Hidden hunger in the hospital?

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CHAPTER 1

GENERAL INTRODUCTION

Malnutrition is a complex and highly prevalent nutrition disorder, particularly in the clinical setting, which continues to impact health and health care on an individual, organizational and population level [3-5]. Historically, malnutrition has mostly been associated with lack of food. Therefore, ongoing efforts have been made to improve food security and aim for the 2030 goal of zero hunger worldwide, particularly directed to developing economies in which malnutrition due to food scarcity is most apparent [8]. However, in traditional high income countries, such as The Netherlands, malnutrition may present itself in a different form and therefore may also require a different approach. Particularly in the context of an ageing society dealing with complex disorders, multi-morbidity and a parallel obesity pandemic [9, 10], current malnutrition care practices may need adjustment. Therefore, the overall aim of the scientific studies presented in this thesis was to evaluate current nutritional care practices with regard to the detection of malnutrition and malnutrition risk in the complex hospital setting, and to identify potential targets for improvement of hospital nutrition care.

Firstly, in this chapter, the broader context of health and disease on a population level, and the role of nutrition therein, is described. Next, the current evidence on the prevalence, causes, characteristics, and consequences of malnutrition and malnutrition risk in the community and clinical setting is briefly summarized. To tackle malnutrition in the clinical setting, different steps in the nutrition care process have previously been identified. Important knowledge gaps with regard to components of this nutrition care process, i.e., screening, assessment, monitoring and post-discharge planning, in the complex hospital population are identified. The example of kidney transplant recipients is presented, as this is a population usually dealing with complex multi-morbidity and may be at risk for multiple nutrition-related conditions at the same time. And at the end of this chapter, an overview is provided of how these knowledge gaps are addressed in the main chapters of this thesis.

Epidemiological changes in health and disease

Human longevity has rapidly increased over the past centuries, with life expectancy doubling from about 40 years in the 19th century to around 80 years in current times [11]. This increase in life expectancy can be attributed to the improved standards of living and important developments in medical care and public health, which can be considered one of the most important achievements of modern society. The massive deaths due to infectious diseases and childbirth have been largely replaced by chronic non-communicable diseases, occurring typically at older age, such as cardiovascular disease, cancer, chronic respiratory disease, chronic kidney disease and diabetes, now accounting for more than 70% of all deaths worldwide [12]. Similar to the global trend, prevalence of chronic diseases in The Netherlands continued to increase over the last two decades, from approximately one-third in 2004 to more than half of the population being affected in 2019 [13, 14]. The disease burden of cancer was shown to be particularly high, followed by cardiovascular disease, and the disease burden of dementia is estimated to strongly increase in the future [15].

Inconveniently, many of the currently prevalent chronic diseases are interrelated and can therefore result in complex comorbidity and a cumulative health risk [16]. For example, presence of diabetes increases the risk of both cardiovascular disease and chronic renal disease, further affecting health outcomes [17, 18]. Prevalence of multi-morbidity rapidly increases with age, affecting 20 to 50% of adults of 50 years and over in Europe [16, 19]. In the Netherlands, prevalence of multi-morbidity showed a relatively large increase compared with prevalence of chronic disease in general, affecting almost one-third of the Dutch population in 2019 [13, 14]. This is well illustrated by data from the Lifelines Cohort Study, a large population-based cohort based on three generations living in the northern region of The Netherlands (**Figure 1**) [9, 20, 21]. Importantly, besides higher risk of mortality, presence of multi-morbidity is associated with functional impairment, lower quality of life, increased care utilization and higher costs [22-27]. These temporal changes in the epidemiology of health and disease thereby pose important challenges for public health and health care to remain manageable and future-proof [28, 29].

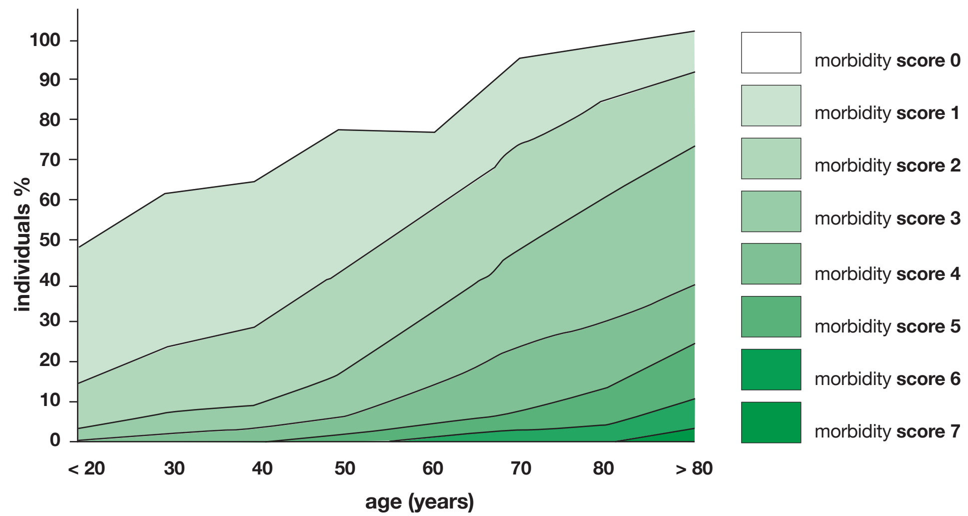

Figure 1. Distribution of number of disease domains in different age categories of subjects from the Lifelines Cohort Study
Contribution per disease domain on total of reported disease domains (%). *Figure by Meems et al. [9], as published in Annals of Medicine (www.tandfonline.com)*

The multiple burden of nutrition-related conditions: food as medicine

The shift from single disorders to multiple chronic conditions warrants a different approach to health and disease. Whereas effective single interventions are usually appropriate for single disorders, the additive effect of multiple treatments for multiple disorders may fall short because of the complex interplay between the different treatments and disease effects [30, 31]. Therefore, there is an urgent need for effective integral interventions targeting multiple diseases at once, rather than all conditions separately. Potential multimodal intervention targets mostly include nutritional and other lifestyle factors, such as weight status and diet, smoking behavior, and physical activity [32-35]. The increasing evidence on the impact of deteriorated weight status, inadequate nutrition and imbalanced diet have given rise to the movement of "Food is medicine" [36]. From the rationale "What is the cause, can also be the cure", this is a potentially highly valuable framework to prevent, cure and manage the increasing chronic care burden.

Different nutrition disorders and nutrition-related conditions have been defined and classified by The European Society of Clinical Nutrition and Metabolism (ESPEN), which are shown in **Figure 2**, including malnutrition, and overweight and obesity. Historically, malnutrition or specifically undernutrition on the one hand, and overweight and obesity on the other hand have mostly been considered as separate conditions at different extremes of the nutrition spectrum ('lack of food' vs. 'excess food'), with separate risk factors and a contrasting geographical distribution (traditional developing economies vs. high income countries). However, more recently, the World Health Organization (WHO) has recognized the growing co-existent presence of malnutrition/undernutrition and overweight or obesity within individuals, households and populations, and its cumulative negative effect on health. This is referred to as '*the double burden of malnutrition*' [37, 38]. A '*multiple burden of malnutrition*' may even be present, when multiple nutrition-related conditions (**Figure 2**), e.g., malnutrition/undernutrition, micronutrient deficiency, and overweight or obesity co-exist [8]. Although current economic models are not designed for estimating the cumulative effect of these multiple burdens of inadequate nutrition properly [39], global action is required to prevent further negative health and economic effects and to achieve the ambitions of the United Nations Decade of Action on Nutrition and the United Nations Sustainable Development Goals for 2030 [8, 40].

However, the recognition of '*the double burden of malnutrition'* until now has been mostly focused on developing economies, rather than on traditional high income countries such as The Netherlands. Although malnutrition due to food scarcity is less common in these countries compared with developing economies, malnutrition due to other causes, particularly disease-related malnutrition, remains highly prevalent. In Dutch care settings, on average, 1 in every 5 patients was considered malnourished in 2007 [41]. At the same time, in The Netherlands, half of the adult population is now overweight, and 1 in every 7 adults is obese [42]. The epidemiology of both malnutrition and overweight or obesity thereby suggests a double burden of malnutrition might also be highly prevalent in The Netherlands and other traditional high income countries, particularly in the care setting. However, empirical evidence in the form of concrete prevalence numbers is yet scarce. If indeed the case, detecting and counteracting malnutrition in this context may require a different approach, as concurrent overweight or obesity may obscure the presence of malnutrition.

Malnutrition and malnutrition risk in the context of the ageing, multi-morbid and obese population

Malnutrition is a complex multifactorial problem, and shares common causal determinants and risk factors with other nutrition-related disorders, including overweight or obesity, such older age, multi-morbidity, polypharmacy and low socio-economic status [43-46]. Prevalence numbers of malnutrition differ largely across geographical areas, settings and definitions used (in this thesis, we adopt the terminology by ESPEN, according to **Figure 2** and **Box 1**). In a multinational study using the Mini Nutritional Assessment (MNA) for malnutrition assessment in more than 4500 older adults, total prevalence of malnutrition was 23%.

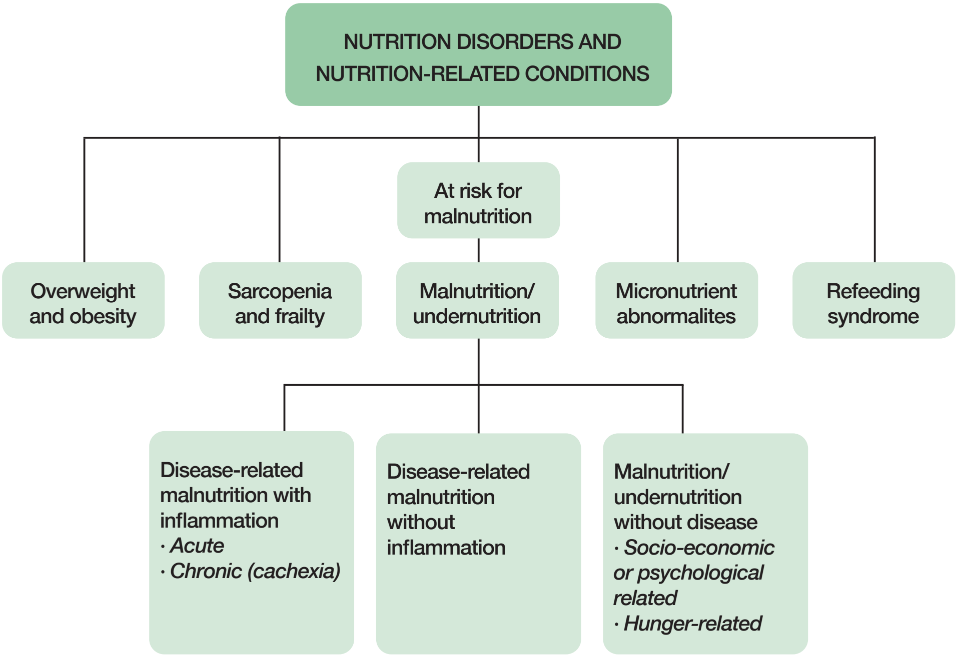

Figure 2. ESPEN terminology and taxonomy of nutrition disorders and nutrition-related conditions, adapted from [6]
** The source of the original figure was published in Clinical Nutrition, Vol 36, T. Cederholm et al., ESPEN guidelines on definitions and terminology of clinical nutrition, Page 49-64, © Elsevier Ltd and European Society for Clinical Nutrition and Metabolism (2017)*

Box 1. *Definition of malnutrition, as endorsed by ESPEN and adopted in this thesis*

"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"

(Sobotka, 2012 – endorsed by ESPEN) [6]

Malnutrition prevalence was the lowest in the community and nursing home setting compared with the hospital and rehabilitation setting, but still present in 6% and 14%, respectively, and an additional 32% and 53% were at risk of malnutrition [47]. In Dutch community-dwelling older individuals, risk of malnutrition determined by the Short Nutritional Assessment Questionnaire 65+ (SNAQ 65+), ranged from 14% in the general practice setting, to 44% in participants receiving home care [48]. Malnutrition and malnutrition risk are associated with higher risk of mortality in community-dwelling older adults, as well as higher risk of falling [49-53], which in turn may further impact functional status negatively, and increase the risk of complications and other adverse outcomes.

In a society dealing with epidemiological changes in health and disease, most prominently ageing and multi-morbidity of non-communicable diseases, the general population increasingly becomes a patient population. To illustrate, nearly 44 per 100 inhabitants of The Netherlands were registered to receive specialist medical care for at least one condition in 2019 [54]. In addition, almost 1.9 million people were admitted to the hospital at least once [55]. Hospital patients, especially those with multiple complex disorders, are likely to be at particular high risk of developing multiple nutrition-related conditions and associated worse outcome, as disease factors can further exacerbate the yet complex interplay of risk factors and underlying biological mechanisms.

This is exactly the case for disease-related malnutrition, which is a specific type of malnutrition (**Figure 2**) caused by a concomitant disease [6]. Inflammation, resulting in catabolism, is an important cause of disease-related malnutrition, which can be present in both acute and chronic forms, for example in trauma or sepsis, and cancer or respiratory disease, respectively. Disease-related malnutrition without inflammation is caused by other disease factors, for example through dysphagia in neurological diseases or malabsorption. Prevalence of disease-related malnutrition is estimated around 30% in the hospital setting, and is associated with a longer length of stay, higher risk of complications, readmission, and in-hospital mortality, as well as mortality after up to 3-years of follow-up [3, 56-58].

Importantly, risk of disease-related malnutrition, as determined by malnutrition screening, is also considered a separate condition by ESPEN [6], that is associated with worse clinical outcomes [59-61]. Furthermore, both disease-related malnutrition and risk thereof are associated with decline of functional status, impaired wound healing and higher risk of pressure ulcers, and lower quality of life [62-65]. Because of the size of the issue and its impact on public health and total care burden, malnutrition (risk) was included in the Dutch National Prevalence Measurement of Care Problems (LPZ) in 2004 and malnutrition risk screening for hospitals was implemented at a national level since 2006 [41]. Based on the data from the LPZ, it was estimated that the total additional costs of managing disease-related malnutrition in The Netherlands were €1.2 billion attributable to the hospital setting in 2011 [4]. Although use of validated malnutrition screening tools is associated with better nutritional care and lower malnutrition rates, effectuation of malnutrition screening in clinical practice remains a challenge and malnutrition care policies need to be continuously and critically evaluated to improve nutritional care and patient outcomes [66],

Specific attention for malnutrition or risk thereof might be required in patients with multiple chronic diseases, polypharmacy, and additional complex needs. In a study of chronic patients with complex needs admitted to two university hospitals in Spain, 83% to 86%

was at risk for malnutrition and malnourished patients had a greater need for home care or intermediate care after discharge, and had a higher risk of in-hospital mortality as well as at 5 months follow up [67]. One of the potential contributing mechanisms is thought to be through a synergistic negative effect of polypharmacy and malnutrition on outcomes [68]. Of note, the mean body mass index (BMI) of the study population was within the overweight range (mean BMI 26.2 kg/m^2), and the malnourished patients were not necessarily underweight (mean BMI 24.9 kg/m^2), which suggests malnutrition might present with different characteristics in a complex hospital population.

Historically, malnutrition has mostly been defined by the presence of underweight/low BMI and/or critical weight loss, but particularly underweight/low BMI may lack validity to identify disease-related malnutrition in an increasingly obese patient population. However, studies that focus specifically on the co-existence of overweight/obesity and disease-related malnutrition and its potential cumulative negative burden for health are still scarce. In a previous study performed in a tertiary hospital in Israel, 23% and 25% of overweight and obese patients, respectively, were at increased risk of malnutrition according to screening by the Nutritional Risk Screening 2002 (NRS 2002) [69]. Moreover, in a secondary analysis of the Australasian Nutrition Care Day Survey, 14% of obese hospitalized patients were found to be malnourished according to assessment by the Subjective Global Assessment (SGA), and the majority (70%) of these patients received no additional nutritional support [70]. These findings show the potential risk of overlooking disease-related malnutrition in the overweight/obese hospitalized patient, but more studies are needed to critically evaluate the efficacy of our current nutritional care practices in light of the changing population characteristics.

The co-existence of overweight or obesity and disease-related malnutrition in hospitalized patients may be characterized by an unfavorable body composition of excess body fat and impaired muscle mass related to inadequate nutrition. Because of its relation to important clinical outcomes, loss of muscle mass has been marked as one of the main challenges in addressing malnutrition in clinical practice [71, 72], and is now included as a diagnostic criterion for malnutrition in the most recent consensus by the Global Leadership Initiative on Malnutrition (GLIM) (**Box 2**) [1]. In hospitalized patients and other patients in which assumptions on the stability of body tissues are often not met, e.g., patients with edema or ascites, body composition assessment is crucial for diagnosing malnutrition, since excess fat mass or fluid accumulation may mask loss of muscle mass [73]. However, to date, there is no consensus on how to assess muscle mass in the clinical setting. Magnetic resonance imaging (MRI) and computed tomography (CT) are considered the gold standard techniques, but are not feasible for routine assessment of muscle mass in clinical practice, because of the high costs, lack of portability, the requirement for highly-trained personnel, and radiation exposure [74]. An alternative body composition assessment technique applicable for bedside measurement in clinical practice and recommended by GLIM and EWGSOP2, is bio-electrical impedance analysis (BIA) [75, 76]. Other potential alternative muscle mass assessment methods include ultrasound [77, 78], and analysis of creatinine from 24-hour urine collection [79], but both methods require further validation in the clinical setting. The GLIM diagnostic framework for malnutrition allows for more consistent diagnosis of malnutrition in research and in clinical practice, and comparison of malnutrition prevalence and characteristics across care settings

Box 2. ***GLIM criteria for the diagnosis of malnutrition*** [1]

Phenotypic criteria
- Non-volitional weight loss
- Low body mass index
- Reduced muscle mass

Etiologic criteria
- Reduced food intake or assimilation
- Disease burden/ inflammatory condition

Malnutrition diagnosis
At least 1 phenotypic + 1 etiologic criterion present

and patient populations. However, more empirical evidence is necessary to evaluate this consensus based framework and its validity and application in clinical practice.

Example: the kidney transplant recipient
The kidney transplant recipient (KTR) is an example of a patient with a complex disorder who is often affected by multiple co-morbidities, and who may be at risk of multiple nutrition-related conditions and worse outcome. In 2017, nearly 700 million people worldwide had chronic kidney disease (CKD), equaling 9% of the world population [80]. The burden of CKD was estimated to result in almost 28 million disability-adjusted life years (DALYs). Nearly one third of the CKD disease burden was accounted for by diabetic nephropathy, illustrating the close relation between different non-communicable diseases and the impact of multi-morbidity.

Renal transplantation is considered the treatment of choice for end-stage renal disease, offering better quality of life and survival chances compared with dialysis treatment [81-83]. In 2018, more than 22.000 kidney transplantations were performed across Europe, and in The Netherlands nearly 17.500 patients were living with a kidney transplant [84]. Although short-term survival of KTR has improved considerably, long-term outcomes are still worse compared with the general population [85, 86]. This is mostly due to a higher risk of cardiovascular mortality in KTR, elicited by conventional risk factors, including unhealthy lifestyle and overweight/ obesity, as well as transplant-specific factors, including side-effects of immunosuppressive medication, complications of the transplantation and previous dialysis therapy [87, 88].

Therefore, in recent years, increasing attention has been paid to preventing weight gain, obesity and associated cardiovascular risk. More than half of the KTR population experiences considerable weight gain after transplantation, with reported estimates of +5 to +9 kg during the first year, primarily due to an increase in fat mass [89-92]. Prevalence of overweight and obesity after kidney transplantation are estimated at 35-40% and 15-25%, respectively [92, 93].

Importantly, weight gain and obesity after transplantation have shown to be associated with higher morbidity, for example post-transplant diabetes mellitus, and higher risk of graft failure and premature mortality [94-98].

In contrast to the risk of weight gain and obesity, less attention is paid to possibly concomitant disease-related malnutrition in KTR. The impact of disease-related malnutrition in the CKD is well-documented in the general CKD population and in CKD patients receiving dialysis therapy [99-101], but studies in KTR are still scarce. The scarce literature available showed that malnutrition risk according to the Malnutrition Inflammation Score (MIS) was associated with lower quality of life and higher risk of graft loss and mortality in KTR [102, 103]. However, the MIS is mostly used within the field of nephrology only, which hampers comparison of the results with other patient populations, and only includes a global assessment of muscle wasting, not a quantification of muscle mass [104]. A previous study from our hospital showed that lower intake of protein was associated with higher risk of graft failure, underscoring the relevance of disease-related malnutrition in KTR [105]. Importantly, the current standard protein recommendation of 0.8 grams per kg body weight, which is the same as for the general population, was associated with a higher risk of worse outcome, compared with a slightly higher intake of approximately 1.0-1.2 grams per kg. A potential factor possibly explaining the association between protein intake and outcomes in KTR, is low muscle mass. Previous quantitative reports on low muscle mass in KTR showed a prevalence of 19% to 50% depending on the cut-off value applied [106, 107]. However, malnutrition according to the full GLIM diagnostic framework has not yet been evaluated in KTR, and identification of KTR with suboptimal muscle status and associated worse outcome warrants further investigation. Better characterization of nutritional status in KTR is needed to further improve long-term outcomes and quality of life in KTR.

The nutrition care process: knowledge gaps in the complex hospital setting
Malnutrition risk screening is the first crucial step in the nutrition care process (**Figure 3**), to identify patients at risk [1, 108]. Multiple screening tools have been developed and validated for this purpose, and malnutrition screening is usually performed upon hospital admission. Traditional screening tools currently used in clinical practice such as the Malnutrition Universal Screening Tool (MUST), include low BMI and/or critical weight loss as main items (**Box 3**). However, in an increasingly obese patient population and in hospitalized patients with fluid accumulation, this may result in underestimation of malnutrition risk. Also, screening for low BMI and critical weight loss alone mainly identifies patients with characteristics of existing malnutrition, rather than those who are at risk for future development of malnutrition. Alternatively, the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF), as part of the PG-SGA Full form (**Box 4**), screens for weight loss irrespective of BMI, as well as food intake, nutrition impact symptoms, and activities and function, enabling a more proactive and BMI-independent approach to identify malnutrition risk [109]. The PG-SGA SF has been validated as a separate screening tool for practice in cancer outpatients receiving chemotherapy and in patients undergoing vascular surgery [110-112]. Although the PG-SGA SF is a potentially valuable tool for malnutrition screening in the complex hospital setting, because of its pro-active and

Box 3. ***MUST, Malnutrition Universal Screening Tool*** [7]

MUST
Score range 0-6
- *BMI*
  (score 0-2)
- *Weight loss*
  (score 0-2)
- *No nutritional intake >5 days due to acute illness*
  (score 0-2)

Box 4. ***PG-SGA, Patient-Generated Subjective Global Assessment*** [2]

PG-SGA Full form
Score range 0-52
Global Assessment Category Stage A/B/C

PG-SGA SF, Short Form
- *Weight loss*
  (score 0-5)
- *Food intake*
  (score 0-4)
- *Nutrition impact symptoms*
  (score 0-24)
- *Activities/functioning*
  (score 0-3)

PG-SGA Professional component
- *Disease and its relation to nutritional requirements*
  (score 0-7)
- *Metabolic demand*
  (score 0-6)
- *Physical exam*
  (score 0-3)

BMI-independent design, it is not yet widely used for malnutrition screening in the general hospital setting and requires further validation in a mixed hospital population.

Whilst risk of malnutrition, as determined by a validated screening instrument, is already an indication for start of nutritional intervention, diagnosis of malnutrition requires further assessment using validated assessment tools and body composition assessment techniques in addition to the malnutrition screening result [1]. The Subjective Global Assessment (SGA) is considered a semi-gold assessment tool and yields a staging of nutritional status based on scored items on weight loss, food intake, gastro-intestinal symptoms, functional status, disease state/comorbidities, and a short physical exam [113]. Being based on the SGA, the PG-SGA also includes scored items on weight loss, food intake, activities and function, disease in relation to nutritional requirements, and a physical exam of muscle deficit/loss, loss of fat stores, and edema. In addition, the PG-SGA includes an item on metabolic demand (fever and use of corticosteroids), and includes more extensive scoring of nutrition impact symptoms, as compared with the SGA. Nutrition impact symptoms, e.g., nausea, altered taste, problems swallowing, have shown to be predictive of future malnutrition [114, 115]. Therefore, including nutrition impact symptoms in malnutrition screening may allow for more pro-active screening through identification of patients at risk of developing future malnutrition. The PG-SGA was originally validated in patients with cancer, but is now more widely adopted as a 4-in-1 instrument for screening, assessment, interdisciplinary triage and monitoring in various patient populations [109, 115-118]. However, larger scale studies on the validity and practical application of the PG-SGA in a mixed hospital population are yet scarce. Since malnutrition care policies are usually organized at an institutional level, studies in a mixed hospital population are particularly relevant for clinical practice, to optimize nutritional care as a whole and for all patients.

To assess whether the next step in the nutrition care process, i.e., intervention, is effective for meeting the intended treatment goals, and to assess whether additional patients require intervention due to deterioration of nutritional status over time, frequent assessment or monitoring of nutritional status is recommended [108]. However, in clinical practice, as well as in the outpatient setting, this is often not performed on a routine basis. This may result in under-detection and undertreatment of malnutrition and malnutrition risk in hospitalized patients, as well as in outpatients with complex disorders and multimorbidity, including KTR. Data on changes in nutritional status during hospitalization, and nutritional status at discharge are therefore also scarce. Particularly the latter, nutritional status at hospital discharge, has received little attention in the scientific literature so far. This may be problematic, considering the usually short length of hospital stay in which nutritional status cannot be fully restored.

Aims and outline of this thesis

Considering the high impact of the multiple burdens of malnutrition, the knowledge gaps regarding detection of malnutrition and malnutrition risk in complex hospital care and in the context of the ageing, increasingly obese and multi-morbid society (**Box 5**), more studies on this topic from a clinical practice perspective are urgently warranted. Therefore, the main aim of this thesis was **to evaluate current nutritional care practices with regard to the detection (i.e., screening, assessment, and monitoring) of malnutrition and malnutrition risk in the complex hospital setting, and identify potential targets for improvement of hospital nutrition care**.

The main aim of this thesis includes two objectives, which are:

- To quantify the issue of malnutrition and malnutrition risk using current standard and alternative screening and assessment methods in the complex hospital setting, 1) across the BMI spectrum, 2) during hospitalization, and 3) in KTR specifically, all of which received little attention in the scientific literature so far;
- To compare different screening and assessment methods that are potentially applicable in clinical practice, for their association with relevant clinical outcomes.

The chapters of this thesis are clustered in two parts: *Part A* - Studies in hospitalized patients (**Chapters 2 to 4)**, and *Part B* - Studies in outpatient KTR (**Chapters 5 and 6**). Additionally, the chapters are structured according to their position in the nutrition care process, as visualized in **Figure 3**.

Starting with **Chapter 2**, the impact of overweight and obesity on the comparative performance of MUST and PG-SGA SF is explored, to detect malnutrition risk in hospitalized patients. In **Chapter 3**, the same screening tools, the MUST and PG-SGA SF, are evaluated for their respective associations with clinical outcomes, i.e., prolonged hospitalization, readmission and mortality after discharge, in our practice-based cohort of hospitalized patients. In **Chapter 4**, nutritional status is monitored using the Full PG-SGA during the course of hospitalization, including at hospital admission, on different time points during hospital stay and before hospital discharge.

In **Chapter 5**, malnutrition is assessed in outpatient KTR with use of data from the TransplantLines Biobank and Cohort Study, applying the international GLIM criteria for the diagnosis of malnutrition, and to determine the relative contribution of each phenotypic criterion (weight loss, low BMI, reduced muscle mass) to the diagnosis. As this study showed that low muscle mass was the predominant phenotypic characteristic of malnutrition in KTR, in **Chapter 6**, the impact of different indices of muscle mass, as well as muscle strength, on all-cause mortality are examined in outpatient KTR.

In **Chapter 7**, the main findings of this thesis are summarized and discussed, and recommendations are made for future research and clinical practice. Additionally, a **Portfolio** section includes other works and activities by the author related to the topic of this thesis and specifically highlighting nutritional care in practice.

Box 5. *Identified knowledge gaps regarding the nutrition care process in complex hospital care*

General complex hospital population

- Traditional BMI-dependent malnutrition screening tools (e.g., MUST) vs. alternative BMI-independent screening tools (e.g., PG-SGA SF): differences in identification and association with clinical outcomes?
- Nutritional status during hospitalization and at hospital discharge

In kidney transplant recipients (KTR)

- Malnutrition in KTR: prevalence, risk factors and characteristics?
- Muscle status in KTR: which measures are associated with clinical outcomes?

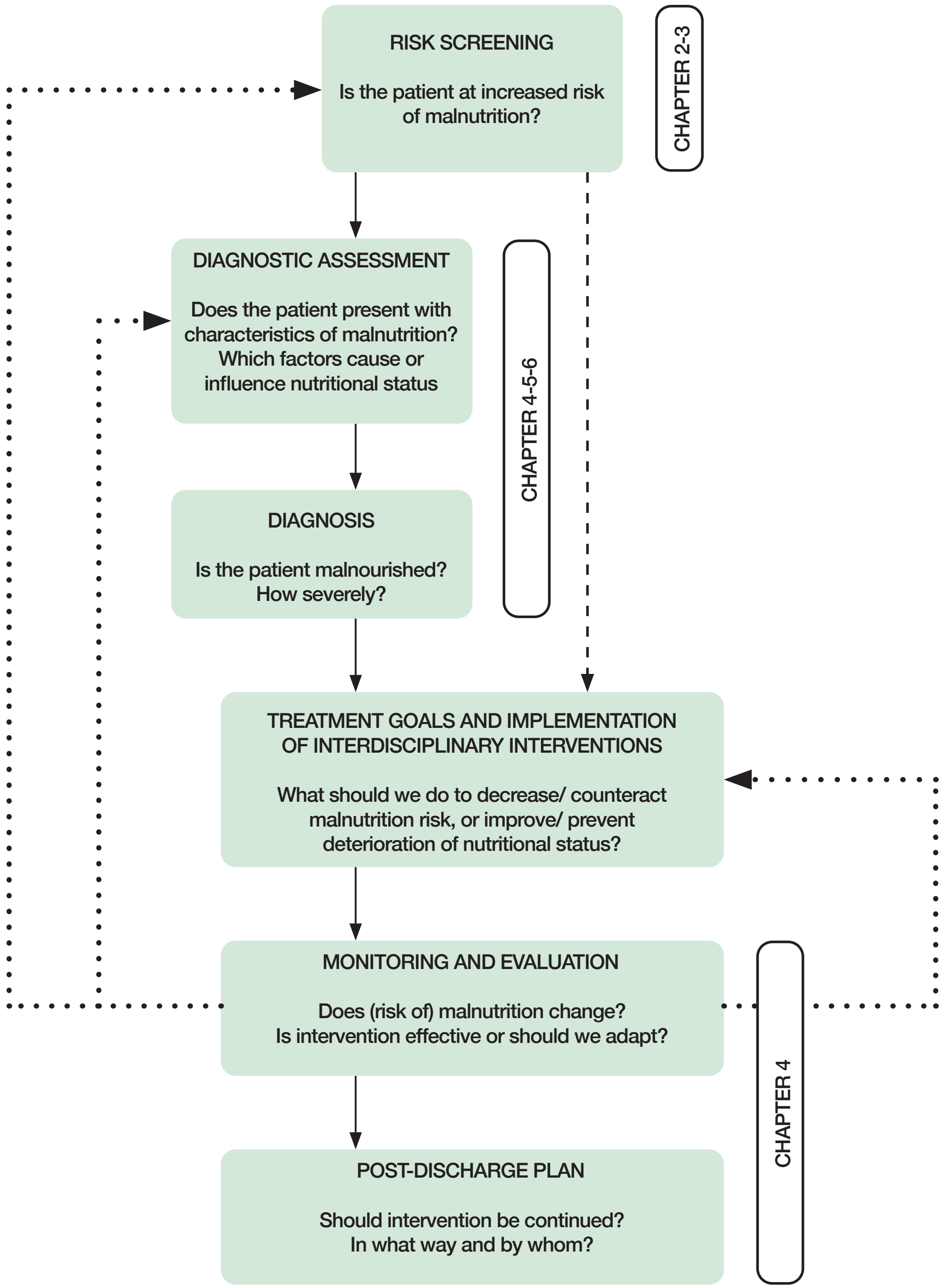

Figure 3. Visualization of the outline of this thesis, in the context of the nutrition care process for hospital patients, adapted from [1] and [108]

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PART A
RECOGNITION OF MALNUTRITION AND MALNUTRITION RISK IN THE HOSPITAL