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 to identify potential targets for improvement of hospital nutrition care. The two objectives of this thesis were:

1. 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,
   3. in kidney transplant recipients (KTR).
2. To compare different screening and assessment methods that are potentially applicable in clinical practice, for their association with relevant clinical outcomes.

Summary of findings

- More than one third (36%) of the overweight or obese hospitalized patients is at increased risk of malnutrition at hospital admission according to the PG-SGA SF, of which 90% is not identified by the currently used screening instrument MUST (Chapter 2);
- Overall, prevalence of high malnutrition risk according to the PG-SGA SF is 2.5 times higher (19% vs. 7%) in hospitalized patients compared with the currently used screening instrument MUST (Chapter 2 and Chapter 3);
- High malnutrition risk according to the PG-SGA SF is independently associated with higher risk of prolonged hospitalization, readmission and mortality, whereas high malnutrition risk according to the MUST is only associated with higher risk of mortality (Chapter 3);
- In patients at low risk of malnutrition according to the MUST, high malnutrition risk according to the PG-SGA SF is also associated with a higher risk of readmission and mortality (Chapter 3);
- Prevalence of malnutrition in hospitalized patients is high (31%) at admission and is also high pre-discharge (36%), according to the PG-SGA (Chapter 4);
- Prevalence of malnutrition is higher in patients with a longer length of stay: at day 5 of hospital admission more than half (56%) of the patients are malnourished and at day 10 two third (66%) of the patients are malnourished (Chapter 4);
- Nutritional status deteriorates from admission to pre-discharge in a quarter (25%) of patients. Of the well nourished patients at admission, 30% is malnourished pre-discharge (Chapter 4);
- One in every seven (14%) KTR outpatients is malnourished according to the GLIM criteria, of which the vast majority (91%) was diagnosed based on the presence of low muscle mass, assessed by BIA, whereas low BMI alone contributed very little to the malnutrition diagnosis. Similar results were found using 24-hour creatinine excretion (operationalized as creatinine-height index, CHI) as a marker for muscle mass: a malnutrition prevalence of 13%, of which 79% based on the presence of low muscle mass (Chapter 5);
- In outpatient KTR, higher 24-hour creatinine excretion as a marker for muscle mass and higher muscle strength by hand grip are strongly associated with lower risk of all-cause mortality, independent of each other and various potential confounders. However, muscle mass as assessed by BIA is not significantly associated with all-cause mortality in these patients (Chapter 6).

Figure 1. Visualization of the main findings and recommendations in this thesis, in the context of the nutrition care process for hospital patients.
These findings and their implications are summarized in Figure 1, within the context of the steps in the hospital nutrition care process according to the patient journey.

**Implications for malnutrition screening**

Malnutrition risk screening, as a first step in the nutrition care process, plays a pivotal role in identifying patients who may benefit from nutritional interventions and/or require further assessment \(^1\) \(^2\). In Chapter 2 and 3 of this thesis, the results of our practice-based study in a mixed sample of adult inpatients are described, to evaluate the current malnutrition screening practice in our university hospital. Our results support the use of the PG-SGA SF, instead of the currently used MUST, as the MUST fails to identify more than half of the patients at high risk of malnutrition and associated worse outcome, i.e., higher risk of prolonged hospitalization and hospital readmission. In the presence of current overweight or obesity, almost all patients with malnutrition are not identified by the MUST. Considering the ongoing increase in prevalence of overweight and obesity worldwide, these findings have far-reaching consequences for the efficacy of malnutrition screening policies now and in the future.

In Chapter 2, we showed that detection of increased malnutrition risk in overweight and obese inpatients using the MUST is very low (5%), compared with the PG-SGA SF (36%). Although the MUST has been validated for the hospital setting in the past and is quick and easy to apply in clinical practice, it is therefore arguable whether it should be applied in a population that is predominantly overweight or obese (60% in our study). Importantly, the use of the PG-SGA SF was supported by the prospective analyses of our practice-based cohort in Chapter 3 of this thesis, in which we showed that high malnutrition risk by the PG-SGA SF is associated with higher risk of prolonged hospitalization, hospital readmission, and mortality during 6-month follow-up, whereas the MUST is only associated with mortality. Moreover, we found that high malnutrition risk by the PG-SGA SF is also associated with worse outcomes in patients who were considered as low risk by the MUST. We consider the difference between the MUST and PG-SGA SF in their association with prolonged hospitalization and hospital readmission as particularly important, since prolonged hospitalization and hospital readmission have far-reaching consequences for patients’ health and wellbeing, as well as for health care expenditure. With the resources/costs and demand balance in health care under increasing pressure, risk of prolonged hospitalization and hospital readmission are arguably relevant endpoints, rather focusing exclusively on mortality. Together with previous health economic and intervention studies \(^1\) \(^2\), our findings thereby suggest a considerable resource and cost-saving potential through better identification of patients at malnutrition risk using the PG-SGA SF.

Our findings in Chapters 2 and 3 highlight the lack of sensitivity of low BMI as criterion to detect patients at malnutrition risk in the clinical setting. Considering that BMI is still a very commonly used parameter in health care settings worldwide, including the hospital setting, we deem it highly important to stress the shortcomings of this parameter for nutritional risk assessment at the individual level. Whereas BMI may still have some value for primary prevention and risk assessment from a public health perspective and on a population level, we recommend moving away from using BMI for nutritional risk assessment for individuals in the clinical setting. Instead, our study suggests that screening for malnutrition risk factors as included in the PG-SGA SF, particularly nutrition impact symptoms, is much more informative in this regard. In other words, our findings support a more pro-active approach to malnutrition risk to identify patients that have a high risk of developing future malnutrition by using the PG-SGA SF, rather than a reactive approach that focuses on patients who already exhibit apparent physical characteristics of malnutrition by using the MUST. Nutrition impact symptoms, such as anorexia, pain and dysphagia, have previously shown to be predictive of reduced dietary intake, weight loss, reduced functional capacity and reduced survival in patients with head and neck cancer \(^7\) \(^8\). Since nutrition impact symptoms are also present in patients with a wide variety of other medical conditions \(^9\) \(^10\) further studies in other hospital patient populations are warranted. Better characterization of these symptom profiles may aid in better tailoring of interventions, and eventually, in improving clinical outcomes.

Although scoring of nutrition impact symptoms is the most prominent item in the PG-SGA SF, this instrument also includes screening for other malnutrition risk factors that are not scored in the MUST, namely food intake and activities/functioning. The use of the PG-SGA SF for malnutrition screening thereby also promotes a more multidimensional and interprofessional approach to malnutrition care in the hospital. Since nutrition impact symptoms and other malnutrition risk factors stretch beyond care disciplines, they may require attention and potentially call for action of multiple health professionals. For example, a dietitian needs to be consulted when food intake is inadequate, but if the patient’s ability to obtain a sufficient food intake is severely hampered by nutrition impact symptoms, such as nausea or problems swallowing, pharmacological interventions by the physician and advice on suitable adaptations by a speech therapist may be effective. Also, when physical functioning is poor, physical therapy might be necessary to enable or optimize the effect of dietary interventions to improve muscle mass and function. All these factors cannot be viewed as separate entities, and need to be addressed in an integrated and interprofessional way. The paradigm of **anabolic competence**, on which the PG-SGA is based, provides a useful basis for such an integrated and interprofessional perspective on malnutrition and malnutrition care (Box 1) \(^7\).

For implementation of the PG-SGA SF instead of the MUST in clinical practice, different practical aspects should be considered, such as time, training of professionals and incorporation in existing workflows, e.g., in the electronic patient file. As mentioned, both BMI and the MUST are very widely used in hospital care worldwide, because of their ease and simplicity. In The Netherlands, malnutrition screening upon hospital admission was made mandatory in 2006 and has been evaluated yearly since then, for quality control and benchmarking by the Dutch national health inspection (Inspectie Gezondheidszorg en Jeugd, IGJ). This has likely resulted in more attention for malnutrition and malnutrition risk among hospital health care providers, and contributed to better in-hospital nutritional care \(^15\) \(^16\). However, as a downside, it has also yielded an additional administrative burden and may have contributed to a culture of ‘checking boxes’, rather than drawing attention to the actual problem and creating time and space for what really matters: caring for the patient, which also entails paying attention to and caring for the patient’s nutritional status. In
Box 1. Definition and visualization of anabolic competence and its three domains

“That state which optimally supports protein synthesis and lean body mass, global aspects of muscle and organ function, and immune response” 1, 2

Figure by 3

* This article was published in Nutrition, Vol 65, G.A.R. Reckman et al., Anabolic competence: Assessment and integration of the multimodality interventional approach in disease-related malnutrition, Page 179-184, Copyright Elsevier (2019).

recognition of the health care professional becoming increasingly buried under administrative burdens, putting the quality of care under even more pressure, different programs to reduce the administrative burden have been set up by governmental institutions (e.g., [Ont]Regel de Zorg, Zinnige Zorg). At first glance, implementation of a more extensive malnutrition screening method may therefore seem contradictory, since, indeed, it may require additional time and effort of health care professional. However, as the PG-SGA SF is suitable and feasible for patients’ self-report, available in multiple culturally adapted translations, and is usually completed within 5 minutes, 17, 18, it may even save valuable time for health care professionals. Moreover, this approach would be in line with the common goal to make health care more patient-centered and enable the patient to self-regulate and manage its own health status more, as filling in the PG-SGA SF has shown to increase patients’ awareness of malnutrition risk. 17 On a more essential level, though, it poses a question to policy makers whether they want care professionals to put their effort in doing something quick that yields little valuable information, or whether they dare to invest in something a little more complex, but also more effective in ‘hitting the target’, that is identifying hospitalized patients at risk of malnutrition and associated worse outcome. Based on the findings in this thesis, the latter option seems to be better aligned with the goals of sensible, meaningful and future-proof health care. Finally, it is important to note that as of 2021, the yearly evaluation of malnutrition quality indicators in the hospital by the Dutch IGJ will no longer be performed. As a consequence, evaluation and updating of the malnutrition care policies can now be considered the sole responsibility of the care institution itself. On the one hand, this gives a certain freedom to design and implement the most optimal, well-tailored policy. On the other hand, there is the pitfall that a lack of external incentive will result in a decline of attention and care quality. Thus, we seemed to have arrived at a crucial stage in the fight against malnutrition: will it become a “hit or miss”? Imlications for nutritional assessment and monitoring: quantity, quality or functionality? Our findings in Chapters 2 and 3 stress the need to adapt malnutrition screening policies to an increasingly obese population dealing with an increasing chronic disease burden, and show that different malnutrition ‘phenotypes’ and risk profiles should therefore be taken into account. This is in line with the most recent GLIM consensus criteria, which allow for different combinations of phenotypic and etiologic criteria to result in a malnutrition diagnosis, also in the case of concomitant overweight or obesity. However, characterization of these phenotypes requires a more in-depth nutritional assessment, which is not yet part of standard routine care during hospitalization or in the outpatient setting, in contrast to malnutrition screening upon hospital admission. Particularly in patients with complex disorders and multi-morbidity, such as KTR, malnutrition phenotypes are not yet well-characterized and a matching approach to nutritional assessment is not yet identified. Therefore, in Chapter 4 of this thesis, we assessed and re-assessed presence of malnutrition during hospital stay, using the Full PG-SGA in our practice-based cohort of hospitalized patients. And in Chapters 5 and 6, we used data from the TransplantLines Biobank and Cohort to assess presence of malnutrition according to the GLIM diagnostic criteria in outpatient KTR, and to evaluate practical measures of muscle status, as an important component of nutritional status, for their association with all-cause mortality in KTR. Our findings in Chapters 4, 5 and 6 show that malnutrition is prevalent in hospitalized patients as well as in outpatient KTR, but is hardly detected ‘at first glance’ when the BMI criterion alone is used. Therefore, an expert approach to nutritional assessment, using BMI-independent assessment instruments such as the PG-SGA, body composition assessment and functional measures, is urgently warranted in routine complex hospital care.

The results of Chapter 4 stress the need for BMI-independent assessment and monitoring of nutritional status in hospital inpatients. We found that prevalence of malnutrition is already high at admission (31%), and is particularly high in patients with a longer length of stay (56% on day 5 and 66% on day 10 of hospitalization). Of note, more than half of the malnourished patients at admission was also overweight or obese, equaling a 17% double burden prevalence. Furthermore, of all the patients who were assessed both at admission and before discharge from the hospital, a quarter deteriorated during hospitalization, and 30% of well-nourished patients were malnourished pre-discharge. These findings show that, even within the scope of one week, patients may develop malnutrition during their hospital stay. This requires extra awareness of all involved health care professionals,
including the physician, nurse, dietitian and nutrition assistant, to adequately detect worsening of nutritional status and start interventions at an early stage to counteract. This can be supported by additional (preventive) nutritional policies and guidelines, which could for example include standard weekly re-assessment of nutritional status, extra provision of enriched foods for patients with a longer length of stay and explicit inclusion of nutritional status in weekly multidisciplinary meetings. Whereas many malnutrition screening and assessment tools are not suitable or practical for monitoring of nutritional status, our findings suggest the Full PG-SGA can be a useful tool for repeated assessment in the inpatient population, also in patients with concomitant overweight or obesity.

Moreover, our findings on malnutrition and muscle status in KTR, as described in Chapter 5 and 6, are illustrative of why nutritional assessment should not be limited to the acute phase of hospitalization alone and is also important in outpatients with complex chronic disorders and multi-morbidity. In Chapter 5, we used data from the TransplantLines Biobank and Cohort study to assess the prevalence of malnutrition in stable outpatient KTR according to the most recent GLIM diagnostic criteria and found that one in every seven KTR is malnourished. Importantly, the predominant phenotypic criterion was low muscle mass. Low BMI contributed very little to the diagnosis of malnutrition in our sample. Similar to our findings on malnutrition risk screening in a mixed inpatient population (Chapter 2), relying solely on BMI and weight loss for assessment of nutritional status does not seem to suffice in outpatient KTR. Moreover, we found that almost a quarter (22%) of malnourished KTR had a BMI in the overweight or obese range, which equals a 7% double burden prevalence when regarding all KTR as meeting the etiologic criterion for disease burden/inflammation. These results show that prevalence of malnutrition is considerable, even in relatively stable outpatient KTR, and is easily overlooked when we fail to look beyond the first glance of outside appearances. Furthermore, other studies have shown that low protein intake and micronutrient insufficiencies, e.g., vitamin B6, are even more common and associated with poorer outcomes in KTR, independent of BMI.10-22 This could be indicative of a poor diet quality and/or a higher nutritional requirement in KTR. Although nutrient deficiencies are considered distinct nutrition-related conditions from malnutrition, these studies shows that nutrition-related conditions are highly prevalent and impactful, but often remain ‘hidden’ under an overweight or obese appearance in KTR. Further characterization of nutritional conditions, nutritional requirements and their complex, potentially interrelated etiology may aid in tailoring nutritional guidelines and interventions for this specific patient group. In the context of this thesis, particularly low protein intake is of interest, as it can result in malnutrition, reduced muscle mass and/or functioning, in turn affecting patient outcomes.

The characterization of nutritional status and nutrition-related conditions has important consequences for the nutritional assessment methods that should be applied. Our finding that malnutrition in outpatient KTR is predominantly characterized by reduced muscle mass was quite striking and was also quite robust, when using either BIA or 24-hour urine samples as a measure for muscle mass, although diagnosis on the individual level differed. Our findings in Chapter 6 show that, when taking into account the association with all-cause mortality, the method of muscle mass assessment matters greatly. A higher muscle mass by 24-hour urinary creatinine excretion rate was associated with a lower risk of mortality, whereas muscle mass by BIA was not. In addition, muscle strength by hand grip was also strongly associated with all-cause mortality, independent from 24-hours urinary creatinine excretion rate and potential other confounders, underscoring the importance of both body composition and functioning assessment. These results suggest that muscle mass and muscle strength are separate domains, that should be assessed in a complementary way to identify KTR at high risk of worse survival who may benefit from interventions. For this purpose, routine assessment using both 24-hours urine samples and hand grip strength measurement in KTR outpatient care is recommended, whereas use of BIA is not. Again, these findings show that a more thorough nutritional assessment is key, instead of relying on BMI alone, particularly in patients with complex disorders.

Implications for post-discharge nutritional care

As of yet, there is no standard policy on post-discharge nutritional care in our hospital, nor in many other hospitals in The Netherlands and worldwide, although ongoing efforts are being made in this area (e.g., ProIntens project in the region of Amsterdam24). This is remarkable, considering the ongoing pressure to shorten hospital stay. Our findings stress the urgent need for such a policy, as we found more than one third of our patients (36%) to be malnourished before discharge (Chapter 4). Considering the often complex (multi-)morbidty of the patients that are admitted to a university hospital, and the short length of hospital stay, i.e. median 4 [1-7] days in our pre-discharge sample, this can hardly be seen as a surprise. Therefore, continuation of interventions after discharge is necessary to restore or improve patients’ nutritional status and to help reducing the risk of associated worse outcomes. Previous intervention studies on continued nutritional support after hospital discharge, particularly the interventions with a multidimensional and multidisciplinary approach, have shown some positive effects on nutritional and functional status, risk of hospital readmission and quality of life, at least on the short term.25-33 However, high-quality intervention studies with clinically relevant endpoints and a longer follow-up are yet scarce.

An important prerequisite for effective post-discharge/transmural nutritional care is adequate transfer of information, in particular adequate transfer from the hospital to the involved health professionals in the home or post-discharge care setting. This starts with adequate discharge planning in the hospital, ensuring that all involved health professionals are ‘in the know’ on the current health status and the planned discharge of the patient, preferably by using both personal communication in multidisciplinary meetings, as well as real-time updates in the electronic patient record. Next, before the actual discharge, it is important to establish which information is required for the transfer and by whom and for whom it should be prepared. For example, the dietitian can prepare a more extensive transfer to the dietitian in the community setting, but should also provide a summary with relevant information for the physician to include in the discharge letter to the general practitioner and for the nurse to include in the transfer to home care if applicable. In clinical practice, the implementation of such a post-discharge planning process for optimal nutritional care is a complex task, which requires input and effort from all involved health professionals, as well as effective arrangements in the electronic patient records. In 2022, two Internal Medicine wards will cooperate with the department of Dietetics
Another prerequisite for effective post-discharge/transmural nutritional care is knowing the region and cooperating with the health care institutions and professionals that work in it. This is also a complex challenge, as the region may stretch across a large geographical area, and the organization and funding of care varies across settings. As a university hospital, we should be a hub for complex care in transmural care networks and have an important task to share our expertise, for example through education, with partners in the region. Vice versa, we rely on our partners in the region to provide a large part of the basic care, preferably close to the patient, to ensure ‘de juiste zorg op de juiste plek’ 34. Examples of transmural dietetic care networks are for example Transmuraal Overleg Amsterdamse Diëtisten (TOAD) and Transmuraal Overleg Diëtisten Utrecht (TODU). There are similar initiatives in the Northern Netherlands, for example through Diëtistenplatform Noord-Nederland (DPNN), but a complete social map or structural transmural network is currently lacking in our region. Also, the current transmural networks have a predominantly monodisciplinary character, including dietitians only or initiated by medical departments or management and excluding dietitians and other care disciplines, which hampers the interdisciplinarity or interprofessional transmural approach that is necessary to counteract malnutrition 35.

Methodological considerations and generalizability

In this thesis, we aimed to evaluate methods for effective screening, assessment and monitoring of malnutrition (risk), under the assumption that improvement of care and patient outcomes can be established by better detection. Although intuitively this assumption is logical, since detection of malnutrition (risk) usually precedes and is the basis for intervention actions, this cannot be concluded based on the findings in this thesis. However, by focusing on the important first steps of the nutrition care process (Figure 1), i.e., malnutrition screening and assessment, we have gained important knowledge on the magnitude of the problem that needs to be targeted and on how to effectively detect malnourished patients or at risk thereof that may benefit from intervention actions. The studies described in this were all observational studies and we did not perform intervention studies to determine effectiveness of interventions to counteract malnutrition (risk) or the feasibility of implementation of these interventions. Therefore, we cannot draw conclusions on causality, nor provide concrete evidence-based recommendations on nutritional interventions other than what has been reported in previous literature.

With regard to malnutrition screening, we recommend to use the PG-SGA SF instead of the MUST on the basis of our findings in Chapters 2 and 3. The comparison of the PG-SGA SF to the MUST was of utmost relevance for our setting, as the MUST is currently used in our hospital. However, there are various other screening instruments that are currently used worldwide that share the same BMI-independency as the PG-SGA SF. In the Dutch hospital setting, for example, the Short Nutritional Assessment Questionnaire (SNAQ) which also does not include scoring of BMI, is most frequently used. However, similar to most other malnutrition screening instruments that are frequently used across the globe, the SNAQ does not include extensive scoring of malnutrition risk factors like nutrition impact symptoms, and most importantly, is not tailored for interprofessional triage. From this perspective, the PG-SGA SF is quite unique, in the sense that it yields concrete information that can be used to triage for interventions, including nutritional, pharmacological, and physical exercise interventions. A recently published study, conducted in another hospital in the Northern Netherlands, showed that the PG-SGA SF was also better able to predict length of hospital stay than the SNAQ 36. For malnutrition screening in the hospital setting, the PG-SGA SF therefore seems to be a valid and practical alternative, preferred above the currently used MUST and SNAQ. However, research on the use of the PG-SGA SF to detect patients at risk in the chronic care setting, and comparisons with dedicated tools for this setting, such as the Mini Nutritional Assessment Short Form (MNA SF) is yet very scarce. As the PG-SGA SF focuses on assessing recent changes in malnutrition risk factors, deterioration of nutritional risk over a long period of time may remain unnoticed, for example in the community-dwelling elderly, but this needs to be further studied. Studies performed in chronic care patients with specific needs, such as the geriatric rehabilitation setting and in hemodialysis patients, have shown that the PG-SGA SF can be useful in detecting patients at high risk of malnutrition and worse outcomes 36, 37.

Underlying the comparison of the performance of malnutrition screening tools, is the ongoing discussion on what components should be included in malnutrition screening and what kind of characteristics should be evaluated to assess the validity and applicability of a malnutrition screening tool. In our study, we focused on the PG-SGA SF as a whole and did not analyze the individual items for their contribution to the total risk score. This was deliberate choice, as the PG-SGA SF was designed as a multidimensional tool, for the purpose of interprofessional triage. In our opinion, further ‘dissecting’ the components of the PG-SGA SF therefore makes little sense for clinical practice, as it would contravene this purpose. Characterization of malnutrition risk factors and intervention targets per domain and in different patient groups, on the other hand, would be more informative. In our studies, we focused on the predictive validity of the PG-SGA SF for malnutrition risk screening. We did not compare the outcomes of malnutrition screening by the PG-SGA SF to semi-gold standard nutritional assessment methods, nor did we assess its content validity, as other studies have previously been performed for this purpose 38, 39. For clinical practice, however, it is of high importance to know whether malnutrition risk assessed by a particular instrument can be reduced by (nutritional) interventions and whether such a therapeutic response can be detected by the instrument. The EFFORT trial showed some promising results of individualized nutritional support for improvement of nutritional intake and outcomes, at least on the short term, in hospitalized patients at risk of malnutrition as determined by the NRS 2002 40. This trial shows the value of nutritional support in hospitalized patients at risk of malnutrition, although it should be noted that the nutritional intervention was compared to a control group receiving only standard hospital food without any nutritional support, which may have emphasized the effect of the intervention and yields some ethical concerns. Intervention studies, preferably with an interprofessional approach, using the PG-SGA SF for identification of patients at risk are needed to evaluate the effectivity of the PG-SGA SF to detect an intervention response.
As with malnutrition risk screening, there is an ongoing discussion on which criteria should be used to diagnose malnutrition. In the studies of this thesis, we used the Full PG-SGA and the GLIM criteria to diagnose malnutrition in hospitalized patients and outpatient KTR, respectively (Chapter 4 and 5). These two approaches may seem inconsistent at first glance, but are not contradictory. The GLIM consensus criteria were determined to create a more uniform malnutrition diagnosis and communication across the globe, but are to be considered a framework with recommendations for methodology, not as a new instrument in itself 7. Therefore, the GLIM framework can be considered as reflective of the diagnostic process, for which existing nutritional screening and assessment instruments can be used. For example, in Chapter 5, we used items of the PG-SGA to operationalize the GLIM criteria in our KTR study population. In addition to the different operationalizations and methodologies that can be used, the GLIM framework allows for different combinations of criteria to result in a malnutrition diagnosis. So although the GLIM criteria have yielded more international consensus, there are still ‘many paths that lead to Rome’ 43 and the scientific debate on the preferred methodologies and valid cut-offs is still ongoing. Part of this discussion is whether subjective measures, such as the PG-SGA, provide sufficient information for the malnutrition diagnosis or if objective measures are necessary, for example through body composition assessment. A previous study in patients with colorectal cancer showed that a physical examination of muscle status using the PG-SGA had the best agreement with presence of low muscle mass as evaluated by CT, compared to mid-upper arm muscle circumference, calf circumference, and BIA 42. These results show that a short non-invasive physical exam as part of the PG-SGA can already provide useful information on body composition and nutritional status. In our studies, we did not compare the physical exam component of the PG-SGA to objective measures of muscle status, but the findings in Chapter 5 and 6 at least suggest that objective measures of both muscle mass and muscle strength are useful to identify outpatient KTR at risk of worse outcome. However, particularly body composition assessment methods may not be available and valid in clinical practice at all times 42, in which case the Full PG-SGA including a short non-invasive physical exam might be a more easily applicable and valid alternative 42, 44, 45.

Our findings on the prevalence of malnutrition and the impact of impaired muscle status in KTR (Chapters 5 and 6) are relevant for KTR and their care providers, and could provide a new therapeutic window to improve the quality of life and survival of KTR. KTR are a specific and relatively small patient group, but previous studies using the GLIM criteria to evaluate malnutrition in other specific university hospital populations 46, 47, as well as in patients with more common conditions such as elderly hospitalized patients with diabetes type 2 48 or heart failure 49, have pointed out malnutrition is even more prevalent in these patient groups. Although the malnutrition phenotypes differ between patient groups, the contribution of the BMI phenotypic criterion to detect malnutrition was low in most of these studies, very similar to our results in Chapter 5. Moreover, there is growing evidence from studies in common outpatient populations and the general population, that shows impaired nutritional and muscle status are also highly prevalent in these populations when looking beyond outside appearances alone. For example, in the DiAbetes and Lifestyle Cohort Twente (DIACOM) of diabetes type 2 outpatients, patients with a higher BMI had a low intake of protein and lower muscle mass as evaluated by 24-hour creatinine excretion rate 50. And in the general population, although mean BMI was well within the overweight range, both low muscle mass and vitamin deficiencies were common 51, 52. These studies show that nutrition-related conditions are indeed pronounced in, but not exclusive to patients with complex disorders and multi-morbidity in the university hospital setting. Therefore, the need for a different approach to adequately detect and treat these conditions is of broad relevance for public health in general.

Implications for the role of dietetics in the university hospital setting: beyond implementation

The high prevalence and impact of malnutrition (risk) and impaired muscle status in university hospital patients presented in this thesis, which often remain undetected with the current assessment practices and treatment guidelines, underscore the importance of a strong position of dietitians in the university hospital, both in the care and knowledge infrastructure. Registered dietitians have specific expertise in the area of nutritional assessment, translation of nutritional treatment goals into personalized advice and other important steps of the nutrition care process. As such, dietitians can offer an important counterweight to prejudices regarding nutritional status based on outside appearance in clinical practice. However, our findings also show recalibrating of current diagnostic and treatment guidelines in response to the increasingly complex and overweight patient...
population is urgently needed. In this area, there seems to be much to gain by embedding dietetics more firmly in the knowledge domain. Particularly in the university hospital, where there is an increasing focus on complex care and is already a strong basis for fundamental research and evidence-based practice, dietitians could play an important role in collecting additional practice-based evidence, to expand the nutrition knowledge base and improve clinical care (Figure 2; see also Portfolio S1 for further reading). As an example, the Department of Dietetics in the UMCG is currently working on implementing nutritional assessment in regular care pathways for patients with complex disorders, i.e., potential lung and heart transplant candidates, yielding important data directly applicable to clinical practice, as well as for scientific and care improvement purposes. Also, the working group Dietetics & Research of the UMCG has been initiated in 2019 by dietitians themselves, to empower and facilitate (practice-based) research by dietitians, and is currently working together with other knowledge institutions, such as the Hanze University of Applied Sciences, to develop in-house training programs. Besides implementation of nutritional assessment and practice-based evidence, there are also other important implementation aspects to be taken into consideration when aiming to improve nutritional care. For example, recent attention has been paid to the importance of addressing food literacy and other potential barriers and facilitators of diet adherence as determinants of nutritional intervention efficacy. These aspects are outside the direct scope of this thesis, but are very relevant for dietetics in the university hospital setting and in other settings. Therefore, summaries of works in this area are included in Portfolio S2 and S3 for further reading.

Although a strong position of dietitians in the hospital is a prerequisite for effective nutritional care, adequate nutritional care in the hospital should not and cannot be the sole responsibility of dietitians alone. Instead, nutritional care should be interprofessional, requiring effort and attention from different stakeholders in the hospital nutrition care process: from managers to physicians, from nurses to physical therapists or other supportive disciplines, from nutrition facilities to nutrition assistants, each with their own expertise and role within the organization. For interprofessional collaboration towards common treatment goals, basic knowledge of each other’s expertise and roles is necessary. In clinical practice, this may be particularly important for physicians, since they are usually tasked with the responsibility to consult other supportive care professionals if needed. However, although nutrition, lifestyle and prevention were already urgent and ‘hot topics’ in 2017, nutritional and lifestyle education for medical students was still very limited, i.e., only 29 hours over the course of 6 years on average \(^1\). Fortunately, this has improved to an average of 57 hours in 2020, although the University of Groningen was still down at the bottom with a total of 13 hours \(^2\). Although initiatives such as Student & Leefstijl show the perceived importance of nutrition and lifestyle and willingness to learn by physicians in training, these numbers show that there are still many steps to be taken for lifestyle medicine and interprofessional nutritional care to be adequately embedded in clinical practice. Ideas for improvement include interprofessional nutritional education, allowing health professionals in training to get familiar with each other and collaborate at an early stage, and continuing this approach throughout their careers. Interesting examples of an interprofessional approach in health care, starting at an early stage of education, can be found in oral health care \(^3\). Extensive discussion of other conditions for effective nutritional care is beyond the scope of this thesis, but during the execution of our studies, we have encountered a few that require further attention (Box 2).

**Box 2. Important conditions for effective nutritional care (non-exclusive)**

- The necessary equipment is available, i.e., scales, measuring tapes, body composition assessment instruments, consulting room and bed;
- Nutritional care is interprofessional and at least includes involvement of physicians, nurses, dietitians, nutrition assistants, physical and speech therapists, pharmacists, facilities and services, policy makers and management;
- All involved professionals have sufficient knowledge and skills, and receive the necessary training to stay up-to-date; interprofessional training is offered at an early stage and is continued throughout health careers;
- Patients and their networks are actively involved;
- The electronic structure is efficient and aligned with the work processes, the necessary stakeholders have easy access to the necessary information;
- Organizational guidelines are clear, up-to-date and accessible, and at least include the agreements on tasks, responsibilities and work processes for each professional involved;
- The involved stakeholders have common goals, and the care professionals are actively supported by management and direction;
- The involved stakeholders generate outreach and visibility, within and outside the own organization;
- Regional care networks are organized and are interprofessional;
- There is willingness and concrete effort by the government and other national institutions, such as health insurance companies, to invest in lifestyle medicine;
- There are (inter)national guidelines based on fundamental, mechanistic studies, RCTs, as well as practice-based studies.

Perspectives for future research and implications for practice

In an increasingly ageing society, dealing with mostly chronic, and nutrition or lifestyle-related disorders and complex multimorbidity, there is an urgent need for (indicated and care-related) preventative actions in the area of nutrition and lifestyle to keep health care sustainable and manageable in the future. The studies in this thesis have made even more clear that tackling malnutrition and risk thereof in hospital care should be an important part of this action plan, which requires further research on remaining knowledge gaps in this area (Box 3), as well as concrete improvement actions for clinical practice based on new insights. It has become increasingly clear that as current hospital care is complex and will probably become even more complex in the future, we probably cannot rely on a
Box 3. Identified knowledge gaps based on the findings in this thesis, to be addressed in future research

- Malnutrition phenotypes and nutritional requirements in patients with specific conditions;
- Valid screening and assessment methods feasible for clinical practice and tailored to the phenotypes and requirements of specific patient populations if needed;
- Cost-effectiveness of pro-active, BMI-independent screening and assessment using the PG-SGA (SF), body composition assessment methods and functional assessment;
- Effective interprofessional and nutritional prevention and treatment intervention strategies for malnourished patients or at risk thereof, particularly in patients with concurrent overweight or obesity and complex disorders, such as KTR;
- Therapeutic response to interprofessional and nutritional intervention in patients at malnutrition risk based on nutrition impact symptoms: indications of disease severity, valid indicators of nutritional intervention response or composite measures?

In recent decades, the rapid developments in the area of information technology has drawn attention to the use of big data for data-driven health care. Although an extensive discussion of this topic is outside the scope of this thesis, this perspective may also provide interesting future opportunities for nutritional care. As illustrated previously in this chapter, nutritional care should preferably be interprofessional, which requires all the involved professionals having access to the same data as a basis for their actions. Furthermore, patient- and population-dashboards, for example the lifestyle dashboard that is currently being implemented in the UMCG, could also allow for data-driven nutritional care improvements. Finally, data-driven nutritional care may put the patient more in the lead, when they receive access to their nutritional data, get real-time feedback on it and can discuss the outcomes with their care professionals. However, effective data-driven nutritional care is still a future perspective, and first requires further study, for example through qualitative studies on the attitudes, wishes and expectations of stakeholders, before proceeding to large-scale implementation.

Concluding remarks
In conclusion, the findings in this thesis show that malnutrition and risk thereof are highly prevalent and impactful in hospital patients with complex disorders, but often remain ‘hidden’ with the current policies – ‘hidden hunger in the hospital’. The current standard practice for detection of malnutrition, often including BMI-dependent malnutrition screening tools at hospital admission only, does not suffice to detect patients at risk of worse outcomes. Importantly, underdetection of malnutrition and risk thereof is most pronounced in overweight or obese patients with complex disorders, which is problematic considering the ongoing obesity pandemic and the growing worldwide chronic disease burden. Therefore, a different approach to malnutrition, not based on first glances of outside appearances to be conducted to what extent these symptoms are also modifiable by and responsive to interprofessional and nutritional interventions.

For clinical practice, an important window of opportunity for care improvement could be implementation of evidence-based nutritional screening and assessment methods suitable for different malnutrition phenotypes. This could be for example supported by a toolbox including some of the instruments used in this thesis, such as the PG-SGA, 24-hour urine samples, and hand grip strength measurement, and could be supplemented by novel methods. For example, ultrasound has recently gained increasing interest as a method for muscle mass assessment, because of its availability, low cost, portability, reliability and potential to assess longitudinal changes in muscle mass. However, further research on standardization of ultrasound protocols and cut-offs is necessary for implementation in routine hospital care. The toolbox also needs to include effective intervention strategies, so that treatment can be initiated immediately when the patients at risk are well-identified using the nutritional screening and assessment methods included in the toolbox. Also, effective prevention strategies should be included in the toolbox, for example targeted at patients visiting for pre-operative consultations or visiting the outpatient clinic in the hospital, or from a transmural perspective, for patients visiting the general practitioner or those receiving home care.
alone, is necessary for better identification of malnutrition (risk), and more efficient allocation of care resources. Several important knowledge gaps have been identified in this thesis that needs to be addressed in future studies to help counteract malnutrition (risk) and manage the increasingly complex and enormous societal disease burden, now and in the future. These include characterization of malnutrition risk profiles and phenotypes in specific complex patient groups and their specific nutritional requirements, evaluation of the cost-effectiveness of BMI-independent and tailored screening and assessment methods, and effective (preventive) interprofessional intervention approaches. Based on the studies in this thesis, we recommend 1) using BMI-independent risk screening that not only identifies characteristics of malnutrition but also risk factors for future malnutrition, 2) structural assessment and monitoring of nutritional status in hospitalized patients, 3) organization of transmural nutritional care pathways, and 4) assessment and monitoring of body composition and muscle function in complex outpatients, such as KTR (Box 4).

Urgent, systemic, and interprofessional action is needed across different domains and professions, which calls for intra- and inter-organizational cooperation and investment in nutrition research that is both fundamental and practice-based.

**Box 4. Identified potential nutritional care improvements for clinical practice, based on the findings in this thesis**

- Substitute traditional BMI-dependent malnutrition screening tools by a BMI-independent screening tool, that includes pro-active screening of risk factors (for example the PG-SGA SF), for malnutrition screening upon hospital admission;
- Re-assess nutritional status during hospital stay, particularly in patients with a longer length of stay, to start interventions early in patients with deteriorating nutritional status;
- Organize transmural care pathways, with adequate transfer of care, to ensure continuation of nutritional care after hospital discharge and potentially improve clinical outcomes;
- Structurally monitor nutritional status and muscle status in kidney transplant recipients (KTR) at the outpatient clinic, using 24-hour urine samples and hand grip strength measurement; work towards an evidence-based and practical toolbox.

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