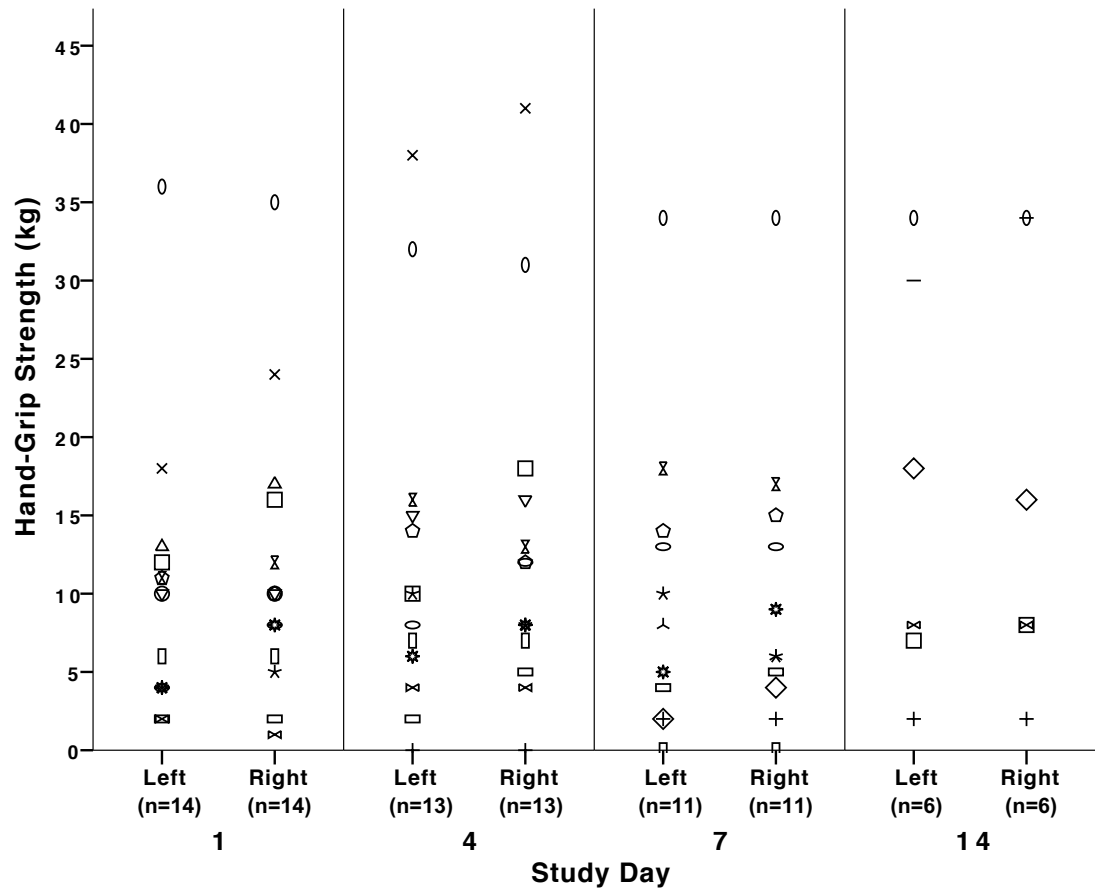
Each symbol represents individual patients. IQR, interquartile range; Min, minimum; Max, maximum.



Median (cm)	L: 30.2 R: 34.1	L: 30.5 R: 35.0	L: 34.7 R: 35.6	L: 34.1 R: 33.5
IQR (cm)	L: 24.5, 42.8 R: 25.5, 42.3	L: 27.2, 39.7 R: 27.0, 35.4	L: 28.0, 41.2 R: 28.7, 42.5	L: 27.7, 38.7 R: 27.4, 39.4
Min, Max (cm)	L: 23.4, 49.1 R: 24.5, 47.9	L: 23.6, 48.5 R: 23.2, 46.9	L: 23.3, 48.4 R: 23.6, 45.9	L: 25.8, 43.3 R: 25.1, 43.6

Figure H - 2 Bilateral mid-upper arm circumference over the duration of the study

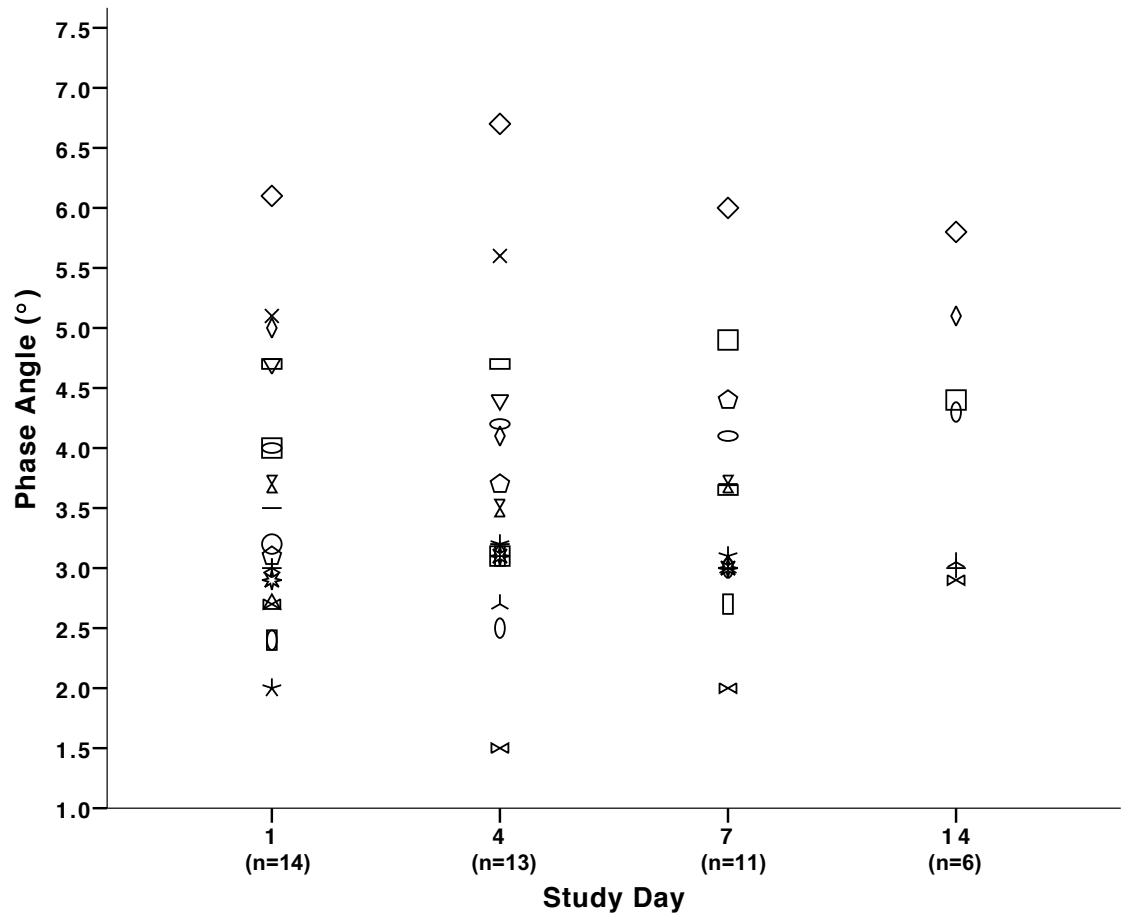
Each symbol represents individual patients. There were no significant differences between left and right arm measurements within patients on study days 1 ($P=0.865$), 4 ($P=0.670$), 7 ($P=0.724$), or 14 ($P=0.752$). IQR, interquartile range; Min, minimum; Max, maximum.



Median (cm)	L: 10 R: 10	L: 10 R: 12	L: 8 R: 8	L: 13 R: 12
IQR (cm)	L: 4, 12 R: 6, 16	L: 5, 16 R: 6, 17	L: 2, 14 R: 4, 15	L: 6, 31 R: 7, 34
Min, Max (cm)	L: 2, 36 R: 1, 35	L: 0, 38 R: 0, 41	L: 0, 34 R: 0, 34	L: 2, 34 R: 2, 34

Figure H - 3 Bilateral hand-grip strength (kg) over the duration of the study

Each symbol represents individual patients. There were no significant differences between left and right hand measurements within patients on study days 1 ($P=0.054$), 4 ($P=0.259$), 7 ($P=0.864$), or 14 ($P=0.593$). IQR, interquartile range; Min, minimum; Max, maximum.

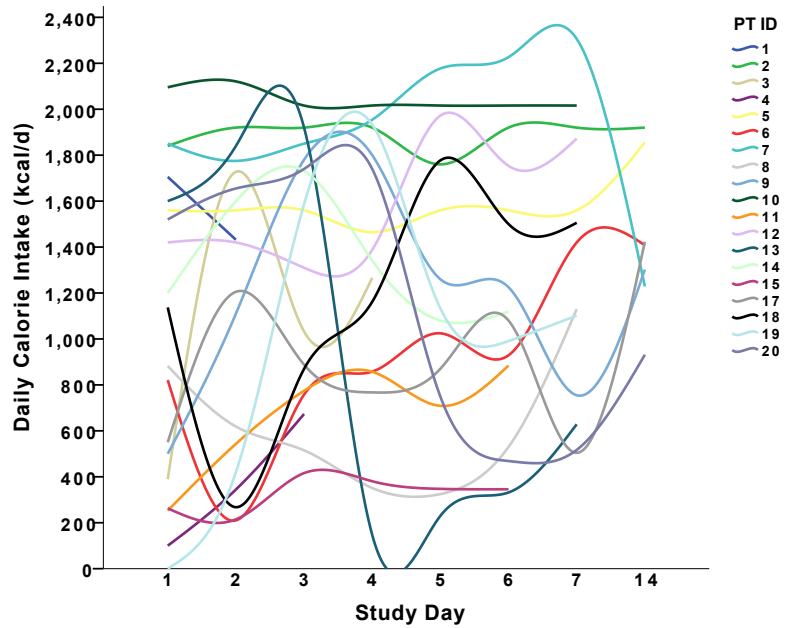
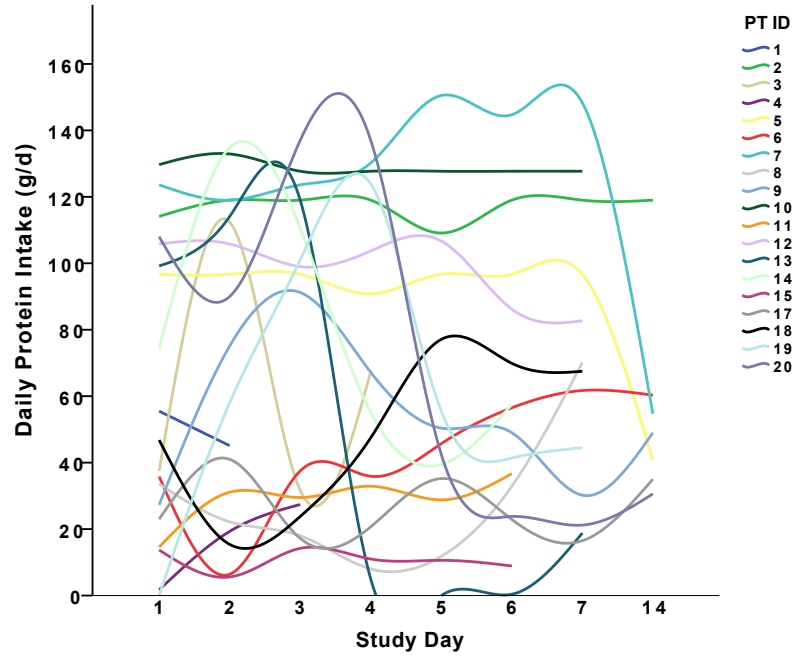


Median (cm)	3.2	3.7	3.4	4.3
IQR (cm)	2.7, 4.7	3.1, 4.3	3.0, 4.2	3.0, 5.1
Min, Max (cm)	2.0, 6.0	1.5, 6.7	2.0, 6.0	2.9, 5.8

Figure H - 4 Phase angle (°) over the duration of the study

Each symbol represents individual patients. IQR, interquartile range; Min, minimum; Max, maximum.

APPENDIX I
INDIVIDUAL DAILY PROTEIN AND ENERGY INTAKE IN
CRITICALLY ILL PATIENTS FOLLOWING LMV



APPENDIX J
DIETARY PRESCRIPTIONS AND TRANSITIONS FOR INDIVIDUAL PATIENTS OVER THE
DURATION OF THE STUDY

Study Day ¹								
ID ²	1	2	3	4	5	6	7	14
1	Regular	Regular						
2	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO
3	EN+NPO	EN+NPO → FF @ Dinner	Regular (Cardiac)	Regular (Cardiac)				
4	NPO → Regular @ lunch	Regular	Regular					
5	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	Minced/ThFl
6	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)	Regular (Cardiac)
7	EN+NPO	EN+NPO	EN+NPO	EN+NPO → EN+Puree/ ThFl @ dinner	EN+Mince/Th Fl → EN+Chop /ThFl @ lunch	EN+Chop/ThFl	EN+Chop/ThFl	Regular

8	EN+Regular (DB)	EN+Regular (DB)	EN+Regular (DB)	EN+Regular (DB)	EN+Regular (DB) → EN+NPO @ dinner	EN+NPO	EN+NPO	
9	EN+NPO	EN+CF (DB) @ breakfast	EN+CF (DB)	EN+CF (DB)	EN+NPO @ breakfast	EN+NPO	EN+NPO	EN+NPO → EN+CF @ dinner
10	EN+NPO → EN+FF/ThFl @ lunch	EN+FF/ThFl → EN+NPO @ dinner	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	
11	NPO → Regular @ lunch	Regular	Regular	Regular	Regular	Regular		
12	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO	
13	EN+NPO	EN+NPO	EN+NPO	EN+CF	CF	CF	CF → Regular @ lunch	
14	EN+NPO	EN+NPO	EN+FF → EN+Chop/ThFl @ dinner	Regular (DB) → Chop (DB)/ThFl @ lunch	Chop/ThFl (DB) → Regular (DB) @ dinner	Regular (DB)		
15	CF → Regular @ dinner	Regular	Regular	Regular	Regular	Regular		
17	EN+NPO → Regular @ dinner	Regular	Regular	Regular	Regular	Regular	Regular	Regular (fluid restriction)

18	EN+NPO → FF @ lunch	FF → NPO @ lunch	NPO → FF @ lunch	FF → Puree @ dinner	Puree	Puree	Puree → Minced @ dinner	
19	EN+NPO	EN+NPO	EN+FF (Renal)	EN+FF (Renal)	FF (Renal)	FF (Renal)	FF (Renal)	
20	EN+NPO	EN+NPO	EN+NPO	EN+NPO	EN+NPO → FF @ dinner	FF → Puree @ dinner	Puree	Mince → Chop @ dinner

¹Cell legend: white cells represent a day that a regular (non-texture or fluid modified) diet is prescribed; orange cells represent days a modified diet has been prescribed; purple cells represent days a patient only receives enteral nutrition; turquoise cells represent days a patient received both enteral nutrition and an oral diet. Cells in which text is bolded refers to days in which a change in dietary prescription occurs. Abbreviations: Chop, chopped food texture; CF, clear fluids; DB, diabetic; EN, enteral nutrition; FF, full fluids; Mince, minced food texture; NPO, *nil per os* (nothing by mouth); Puree, pureed food texture; Regular, regular diet with no therapeutic attachment; ThFl, thickened fluids

²Total sample size: n=19. Note, PT16 is omitted as this patient expired on day 1 prior to the collection of any data