Master thesis in clinical nutrition

Malnutrition in a population of inpatients; From screening with NRS2002 to a diagnosis. Comparing ICD-10 with the GLIM criteria.

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Abstract

Background: Malnutrition is highly prevalent in hospital settings, with adverse effects on patient outcomes. Up until recently, there have been no universally accepted diagnostic criteria for malnutrition to aid clinical practice. In response to the needs of the clinical nutrition and medical communities, the Global Leadership Initiative on Malnutrition (GLIM) has proposed a set of core diagnostic criteria for diagnosing adult malnutrition across different healthcare settings. These criteria are consensus based and need validation.

Aims and objectives: This study aimed to investigate the criterion validity of the GLIM criteria for the malnutrition diagnosis using ICD-10 diagnostic codes E.44.0 and E.43 as reference, and to investigate the prevalence of malnutrition and nutritional risk as identified by NRS-2002 among hospitalized patients at Haukeland University Hospital.

Methods: This study is a cross-sectional analysis of anthropometrical and nutritional indicators from inpatients at six departments at Haukeland University Hospital, collected as part of the MALNUTRA-study. Nutritional risk status was determined based on NRS-2002 scores collected from previous study personnel. Based on the available data, patients were assessed retrospectively using the ICD-10 diagnostic codes E.44.0 and E.43, and by applying six combinations of GLIM's phenotypic and etiologic criteria: A) Weight loss and reduced food intake B) Weight loss and inflammation C) Low BMI and reduced food intake D) Low BMI and inflammation E) Reduced muscle mass and reduced food intake F) Reduced muscle mass and inflammation. Reduced muscle mass was assessed by mid arm muscle circumference, and CRP $\geq$ 5 mg/dl was used as an indicator of inflammation. Agreement (Cohen's Kappa, percent agreement) and validity (sensitivity, specificity, positive predictive value and negative predictive value) statistics were performed to assess criterion validity.

Results: 326 patients (71 years (IQR 18), 53% men) were assessed. NRS-2002 identified 44% as in nutritional risk. ICD-10 identified 37% as malnourished, of which 28% were moderately malnourished (E.44.0) and 9.5% were severely malnourished (E.43). GLIM identified 35% as malnourished, of which 13% were moderately malnourished and 22% were severely malnourished. The GLIM criteria displayed fair criterion validity (sensitivity 59.0%, specificity 79.4%) and agreement (k=0.389, agreement 72%) when compared to the ICD-10 diagnostic codes E.44.0 and E.43. When compared based on moderate malnutrition status,

GLIM's criterion validity was rated as poor (sensitivity 18.7%, specificity 89.8%) and agreement was poor (k=0.102, agreement 70%) when compared to ICD-10 E.44.0. However, when compared based on severe malnutrition status the GLIM criteria displayed good criterion validity (sensitivity 87.1%, specificity 84.4%) and moderate agreement (k=0.445, agreement 85%) when compared to ICD-10 E.43.

Conclusion:

The newly proposed GLIM criteria displayed fair criterion validity and agreement for the diagnosis of malnutrition, using ICD-10 as reference. However, this was not consistent across severity grades.

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Abbreviations

AND	Academy on Nutrition and Dietetics
ASPEN	American Society of Parenteral and Enteral Nutrition
BIA	Bioelectrical impedance
BMI	Body mass index
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CT	Computed tomography
DIPS	Distribuert Informasjons og Pasientdatasystem
DRM	Disease-related malnutrition
DXA	Dual-energy absorptiometry
ESPEN	European Society for Clinical Nutrition and Metabolism
ER	Estimated requirements
FELANPE	Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo
FFQ	Food frequency questionnaire
FFMI	Fat free mass index
GI	Gastro- intestinal
GLIM	Global Leadership Initiative on Malnutrition
HUH	Haukeland University Hospital
IBD	Irritable bowel disease
IRR	Inter-rater reliability
IQR	Interquartile range
ICD-10	The International Statistical Classification of Diseases and Related Health Problems, 10th edition.
LOS	Length of Stay
MNA-(SF)	Mini Nutritional Assessment (Short form)
MUST	Malnutrition Universal Screening Tool
MRI	Magnetic resonance imaging
MUAC	Mid upper arm circumference
MAMC	Mid arm muscle circumference
NRS-2002	Nutritional Risk Screening 2002

N/A	Not available
NPV	Negative predictive value
PPV	Positive predictive value
(PG-) SGA (SF)	(Patient Generated) Subjective Global Assessment (Short Form)
PENSA	Parenteral and Enteral Nutrition Society of Asia
REC	Regional Ethical Committee
SOP	Standard operating procedures
SFT	Skinfold thickness
SD	Standard deviation
Se	Sensitivity
Sp	Specificity
WHO	World Health Organization

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1. Introduction

Malnutrition in hospitalized patients predisposes to disease, impairs recovery from disease, and adversely affects both body and mental function, as well as clinical outcome (1). Still, malnutrition is a highly prevalent condition in hospitals (2), often left unrecognized and untreated (3). Up until recently, there have been no universally accepted diagnostic criteria for malnutrition to aid clinical practice. In response to the needs of the clinical nutrition and medical communities, the Global Leadership Initiative on Malnutrition (GLIM) (4) has proposed a consensus-based set of core diagnostic criteria for diagnosing adult malnutrition across different healthcare settings.

1.1. Definition

There is a variety of proposed definitions and diagnostic criteria for malnutrition in the literature (4-12). A universally accepted definition that adequately reflects the pathophysiology and clinical outcome of malnutrition is still wanted by global nutrition and medical societies (13, 14). Simply put, malnutrition translates to "bad nutrition" (1). By this definition, malnutrition is an umbrella term that includes a wide range of nutritional disorders. One common approach is to distinguish between over-or undernutrition, i.e. excess or lack of dietary protein or energy, also referred to as protein-energy malnutrition. Malnutrition can also refer a lack of specific vitamins and minerals, therefore including micronutrient deficiencies. For the current thesis, the following definition of malnutrition will be used:

> *"Malnutrition is 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"*

By this definition, malnutrition will be interpreted in the "undernourished" as a result of "a lack of protein or energy" sense of the term. Furthermore, it will be used synonymously with disease-related malnutrition (DRM), which is the sub-classification of malnutrition primarily encountered among adult and elderly in a hospital setting (15).

1.1.1. Sub-classifications of malnutrition

Following the general definition, malnutrition in a clinical setting can be further classified based on etiology (6), as, illustrated in Figure 1.

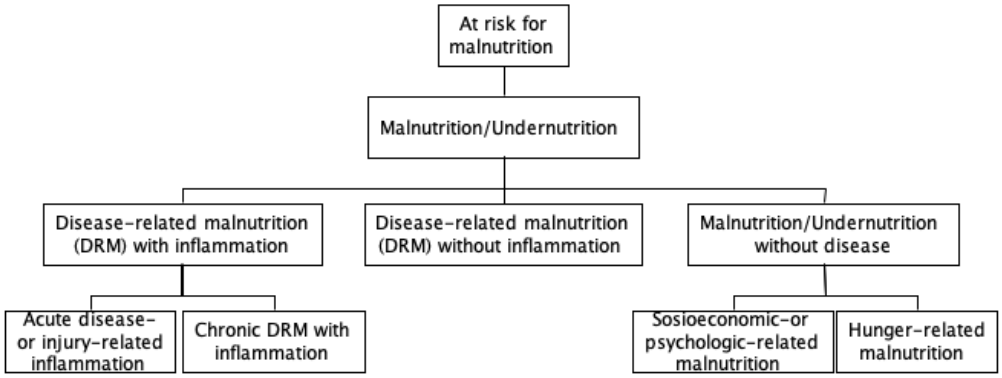


Figure 1. The diagnosis tree of malnutrition. From (10).

In a clinical setting malnutrition mainly arises as a consequence of disease (5, 15), therefore termed disease-related malnutrition (DRM). DRM can develop as a result of 1) Pure starvation without inflammation, typically seen in conditions such as dysphagia, dementia or anorexia nervosa 2) Chronic disease with prolonged inflammation of a mild or moderate degree e.g. in cancer or chronic lung disease 3) Acute disease or injury with severe inflammation such as in patients undergoing extensive surgery or treatment for extensive burns. There is also malnutrition without disease, which is seen more frequently in developing countries and will not be discussed further in this thesis. It is important to correctly identify the different sub-classifications of malnutrition, as it has consequences for planning of treatment and patient prognosis (8).

1.2. Prevalence

Malnutrition is common in hospitalized patients. Prevalence rates vary depending on which nutritional screening or assessment tools are used to define it, and which population is being investigated. Particularly the lack of a universal definition of malnutrition has been pointed to as part of the issue, as different criteria and cut-off values make comparisons difficult (7, 16). Therefore, the actual prevalence of malnutrition in hospitals is unknown. Global estimates range between 10- 70% (5, 15, 17-19). As for Norway, it has been reported that 29-60% of hospitalized patients are at risk of malnutrition (20-22) and 39-65% are malnourished (23, 24). Although malnutrition can occur at any age or condition, malnutrition is more frequent in the elderly, patients with multiple comorbidities, critically ill, and in specific diseases or conditions such as dementia, malignant-, GI-, renal -, respiratory and heart disease (10, 25).

1.3. Consequences of malnutrition

It is well established that malnutrition has negative implications for hospitalized patients' clinical outcomes. Malnutrition is associated with increased morbidity, risk of complications (26) and infections (27), increased mortality (28), longer length of stay (LOS) at the hospital, and more hospital readmissions (7, 17). It is of important note, that this also applies to patients at risk of developing malnutrition. Tangvik et. al. (29) found that patients answering positively on the initial screening of NRS-2002 had significantly longer LOS, increased mortality and morbidity, and were more likely to be readmitted compared to patients not at risk. As a result, malnutrition has a significant economic impact on health care services (17, 30). In a Dutch study (31) it was estimated that the total additional cost of treating adult DRM was €1.9 billion per year or 2.1% of the total national health expenditure (2011 figures). Furthermore it has been estimated Norwegian Specialiced Health Services can save 800 million NOK, or approximately 1% of its total expenditures, by preventing and treating malnutrition through individualized nutrition care (2010 figures) (32).

1.4. Etiology

The underlying reasons for the development and exacerbation of DRM are many and not fully understood. Central factors include inadequate dietary intake, together with increased nutritional requirements or an impaired absorption/assimilation of nutrients (33). The underlying mechanisms differ based on the presence or absence of inflammation.

1.4.1. DRM with inflammation

DRM with inflammation is described as a catabolic condition characterized by an inflammatory response due to an underlying disease (10). The inflammatory state has several negative implications. Inflammation influences metabolism, shifting it towards a catabolic state of increased breakdown of body fat and muscle (34). Breakdown of muscle mass is more rapid in acute disease and injury but will also occur in chronic disease at a slower rate over a longer period (35). Inflammation also increases energy and protein requirements, by elevating resting energy expenditure and nitrogen excretion. Furthermore, inflammation associated loss of appetite (anorexia) can limit dietary intake so that nutritional requirements are not met. This contributes to worsening losses of total body weight and muscle mass, thus making malnutrition associated with impaired functional status and worsened clinical outcome (15).

1.4.2. DRM without inflammation

DRM without inflammation is caused by etiologic mechanisms not driven by inflammation (10). Common examples include conditions that obstruct food intake such as dysphagia or neurologic disorders such as stroke or dementia. Conditions like anorexia nervosa or depression can negatively impact appetite, and malabsorptive conditions like IBD or Crohn's disease can limit nutrient uptake from the GI-tract. DRM without inflammation differs from its inflammatory counterpart in that metabolism decreases in response to inadequate nutritional intake (35). Therefore, loss of body weight is slower than in inflammatory-driven DRM.

1.4.3. Other etiologic factors

Several factors contribute to the development of DRM, irrespective of the presence or absence of inflammation. Age-related decrease in appetite and/or dietary intake, coined "anorexia of ageing", is frequently seen in the elderly (36). Common symptoms related to disease or medical treatment, such as nausea, sore mouth, diarrhea or constipation, will also contribute to loss of appetite and impaired nutrient absorption (4). Nutritional status has also been shown to deteriorate during the hospital stay (25). Lack of knowledge and interest among health personnel regarding the patients nutritional status and requirements has been described as contributing factors (37). In a 2006 study (38) regarding the quality of health care provided to hospitalized or institutionalized elderly in Norway, doctors and nurses reported that they thought patients nutritional requirements were inadequately looked after. The main reason provided was a lack of resources and access to qualified health personnel, dietitians.

1.5. Nutritional screening and nutritional assessment

The first step of a systematic nutrition care process is screening for nutritional risk. Risk screening can be defined as "a rapid process performed to identify subjects at nutritional risk" (10). Patients' nutritional status will often deteriorate due to unrecognized nutritional risk (37). Therefore, risk screening should be carried out at first contact, or within the first 24-48 hours after hospital admission (10). Thereafter, patients should be reassessed weekly. Thus, risk screening helps to rapidly determine if further action is needed in order to prevent deterioration of a patient's nutritional status. Patients identified as being at nutritional risk should always proceed to a full nutritional assessment. A nutritional assessment can be defined as "a more detailed, more specific, and in-depth evaluation of a patient's nutritional

state" (39). A nutritional assessment should be carried out by health personnel with nutritional competence, such as dietitians. The assessment forms the basis for a malnutrition diagnosis, and for specific nutritional care plans adapted to the individual patient (10). Obtaining an accurate assessment of nutritional status is complicated by the lack of universally accepted diagnostic criteria with clearly defined cut-off values (14). In other words, there is no "gold standard" available to diagnose malnutrition (40). As a result there is published more than 50 tools for risk screening and nutritional assessment (39). Which diagnostic criteria are used, how the selection criteria are weighed, how much time is needed to perform the screening or assessment, or whether the tool is validated in the population under question, are some of the factors that a clinician should consider when choosing a tool. A selection of widely accepted screening and assessment tools, along with some of the most common indicators used to assess nutritional status, is presented in Table 1.

Table 1. Indicators used in selected tools for risk screening and nutritional assessment. Adapted from (4).

	NRS-2002 [a] (41)	MNA-SF [a] (42)	MUST [a] (43)	ESPEN 2015 [b] (8)	ASPEN/ AND [b] (7)	SGA [b] (44)
Etiologic						
Reduced food intake	X	X	X	X	X	X
Disease burden/ inflammation	X	X	X	X	X	X
Symptom						
Anorexia		X				X
Weakness		X				X
Phenotypic						
Weight loss	X	X	X	X	X	X
BMI	X	X	X	X		
Fat free mass		X		X	X	X
Fat mass					X	X
Fluid retention/ ascites					X	X
Muscle function					X	X

"X" marks the use of an indicator by a tool.
[a] Tool used for screening
[b] Tool used for assessment
Abbreviations: NRS-2002, Nutritional Risk Screening 2002; MNA-SF, Mini Nutritional Assessment- Short Form; MUST, Malnutrition Universal Screening Tool; ESPEN, European Society for Clinical Nutrition and Metabolism; ASPEN, American Society of Parenteral and Enteral Nutrition; AND, Academy on Nutrition and Dietetics; SGA, Subjective Global Assessment.

1.6. Diagnostic criteria

1.6.1. Reduced food intake

The role of reduced food intake in the development of malnutrition is well established. It can have multiple causes, which are further elaborated in Section 1.4. In a hospital setting, questions regarding food intake before admission can provide useful information. Bedside food records that are filled out by health personnel or the patients themselves, preferably for more than two days, can also be used for quantifying food intake (10). Other methods include 24-hour recalls and food frequency questionnaires (FFQs) (45).

1.6.2. Involuntary weight loss

Measurement of body weight is part of routine clinical practice when assessing nutritional status (46). Body weight equals the sum of both fat-free mass and fat mass, therefore changes in body weight can represent changes in muscle and fat, as well as changes in fluid balance. Depending on the situation, this should be considered when assessing the clinical impact of changes in weight. For example, day to day physical fluctuations in fluid balance in healthy individuals are not likely to significantly impact measurements, but excess fluid (ascites or oedema) related to liver- or kidney disease has the potential for obscuring changes in muscle or fat mass (46) Which cut-offs used for percentage weight loss over a given time period, will vary between screening or assessment tools. Unintentional weight loss > 10% over 3-6 months is generally considered as clinically significant as it implies underlying disease and loss of functional status (39). For inpatients, weight should be measured at least once a week, and repeatedly over time in order to follow development (10).

1.6.3. BMI

Body mass index (BMI) is widely used in clinical practice as a quick and relatively easy to use indicator of nutritional status (39). BMI has well established validity, and low BMI is associated with increased mortality, complications after surgery, risk of infection and LOS (46). While there are regional differences, WHO provide generally accepted cut-off values (47) where underweight is defined as BMI under 18.5 kg/m^2. Due to the increasing prevalence of overweight and obesity in large parts of western populations, it has been noted that the use of BMI in nutritional assessment can be limited (4). In some cases, a substantial weight loss would be required before being identified as malnourished based on solely BMI as an indicator.

1.6.4. Disease burden/inflammation

Malnutrition is associated with metabolic changes caused by an inflammatory response triggered by disease or injury (48). This has been described in more detail in Section 1.4.1. Thus, inflammation, often used interchangeably with disease burden, has become a widely accepted component of nutritional assessment (4). How to best measure inflammation in clinical settings is not agreed upon. A subjective approach would be to assess the clinical diagnosis and use clinical judgement to consider the degree of associated inflammatory response. For example, diseases such as cancer, chronic obstructive pulmonary disease (COPD), inflammatory bowel diseases, congestive heart failure, or chronic kidney disease are usually associated with systemic inflammation of a mild- to moderate degree (10). Patients suffering from acute disease, injury or trauma, such as major burns or infections, are in a highly catabolic state with high levels of inflammation (49). The degree of inflammation can also be assessed using objective biochemical markers as supportive measures. ESPEN guidelines suggest elevated serum C-reactive protein (CRP) and reduced serum concentrations of albumin or pre-albumin (10). Although these biochemical markers have been shown to predict adverse health outcomes, they are primarily markers of inflammation, and not nutritional status (50). Therefore, they should not be used in isolation when assessing nutritional status.

1.6.5. Reduced muscle mass

An accurate and valid assessment of body composition is considered essential when assessing nutritional status (46). Loss of muscle mass, or fat free mass, is considered a reliable indicator for assessing the severity of malnutrition, and for predicting adverse health outcomes (51). Furthermore, loss of muscle mass is generally accompanied by a loss of muscle function. Studies show that reduced muscle function, measured by grip strength, is associated with a loss of functional status in hospitalized patients (52). There is currently no agreement on which method best measures the loss of muscle mass, or which cut-off values to apply (4). Some methods include imaging techniques such as Dual-energy absorptiometry (DXA), ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI). Bioelectrical impedance (BIA) is considered a less invasive, less expensive and more available bedside assessment method (53). Anthropometric measurements such as calf or arm muscle circumference can also be used to assess nutritional status, as muscle size reflects protein

reserves (54). Choice of methods may vary according to available resources and time. It has been shown that different ways to measure muscle mass may provide different results (55).

1.7. Tools used to identify nutritional risk and malnutrition

1.7.1. NRS-2002

Nutritional risk screening (NRS) 2002 is a tool developed for nutritional risk screening in adult hospitalized patients, and recommended by ESPEN (41). The screening tool is two-part, with a quick to use initial screening consisting of only four questions for easier identification of patients that could be at nutritional risk. These questions are simple (yes or no) and assess the patients BMI, involuntary weight loss during the last 3 months, reduced food intake during the last week, and disease severity. If the answer is "yes" to any of the initial questions, a more comprehensive evaluation follows where the patient is scored based on the degree of nutritional impairment, disease severity and age (over or under 70 years old). A patient is classified as being at nutritional risk if the total score is over or equal to 3. The full NRS-2002 questionnaire is presented in Table 2. At Haukeland University Hospital (HUH), risk screening using NRS-2002 is incorporated into a larger risk assessment tool called "Trygg pleie". "Trygg pleie" was implemented by the Norwegian Patients Safety Programme "In Safe Hands 24-7" (56) as one of the nutrition strategies described in the National Guidelines for Prevention and Treatment of Malnutrition (25).

Table 2. Identification of nutritional risk using Nutritional Risk Screening 2002 (NRS-2002)

Score		Nutritional status (≈ degree of impairment)	Disease severity (≈ stress metabolism)
	0 – Absent	Normal nutritional status	Normal nutritional requirements
	1 – Mild	Weight loss > 5% last 3 months, or food intake 50-75% of normal requirements the last week.	Hip fracture*, patients with chronic diseases/conditions*, in particular those with acute complications: liver cirrhosis, COPD*. *Chronic hemodialysis, diabetes, cancers.*
	2 – Moderate	Weight loss > 5% last 2 months, or BMI 18.5-20.5 + impaired general condition, or food intake 25-50% of normal requirements the last week.	Major abdominal surgery*, stroke*. *Severe pneumonia, hematologic malignancies*
	3 – Severe	Weight loss > 5% last 1 month (> 15% last 3 months), or BMI < 18.5 + impaired general condition, or food intake 0-25% of normal requirements the last week.	Head trauma*, bone marrow transplantations* *Intensive care patients (APACHE score > 10)*
Total score		Calculation procedure: 1) Score 0-3 based on nutritional status + score 0-3 based on disease severity (Only one score from each component, the most severe score should be selected). 2) If age ≥ 70 years, add 1 to the total score. 3) If age corrected total score ≥ 3, patient is at nutritional risk and nutritional support must be implemented.	

* Indicates that a study directly supports the categorization of patients based on the specific disease. Diagnoses in *italics* are based on the prototypes described below:
Score 1: A patient with chronic disease hospitalized due to complications associated with a chronic disease. The patient is weak, but not bedridden. Protein requirements are increased but can be covered by food intake per os and/or oral nutrition support in most cases.
Score 2: A patient bedridden due to disease e.g. after major abdominal surgery. Protein requirements are substantially increased, but can be covered, even if artificial nutrition support is required in many cases.
Score 3: An intensive care patient requiring e.g. assisted ventilation. Protein requirements are increased and cannot be covered by artificial nutrition support. Catabolism of body protein and associated nitrogen losses can be significantly reduced by nutrition support.
Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; APACHE, acute physiology and chronic health evaluation.

1.8. Subjective global assessment

Subjective global assessment (SGA) is a comprehensive tool considered by some as a semi-gold standard in nutritional assessment of hospitalized patients (57). SGA was originally developed in an adult surgical population (44) but has been widely used in hospital nutritional assessment since. It has been validated and is predictive of health outcomes associated with impaired nutritional status in hospitalized patients (58). SGA is also two-part, assessing nutritional status based on 1) clinical history and 2) physical examination. When assessing the clinical history, information is collected weight loss, food intake, GI-symptoms, functional status and metabolic demand related to the disease/condition. During the physical exam, loss of muscle mass, subcutaneous fat and presence of oedema is evaluated. This information forms the basis from which the health personnel subjectively categorize patients as well nourished (SGA A), moderately or suspected of being malnourished (SGA B) or severely malnourished (SGA C).

1.9. ICD-10

The International Statistical Classification of Diseases and Related Health Problems (ICD) is a classification- and diagnostic system owned and published by the World Health Organization (WHO) (59). Available to all member countries, the ICD provide diagnostic codes for easy comparison of health-related data between countries. The ICD system is periodically updated and is currently on the 10th edition (ICD-10). ICD-10 is currently being used by the Norwegian Specialist Health Service and include three codes for malnutrition: E.46 Unspecified protein-/energy malnutrition, E.44.0 Moderate protein-/energy malnutrition and E43 Severe protein-/energy malnutrition. The diagnostic code E.46 is used interchangeably with nutritional risk, is based upon scores from select nutritional screening or assessment tools, for example, a total NRS-2002 score ≥ 3. The diagnoses of E.44.0 and E.43 are based on an assessment of involuntary weight loss and BMI, either separately or in combination. For E.44.0 food intake with concurrent inflammation is also considered. The diagnostic criteria for E.46, E.44.0 and E.43 are presented in full in Table 3.

Table 3. Criteria for ICD-10 malnutrition diagnoses E.46, E.44.0 and E.43.

Code	Term	Criteria [a]				
		Weight loss (%)	Low body mass index (kg/m^2)	Low body mass index and weight loss	Reduced food intake and inflammation	Nutritional screening-or assessment tool scores
E.46	Unspecified protein-/energy malnutrition	N/A	N/A	N/A	N/A	NRS-2002: ≥ 3 MUST: ≥ 2 MNA Part 1: ≤ 11 PG-SGA SF: ≥ 2
E.44.0	Moderate protein-/energy malnutrition	> 10% last 3-6 months, or > 5% last 2 months	< 18.5 if < 70 years or < 20 if >70 years	< 20.5 (< 22 if > 70 years) and concurrent weight loss > 5% last 6 months	< 50% of ER last week and concurrent acute/chronic inflammatory condition.	PG-SGA grade B
E.43	Severe protein-/energy malnutrition	> 15% last 3-6 months, or > 5% last 1 month	< 16 if < 70 years or < 18.5 if >70 years	< 18.5 (< 20 if > 70 years) and concurrent weight loss > 5% last 3 months	N/A	PG-SGA grade C

[a] Requires at least 1 criterion for diagnosis.

Abbreviations: N/A, not available; NRS2002, Nutritional Risk Screening 2002; MUST, Malnutrition Universal Screening Tool; MNA, Mini Nutritional Assessment; PG-SGA (SF), Patient Generated Subjective Global Assessment (Short Form); ER, estimated requirements.

1.10. The Global Leadership Initiative on Malnutrition

1.10.1. Background

It is evident that there is a lack of consensus on a definition of malnutrition, and subsequently diagnostic criteria for use in both clinical settings and in nutrition research (4, 10, 14). Although most approaches to define malnutrition are similar and largely use the same diagnostic criteria (13), one universally accepted approach to define malnutrition is needed in order to standardize clinical practice. In response to the needs of the clinical nutrition and medical communities, the Global Leadership Initiative on Malnutrition (GLIM) (4) recently proposed a consensus- based approach, describing core diagnostic criteria for diagnosing adult protein-energy malnutrition across different healthcare settings worldwide.

1.10.2. Development

The GLIM criteria were developed over a 3-year period between 2016 and 2018, as a collaborative initiative between four of the major global clinical nutrition societies: American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo (FELANPE), Parenteral and Enteral Nutrition Society of Asia (PENSA). GLIM consisted of a core leadership committee and a supporting working group of representatives from diverse disciplines. The consensus procedure consisted of a series of face-to-face meetings, telephone conferences and e-mail communications. In 2019 the results were published in a statement paper (4), presenting a three-step approach for detecting and diagnosing malnutrition.

1.10.3. A three-step approach

Originally presented as a two-step approach, GLIM is in practice more of a three-step approach. Starting with screening for nutritional risk, followed by diagnostic assessment and lastly severity grading of malnutrition. An overview of the framework is illustrated in Figure 2.

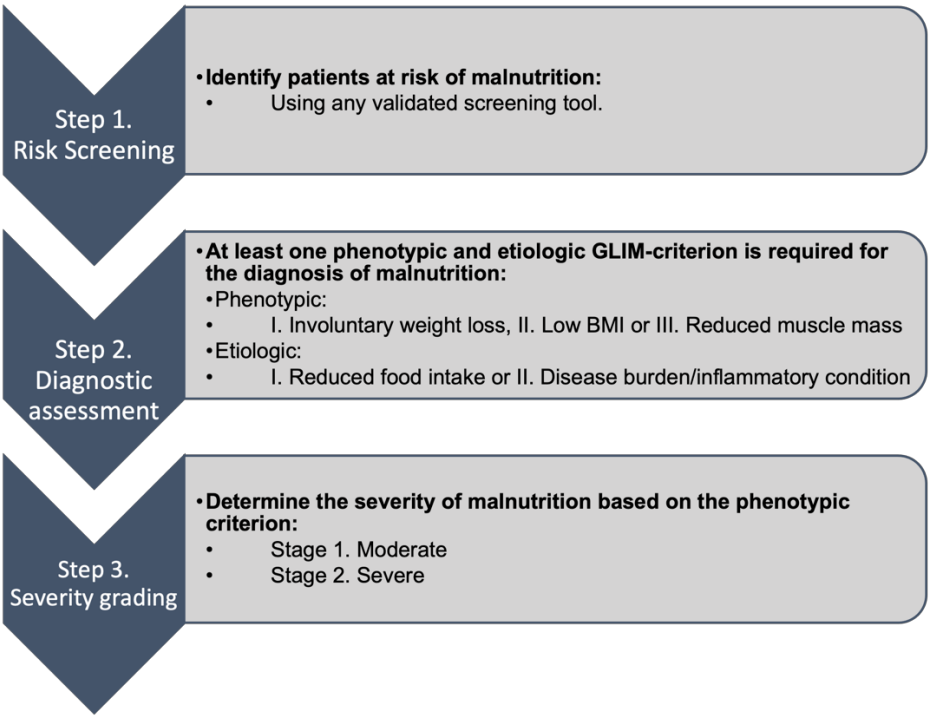


Figure 2. The GLIM-approach for the diagnostic assessment of malnutrition. Modified from (4).

Similar to previously described approaches, GLIM also recommends that the first step of the process should always be to identify patients at nutritional risk using any validated screening tool. Patients at risk of developing malnutrition should then continue to the second step of a more in-depth diagnostic assessment based on the consensus based diagnostic criteria, referred to as the GLIM criteria. For the diagnosis of GLIM defined malnutrition a minimum of one phenotypic and one etiologic criterion must be present. The phenotypic criteria are clinical features that reflect the severity of malnutrition and include involuntary weight loss, low BMI and reduced muscle mass. The etiologic criteria include reduced food intake or assimilation of nutrients, and the presence of inflammation due to disease. Lastly, GLIM recommends grading the severity of malnutrition based upon the relevant phenotypic criteria from the previous step. See Table 4 for more detail on the GLIM criteria, including suggested methods to assess the criteria and cutoff points.

Table 4. Phenotypic and etiologic criteria for the GLIM diagnosis of malnutrition. With thresholds for severity grading into Stage 1. Moderate and Stage 2. Severe Malnutrition. From (4).

	Phenotypic Criteria			Etiologic Criteria	
	Weight loss (%)	Low body mass index (kg/m^2)	Reduced muscle mass [a]	Reduced food intake or assimilation [b-c]	Inflammation [d-f]
Malnutrition [g]	>5% within past 6 months, or >10% beyond 6 months	<20 if <70 years or < 22 if > 70 years	Reduced by validated body composition measuring techniques [a]	<50% of ER > 1 week, or any reduction for >2 weeks, or any chronic GI condition that adversely impacts food assimilation/absorption [b-c]	Acute disease/ injury [d-f], or chronic disease-related [e-f]
Stage 1. Moderate Malnutrition [h]	5-10% within past 6 months or 10-20% beyond 6 months	<20 if <70 years or < 22 if > 70 years	Mild-to-moderate deficit (per validated assessment methods) [a]		
Stage 2. Severe Malnutrition [h]	>10% within past 6 months or >20% beyond 6 months	<18,5 if <70 years or < 20 if > 70 years	Severe deficit (per validated assessment methods) [a]		

[a] E.g., Fat free mass index (FFMI, kg/m^2) by dual-energy absorptiometry (DXA), or other corresponding body composition methods such as bioelectrical impedance analysis (BIA), CT or MRI. When not available or by regional preference, physical examination or standard anthropometric measures like mid-arm muscle or calf circumferences may be used. Functional assessments like hand-grip strength may be considered as a supportive measure.
[b] Consider gastrointestinal symptoms as supportive indicators that can impair food intake or absorption e.g., dysphagia, nausea, vomiting, diarrhea, constipation or abdominal pain. Use clinical judgment to discern severity based upon the degree to which intake or absorption are impaired. Symptom intensity, frequency, and duration should be noted.
[c] Reduced assimilation of food/nutrients is associated with malabsorptive disorders like short bowel syndrome, pancreatic insufficiency and after bariatric surgery. It is also associated with disorders like esophageal strictures, gastroparesis, and intestinal pseudo-obstruction. Malabsorption is a clinical diagnosis manifest as chronic diarrhea or steatorrhea. Malabsorption in those with ostomies is evidenced by elevated volumes of output. Use clinical judgment or additional evaluation to discern severity based upon frequency, duration, and quantitation of fecal fat and/or volume of losses.
[d] Acute disease/injury related. Severe inflammation is likely to be associated with major infection, burns, trauma or closed head injury. Other acute disease/injury-related conditions are likely to be associated with mild to moderate inflammation.
[e] Chronic disease related. Chronic or recurrent mild to moderate inflammation is likely to be associated with malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease or any disease with chronic or recurrent inflammation. Transient inflammation of a mild degree does not meet the threshold for this etiologic criterion.
[f] C-reactive protein may be used as a supportive laboratory measure.
[g] Requires at least 1 phenotypic criterion and 1 etiologic criterion for diagnosis of malnutrition.
[h] Severity grading is based upon the noted phenotypic criteria while the etiologic criteria are used to provide the context to guide intervention and anticipated outcomes.
Abbreviations: GI, gastro-intestinal; ER, energy requirements.

1.10.4. Assessing the validity of GLIM

Assessing validity of a tool refers to testing if the tool detects what the tool is indented to detect (60), which in the case of GLIM is protein-energy malnutrition (4). Valid tools are important as they provide accurate identification of patients at nutritional risk or malnourished or nutritional risk or that are malnourished, which in turn promotes referral to a dietitian (61). There are different types of validity, which are defined in Table 5. Criterion validity is considered the superior type of validity (60).

Table 5. Definitions of types of validation. From (40, 62).

	Definition	Description
Content validity	Assesses the relevance and completeness of a tool's content.	E.g. If the selected GLIM criteria are relevant for assessing malnutrition.
Construct validity	Assesses the extent to which a tool performs in accordance with theoretical expectations.	E.g. If prevalence of GLIM defined malnutrition differs among groups in which prevalence is expected to vary, such as between hospital and community.
Criterion validity	Assesses the ability of a tool to detect what it is intended to detect by comparing it to a gold standard procedure.	Comparison of GLIM's identification of malnutrition to the identification obtained using a gold standard procedure.
Predictive validity	Assesses the ability of the tool to predict future outcomes expected to be associated with the construct.	E.g. mortality and LOS, which are known to be associated with malnutrition.

Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; LOS, length of stay.

1.11. Clinical relevancy statement

It is well established that malnutrition is prevalent in hospitalized patients, adversely affecting patient health outcomes and healthcare utilization. Still, clinical practice and nutrition research is limited by a lack of universally accepted diagnostic criteria. The newly published GLIM criteria provide a globally accepted approach to define malnutrition across care settings. As the proposed GLIM criteria are consensus based, they need to be applied to clinical practice for validation and further improvement (4, 62). Currently, the literature on the GLIM criteria's diagnostic accuracy is scarce.

2. Study aims

2.1. Primary aims

- To investigate the GLIM criteria's criterion validity in a hospital setting when compared to the ICD-10.
- To investigate the prevalence of malnutrition among hospitalized patients at HUH according to the GLIM criteria and ICD-10.

2.2. Secondary aim

- To investigate which diagnostic criteria contribute most to the GLIM and ICD-10 defined malnutrition diagnosis.

2.3. Hypotheses

H_0: GLIM has satisfactory criterion validity for the diagnosis of malnutrition and agrees with the ICD-10 diagnostic codes E.44.0 and E.43.

H_A: GLIM has unsatisfactory criterion validity for the diagnosis of malnutrition and is not in agreement with the ICD-10 diagnostic codes E.44.0 and E.43.

3. Materials and methods

3.1. Study design

The present study is a cross-sectional analysis of data collected from the matched cohort study called the MALNUTRA-study. The MALNUTRA-study was conducted from September 2017 to December 2019, as a collaboration between Haukeland University Hospital (HUH) and the University of Bergen, aiming to assess determinants and consequences of malnutrition. The present study is conducted at the Department of Clinical Science, University of Bergen, as part of the ongoing MALNUTRA-project.

Sections 3.2-3.3 will describe MALNUTRA study procedures carried out by study personnel, with relevance for this thesis.

3.2. MALNUTRA study population and recruitment process

The MALNUTRA study population consists of inpatients mainly from the Department of Thoracic Medicine and Heart Disease, the Departments of Dermatology/ Rheumatology, Internal Medicine (Gastroenterology and Endocrinology), and the Orthopedic Clinic. In brief, the study population was recruited following a matched cohort design. Patients at nutritional risk ("at risk") and patients not at nutritional risk ("not at risk") were matched for age (+/- 10 years), gender and diagnosis. Eligible at risk patients and suitable not at risk matches were asked to participate based on criteria described in Table 6. The same eligibility and exclusion criteria were extended onto the current thesis, with the added criteria that all participants had to have anthropometrical and nutritional data on at least one phenotypic and etiologic GLIM criterion necessary to perform a nutritional assessment (see section 3.4.1 for further elaboration).

Table 6. Eligibility and exclusion criteria used in the MALNUTRA recruitment process.

Eligibility criteria	Exclusion criteria
Age ≥ 18 years	Current cancer diagnosis
Nutritional risk assessed using NRS-2002	Patients from intensive care unit
Understanding the Norwegian language	Patients with transmissible infectious disease
Cognitive abilities to understand the study purposes	Insufficient data for GLIM assessment [a]
Time to participate in the additional measurements	
Willingness to participate	

[a] Additional exclusion criteria for the current thesis, and not used in the original MALNUTRA recruitment process.
Abbreviations: NRS-2002, Nutritional Risk Screening 2002; GLIM, Global Leadership Initiative on Malnutrition.

3.3. MALNUTRA data collection

3.3.1. The MALNUTRA screening-procedure

Information regarding patient nutritional risk status was obtained from the medical journal Distribuert Informasjons og Pasientdatasystem (DIPS). The study procedures then included a re-screening by the study personnel, also using NRS-2002. The study re-screening used measured weight and height, information on weight history and food intake from a study questionnaire (Appendix I), and information on diagnosis from the discharge letters in the medical records. Information on length of stay at the ward was also extracted from the patients discharge letters. Anthropometrical measurements and data for nutritional assessment in the present thesis, are further elaborated below.

3.3.2. Anthropometrical measurements.

All anthropometrical measurements were collected in the patient room according to standard operating procedures (SOPs), while the patients were in hospital clothes without shoes. Weight was measured once in kilograms using a portable flat scale, Seca model 877 (Hamburg, Germany). Height was measured twice in centimeters at maximal inspiration using a portable stadiometer, Seca model 217 (Hamburg, Germany). The mean value was used for further analysis. If height measurements could not be conducted, self-reported height was used. Skinfold thickness (measured in millimeters) was measured three times using a Lange skinfold caliper (Santa Cruz, USA). The mean value was used for further analysis. Mid upper arm circumference (measured in centimeters) was measured twice using a non-elastic ergonomic measuring tape, Seca model 201 (Hamburg, Germany). Each measurement was

noted at the nearest 0.1 centimeter, and the mean value of the two measurements was used for further analysis. For further detail regarding the execution of the anthropometrical measurements, see SOPs listed in Appendix II-V.

3.3.3. Weight history and food intake

During the re-screening procedure, the patients were asked to answer a general questionnaire, called the MALNUTRA- questionnaire. The MALNUTRA- questionnaire was made specifically for the study and contained questions regarding health, lifestyle and social factors Page 1 (see Appendix I) contained questions regarding weight history and food intake, which was used in the present thesis for the diagnostic assessment of malnutrition as described in section 3.4.

3.3.4. Blood samples

Biochemical and haematological parameters including serum C-reactive protein (CRP) were measured usually from morning blood samples and analysed at the central laboratory at the Haukeland University Hospital using standard methods.

3.4. Diagnostic assessment of Malnutrition

3.4.1. Data collection from the MALNUTRA-database

For the assessment of malnutrition using ICD-10 and GLIM as diagnostic tools, the following data were extracted from the MALNUTRA- database: Height, weight, BMI, self-reported weight loss the last 3 months, self-reported food intake the last week, skinfold thickness (SFT), mid-upper arm circumference (MUAC) and serum CRP. BMI was calculated using the formula: BMI= bodyweight in kg/ (height in m)^2. Weight loss was reported in kilograms, and percentage weight loss was calculated based on measured weight during the study re-screening using the formula: [(Weight loss in kg/ (Measured weight in kg + weight loss in kg) *100) = Weight loss in percent]. Mid arm muscle circumference (MAMC) was calculated using the formula: MUAC- (3.14 x SFT x 0.1).

3.4.2. Diagnostic procedure

Based on the information extracted from the MALNUTRA-database, diagnostic assessment of malnutrition was conducted as illustrated in Figure 3. The assessment was carried out blinded for patient nutritional risk status. The whole set of patients were assessed using GLIM

criteria first, before re-assessing using the ICD-10 criteria while blinded to the outcome of the GLIM assessment.

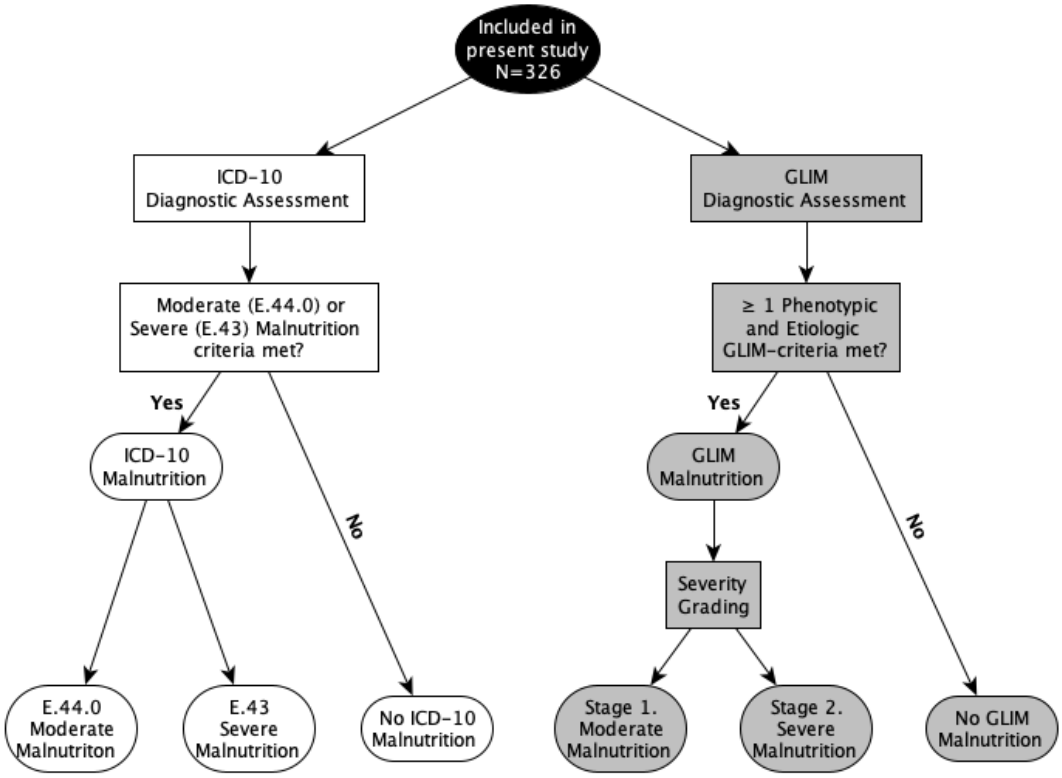


Figure 3. Flow chart over the GLIM and ICD-10 diagnostic assessment process.

3.4.2.1. GLIM diagnostic assessment

The GLIM criteria were applied based on available data from the MALNUTRA- database. For the diagnosis of I. GLIM Malnutrition, II. GLIM Stage 1. Moderate malnutrition, or III. GLIM Stage 2. Severe malnutrition, the phenotypic and etiologic criteria presented in Table 7 were used. Calculations of MAMC were used in the assessment of the phenotypic criteria of reduced muscle mass. The cut-off points applied (63) are presented in Table 8. For the etiologic criteria, presence of inflammation was defined as CRP ≥ 5, and reduced food intake was defined as < 50% of ER last week based on answers from the MALNUTRA-questionnaire (Appendix I) where "less than half of normal" was interpreted as < 50% of ER and "less than a quarter of normal" was interpreted as < 25% of ER.

Table 7. Phenotypic and etiologic criteria applied in the assessment process for the GLIM diagnosis of malnutrition, with thresholds for severity grading into Stage 1. Moderate and Stage 2. Severe Malnutrition.

	Phenotypic Criteria			Etiologic Criteria	
	Weight loss (%)	Low body mass index (kg/m^2)	Reduced muscle mass [c]	Reduced food intake [d]	Inflammation
Malnutrition [a]	>5% within past 3 months	<20 if <70 years or < 22 if > 70 years	Any reduction in MAMC below 10th or 5th percentile [c]	<50% of ER > 1 week [d]	CRP ≥ 5 mg/dl
Stage 1. Moderate Malnutrition [b]	5-10% within past 3 months	<20 if <70 years or < 22 if > 70 years	Reduction in MAMC < 10th percentile [c]		
Stage 2. Severe Malnutrition [b]	>10% within past 3 months	<18,5 if <70 years or < 20 if > 70 years	Reduction in MAMC < 5th percentile [c]		

[a] At least 1 phenotypic criterion and 1 etiologic criterion was required for the diagnosis of malnutrition.
[b] Severity grading was based upon the most severe phenotypic criteria.
[c] MAMC cut-off points used to assess reduced muscle mass are presented in Table 8.
[d] Data on food intake was based on self-reported answers from the MALNUTRA-questionnaire (Appendix I).
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; MAMC, mid arm muscle circumference; ER, estimated requirements; CRP, C-reactive protein.

Table 8. Mid arm muscle circumference (MAMC) cutoff points in centimeters, used for GLIM malnutrition assessment. From (63).

Sex	**Age**	**Moderate malnutrition** (10th percentile) [a]	**Severe malnutrition** (5th percentile) [a]
Women	20-79	19	18
	80-89	18	17
Men	20-79	23	22
	80-89	21	20

[a] Values in cm.

Patients were categorized as malnourished by GLIM if at least one phenotypic and one etiologic criterion were met. The category "GLIM malnourished" was created in order to provide a dichotomous response for analysis, and includes all patients identified as malnourished by GLIM prior to severity grading. The GLIM criteria combinations used for the diagnosis of malnutrition were A) Weight loss and reduced food intake B) Weight loss and inflammation C) Low BMI and reduced food intake D) Low BMI and inflammation E) Reduced muscle mass and reduced food intake F) Reduced muscle mass and inflammation (Figure 4). If a patient met more than one phenotypic criterion, the most severe criterion was used. If a patient met more than one equally severe phenotypic criterion, e.g. severely low BMI and muscle mass, the diagnosis was based on the prioritized order of 1) Low BMI 2) Weight loss 3) Reduced muscle mass. If a patient met more than one etiologic criterion, diagnosis was based on the prioritized order of 1) Reduced food intake and 2) inflammation. After selecting the most appropriate GLIM criteria combination, patients were categorized as moderately or severely malnourished based on the selected phenotypic criterion.

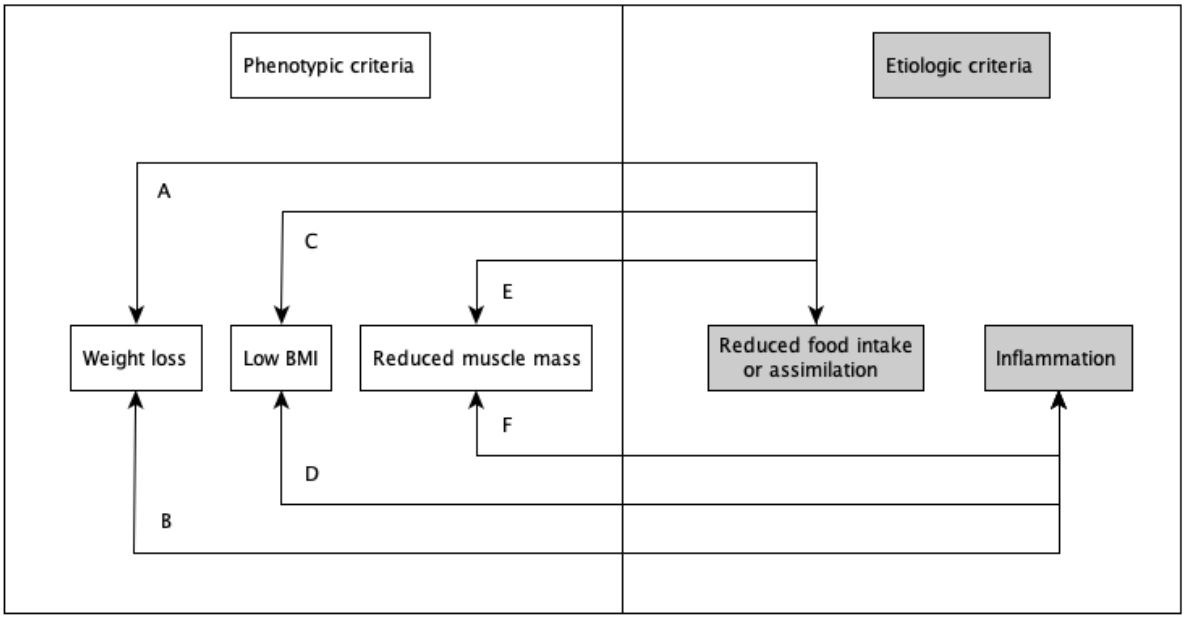


Figure 4. GLIM criteria combinations used for diagnostic assessment of malnutrition. A) weight loss and reduced food intake B) weight loss and inflammation C) low BMI and reduced food intake D) low BMI and inflammation E) reduced muscle mass and reduced food intake F) reduced muscle mass and inflammation. Adapted from (62).

3.4.2.2. ICD-10 diagnostic assessment

Criteria for the ICD-10 malnutrition diagnoses E.44.0 and E.43 were then applied based on available data from the MALNUTRA-database. For further analysis, ICD-10 E.44.0. Moderate protein-/energy malnutrition will be referred to as "ICD-10 moderate malnutrition", and ICD-10 E.43 Severe protein-/energy malnutrition as "ICD-10 severe malnutrition". The criteria presented in Table 9 were used for the diagnosis of 1) ICD-10 moderate malnutrition, or 2) ICD-10 severe malnutrition. As with GLIM, an extra category called "ICD-10 malnourished" was created, including all patients identified as moderately or severely malnourished by ICD-10. If a patient met more than one criterion, the most severe criterion was used. If a patient met more than one equally severe criterion, the diagnosis was given based on a prioritized order of 1) Low BMI 2) Weight loss 3) Low BMI and weight loss 4) Reduced food intake.

Table 9. Criteria applied in the nutritional assessment process for the ICD-10 diagnoses of moderate (E.44.0) and severe (E.43) malnutrition.

Code	Term	Criteria [a]			
		Weight loss (%)	Low body mass index (kg/m^2)	Low body mass index and weight loss	Reduced food intake
E.44.0	ICD-10 Moderate malnutrition	> 10% last 3 months	< 18.5 if < 70 years or < 20 if >70 years	< 20.5 (< 22 if > 70 years) and weight loss > 5% last 3 months	< 50% of ER last week
E.43	ICD-10 Severe malnutrition	> 15% last 3 months	< 16 if < 70 years or < 18.5 if >70 years	< 18.5 (< 20 if > 70 years) and weight loss > 5% last 3 months	N/A

[a] Requires at least 1 criterion for diagnosis.
Abbreviations: ICD-10, International Classification of Diseases 10th edition; N/A, not available; ER, estimated requirements.

3.4.2.3. Nutritional risk assessment

Lastly, the NRS-2002 score from the re-screening (see Section 3.3.1) was used to determine patient nutritional risk status. Patients were categorized as being at nutritional risk if the NRS-2002 score ≥ 3. Nutritional risk corresponds to ICD-10 E.46 Unspecified protein-/energy malnutrition, which will be referred to as "Nutritional risk" in further analysis and considered separate from the ICD-10 malnutrition diagnoses described in Section 3.4.2.2.

3.5. Ethical considerations

The MALNUTRA study protocols were approved by the Regional Ethical Committee (REC number 2016/792) and conducted according to the Declaration of Helsinki ethical principles

for medical research (64). All participants received verbal or written information regarding the study, and informed consent was obtained before participation. In order to secure patient privacy, personal data were pseudo- anonymized and stored at a research sever with restricted access only for authorized study personnel. The ID-key was stored in a separate location on the research server, only accessible to the project leader.

3.6. Statistical analysis

All analyses were performed using IBM SPSS statistics version 26 (IBM corp., Armonk, NY, USA). A p-value of less than 0.05 was considered significant.

3.6.1. Descriptive statistics

Continuous variables were presented as mean and standard deviation (SD) when normally distributed, or as median and interquartile range (IQR) if non-normally distributed. The normality of the data was analyzed using the Shapiro-Wilk test. Categorical variables were presented as numbers and percentages. The Chi-square test was used to compare categorical variables, and the independent samples t-test or the Mann Whitney U-test were used for quantitative variables.

3.6.2. Validity and agreement statistics

In order to validate the GLIM criteria, validity statistics were performed using ICD-10 as a "semi-gold standard" for detecting the presence and severity of malnutrition. First, the proportion of patients identified as malnourished by each tool was calculated. Then sensitivity (Se), specificity (Sp), negative predictive values (NPVs) and positive predictive values (PPVs) were calculated. In order to rate the outcome, the following cut-off values were applied (65): "Good", Se AND Sp > 80%; "Fair", Se OR Sp > 80%, but both > 50%; "Poor", Se OR Sp < 50%. Cohen's kappa (κ) was used to measure agreement between ICD-10 and GLIM as diagnostic tools. In order to rate the strength of agreement, cutoff values for Cohen's kappa (κ) were applied (66, 67): "Poor", 0.0-0.2; "Fair", 0.21-0.40; "Moderate", 0.41-0.60; "Good", 0.61-0.80; "Very good", 0.81-1.00.

4. Results

4.1. General population characteristics

Out of 992 patients asked to participate in the MALNUTRA-study, a total of 326 patients (approximately 33%) were included in the current study. Patients who declined participation were 55% women with a median age of 79 years, and the men were at median 75 years old. Reasons for non-participation, exclusion and withdrawal are listed in the flow chart below (Figure 5).

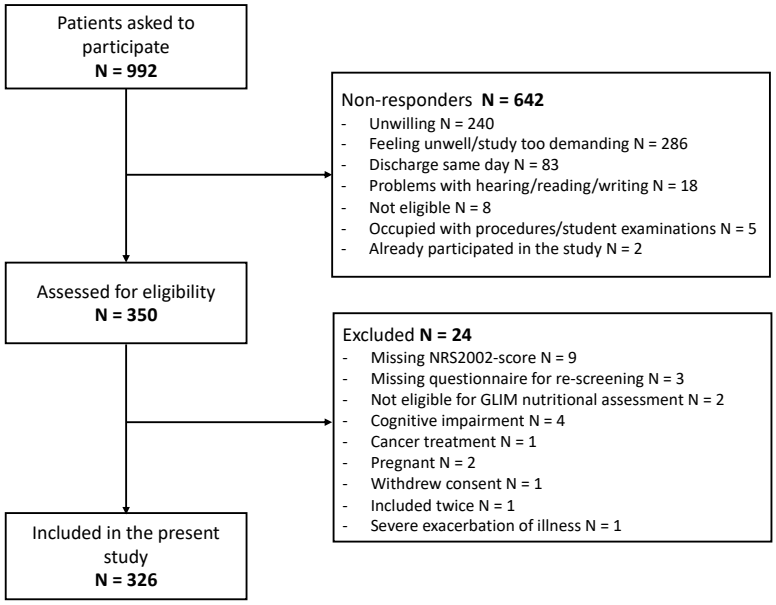


Figure 5. Flow chart over participant inclusion and exclusion process.

Of the included patients, 53% were men and the median age of inclusion was 71 years (IQR 18). Most patients were from the Department of Thoracic medicine (n=136; 42%) and the Department of Heart disease (n=110; 34%), while the remainder (n=80; 25%) were from the departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the orthopedic clinic. Median length of stay at the ward was 7 days (IQR 8) and the patients had a median of 3 diagnoses (IQR 2) reported in their medical records.

Of the parameters used to assess nutritional status, some information was missing. Information on bodyweight and BMI was available for 322 patients (98.7%), MAMC could be calculated based on MUAC and SFT measured in 304 patients (93.3%), CRP was available for 323 patients (99.1%), information on food intake the last week was reported by 302 patients (92.6%), and information on weight loss was reported by 306 patients (93.9%).

4.2. Comparison of patients according to nutritional status

4.2.1. Nutritional risk

Of the total population, 142 (43.6%) were identified as being at nutritional risk and 184 (56.4%) as not being at nutritional risk based on the re-screening using NRS-2002. Full patient characteristics according to nutritional risk status are presented in Table 10. The patients at nutritional risk were older (median age 74 vs. 68 years) and had longer length of stay at the ward (median 8 vs. 7 days) when compared to patients not at risk. Distribution based on sex was even, with 50% women of patients categorized to be at nutritional risk, and 45% women among the patients not at risk. Patients from both categories had median 3 diagnoses in total. Patients at nutritional risk had lower bodyweight (median 63 vs. 78 kg), lower BMI (median 23 vs. 27 kg/m^2) and reported weight loss above 5,10 and 15% for the last 3 months was consistently higher compared to patients not at risk. Among the patients at nutritional risk, 28% (n=52) reported a food intake below half of the ER last week, compared to 5% (n=7) of the patients not at risk. When considering the nutritional indicators not incorporated in NRS-2002, patients at nutritional risk had lower muscle mass as assessed by MAMC (median 21 vs. 24 cm), and a higher degree of inflammation as assessed by CRP (median 22 vs. 12 mg/dl) when compared to patients not at risk.

Table 10. Patient characteristics according to nutritional risk status.

	All patients	At nutritional risk	Not at nutritional risk	P-value [e]
	N (%)	**N (%)**	**N (%)**	
Total	326 (100)	142 (100)	184 (100)	
Sex				
Women	153 (47)	71 (50)	82 (45)	0.330 [f]
Departments				
Heart Disease	110 (34)	40 (28)	70 (38)	
Thoracic Medicine	136 (42)	68 (48)	68 (37)	
Others [a]	80 (25)	34 (24)	46 (25)	
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	
Age, years	71 (18)	74 (16)	68 (18)	0.000
Length of stay, days	7 (8)	8 (9)	7 (7)	0.016
Diagnoses, number	3 (2)	3 (3)	3 (3)	0.000
BMI, kg/m^2 [b]	25 (7)	23 (6)	27 (7)	0.000
Bodyweight, kg [b]	71 (22)	63 (18)	78 (19)	0.000
MAMC, cm [c]	23 (5)	21 (4)	24 (5)	0.000
CRP, mg/L [d]	15 (45)	22 (69)	12 (34)	0.001
	N (%)	**N (%)**	**N (%)**	
Low food intake [e]	59 (18)	52 (28)	7 (5)	0.000 [f]
Weight loss [f]				
>5%	68 (21)	53 (29)	15 (11)	0.181 [f]
>10%	36 (11)	27 (15)	9 (6)	0.921 [f]
>15%	13 (4)	12 (7)	1 (1)	0.110 [f]

[a] Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic.
[b] n=322 patients with information on BMI and bodyweight.
[c] n= 304 patients with information on MAMC.
[d] n=323 patients with information on CRP.
[e] n= 302 patients with information on food intake, low food intake was defined as < 50% of ER the last week.
[f] n=306 patients with information on weight loss the last 3 months.
[g] P-value is calculated using Mann-Whitney U-test for nonparametric independent samples, significance level: $p < 0.05$
[h] P-value is calculated using Pearson's chi-square test, significance level: $p < 0.05$
Abbreviations: NRS-2002, Nutritional Risk Screening 2002; BMI, Body mass index; MAMC, Mid arm muscle circumference; CRP, C-reactive protein; IQR, Interquartile range; ER, estimated requirements.

4.2.2. Malnourished according to ICD-10.

In the retrospective application of the ICD-10 codes E.44.0 and E.43, 122 (37.4%) were identified as being malnourished, and 204 (62.6%) as well-nourished. Full population characteristics according to the nutritional assessment using ICD-10 are presented in Table 11. There was no difference in age (median 71 vs. 71 years), LOS (median 3 vs. 3 days), number of diagnoses (median 3 vs. 3 diagnoses in total) and distribution based on sex (49% vs. 46% women) between malnourished and well-nourished, respectively. Almost half of the malnourished patients (n=60) were from The Department of Thoracic Medicine, while the remaining half was evenly distributed between the Department of Heart Disease (n=26) and the Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic (n=30). The malnourished patients had lower bodyweight (median 61 vs. 76 kg), a higher weight loss the last 3 months (median 6 vs. 3 kg) lower BMI (median 21 vs. 27 kg/m^2), lower muscle mass as assessed by MAMC (median 21 vs. 23 cm), and a higher degree of inflammation as assessed by CRP (median 17 vs. 13 mg/dl) when compared to the well-nourished. Of the malnourished patients, 48% (n=58) reported having a food intake below half of the ER the last week, while less than 1% (n=1) of the well-nourished reported the same.

Malnourished patients were further grouped as moderately (E.44.0) and severely (E.43) malnourished. Of the total population, 28% (n=91) were identified as moderately malnourished and 9.5% (n=31) as severely malnourished using ICD-10. There was no difference in number of diagnoses (median 3 vs. 3 diagnoses in total) and in distribution based on sex (50% vs. 48% women) between the moderately and severely malnourished patients, respectively. The severely malnourished patients were older (median 73 vs. 68 years) and had a shorter LOS (median 7 vs. 8 days) when compared to the moderately malnourished. The Department of Thoracic Medicine had the most moderately (n=41) and severely (n=19) malnourished patients. The severely malnourished patients had lower bodyweight (median 52 vs. 66 kg), larger weight loss the last 3 months (median 9 vs. 6 kg) lower BMI (median 18 vs. 23 kg/m^2), and lower muscle mass as assessed by MAMC (median 20 vs. 22 cm) when compared to the moderately malnourished. There was a higher degree of inflammation in the moderately malnourished compared to the severely malnourished, as assessed by CRP (median 18 vs. 15 mg/dl). Of the moderately malnourished patients, 56% (n=51) reported having a food intake below half of the ER the last week, while 23% (n=7) of the severely malnourished reported the same.

Table 11. Patient characteristics according to nutritional status assessed by ICD-10.

	No malnutrition	Malnutrition	P-value [d]	Moderate Malnutrition	Severe Malnutrition	P-value [d]
	N (%)	**N (%)**		**N (%)**	**N (%)**	
Total	204 (100)	122 (100)		91 (100)	31 (100)	
Sex						
Women	93 (46)	60 (49)	0.529 [e]	45 (50)	15 (48)	0.919 [e]
Departments						
Heart Disease	78 (38)	32 (26)		24 (26)	8 (26)	
Thoracic Disease	76 (37)	60 (49)		41 (45)	19 (61)	
Others [a]	50 (25)	30 (25)		26 (29)	4 (13)	
	Median (IQR)	**Median (IQR)**		**Median (IQR)**	**Median (IQR)**	
Age, years	71 (17)	71 (19)	0.850	68 (26)	73 (11)	0.195
Length of stay, days	7 (8)	7 (8)	0.586	8 (7)	7 (8)	0.800
Diagnoses, number	3 (2)	3 (2)	0.117	3 (2)	3 (3)	0.328
BMI, kg/m^2	27 (7)	21 (6)	0.000	23 (6)	18 (3)	0.000
Bodyweight, kg	76 (21)	61 (19)	0.000	66 (18)	52 (11)	0.000
Weight loss, kg [b]	3 (3)	6 (6)	0.000	6 (5)	9 (8)	0.030
MAMC, cm	23 (5)	21 (4)	0.000	22 (4)	20 (3)	0.000
CRP, mg/L	13 (41)	17 (66)	0.076	18 (92)	15 (51)	0.426
	N (%)	**N (%)**		**N (%)**	**N (%)**	
Low food intake [c]	1 (<1)	58 (48)	0.000 [e]	51 (56)	7 (23)	0.001 [e]

[a] Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic.
[b] Weight loss the last 3 months.
[c] Low food intake defined as < 50% of ER
[d] P-value is calculated using Mann-Whitney U-test for nonparametric independent samples, significance level: $p < 0.05$
[e] P-value is calculated using Pearson's chi-square test, significance level: $p < 0.05$
Abbreviations: ICD-10, International Classification of Diseases 10th edition.; BMI, Body mass index; MAMC, Mid arm muscle circumference; CRP, C-reactive protein; IQR, Interquartile range; ER, estimated requirements.

4.2.3. Malnourished according to the GLIM criteria.

In the retrospective application of the GLIM criteria, 114 (34.9%) were identified as being malnourished, and 212 (65.0%) as well-nourished by GLIM. For the category of malnourished, moderately and severely malnourished patients were grouped. Full population characteristics according to the nutritional assessment by GLIM are presented in Table 12. There was no difference in age (median 72 vs. 70 years) and number of diagnoses (median 3 vs. 3 diagnoses in total) between malnourished and well-nourished, respectively. Malnourished patients had one day longer length of stay at the ward (median 8 vs. 7 days) and consisted of fewer women (37% vs. 52% women) when compared to the well-nourished patients. Half of all malnourished patients (n=57) were from The Department of Thoracic Medicine, followed by the Department of Heart Disease (n=35) and the Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic (n=22). The malnourished patients had lower bodyweight (median 64 vs. 76 kg), larger weight loss the last 3 months (median 6 vs. 5 kg) lower BMI (median 21 vs. 27 kg/m^2), lower muscle mass as assessed by MAMC (median 21 vs. 24 cm), and a higher degree of inflammation as assessed by CRP (median 28 vs. 11 mg/dl) when compared to the well-nourished. Of the malnourished patients, 26% (n=30) reported having a food intake below half of the ER the last week, while less than 14% (n=29) of the well-nourished reported the same.

GLIM identified 12.6% (n=41) as moderately malnourished and 22.4% (n=73) as severely malnourished. There was no difference in age (median 69 vs. 72 years), distribution based on sex (39% vs. 36% women, or length of stay at the ward (median 8 vs. 8 days) between the moderately and severely malnourished patients, respectively. The severely malnourished patients had more diagnoses in total (median 4 vs. 3) when compared to the moderately malnourished. The Department of Thoracic Medicine had the most moderately (n=19) and severely (n=38) malnourished patients. The severely malnourished patients had lower bodyweight (median 59 vs. 69 kg), larger weight loss the last 3 months (median 8 vs. 5 kg) lower BMI (median 20 vs. 23 kg/m^2), and lower muscle mass as assessed by MAMC (median 20 vs. 22 cm) when compared to the moderately malnourished. The degree of inflammation as assessed by CRP was similar in the moderately malnourished compared to the severely malnourished (median 29 vs. 28 mg/dl). Of the moderately malnourished patients, 34%

(n=14) reported having a food intake below half of the ER the last week, while 22% (n=16) of the severely malnourished reported the same.

Table 12. Patient characteristics according to nutritional status assessed by GLIM.

	No malnutrition	Malnutrition	P-value [d]	Moderate malnutrition	Severe malnutrition	P-value [d]
	N (%)	**N (%)**		**N (%)**	**N (%)**	
Total	212 (100)	114 (100)		41 (100)	73 (100)	
Sex						
Women	111 (52)	42 (37)	0.007 [e]	16 (39)	26 (36)	0.717 [e]
Departments						
Heart Disease	75 (35)	35 (31)		14 (34)	21 (29)	
Thoracic Disease	79 (37)	57 (50)		19 (46)	38 (52)	
Others [a]	58 (27)	22 (19)		8 (20)	14 (19)	
	Median (IQR)	**Median (IQR)**		**Median (IQR)**	**Median (IQR)**	
Age, years	70 (20)	72 (14)	0.307	69 (12)	72 (15)	0.207
Length of stay, days	7 (8)	8 (9)	0.041	8 (11)	8 (8)	0.794
Diagnoses, number	3 (2)	3 (3)	0.000	3 (2)	4 (2)	0.018
BMI, kg/m^2	27 (6)	21 (5)	0.000	23 (5)	20 (4)	0.000
Bodyweight, kg	76 (21)	64 (17)	0.000	69 (17)	59 (17)	0.000
Weight loss, kg [b]	5 (6)	6 (6)	0.052	5 (2)	8 (6)	0.011
MAMC, cm	24 (5)	21 (4)	0.000	22 (4)	20 (3)	0.000
CRP, mg/L	11 (40)	28 (76)	0.000	28 (95)	29 (61)	0.820
	N (%)	**N (%)**		**N (%)**	**N (%)**	
Low food intake [c]	29 (14)	30 (26)	0.012 [e]	14 (34)	16 (22)	0.156 [e]

[a] Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic.
[b] Weight loss the last 3 months.
[c] Low food intake defined as < 50% of ER
[d] P-value is calculated using Mann-Whitney U-test for nonparametric independent samples, significance level: $p < 0.05$
[e] P-value is calculated using Pearson's chi-square test, significance level: $p < 0.05$
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; BMI, Body mass index; MAMC, Mid arm muscle circumference; CRP, C-reactive protein; IQR, Interquartile range; ER, estimated requirements.

4.2.4. Combinations of GLIM and ICD-10 malnourished

ICD-10 identified 50 patients (15.3%) as malnourished, which GLIM identified as well-nourished. Likewise, GLIM identified 42 patients (12.8%) as malnourished which ICD-10 identified as well-nourished. Full population characteristics according to the nutritional assessment by GLIM and ICD-10 are presented in Table 13. The patients identified as both malnourished by GLIM and well-nourished by ICD-10 were older (72 vs. 67 years), consisted of fewer women (12% vs. 30% women), had longer length of stay at the ward (9 vs. 7 days), and more diagnoses (3 vs. 2 diagnoses in total), when compared to the patients identified as both malnourished by ICD-10 and well-nourished by GLIM. Furthermore, the patients identified as both GLIM malnourished and ICD-10 well-nourished had higher bodyweight (median 69 vs. 67 kg), lower weight loss the last 3 months (median 5 vs. 6 kg) lower BMI (median 23 vs. 24 kg/m^2), lower muscle mass as assessed by MAMC (median 21 vs. 22 cm), and a higher degree of inflammation as assessed by CRP (median 27 vs. 5 mg/dl) when compared to patients identified as both ICD-10 malnourished and GLIM well-nourished. Of the patients identified as both malnourished by ICD-10 and well-nourished by GLIM, 58% (n=29) reported having a food intake below half of the ER the last week. This was not reported in any of the patients identified as both GLIM malnourished and ICD-10 well-nourished.

Table 13. Patient characteristics according to nutritional status assessed by GLIM and ICD-10.

	ICD-10 malnourished and and GLIM well-nourished	**GLIM malnourished and ICD-10 well-nourished**
	N (%)	**N (%)**
Total	50 (100)	42 (100)
Sex		
Women	30 (60)	12 (29)
Departments		
Heart Disease	14 (28)	17 (41)
Thoracic Disease	20 (40)	17 (41)
Others [a]	16 (32)	8 (19)
	Median (IQR)	**Median (IQR)**
Age, years	67 (28)	72 (13)
Length of stay, days	7 (8)	9 (10)
Diagnosis, number	2 (1)	3 (2)
BMI, kg/m^2	24 (6)	23 (5)
Bodyweight, kg	67 (22)	69 (15)
Weight loss, kg [b]	6 (7)	5 (3)
MAMC, cm	22 (5)	21 (3)
CRP, mg/L	5 (38)	27 (58)
	N (%)	**N (%)**
Low food intake [c]	29 (58)	0 (0)

[a] Departments of Gastroenterology, Endocrinology, Dermatology and Rheumatology, and the Orthopedic Clinic.
[b] Weight loss the last 3 months.
[c] Low food intake defined as < 50% of ER
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; ICD-10, International Classification of Diseases 10th edition.; BMI, Body mass index; MAMC, Mid arm muscle circumference; CRP, C-reactive protein; IQR, Interquartile range.

4.3. GLIM criteria combinations

For the diagnosis of malnutrition, GLIM requires at least one phenotypic and etiologic criteria be present. The GLIM criteria combinations used to support the 114 malnutrition diagnoses are presented in Figure 6.

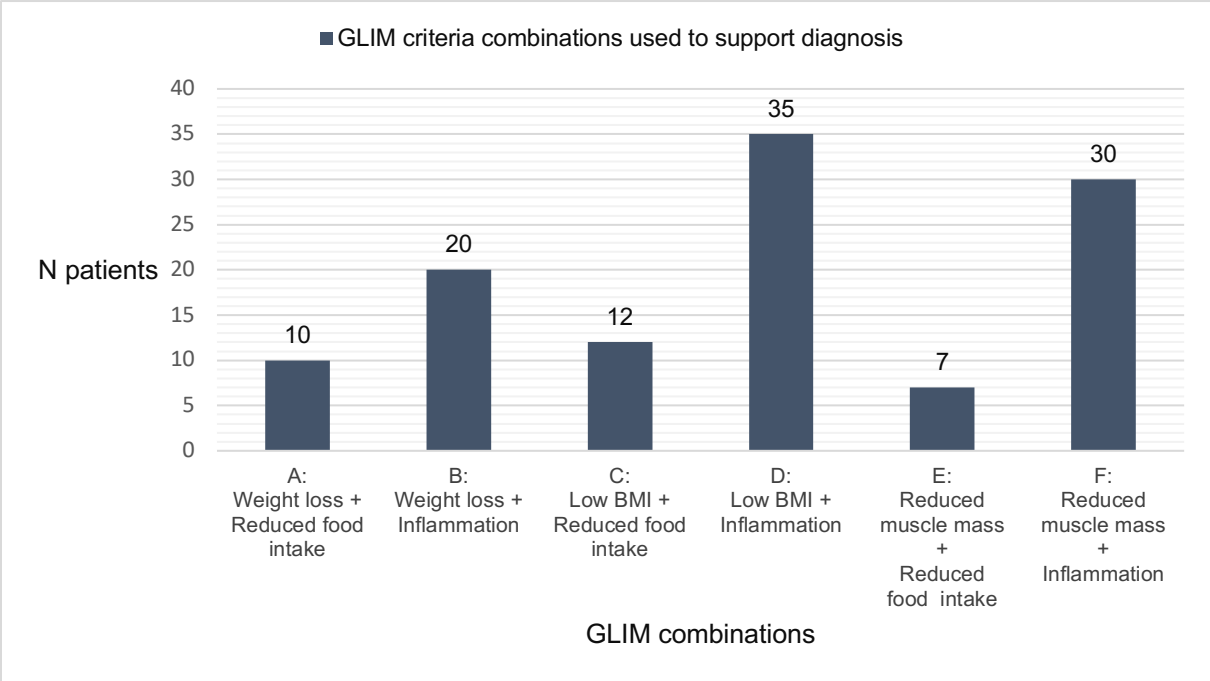


Figure 6. Distribution of GLIM combinations (A-F) of phenotypic and etiologic criteria used to support the diagnosis of malnutrition. A) Weight loss and reduced food intake B) Weight loss and inflammation C) Low BMI and reduced food intake D) Low BMI and inflammation E) Reduced muscle mass and reduced food intake F) Reduced muscle mass and inflammation.

From most to least frequent, the combinations used for diagnosis were: D “low BMI and inflammation” 30.7% (n=35); F “reduced muscle mass and inflammation” 26.3% (n=30); B “weight loss and inflammation” 17.5% (n=20); C “low BMI and reduced food intake” 10.5% (n=12); A “weight loss and reduced food intake” 8.8% (n=10); E “reduced muscle mass and reduced food intake” 6.1% (n=7).

4.4. Diagnostic criteria for moderate and severe malnutrition

The diagnostic criteria used to support a malnutrition diagnosis when retrospectively applying the ICD-10 (Table 9) and GLIM (Table 7) criteria are presented in Figure 7.

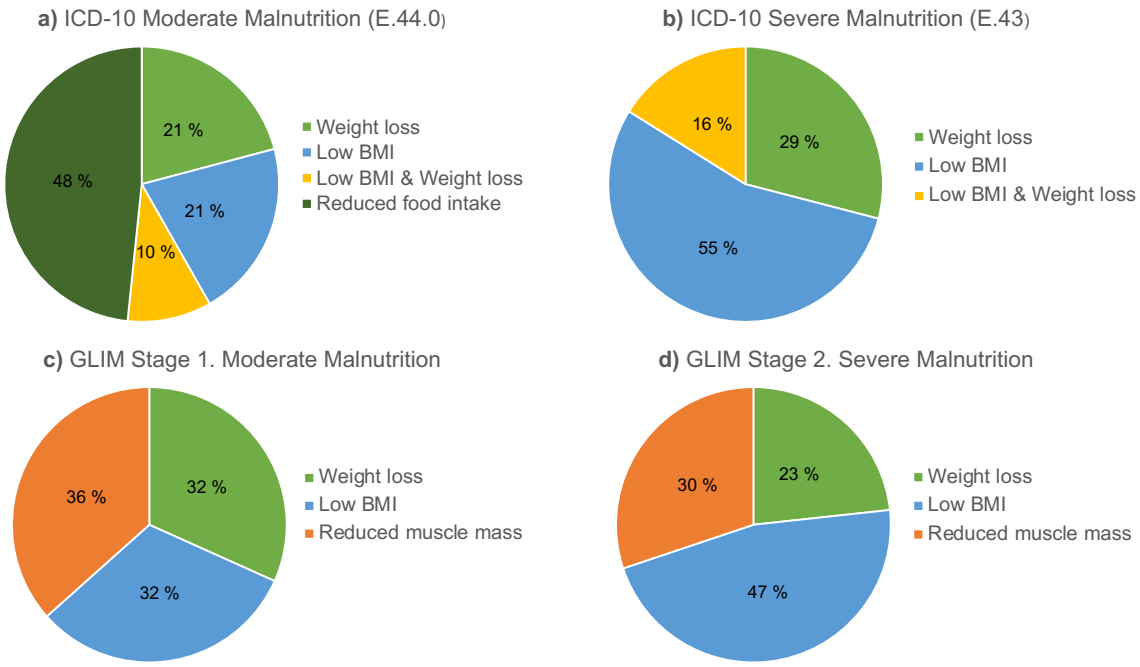


Figure 7. Distribution of criteria used to diagnose a) ICD-10 moderate malnutrition (E.44.0), b) ICD-10 severe malnutrition (E.43), and distribution of phenotypic criteria used to categorize GLIM-defined malnutrition into c) Stage 1 moderate malnutrition, and d) Stage 2 severe malnutrition.

In the ICD-10 moderately malnourished (E.44.0) patients, diagnosis was based according to the criterion for reduced food intake in 48% (n=44), low BMI in 21% (n=19), weight loss in 21% (n=19), and low BMI and weight loss in 10% (n=9), In the ICD-10 severely malnourished (E.43) patients, diagnosis was based on the criterion for low BMI in 55% (n=17), weight loss in 29% (n=9), and weight loss and low BMI in 16% (n=5).

In the GLIM malnourished patients, the severity grading for moderate malnutrition was based on the phenotypic criteria of low BMI in 22.7% (n=74) of patients, weight loss in 9.8% (n=32), and reduced muscle mass identified in 8.6% (n=28) of patients. As for GLIM severely malnourished, severity grading was based on the phenotypic criterion of reduced muscle mass in 16.6% (n=54), low BMI in 13.2% (n=43) and weight loss in 11% (n=36) of patients.

In 104 cases an ICD-10 malnutrition diagnosis was based on solely one criteria of the most severe degree. 13 patients met two equally severe diagnostic criteria, and 4 patients met three equally severe diagnostic criteria. As per GLIM, 83 patients met only one phenotypic criterion of equal severity, 47 patients met two, and 15 patients met three. As for the etiologic criteria, 200 patients met one, and 52 patients met two.

4.5. Prevalence of nutritional risk and malnutrition

The prevalence of nutritional risk as per NRS-2002 was 44% (n=142). Table 14 shows the proportion of patients identified as at nutritional risk by the screening, and the proportion of at- risk patients who were identified by GLIM and ICD-10 as malnourished. Out of the patients identified as being at nutritional risk GLIM identified 54% (n=77) as malnourished, of which 14% (n=20) was moderately and 40% (n=57) was severely malnourished. Likewise, ICD-10 identified 73% (n=104) of the at-risk patients as being malnourished, of which 54 % (n=77) and 19 % (n=27) were categorized as being moderately or severely malnourished respectively.

Table 14. Number of patients identified as being in nutritional risk by NRS-2002 and malnourished, moderately malnourished or severely malnourished by GLIM and ICD-10.

	Nutritional Risk [a]		
	Yes	No	Total, N (%)
GLIM Malnutrition [b]			
Yes	77	37	114 (35)
No	65	147	212 (65)
GLIM Moderate Malnutrition			
Yes	20	21	41 (13)
No	122	163	285 (87)
GLIM Severe Malnutrition			
Yes	57	16	73 (22)
No	85	168	253 (78)
Total, N (%)	142 (44)	184 (56)	326 (100)

	Nutritional Risk [a]		
	Yes	No	Total, N (%)
ICD-10 Malnutrition [c]			
Yes	104	18	122 (37)
No	38	166	204 (63)
ICD-10 Moderate Malnutrition			
Yes	77	14	91 (28)
No	65	170	235 (72)
ICD-10 Severe Malnutrition			
Yes	27	4	31 (9.5)
No	115	180	295 (90.5)
Total, N (%)	142 (44)	184 (56)	326 (100)

[a] Patients with a total NRS-2002 score ≥ 3 were classified as at nutritional risk.
[a] Patients were classified as malnourished by GLIM if at least one phenotypic and one etiologic criterion were met; moderately malnourished if at least one moderate phenotypic criterion and one etiologic criterion were met; and severely malnourished if at least one severe phenotypic criterion and one etiologic criterion were met (Table 7).
[b] Patients were classified as malnourished by ICD-10 if at least one criterion for moderate protein-/energy malnutrition (E.44.0) or severe protein-/energy malnutrition (E.43) were met; moderately malnourished if at least one criterion for moderate protein-/energy malnutrition (E.44.0) were met; or severely malnourished if at least one criterion for severe protein-/energy malnutrition (E.43) were met (Table 9).
Abbreviations: NRS-2002, Nutritional Risk Screening 2002; GLIM, Global Leadership Initiative on Malnutrition; ICD-10, International Classification of Diseases 10th edition.

Table 15 shows the proportion of patients identified as malnourished by both GLIM and ICD-10, and those who were categorized as moderately or severely malnourished by GLIM and ICD-10. The prevalence of GLIM-defined malnutrition was 35% (n=114). Based on ICD-10 the prevalence of malnutrition was 37% (n=122) GLIM identified 13% (n=41) as moderately malnourished, and 22% (n=73) as severely malnourished. ICD-10 identified 28% (n=91) as moderately malnourished and 9.5% (n=31) as severely malnourished.

Table 15. Number of patients identified as being malnourished, moderately malnourished or severely malnourished by ICD-10 and GLIM.

	ICD-10 Malnutrition [a]		
	Yes	No	Total, N (%)
GLIM Malnutrition [b]			
Yes	72	42	114 (35)
No	50	162	212 (65)
Total, N (%)	122 (37)	204 (63)	326 (100)
	ICD-10 Moderate Malnutrition		
	Yes	No	Total, N (%)
GLIM Moderate Malnutrition			
Yes	17	24	41 (13)
No	74	211	285 (87)
Total, N (%)	91 (28)	235 (72)	326 (100)
	ICD-10 Severe Malnutrition		
	Yes	No	Total, N (%)
GLIM Severe Malnutrition			
Yes	27	46	73 (22)
No	4	249	253 (78)
Total, N (%)	31 (9.5)	295 (90.5)	326 (100)

[a] Patients were classified as malnourished by GLIM if at least one phenotypic and one etiologic criterion were met; moderately malnourished if at least one moderate phenotypic criterion and one etiologic criterion were met; and severely malnourished if at least one severe phenotypic criterion and one etiologic criterion were met (Table 7).
[b] Patients were classified as malnourished by ICD-10 if at least one criterion for moderate protein-/energy malnutrition (E.44.0) or severe protein-/energy malnutrition (E.43) were met; moderately malnourished if at least one criterion for moderate protein-/energy malnutrition (E.44.0) were met; or severely malnourished if at least one criterion for severe protein-/energy malnutrition (E.43) were met (Table 9).
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; ICD-10, International Classification of Diseases 10th edition.

4.6. Criterion validity of the GLIM criteria

4.6.1. Sensitivity, specificity, NPV and PPV

When comparing GLIM malnutrition to ICD-10 malnutrition based on the categories well-nourished or malnourished, sensitivity (59.0%) and specificity (79.4%) was fair, the PPV was 63.2% and the NPV was 76.4%. When comparing GLIM moderate malnutrition to ICD-10 moderate malnutrition, based on the categories moderately malnourished or not, sensitivity (18.7%) and specificity (89.8%) was poor. PPV fell to 41.5% and NPV fell slightly to 74.0%. Lastly, comparing only GLIM severe malnutrition to ICD-10 severe malnutrition, based on the categories severely malnourished or not, sensitivity (87.1%) and specificity (84.4%) was good. PPV fell to 37.0% and NPV increased to 98.4%. All values of sensitivity, specificity, PPVs and NPVs are presented in Table 16.

Table 16. Sensitivity, specificity, PPV and NPV of the GLIM-criteria for malnutrition, using ICD-10 as criterion.

	GLIM Malnutrition [a, c] vs. ICD-10 Malnutrition [b, c]	GLIM Moderate Malnutrition [a, d] vs. ICD-10 Moderate Malnutrition [b, d]	GLIM Severe Malnutrition [a, e] vs. ICD-10 Severe Malnutrition [b, e]
Sensitivity, %	59.0	18.7	87.1
Specificity, %	79.4	89.8	84.4
PPV, %	63.2	41.5	37.0
NPV, %	76.4	74.0	98.4

[a] Patients were classified as malnourished by GLIM if at least one phenotypic and one etiologic criterion were met; moderately malnourished if at least one moderate phenotypic criterion and one etiologic criterion were met; and severely malnourished if at least one severe phenotypic criterion and one etiologic criterion were met (Table 7).
[b] Patients were classified as malnourished by ICD-10 if at least one criterion for moderate protein-/energy malnutrition (E.44.0) or severe protein-/energy malnutrition (E.43) were met; moderately malnourished if at least one criterion for moderate protein-/energy malnutrition (E.44.0) were met; or severely malnourished if at least one criterion for severe protein-/energy malnutrition (E.43) were met (Table 9).
[c] Categories: Not malnourished or malnourished (moderately and severely malnourished grouped).
[d] Categories: Moderately malnourished or not moderately malnourished (well-nourished and severely malnourished grouped)
[e] Categories: Severely malnourished or not severely malnourished (well-nourished and moderately malnourished grouped)
Abbreviations: PPV, positive predictive value; NPV, negative predictive value; GLIM, Global Leadership Initiative on Malnutrition; ICD-10, International Classification of Diseases 10th edition.

4.6.2. Agreement between GLIM and ICD-10

Cohen's kappa was calculated to determine if there was agreement between GLIM and ICD-10 on which patients were malnourished, and further if there was agreement on which patients were moderately or severely malnourished. The results are presented in Table 17.

Table 17. Agreement between GLIM-criteria and ICD-10 for the diagnosis of malnutrition.

	Crude agreement, (%)	Cohen's κ coefficient	Standard error of κ	P-value	Strength of agreement
GLIM Malnutrition [a, c] vs. ICD-10 Malnutrition [b, c]	72	0.389	.053	.000	Fair
GLIM Moderate Malnutrition [a, d] vs. ICD-10 Moderate Malnutrition [b, d]	70	0.102	.054	.039	Poor
GLIM Severe Malnutrition [a, e] vs. ICD-10 Severe Malnutrition [b, e]	85	0.445	.062	.000	Moderate

[a] Patients were classified as malnourished by GLIM if at least one phenotypic and one etiologic criterion were met; moderately malnourished if at least one moderate phenotypic criterion and one etiologic criterion were met; and severely malnourished if at least one severe phenotypic criterion and one etiologic criterion were met, according to Table 7.
[b] Patients were classified as malnourished by ICD-10 if at least one criterion for moderate protein-/energy malnutrition (E.44.0) or severe protein-/energy malnutrition (E.43) were met; moderately malnourished if at least one criterion for moderate protein-/energy malnutrition (E.44.0) were met; or severely malnourished if at least one criterion for severe protein-/energy malnutrition (E.43) were met, according to Table 9.
[c] Categories: Not malnourished or malnourished (moderately and severely malnourished grouped).
[d] Categories: Moderately malnourished or not moderately malnourished (well-nourished and severely malnourished grouped)
[e] Categories: Severely malnourished or not severely malnourished (well-nourished and moderately malnourished grouped)
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; ICD-10, International Classification of Diseases 10th edition.

Comparing GLIM malnutrition to ICD-10 malnutrition based on the categories well-nourished or malnourished, both tools agreed on 72 patients being categorized as malnourished (true positives), and 162 patients as not malnourished (true negatives). However, GLIM categorized 42 patients as malnourished when ICD-10 categorized them as not (false positives), and ICD-10 categorized 50 patients as malnourished when GLIM categorized them as not (false negatives). There was fair agreement between GLIM and ICD-10 for the diagnosis of malnutrition, kappa = 0.389 (p = .000), percent agreement 72%. When agreement between GLIM and ICD-10 was evaluated considering all three categories for the malnutrition diagnosis (i.e. no malnutrition, moderate malnutrition and severe malnutrition) there was fair agreement, kappa =0.314 (p = .000), percent agreement 63% (Data not presented).

Comparing GLIM moderate malnutrition to ICD-10 moderate malnutrition, based on the categories moderately malnourished or not, both agreed on 17 patients being classified as moderately malnourished (true positives), and 211 patients as not moderately malnourished (true negatives). However, GLIM identified 24 patients as moderately malnourished when ICD-10 identified them as not (false positives), and ICD-10 identified 74 patients as moderately malnourished when GLIM identified them as not (false negatives). There was poor agreement between GLIM and ICD-10 for the diagnosis of moderate malnutrition, kappa = 0.102 (p = .039), percent agreement 70%.

Comparing GLIM severe malnutrition to ICD-10 severe malnutrition, based on the categories severely malnourished or not, both agreed on 27 patients being classified as severely malnourished (true positives), and 249 patients as not severely malnourished (true negatives). However, GLIM identified 46 patients as severely malnourished when ICD-10 identified them as not (false positives), and ICD-10 identified 4 patients as severely malnourished when GLIM identified them as not (false negatives). There was moderate agreement between GLIM and ICD-10 for the diagnosis of severe malnutrition, kappa = 0.445 (p = .000), percent agreement 84%.

5. Discussion

5.1. Main findings

The overall aim of this thesis was to test the GLIM's criterion validity in an inpatient population screened for nutritional risk, by using the ICD-10 diagnostic codes for moderate (E.44.0) and severe (E.43) malnutrition as reference; and to investigate the prevalence of malnutrition in the same population. For this section the main findings will be reviewed, followed by a discussion of the results and methods. Finally, a conclusion and implications for further research will be presented.

GLIM's overall ability to identify malnutrition was rated as fair (sensitivity 59.0%, specificity 79.4%, k=0.389, fair agreement) when compared to ICD-10 (E.44.0 and E.43). GLIM's performance was poor at identifying moderate malnutrition, as sensitivity fell to 18.7% with a specificity of 89.8% (k=0.102, poor agreement). However, GLIM was rated as good at identifying severely malnourished patients, with a sensitivity of 87.1% and specificity of 84.4% (k= 0.445, moderate agreement). Of the potential combinations of phenotypic and etiologic criteria required for a GLIM malnutrition diagnosis, combination D: Low BMI (< 20 or < 22 if > 70 years) and inflammation (CRP≥ 5 mg/dl) was the most frequent. For the GLIM diagnosis of moderate and severe malnutrition, the predominant phenotypic criteria were reduced muscle mass (MAMC < 10^{th} percentile) and low BMI (< 18.5 or <20 if > 70 years), respectively. For the ICD-10 diagnoses of moderate (E.44.0) and severe (E.43) malnutrition, the predominant diagnostic criteria were reduced food intake (< 50% of ER for > 1 week) and low BMI (< 16 or < 18.5 if >70 years,) respectively.

In this population of hospitalized patients at Haukeland University Hospital (HUH) 44% were identified as at nutritional risk by NRS-2002. Using the ICD-10 E.44.0 and E.43 criteria for malnutrition, 37% were identified as malnourished. Similar results were found applying the newly proposed GLIM criteria which identified 35% as malnourished. When considering malnutrition severity, ICD-10 identified a larger proportion as moderately malnourished (28%) than GLIM (13%), whereas GLIM identified a larger proportion as severely malnourished (22%) than ICD-10 (9.5%). Thus, estimates of overall malnutrition prevalence were approximately equal between both approaches, but it would seem as though GLIM is more likely to identify severely malnourished patients.

5.2. Discussion of results

5.2.1. Population characteristics according to nutritional risk status

With a few exceptions, the differences between the patients based on nutritional risk status are as expected. Being at nutritional risk is significantly associated with higher age, longer LOS, more comorbidity (higher number of diagnoses in total), as well as significantly lower total bodyweight, BMI and MAMC. These results are consistent with previous findings. Tangvik et. al. (20) investigated the nutritional status of inpatients at HUH, based on repeated prevalence surveys as part of a quality improvement project between 2008-2009. The study found that nutritional risk as defined by NRS-2002 was most prevalent in the very old (>80 years), patients with low BMI (< 20.5 kg/m2) and patients with high comorbidity (> 7 diagnoses). In another study conducted by Tangvik et al. (29), patients at nutritional risk had significantly longer LOS than those not at risk (mean 8.3 versus 5 days).

5.2.2. According to malnutrition status

The anthropometrical and nutritional features of the malnourished patients identified by ICD-10 or GLIM are largely in line with expectations. For example, it is expected that malnourished patients have lower BMI than well-nourished and that BMI is further reduced with increasing degree of severity. This general trend was present for both diagnostic tools, except for no statistically significant difference in involuntary weight loss between GLIM well-nourished and malnourished. Interestingly, there is not found any difference in age, LOS, or comorbidities between ICD-10 well-nourished and malnourished, or between the moderately and severely malnourished. As for GLIM, the malnourished patients have longer LOS and more comorbidities than the well-nourished, and the severely malnourished have more comorbidities than the moderately malnourished. The number of well-nourished patients reporting food intake below 50% of ER the last week is higher in GLIM than in ICD-10. This is most likely explained by the ICD-10 E.44.0 criterion “Reduced food intake below 50% of ER the last week”, which is required to be matched with a phenotypic criterion to receive a GLIM diagnosis.

The patient characteristics seen in Table 13 were presented in order to further investigate differences or similarities between patients identified as malnourished *exclusively* by GLIM or ICD-10. These findings suggest that exclusively GLIM malnourished are likely to be older, have longer LOS, and more comorbidity than exclusively ICD-10 malnourished. Furthermore,

the exclusively GLIM malnourished have lower BMI, more loss of muscle mass (assessed by MAMC), and more inflammation (assessed by CRP). On the other hand, exclusively ICD-10 malnourished display lower total bodyweight and higher weight loss. Of note, these are observed differences and have not been tested statistically.

5.2.3. Prevalence of nutritional risk and malnutrition

The 44% prevalence of patients at nutritional risk is within the range (18.2-58.6%) of what has been reported in some studies of hospitalized patients using NRS-2002 (29, 68-71) (Kilder). In a study of 705 hospitalized patients in Brazil (71), 27.9% were classified as at nutritional risk by NRS-2002. The study also found that 38.9% of the at risk patients were malnourished according to SGA (classified as SGA B moderately or SGA C severely malnourished). In contrast, the results from this thesis show that GLIM and ICD-10 identified a higher proportion of the of the at-risk patients as malnourished, 54% and 73% respectively.

The 35% prevalence of GLIM defined malnutrition is also within range (13.9-80%) of what has been reported in most studies applying the GLIM criteria in a hospital setting (26, 72-76). The highest prevalence (80%) is seen in advanced-stage cancer patients (72), however it is also prevalent in in hospitalized elderly (74), which is in line with a growing body of evidence that malnutrition is frequently seen in higher age (77). As the average age is increasing in developed countries, there is subsequently more elderly being hospitalized (78). Henriksen et al. (79) highlighted an important challenge in the GLIM process. By applying four different validated screening tools (NRS 2002, MST, MUST, PG-SGA Short Form) to a population of patients with colorectal cancer, they found that depending on the screening tool, 21-36% of patients were identified as at risk of malnutrition, and furthermore that 13-24% were diagnosed as malnourished by GLIM. This implies that the choice of screening used for the first step of the GLIM process, can influence the diagnostic outcome and therefore prevalence estimates. This potential limitation has been avoided for the current thesis. All patients were assessed using the GLIM criteria, skipping the first step of risk screening while being blinded to the NRS-2002 outcomes in order to avoid a biased assessment. However, the crosstabulations (Table 14) show that 37 patients were identified as not at nutritional risk by NRS-2002, while also identified as malnourished by GLIM. This suggests that some patients would not have been detected by GLIM, had the diagnostic assessment been based on the NRS-2002 outcome. Additionally, prevalence estimates are influenced by which methods are applied to assess the muscle mass and inflammation criteria. This was demonstrated in a

retrospective analysis of community-dwelling elderly, where applying seven different approaches to measure reduced muscle mass resulted in GLIM malnutrition prevalence between 13.9% to 20.9% (80).

5.2.4. Validity and agreement.

The current study has demonstrated that GLIM has fair agreement (k=0.389) with ICD-10 (E.44.0 and E.43), with a sensitivity of 59%, specificity of 79.4%, and PPV of 63.2% and of NPV 76.4%. These results suggest that GLIM has fair criterion validity for the diagnosis of malnutrition. However, when considering GLIM's accuracy in identifying severity grades of malnutrition the results are inconsistent. The discrepancy between GLIM and ICD-10 could be explained by a difference in indicators included, and their cut-offs. The GLIM criteria consist of five indicators of malnutrition, while ICD-10 consists of four indicators of moderate malnutrition and three indicators of severe malnutrition. Exclusive to GLIM is the phenotypic criteria of muscle mass, and the etiologic criteria of inflammation. As for ICD-10, low food intake as an indicator is only used for moderate malnutrition. Furthermore, the common indicators used by the two tools use different cut-offs to distinguish between severity grades. For example GLIM requires a BMI below 18 kg/m^2 for the diagnosis of severe malnutrition, while ICD-10 requires a BMI below 16 kg/m^2 for the same diagnosis. Thus, GLIM will be more sensitive to changes in BMI and potentially identify more people as severely malnourished as a result, while a much larger reduction in BMI would be required for the same diagnosis by ICD-10.

According to the GLIM committee recommendations for validation studies (62), criterion validity should be assessed using SGA as a semi-gold standard reference. Although the literature is scarce, there are some published studies assessing the validity of the GLIM criteria in hospitalized patients using SGA as reference.

In a prospective cohort study (75) on adult/elderly patients from all units (excluding emergency and intensive care units) found that GLIM had satisfactory criterion validity, with a sensitivity of 86.6%, specificity of 81.6%, PPV of 70.8%, NPV of 92.3%, and k= 0.648 ($p<0.001$) when using SGA as reference. These results are an improvement to the ones found in the present thesis. However, when comparing GLIM severity grading with SGA, similar results were found with crude agreement between the two tools in 64.5% and 76.6% of moderately (GLIM Stage 1 and SGA-B) and severely (GLIM Stage 2 and SGA-C)

malnourished patients, respectively. Here the GLIM criteria were applied in full. The presence of inflammation was indicated by CRP > 5 mg/dl, and reduced muscle mass was assessed by a full physical assessment as well as calf-circumference (CC). However, reduced muscle mass was not used in the severity grading due to a lack of guidelines on relevant cut-off values for CC. Furthermore, the study found that the most predominant phenotypic criteria was reduced muscle mass which was observed in 86.8% of malnourished patients. Due to differences in methods, the descriptives on phenotypic criteria from the present thesis cannot be directly compared. However, loss of muscle mass was the most severe phenotypic criterion used for classification in 36% of moderately and 30% of severely malnourished patients in the present thesis. Taken all together, this implies that low muscle mass is frequent in malnourished patients and is an important component of a nutritional assessment.

In an Australian cross-sectional observational study (81) of adult ambulatory cancer care patients, it was concluded that GLIM had fair criterion validity with a sensitivity of 76%, specificity of 73%, PPV of 34%, NPV of 94% and kappa= 0.32, when using PG-SGA as reference. This study was limited in that only weight history the last six months and BMI could be assessed of the phenotypic criteria, and the etiologic criterion of inflammation was assumed present on the basis of cancer as an inflammatory condition.

A similar approach to the present thesis was applied in a retrospective analysis of nutritional parameters from a prospective cohort study assessing malnutrition at admission to 18 Canadian hospitals (73). The study did not have data on the phenotypic criterion for loss of muscle mass, so four combinations of the phenotypic criteria “weight loss” and “low BMI”, coupled with the etiologic criteria “low food intake” and “inflammation”, was compared to SGA. A CRP > 8 mg/dl was used to determine the presence of inflammation. The study found that GLIM had fair criterion validity regardless of severity status, with a sensitivity of 61.30% specificity of 89.77%, PPV of 83.14% and NPV of 73.80%. Similarly, (Kappa was not reported). Although the results differ somewhat from the present thesis, the authors found that when comparing only GLIM severely malnourished with SGA C (severely malnourished) sensitivity improved to 76.09%, specificity to 87.7%, and NPV to 96.5%, while PPV was reduced to 45.2%. These findings support the ones from the present thesis, that GLIM tends to have better diagnostic accuracy towards the severely malnourished patients. Furthermore, when using combinations of phenotypic and etiologic criteria on their own, e.g. only low BMI and reduced food intake versus SGA, all phenotypic/etiologic combinations were rated as

poor, as no combination had a sensitivity above 50%. The authors therefore concluded that all GLIM criteria combinations should be assessed in order to correctly identify malnutrition. This strengthens the current thesis, as all GLIM criteria were applied during assessment.

5.3. Discussion of methods

5.3.1. Study design

The patient population used for analysis in the current thesis was originally recruited to the MALNUTRA-study. The MALNUTRA-study had a matched cohort design, utilizing a non-probability sampling technique. This can lead to selection bias, as it is no longer a randomized participant recruitment process (54). Sampling at the wards was done by convenience, meaning that potential and available participants at the wards were informed in writing or orally regarding the study procedure, before consenting or not. Patients who declined participation were older (median 77 vs. 71 years) than the patients who consented, and one of the most frequent reasons for non-participation was "feeling unwell/study too demanding". Therefore, it is not unlikely that the point prevalence estimate of malnutrition could be suppressed by selection bias, as it is well documented that malnutrition is more common in the elderly and in patients with multiple comorbidities (20). Selection bias is also displayed by the exclusion of patient populations known to have a higher proportion of nutritional risk or malnutrition (e.g. cancer and acute care patients (20) and by the fact that 76% of the patient population was recruited from two departments alone. Taking this into account, extrapolating the results to a general inpatient population may be inappropriate.

The present thesis is a retrospective cross-sectional analysis of inpatient data collected at the time of inclusion to the MALNUTRA-study. Applied to the context of the current thesis, a cross-sectional design can be utilized to determine the presence or absence of nutritional risk or malnutrition for all patients in a sample population at a single point in time, often compared to a "snapshot", e.g. at inclusion. The cross-sectional design is also subject to certain limitations. The "snapshot" characteristic implies that associations can be investigated, but causality cannot be established. For example, patients identified as malnourished by both GLIM and ICD-10 reported significantly lower food intake compared to the well-nourished patients. Thus, reported low food intake at inclusion is associated with malnutrition, but it cannot be deduced as the causal factor for the patients' malnourished state. Nonetheless, the

cross-sectional is suitable for descriptive analysis and determining point prevalence of nutritional risk and malnutrition.

5.3.2. Statistics

5.3.2.1. Validity statistics

In line with the GLIM committee recommendations for validation studies (62), sensitivity, specificity, positive predictive value and negative predictive value has been reported in the assessment of GLIM's criterion validity. The literature lacks guidelines for optimal cutoff points for sensitivity and specificity (82). This is because diagnostic tests optimal sensitivity and specificity is dependent on the consequences of identifying false negatives and false positives (54). Ideally, a tool has both high sensitivity (i.e. a low number of truly well-nourished wrongly classified as malnourished) and high specificity (i.e. a low number of truly malnourished classified as well-nourished). In clinical practice a balance has to be struck between the two (54). For this thesis, cut-off values for sensitivity and specificity described by van Bokhorst-de van der Schueren et. al (65), was applied in order to rate the GLIM criteria's performance. Alternatively, the GLIM committee recommendations require Se, Sp and kappa > 80% for the GLIM criteria's diagnostic performance to be acceptable (62). Had this cut-off been applied to the current thesis, then only the sensitivity and specificity found when comparing GLIM and ICD-10 severely malnourished would have been satisfactory. It could be argued that these values are chosen somewhat arbitrarily, and therefore the sensitivity and specificity percentages are presented in full so that individual interpretation is possible. As for NPV's and PPV's of a test, it is important to consider the impact of prevalence (83). When prevalence decreases, so does PPV, while NPV increases. Reversely, when prevalence increases, so does PPV, while NPV decreases.

5.3.2.2. Agreement statistics

A screening or assessment tools reliability can be defined as the measure of agreement between the results of the tool when more than one user applies it to the same subject (84). This is commonly referred to as inter-rater reliability (IRR). For the present thesis, there was only one rater, assessing the agreement between two methods of assessment i.e. ICD-10 and GLIM. Therefore, the term "agreement" has been used instead of IRR. The simplest measure or agreement is by calculating the "Percent Agreement" i.e. the number of patients in which both tools agreed divided by the total number of agreements and disagreements. However,

this method does not account for chance agreement. To account for this, Cohen's Kappa has been calculated. There are several proposed ways to interpret kappa values in the literature, varying in both numerical cut-off values as well as in rating. For example, an alternative way to interpret a kappa value between 0.4 and 0.6 is as "weak" (85) and not "good" as in the current thesis. Thus, ratings of agreement can vary between studies despite identical kappa-values.

5.3.3. Using ICD-10 as reference

For the assessment of criterion validity of any tool, there should be a comparison of the new tool's assessment of nutritional status with an assessment obtained by a gold standard procedure (60). By this definition, the GLIM criteria would have to be compared to a gold standard reference for diagnosing malnutrition. As previously mentioned, a gold standard for defining malnutrition is absent. However, a full nutritional assessment by e.g. a dietitian, has been proposed as a "semi-gold standard (57). In addition, more comprehensive assessment tools such as the SGA, has been validated against full nutrition assessment by a clinician and is therefore considered more appropriate, albeit less conclusive, than a full clinical assessment (40). For the present thesis, ICD-10 has been used as reference for all analysis. This is in part because of the available parameters from the MALNUTRA-database. The comprehensive and subjective assessments that are part of the SGA also made this tool unapplicable in a retrospective analysis. This is limiting the overall results of the assessment of GLIM's criterion validity. A tool can only be as good as the reference it is measured by, and ICD-10 is likely to be outdated as the understanding of malnutrition has grown and the definition evolved since it was first published. Nonetheless, the ICD-10 is what clinicians are using every day and therefore it is of value to investigate how well the two diagnostic approaches agree. It is worth noting that the GLIM committee is working with the WHO to incorporate the GLIM criteria into the new ICD-11 (4).

5.3.4. The nutritional assessment procedure

The current thesis is a retrospective analysis of nutritional and anthropometric data collected in the MALNUTRA-study. As the available data was not originally intended for diagnostic assessment, some modification/simplification of the ICD-10 and GLIM criteria had to be made. With relevance for the ICD-10 criteria, weight loss beyond 3 months or during specific time intervals (e.g. 1 or 2 months) within 3 months could not be assessed. The presence or

absence of any acute/chronic inflammatory condition concurrent with a reduction in reduced food intake the last week has not been considered either. This is due to the design of the MALNUTRA-questionnaire, where patients reported weight history for the last 3 months only, and questions regarding food intake the last week did not include assessment of simultaneous disease activity. Since CRP was measured at admission to the hospital, this could not be applied as a measure of disease-related inflammation for the week prior to hospitalization. Similarly, the GLIM assessment did not consider weight loss beyond 3 months, reductions in food intake beyond 1 week, or the presence or absence of chronic GI conditions that could adversely affect absorption of nutrients. Obtaining information regarding patients' medical history and disease activity is a common part of any clinical nutritional assessment process. However, this is highly subjective, and it is difficult to draw any conclusions as to the impact of a condition based on a diagnosis alone. For example, it would be impossible to know retrospectively if a patient with Crohn's disease was in remission or in an active phase at the time of inclusion, which would impact nutrient absorption. Thus, information regarding patients' diagnoses was not included in the nutritional assessment. Taken together, the validation of GLIM is limited by the fact that the criteria were not applied fully as described in the consensus report.

When assessing the patients using the GLIM and ICD-10 criteria, the criteria of most severe degree would be used to support a diagnosis. As in clinical practice, malnutrition does not necessarily present only as low BMI, or only as a consequence of low food intake. Therefore a prioritized sequence was made in advance, guiding the selection of diagnostic criteria in cases with multiple equally severe criteria. The sequence was made to reflect clinical practice where it could be argued that the easiest, most attainable criteria are more likely to be used. This introduces bias to the results, as they only describe the select criteria for diagnosis, and do not reflect the total prevalence of any given criterion. Thus, it is expected that the prevalence of malnutrition defined by e.g. reduced muscle mass is underreported as it is placed last in the aforementioned sequence. However, this does not affect the overall prevalence estimates of malnutrition, nor the result of the severity classification.

The following section will discuss the applied methods for measuring the nutritional and anthropometrical data used in the diagnostic process.

5.3.5. Reduced muscle mass

According to GLIM, loss of muscle mass can be measured by any validated body composition method (4). The anthropometric measure of mid arm muscle circumference (MAMC) was used for assessment of reduced muscle mass. MAMC is calculated from skinfold thickness (SFT) and mid upper arm circumference (MUAC). MAMC is a simple, non-invasive and inexpensive procedure that used to assess malnutrition by using muscle size as an index of protein reserves (54). Low MAMC has been shown to be an independent predictor of mortality in hemodialysis patients (86), and in a study on community dwelling elderly (>80 years) higher MAMC was associated with lower mortality risk and better functional status (87). As any anthropometric measurement, MAMC suffers from some limitations. Random measurement errors in measuring SFT and MUAC cannot be excluded, although standardized procedures were carried out by trained dietitians and masters' students. Perhaps most importantly, is the choice of reference values to interpret the results. There are no international population standards available for MAMC (46). Published cut-off values by Symreng et al. (63) were applied. Here values below the 10^{th} percentile and the 5^{th} percentile are interpreted as moderate and severe malnutrition, respectively. The values are based on a Swedish reference population of 1860 healthy men and women between 20 and 101 years, later validated in a gastroenterological population. Although not validated in the current population, the reference data should be more appropriate in terms of ethnicity than values from e.g. American populations. Another strength is its wide age band (20-89 years).

5.3.6. Inflammation

CRP was selected as a biochemical indicator for the presence of inflammation. The chosen cut-off was in line with ESPEN guidelines (10) which suggest CRP > 5 mg/L as the lowest limit of inflammation that is relevant for DRM with inflammation. However, GLIM (4) recommends to primarily assess the clinical diagnosis and associated inflammation and to use CRP as a supportive measure. This subjective approach requires some degree of clinical experience and is difficult to accomplish retrospectively. Thus, an objective assessment of CRP was considered a better approach for this thesis. Other studies have defined cut-off values of CRP > 2 mg/dl (88) or CRP > 8 mg/dl (73), which underscores that there is a lack of guidelines on how to best objectively assess not only the etiologic criterion of inflammation, but also CRP as a biomarker in relation to malnutrition.

5.3.7. Weight loss and food intake history

Data on weight loss and food intake used in the nutritional assessment is self-reported data from the MALNUTRA-questionnaire (Appendix 1). These data are dependent on the patient's memory and could suffer from measurement error and their value be discussed. Furthermore, the questionnaire was not validated prior to use.

5.4. Conclusion

The GLIM criteria displayed fair criterion validity (Se 59.0%, Sp 79.4%) and agreement (k=0.389, agreement 72%) when compared to the ICD-10 diagnostic codes E.44.0 and E.43. When compared based on moderate malnutrition status, the GLIM criteria's criterion validity fell to poor rating (Se 18.7%, Sp 89.8%) and agreement was poor (k=0.102, agreement 70%) when compared to ICD-10 E.44.0. However, when compared based on severe malnutrition status the GLIM criteria displayed good criterion validity (Se 87.1%, Sp 84.4%) and moderate agreement (k=0.445, agreement 85%) when compared to ICD-10 E.43. In this population of inpatients at Haukeland University Hospital, the prevalence of nutritional risk (E.46) as identified by NRS-2002 was 44%. The prevalence of malnourished as identified by ICD-10 was 37%, of which 28% were moderately malnourished (E.44.0) and 9.5% were severely malnourished (E.43). The newly proposed GLIM criteria identified 35% as malnourished, of which 13% were moderately malnourished and 22% were severely malnourished. Taken together, while GLIM seems to identify a similar total number of malnourished patients as ICD-10, the approach can also result in a higher proportion of severely malnourished patients. Lastly, the predominant criteria for diagnosing moderate and severe malnutrition using ICD-10, was "reduced food intake" (45% of diagnoses) and low BMI (55% of diagnoses), respectively. As for GLIM, the predominant phenotypic criteria used for severity grading into moderate and severe malnutrition was "reduced muscle mass" assessed by MAMC (36% of diagnoses), and "low BMI" (47% of diagnoses), respectively.

5.5. Implications for future research

Guidelines from the GLIM committee on how to best assess muscle mass and disease-related inflammation in a clinical setting are warranted. Preferably, this should include consulting clinicians to identify methods that are readily available and easily applied to clinical practice. Furthermore, these guidelines should provide cut-off points for severity grading based on the extent of muscle mass loss. Following such guidelines, there should be more prospective studies designed to validate the full GLIM criteria, as it seems that retrospective studies are limited by the combability of available parameters. It is evident that assessment of body composition, especially muscle mass, is of importance when evaluating nutritional status. An important question is whether this should be better implemented in routine nutritional assessment along with more traditional indicators such as BMI, weight loss or food intake. Lastly, there should be more prospective studies investigating if the patients identified as malnourished by GLIM, also benefit from nutritional support.

6. Appendix

Appendix I: MALNUTRA general questionnaire (page 1)

Pasient ID: Dato:

Kjønn:

Vekt: _____kg

Vekten din for 5 år siden? _____kg vet ikke ◯

Vekt din da du var 18 år gammel? _____kg vet ikke ◯

Er du fornøyd med vekten din nå? Ja ◯ nei, for lett ◯ nei, for tung ◯

Har du prøvd å slanke deg i løpet av de siste 10 årene?

Nei ◯ ja, en gang ◯ ja, mange ganger ◯

Har du hatt ufrivillig vekttap siste 3 måneder?

Ja ◯ nei ◯ nei, jeg har gått opp i vekt ◯ jeg vet ikke ◯

Hvis ja, hvor mange kilo har du gått ned? Ca. _____kg

Hvor mye har du spist den siste uken

Normalt ◯ litt mindre enn normalt ◯

mindre enn halvparten av normalt◯ mindre enn en fjerdedel av normalt◯

Jeg spiste mindre fordi

Jeg hadde ikke matlyst ◯ jeg er kvalm ◯

Jeg har problemer med å tygge/svelge ◯ annet _____

Syns du at det er greit med vektnedgang? Ja ◯ nei ◯

Hvor fornøyd er du med dine spisevaner?

Svært fornøyd 1 2 3 4 5 6 7 8 9 10 svært misfornøyd

Har du følt at du veier for mye?

Ikke i det hele tatt 1 2 3 4 5 6 7 8 9 10 hver dag

Høyde: _____cm

Din høyde da du var 18 år gammel? _____cm vet ikke ◯

Appendix II: SOP Height measurement

Universitetet i Bergen

Prosedyre MÅLING AV HØYDE MED STADIOMETER,SECA 217		Saks- og dokumentnr. i ePhorte: **A-004**	
		Version:	001
Skrevet av : Marte Almenning Trollebø & Camilla Børsheim	Godkjent av: Jutta Dierkes	Date:	24.10.2017
		Page:	1 of 2

1. INTRODUKSJON

Denne prosedyren skal benyttes ved måling av høyde, med mål om å sikre korrekte og ensartede målinger.

2. ANSVAR

Det er den som gjennomfører målingen som har ansvar for at denne prosedyren benyttes ved måling av høyde. Det er leder for studien som har ansvar for at ansatte som jobber med studien har tilstrekkelig erfaring for å kunne gjøre dette.

3. UTSTYR

Målinger gjennomføres med Seca modell 217 (Figur 1).

Figur 1. Stadiometer

Om instrumentet:

Det mobile stadiometeret består av 7 deler som settes sammen før måling. Øverst festes et toppstykke som holder målestangen i avstand fra veggen, og forhindrer bevegelse som kan gjøre målingen unøyaktig.

4. BESKRIVELSE OG PROSEDYRE

Kontraindikasjoner:
Dersom deltageren ikke er i stand til å stå oppreist, kan ikke måling gjennomføres.

Deltagerforberedelser: Informer om prosedyre og gjennomføring.

Gjennomføring av måling:
1. Høyde skal måles uten sko med lette klær til nærmeste 0,1 cm.
2. Deltageren må ha føttene samlet, armene langs siden, strake bein og avslappede skuldre. Hodet må være i Frankfurt horisontale plan (ser rett framover; figur 2). Heler, rumpe, skulderblader og baksiden av hodet må være inntil den vertikale målestolpen.
3. Måling gjennomføres en gang, ved maksimal inspirasjon.
4. Dersom deltageren ikke er i stand til å stå oppreist kan man spørre etter hvilken høyde som står i passet.
5. Måling gjennomføres x2.

Figur 2. Måling av høyde med korrekt hodeplassering

Avvik og nøyaktighet:
Måling av høyde gjennomføres til samme tid hver dag, helst ettermiddag.
I tilfeller der overvekt forhindrer deltageren å ha heler, rumpe og skuldre inntil stadiometeret, bes deltageren om å stå strak (1, s. 247-248).

Se Vedlegg 2 for informasjon om variasjon i målemetoden.

5. RENGJØRING

Stadiometeret kan vaskes med en fuktig klut.

6. REFERANSER

1. Gibson RS. Principles of Nutritional Assessment. 2nd ed. New York: Oxford University Press; 2005.

7. VEDLEGG

Vedlegg 1: Bruksanvisning, Seca 217
Vedlegg 2: Kvalitetskontroll, høyde

Appendix III: SOP Weight measurement

Universitetet i Bergen			
Prosedyre MÅLING AV VEKT MED SECA 877		Saks- og dokumentnr. i ePhorte: **A-006**	
		Version:	001
Skrevet av : Marte Almenning Trollebø & Camilla Børsheim	Godkjent av: Jutta Dierkes	Date:	24.10.2017
		Page:	1 of 2

1. INTRODUKSJON

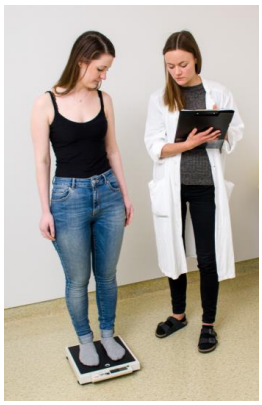
Denne prosedyren skal benyttes ved måling av vekt, med mål om å sikre korrekte og ensartede målinger.

2. ANSVAR

Det er den som gjennomfører målingen som har ansvar for at denne prosedyren benyttes ved måling av vekt. Det er leder for studien som har ansvar for at ansatte som jobber med studien har tilstrekkelig erfaring for å kunne gjøre dette.

3. UTSTYR

Veiing gjøres med Seca, model 877 (Figur 1).



Figur 1. Veiing

Om vekten:

Vekten bør plasseres på en hard overflate. Den skrus på ved å tråkke lett på overflaten. Før måling må man se til at den viser 0 kg.

4. PROSEDYRE

Kontraindikasjoner:
Måling gjennomføres ikke dersom deltageren ikke kan stå selv, evt. at det ikke er tilgjengelig stolvekt eller sengevekt. Maks vekt er 200kg.

Deltagerforberedelser:
Forklar prosedyren til deltageren, og be deltageren ta av seg tunge klesplagg og sko.

Gjennomføring av veiing:

1. Dersom deltageren ikke kan stå selv, men det er tilgjengelig en stolvekt på avdelingen, kan denne benyttes. Sjekk da at vektene viser samme vekt, ved at prosjektmedarbeider selv måler seg på begge vekter.
2. Måling gjennomføres en gang.

Avvik og nøyaktighet:

Måling av vekt bør helst gjennomføres om morgenen etter at blæren er tømt, og før første måltid. Dersom deltageren har ødemer må dette noteres (1, s. 252-253).

Se Vedlegg 2 for informasjon om variasjon i målemetoden.

5. RENGJØRING

Desinfiseres med kommerstelt tilgjengelig middel.

6. KALIBRERING:

Ved behov for kalibrering kontaktes:

Teck-Ho Service AS
Mailadresse: post@teckhoservice.no
Telefon: 55 29 22 03 / 92 06 83 26

7. REFERANSER

1. Gibson RS. Principles of Nutritional Assessment. 2nd ed. New York: Oxford University Press; 2005.

8. VEDLEGG

Vedlegg 1: Bruksanvisning, Seca 877.
Vedlegg 2: Kvalitetskontroll, vekt.

Appendix IV: SOP Skinfold thickness measurement

Universitetet i Bergen			
Prosedyre MÅLING AV HUDFOLDTYKKELSE MED LANGE HUDFOLD KALIPPER		Saks- og dokumentnr. i ePhorte: **A-002**	
		Version:	001
Skrevet av : Marte Almenning Trollebø & Camilla Børsheim	Godkjent av: Jutta Dierkes	Date:	24.10.2017
		Page:	1 of 2

1. INTRODUKSJON

Denne prosedyren skal benyttes ved måling av hudfoldtykkelse, med mål om å sikre korrekte og ensartede målinger.

Kalipperen brukers til å måle tykkelse av det subkutane fettvevet på ulike områder på kroppen som for eksempel: biceps, triceps, hofte, skulder og mage. Som kan gi et indirekte estimat av totalt kroppsfett.

2. ANSVAR

Det er den som gjennomfører målingen som har ansvar for at denne prosedyren benyttes ved måling av hudfoldtykkelse. Det er leder for studien som har ansvar for at ansatte som jobber med studien har tilstrekkelig erfaring for å kunne gjøre dette.

3. UTSTYR

Målinger gjennomføres med Lange skinfold kaliper

Om instrumentet:
Tallskivene viser i milimeter fra 0- 67. For å åpne kalipperen trykker en inn den grønne hendelen og når en skal lukke denne skal en slippe forsiktig.

4. PROSEDYRE

Adaptert og oversatt fra brukerveiledning (vedlegg 1).

Kontraindikasjoner: Måling skal ikke gjennomføres dersom deltageren har ødemer i armene.

Deltagerforberedelser: Forklar deltager hva målingen går ut på. Be så deltageren om å reise seg opp å stå oppreist gjennom prosedyren.

Gjennomføring av måling: triceps og biceps:
1. Deltagerens arm skal hvile langs kroppen med håndflaten mot kroppen.
2. Ta tak i hud og underhudsfett med pekefinger og tommel 1 cm over merket fra MUAC-måling.
3. Plasser kaliperen 1 cm under der men holder på baksiden av armen. Huden holdes fast mens målingen avleses. Vent 2-3 sek fra kaliperen er plassert til avlesning.
4. Vent min. 15 sek før neste måling gjennomføres.
5. Biceps hudfoldtykkelse måles på tilsvarende måte, men på forsiden av armen.
6. Begge måles tre ganger, en bruker gjennomsnittet som resultat

Avvik og nøyaktighet:
Se Vedlegg 2 for informasjon om variasjon i målingene.

Figur 2. Korrekt plassering av kaliper

5. RENGJØRING

Kan tørkes av med en fuktig klut. Klypene kan desinfiseres.

6. KALIBRERING

Gjennomføres ved hjelp av måleblokk. Plasser kalipperen på de ulike trinnene av måleblokken og sammenlign målingene med mål på blokken.

Ta kontakt med medisinsk teknisk avdeling på Haukeland sjukehus for kontroll av måleblokk.

7. VEDLEGG

Vedlegg 1: Lange skinfold caliper, Beta Technology
Vedlegg 2: Kvalitetskontroll, hånddynamometer

Appendix V: SOP Mid upper arm circumference measurement

Universitetet i Bergen

Prosedyre MÅLING AV MID UPPER ARM CIRCUMFERANCE (MUAC) MED MÅLEBÅND SECA 203 OG 201		Saks- og dokumentnr. i ePhorte: **A-005**	
		Version:	001
Skrevet av : Marte Almenning Trollebø & Camilla Børsheim	Godkjent av: Jutta Dierkes	Date:	24.10.2017
		Page:	1 of 2

1. INTRODUKSJON

Denne prosedyren skal benyttes ved måling av MUAC, med mål om å sikre korrekte og ensartede målinger.

2. ANSVAR

Det er den som gjennomfører målingen som har ansvar for at denne prosedyren benyttes ved måling av MUAC. Det er leder for studien som har ansvar for at ansatte som jobber med studien har tilstrekkelig erfaring for å kunne gjøre dette.

3. UTSTYR

Målinger gjennomføres med målebånd; Seca målebånd 201 cm (Figur 1).

Figur 1. Målebånd

4. PROSEDYRE

Kontraindikasjoner:
Om deltageren ikke kan sitte eller stå.

Deltagerforbedederedelser:
Informer deltageren om gjennomføringen av målingen og be deltageren ta av seg genser eller jakke.

Gjennomføring av måling:

1. Marker midten av overarmen: Deltagerens arm skal være i 90 graders vinkel med håndflaten opp. Punktet finnes midt mellom acromion på scapula og ytterst på albuen, oclecranon på ulna.
2. Deltageren skal stå oppreist, beina litt fra hverandre og armene avslappet ned langs siden med håndflaten innover. Om en må ta målingen liggende skal en plassere et brettet håndkle eller pute under albuen slik at armen kommer opp fra underlaget.
3. En skriver ned målingen til nærmeste 0,1 cm.
4. Gjennomfør måling x 2.

Figur 2. Korrekt plassering av målebånd

5. RENGJØRING

Bruk av desinfiseringsmiddel, tørk av målebånd og beholder.

6. VEDLEGG

Vedlegg 1: Bruksanvisning, Seca 203 og 201

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