The Dormant Triad

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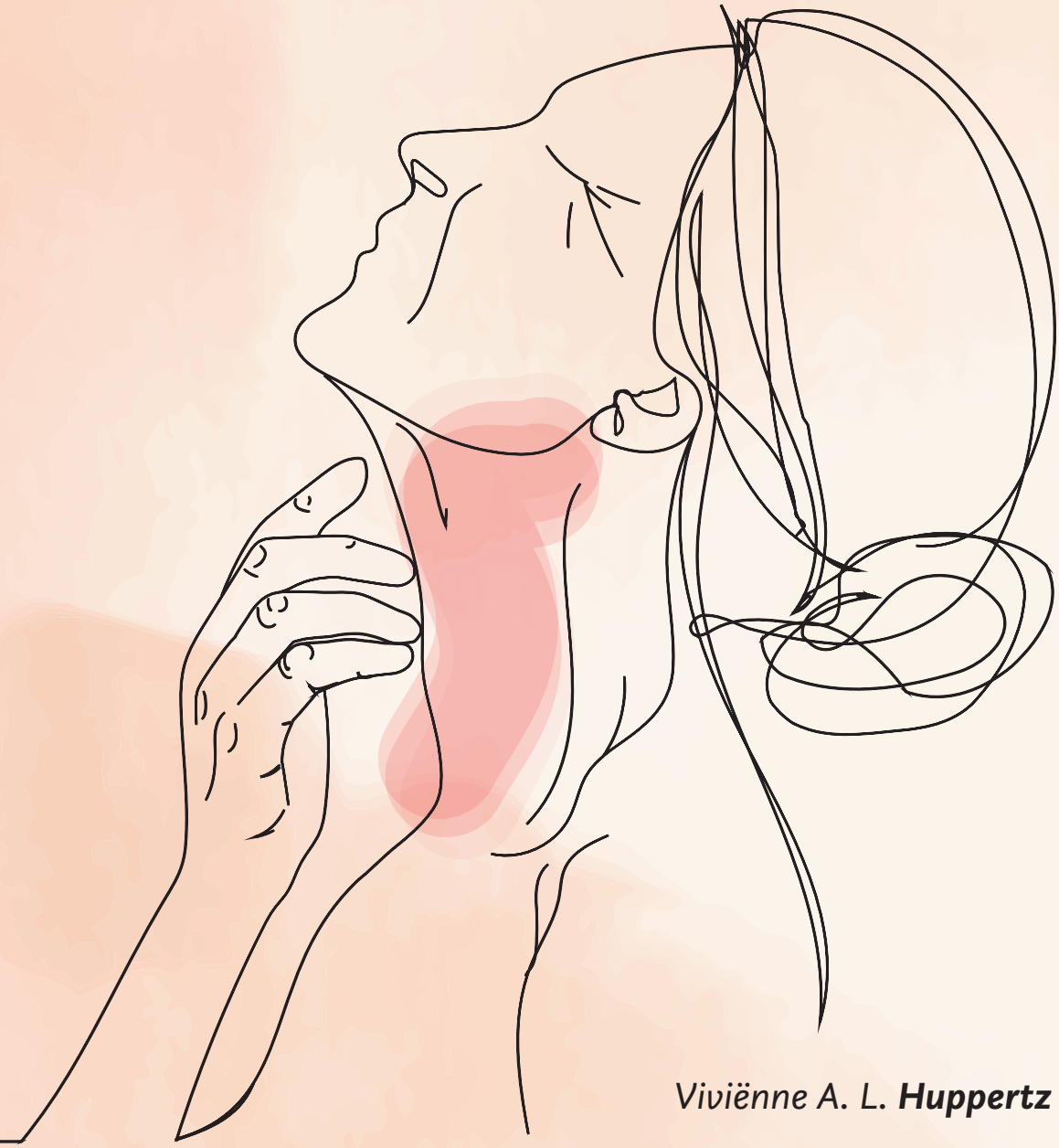
Exploring Dysphagia, Oral health and Malnutrition in stroke and nursing home patients



Viviënne A. L. ***Huppertz***

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Contents

Chapter 1

General Introduction

Healthcare systems worldwide are challenged in the provision of continuous high quality healthcare for a growing population of chronically ill patients and geriatric patients e.g., patients with neurological disorders and nursing home residents [1, 2]. These patients often show a profile of multimorbidity and comorbidities with associated disabilities and handicaps which interfere with their recovery and rehabilitation. Therefore, they are considerably care dependent [3] and in need of long - term multidisciplinary care.

In these patients, malnutrition as a complicating problem is associated with poor clinical outcomes, including impaired effectiveness of the immune system or medication [4], mortality [5], increased length of hospitalization [6], and impaired health - related quality of life [7]. Oropharyngeal dysphagia and poor oral health are also commonly seen comorbidities of neurological disorders and ageing [8-11], and there is evidence of associations between malnutrition, oropharyngeal dysphagia, and poor oral health [12-15].

The present dissertation targets at malnutrition in stroke patients and in nursing home residents in relation to oropharyngeal dysphagia on the one hand, and poor oral health on the other hand.

Malnutrition

The definition of malnutrition has been a point of discussion ever since the term was used for the first time [16]. The present dissertation refers to undernutrition as a type of malnutrition. This type of malnutrition encompasses underweight, or a deficiency, or imbalance of macro - and micronutrients [17, 18]. Recently, a global consensus was reached on diagnostic criteria of malnutrition in adults, covering the following five phenotypic and etiologic health criteria: involuntary weight loss, body mass index, decreased muscle mass, reduced nutritional intake or absorption, and disease - induced burden or inflammation [19, 20]. These criteria are defined for use in all healthcare settings and by all healthcare professionals.

Older people [21, 22] and patients with neurological disorders [23, 24] are particularly at risk of malnutrition as they suffer from multiple physical and / or mental deteriorations, e.g., low nutrient intake, elevated nutrient needs, and reduced nutrient bioavailability, that directly or indirectly promote malnutrition [25]. The provision of high quality nutritional care is important for these patients to prevent or minimize the risk of malnutrition. Nutritional care is comprehensive and includes valid nutritional screening and diagnostic measurements to assess the extent and severity of the problem, treatment (e.g., the provision of foods, supplementation or nutritional information), and monitoring. Nutritional care is particularly important in care dependent patients. A previous multicenter study suggests that the prevalence of malnutrition in hospitals may reflect the quality level of the nutritional care that is provided [26].

Prevalence rates of malnutrition in hospitals and residential care facilities European - wide reach up to 28.0% and 17.5% respectively [27]. In Dutch hospitals,

up to 14.9% of the patients were defined as being malnourished [28]. The prevalence of malnutrition in Dutch nursing homes remained unchanged around 16.0% over the past decade [29]. Thus, attention for the patients' nutritional status, nutritional intake, and nutritional care remains important in these healthcare facilities and patient populations.

Mechanisms of oral nutritional intake and swallowing

Oral nutritional intake requires well - coordinated sensory, cognitive, and motor functions controlled by the central nervous system [30]. A schematic representation of the upper aerodigestive tract, the senses involved in swallowing, and the swallow – specific central nervous system control is provided in figure 1. Several cranial nerves [31] are crucial for oral bolus preparation and subsequently for swallowing the bolus from the oral cavity to the stomach. In healthy persons, swallowing and breathing alternate and are well coordinated [32]. Well - functioning and well - coordinated swallowing and upper airway mechanisms prevent the unintended entrance of bolus particles, microbial pathogens, and commensal microbes [33, 34] from the upper digestive tract into the lower respiratory system. This is of vital importance as the entrance of bolus particles and / or microbes into the lower respiratory tract system may lead to adverse effects including choking and aspiration pneumonia [35, 36]. These adverse effects are commonly seen in patients with oropharyngeal dysphagia and poor oral health and can be fatal [37], impact the patients' quality of life [38, 39], or the length of hospitalization [40].

The preparation of the bolus relies on structures of the oral cavity (e.g., salivary glands, integrity of the mucosa), the microbiome of the oral cavity, and the functionality of the masticatory system. Several exogenous and endogenous factors may affect oral health. These factors are, amongst others, medication use [41], diet [42], care dependency, access to oral care [11], and immune responsiveness [43]. Poor oral health can cover a wide variety of oral health problems, e.g., dental caries, periodontal disease, edentulousness, and hyposalivation [44].

Swallowing relies on the integrity of skeletal muscles, sensory perception (e.g., taste perception), and saliva production in the upper aerodigestive tract [45, 46]. Furthermore, swallowing is a complex process consisting of a combination of voluntary and involuntary (reflexive) activities allowing part of the swallowing process to be performed consciously (e.g., chewing more carefully, swallowing smaller sips of an oral bolus) and part of the swallowing process reflexively without the possibility of modulation of this part (e.g., esophageal bolus transport) [45, 46]. Difficulties in the oral preparation of solid and liquid foods into a ready - to - transport food bolus (e.g., hyposalivation or poor fitting dentures), impaired oral bolus control (pre - swallow posterior pharyngeal spill), or poor swallow response (weak or inefficient oral bolus transport) may hinder the transfer of the bolus from the oral cavity towards the pharynx. A bolus can enter the larynx in case of impaired airway protective mechanisms but may remain on or above the true vocal folds

(penetration) [47]. The bolus can also enter the trachea so below the level of the true vocal folds (aspiration) [47] and / or remain in the pharynx after swallowing (pharyngeal residue) [48]. Penetration, aspiration, and pharyngeal residue are symptoms of oropharyngeal dysphagia [45, 46, 49, 50].

Both, oropharyngeal dysphagia and poor oral health are highly prevalent in stroke patients [51] and in geriatric patients, such as nursing home residents with neurological disorders and somatic health conditions [10, 11, 52, 53]. International reviews investigating the prevalence rates of oropharyngeal dysphagia or clinically relevant symptoms of oropharyngeal dysphagia report rates between 8.1% and 80.0% in stroke patients [51] and between 5.4% and 83.7% in nursing home residents [53]. Approximately half of the stroke patients with oropharyngeal dysphagia in the acute phase after stroke still suffer from oropharyngeal dysphagia at three months post - stroke [54]. Up to 25% show symptoms of oropharyngeal dysphagia at six months post - stroke [55, 56].

Pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in patients with neurological disorders and in nursing home residents

In patients with neurological disorders, the brain, spinal cord, and / or the peripheral neuromuscular system are affected. Patients may suffer from (partial) paralysis, muscle weakness or alterations in sensory, cognitive, and motor systems that affect oral feeding ability, swallowing, and the breathing - swallowing coordination [57-59]. Malnutrition, oropharyngeal dysphagia, and poor oral health are mutually reinforcing conditions as malnutrition may affect muscle mass and strength which in turn can affect the swallowing function and oral health leading to a decreased nutritional intake [60, 61].

In geriatric patients, age - related physiologic changes (e.g., sarcopenia, presbyphagia, loss of teeth, or changes in taste and smell), cognitive decline, and social factors (e.g., bereavement, social isolation) do accommodate risk factors of malnutrition, oropharyngeal dysphagia, and poor oral health [21, 62-67].

Malnutrition, oropharyngeal dysphagia, and poor oral health thus form a complex pathophysiological triad occurring throughout the continuum of care of patients with neurological disorders and geriatric patients. These patients may benefit from a multidimensional treatment protocol [68], including interventions targeting oral health and oral hygiene (e.g., daily teeth brushing) [15, 69], the swallow physiology (e.g., muscle strength training, compensatory body posture strategies while eating) [59], and the nutritional status (e.g., texture modified foods, fortified foods, oral nutritional supplementation [ONS]) [70-72]. Furthermore, environmental factors of eating such as mealtime ambiance or healthcare professionals' knowledge and skills on nutrition and nutritional care are important [73].

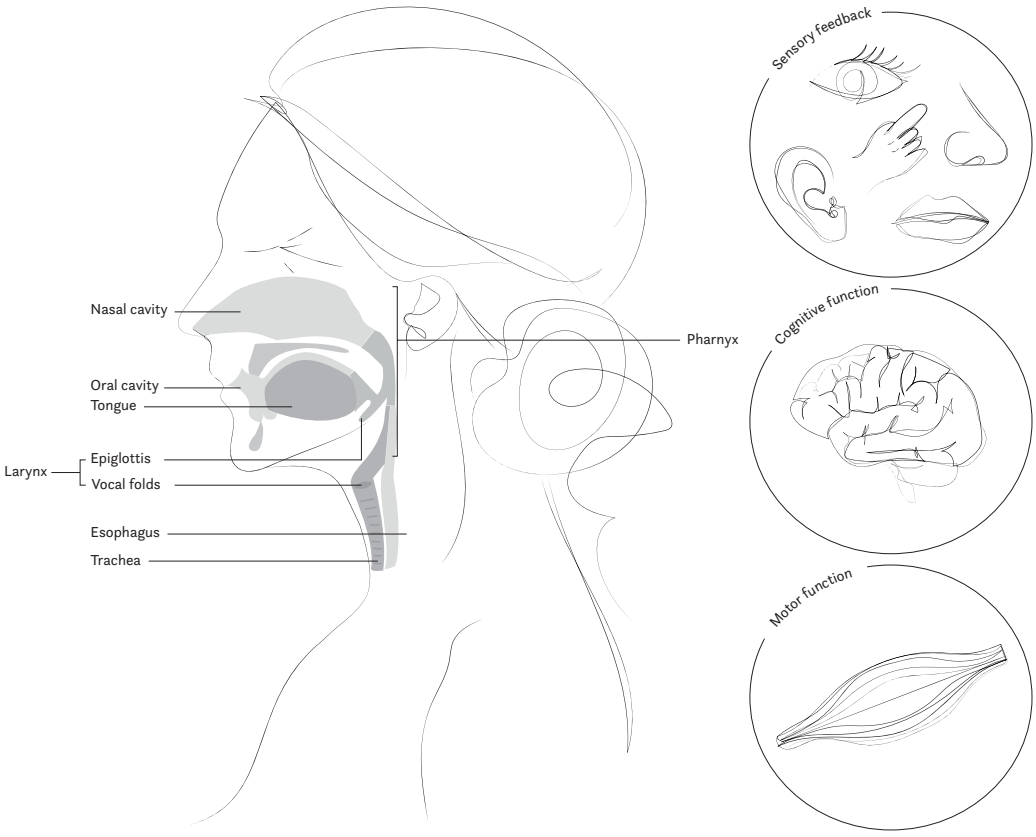

Figure 1. Schematic representation of the upper aerodigestive tract, the senses involved in swallowing, and the swallow – specific central nervous system control.

Aim and outline of this dissertation

Prevalence rates of malnutrition, oropharyngeal dysphagia, and poor oral health show that these detrimental conditions are highly present in all healthcare settings [10, 11, 27, 51-53]. Associations between malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents seem logic. A multidimensional approach, including two or all three of these conditions, has already been incorporated in a few clinical guidelines [23, 74]. Yet, more research is needed to further explore these associations in stroke patients and in nursing home residents, create awareness on consequences for the patients' health and health - related quality of life, and provide evidence to optimize clinical guidelines.

The present dissertation aims to gain knowledge and reflect on the associations within the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents with somatic and psychogeriatric diseases (including stroke and all types of dementia as main diagnosis). Multiple objectives are discussed, targeting at the

assessment of quality indicators of nutritional care in hospitals and the prevalence rates and associations between malnutrition and oropharyngeal dysphagia on the one hand, and poor oral health on the other hand.

The order of chapters in this dissertation follows the patient's care trajectory; starting at the acute care setting in the hospital, followed by a visit to the outpatient clinic in the aftermath of illness, or admission to a long - term care facility. Figure 2 provides a schematic overview of the associations within the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health that are assessed in the present dissertation.

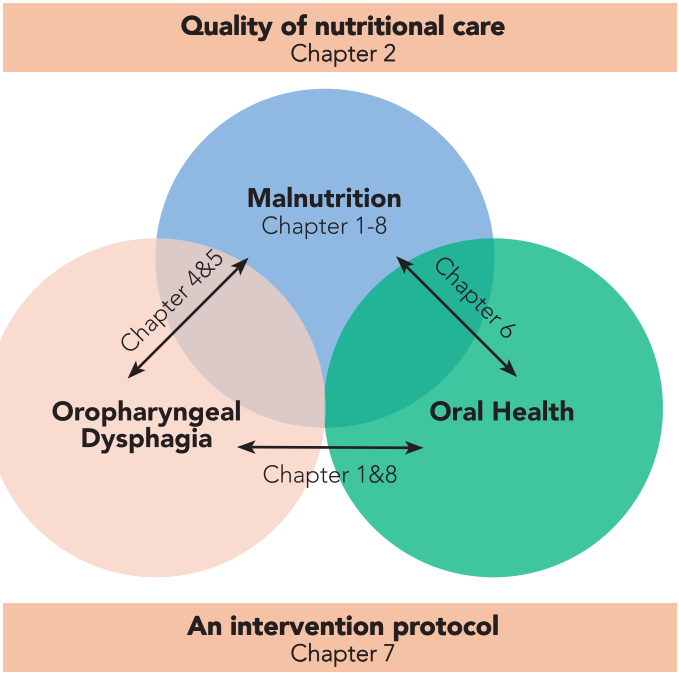

Figure 2. Overview of the associations within the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health that are assessed within the present dissertation

In part I of this dissertation, the prevalence of the risk of malnutrition and the quality of nutritional care in hospitals in three European countries is investigated. A retrospective cross - sectional study using data from an international collaborative project, the National Prevalence Measurement of Quality of Care (Landelijke Prevalentiemeting Zorgkwaliteit [LPZ]) [75] is conducted to compare the prevalence of the risk of malnutrition and the fulfillment of quality indicators of nutritional care on a structure, process, and outcome level in Austrian, Swiss, and Turkish hospitals (**chapter 2**). At the structure level, it is investigated how hospitals in Austria, Switzerland, and Turkey differ in the fulfillment of structural quality indicators on

ward and institutional level, e.g., the presence of a multidisciplinary nutritional expert committee (institutional level), and the performance of multidisciplinary team consultations for patients at risk of malnutrition (ward level). At process level, it is investigated what the differences between hospitals in Austria, Switzerland, and Turkey are regarding interventions for prevention or treatment of malnutrition risk. On outcome level, the differences in the prevalence rate of malnutrition risk between Austrian, Swiss, and Turkish hospitals are addressed.

In part II of this dissertation, the nutritional status in relation to oropharyngeal dysphagia in stroke patients is examined. A systematic literature review and meta - analysis is performed to investigate the prevalence of stroke patients with an impaired nutritional condition across the continuum of care (**chapter 3**). The term impaired nutritional condition refers to not well - nourished patients and has been introduced due to a lack of consensus in terminology and nutritional screening and diagnostic measurements in the literature. Additionally, a cross - sectional study was conducted to assess the prevalence of malnutrition risk, and explore the relationship between malnutrition risk and the severity of oropharyngeal dysphagia in stroke patients in an interdisciplinary outpatient clinic for dysphagia (**chapter 4**).

In part III of this dissertation, malnutrition is investigated in relation to oropharyngeal dysphagia and poor oral health in nursing home residents (**chapter 5** and **chapter 6**). Two cross - sectional studies using data from the LPZ measurements in Dutch nursing homes were conducted. In addition, a randomized controlled trial, the DYNAMO study, was developed (**chapter 7**). The DYNAMO study aimed to investigate the effect of daily use of a range of pre - thickened ONS for 12 weeks on the body weight of nursing home residents with oropharyngeal dysphagia and malnutrition (risk) compared to standard oropharyngeal dysphagia and nutritional care. However, early termination of this trial was inevitable during the COVID - 19 pandemic due to the associated health risks for nursing home residents and increased workload for the staff. An evaluation of the effect of a pre - thickened ONS on the body weight of nursing home residents using primary data from the randomized controlled trial is therefore lacking in this dissertation.

This dissertation is completed with a discussion on the findings of this dissertation, implications for clinical practice, education, and future research and a reflection on the methodologies used in this dissertation (**chapter 8**).

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Part I

Chapter 2

The quality of nutritional care in hospitals: Austria, Switzerland, and Turkey compared

Doris Eglseer*, Viviënne A.L. Huppertz*, Leonie Kammer, Bulent Saka, Jos M.G.A Schols, Irma Everink

*authors contributed equally

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Abstract

Objective The aim of this study was to investigate the differences in the quality of nutritional care among hospitals in Austria, Switzerland, and Turkey.

Methods This was a cross - sectional multicenter study. Data were collected using a standardized questionnaire. Descriptive statistics, as well as univariable and multivariable logistic regression (adjusted for age, sex, number of diagnoses, and care dependency) analyses were performed.

Results Taking part in the study were 6,293 patients from 62 hospitals. The prevalence of malnutrition risk was 14.5% in Austrian, 16.5% in Swiss, and 33.7% in Turkish patients. Standardized screening procedures were applied in 51.3% of Austrian, 53.6% of Swiss, and 38.4% of Turkish patients. The interventions applied in risk patients varied significantly between Austrian, Swiss, and Turkish hospitals for all but two interventions. Referrals to dietitians were lower in Austria (35.8%) and Switzerland (37.7%), as compared to Turkey (61%). Turkish patients received more frequently ONS, an energy or protein enriched diet, or parenteral nutrition, as compared to patients in Austrian or Swiss hospitals. The differences in the quality of nutritional care between Austrian and Swiss hospitals were only marginal. Of at-risk patients, 15.3% in Austria, 11.4% in Switzerland, and 5.5% in Turkey did not receive any intervention.

Conclusions The findings of this study indicated that significant differences exist in the prevalence, the identification and treatment of malnutrition, as well as the fulfillment of structural quality indicators. Standards and guidelines need to be developed that can be used by all countries. The severity of the situation in hospitals with regard to malnutrition needs further attention in future management policies.

Introduction

Malnutrition is a highly prevalent condition in hospitalized patients worldwide, which is defined as "*a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function, and impaired clinical outcome from disease*" [1]. Approximately every second hospitalized patient is at risk of malnutrition, which has a decisive impact on patient outcomes [2-4]. Studies have demonstrated that malnourished patients have higher rates of complications, more hospital readmissions, longer lengths of hospital stays (LOS), higher mortality rates, and a lower quality of life than patients without malnutrition [4-8]. Furthermore, malnutrition leads to additional costs of up to € 5829 for every patient per hospitalization [9, 10].

Several guidelines have been developed to provide recommendations on how to deliver optimal nutritional care in hospitals [1, 11, 12]. The use of a valid and reliable malnutrition screening tool is fundamental for identifying patients at risk. The primary guidelines also include recommendations for nutritional assessments, comprehensive diagnostic procedures, nutritional care planning, adequate nutritional interventions, monitoring and evaluating the effects of these interventions, and adequate documentation of the nutritional care provided [1]. The early recognition and treatment of malnutrition leads to an improvement in the patient's body weight, body composition and physical function [13], and it may be effective in reducing complications, readmission rates, LOS, mortality, and associated costs [13-16].

According to Donabedian's "Quality of care" health model, quality indicators on three levels may have an impact on the quality of care offered by organizations. These include structure, process, and outcome indicators [17]. In the context of the present study, a structural indicator for the quality of nutritional care is considered as the use of guidelines or the availability of a multidisciplinary nutrition support team in the hospital. Following protocols or guidelines may improve safety and efficiency of care [18, 19], and a multidisciplinary nutrition team may increase the knowledge and expertise of hospital staff, and provide support with treatment planning [20].

Process indicators include the use of a malnutrition screening tool or the provision of different interventions, such as nutritional counselling or providing oral nutritional supplements (ONS). Outcome indicators may comprise the nutritional intake of the affected persons or their nutritional status (risk of malnutrition) [21, 22].

It is necessary to regularly assess these quality indicators. They can serve as benchmarking tools and be used to initiate improvement projects [21-23]. Furthermore, hospitals need to transparently report the outcomes of these assessments, supporting mutually reinforcement and enrichment between hospitals. Thus, care performance and patient outcomes can be optimized [21, 24, 25]. By comparing the nutritional care provided in hospitals in different countries, researchers can explore and recognize differences among the existing structures and processes, identifying possibilities for improvements. Within this study, measurements were undertaken in hospitalized patients admitted to hospitals participating in the International Prevalence Measurement of Care Quality (LPZ

study) in November 2018 in three countries (Switzerland, Austria, and Turkey). Therefore, in the present study, differences in the fulfillment of quality indicators of nutritional care in three countries are investigated.

The research questions asked were:

- How does fulfilling structural quality indicators of nutritional care differ among hospitals in Austria, Switzerland, and Turkey? (structure)
- What are the differences in the conducted interventions for the prevention and / or treatment of malnutrition risk used in hospitals in Austria, Switzerland, and Turkey? (process)
- What are the differences in the prevalence of malnutrition risk among hospitals in Austria, Switzerland, and Turkey? (outcome)

Methods

Study design

The present cross - sectional study represents a secondary analysis of data collected during the annual LPZ study [23]. The LPZ study addresses six nursing problems (LPZ - modules): pressure injuries, falls, malnutrition, incontinence, pain, and restraints. Data were collected in November 2018 from a representative sample of hospitalized patients in Austria, Switzerland, and Turkey. A standardized questionnaire was used to assess quality indicators of care, the application of nutritional interventions and the prevalence of malnutrition risk among hospitalized patients [23].

Ethical considerations

The Medical Research Ethics Committee of the Maastricht University and the Academic Hospital of Maastricht approved the study. Additional ethical approvals were obtained from ethics committees in Austria (20 - 192 ex 08 / 09) and Turkey (22 / 01 / 2016, 02 - 153). Swiss ethics and the cantonal ethics committees had classified the measurement in 2012 as a quality measurement and therefore declared that the LPZ study is not within their purview, as it does not fall under the Swiss Human Research Act. The LPZ study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Hospitals participated on voluntary basis.

Study participants

LPZ study measurements were undertaken in participating countries (Austria, Switzerland, and Turkey) in November 2018. The present study therefore includes hospital patients from these three countries. To participate in the study, hospitalized patients had to be ≥ 18 years of age and had to provide their informed consent.

Data collection

Data were collected on the hospital level by the LPZ coordinators and on the ward level by ward nurses. On patient level, trained nurses from the participating

hospitals collected the data. To improve study reliability, two nurses were always involved in the data collection process; one nurse belonging to the respective ward and knew the patient, and one nurse was from another ward. Participating wards could choose to use either printed paper questionnaires and enter the information afterwards into an online data entry program or enter the data directly into the online data entry program.

Assessment methods

A questionnaire was used to assess all three levels (structure, process, and outcome) of the quality of care. Structure level indicators and process level indicators were assessed using binary data (i.e., yes / no). The outcome level indicator was assessed using continuous data (i.e., length, body weight, unintended body weight loss).

Structure level - quality indicators

Quality indicators assessed on an institutional level were: (1) the presence of an accepted protocol or guideline with regard to nutritional care and (2) the presence of a multidisciplinary nutritional expert committee.

Quality indicators assessed on a ward level were: (1) the performance of regular audits of the nutrition guideline used, (2) the performance of multidisciplinary team consultations for patients at risk of malnutrition, (3) the documentation of malnutrition risk assessment in each patient file, (4) the participation of caregivers in a refresher course about malnutrition, (5) and the presence of a standard policy for the transfer of malnutrition risk assessment documentation during the admission, transfer and discharge of the patient.

Process level - prevention or treatment

Prevention or treatment methods assessed included: (1) performing a malnutrition screening, (2) referring the patient to a dietitian, (3) enriching diet or snacks, (4) adjusting meal consistencies and mealtime ambiance, (5) taking into account the food preferences of the patient, (6) providing support at mealtimes if necessary, (7) providing information on nutritional problems and measurements to patients and relatives, (8) monitoring the fluid and nutritional intake, (9) providing oral nutritional supplements (ONS), (10) providing tube feeding, (11) providing parenteral nutrition, and (12) noting the absence of interventions.

Outcome level - prevalence

Malnutrition risk was assessed using the Body Mass Index (BMI) < 18.5 kg / m^2 (and in patients ≥ 65 years old ≤ 20 kg / m^2) and / or unintended weight loss of > 10% respectively within the last six months or > 5% within the last month.

Data analysis

All data were analyzed using SPSS version 26.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). Data cleaning was performed, and patients with unlikely BMI values (< 10 and > 60 kg / m^2) were excluded from the analysis. Descriptive

statistics was applied; dichotomous data are presented as absolute and relative frequencies, and continuous data are presented as mean (± SD) or median (IQR). Differences between the countries were calculated with chi – square (χ^2) tests with dichotomous outcomes and Kruskal - Wallis *H* tests with metric outcomes. To consider influencing factors with regard to the differences in the prevalence of malnutrition risk for the countries, both univariable and multivariable logistic regression analyses were performed; the latter was adjusted for age, sex, number of diagnoses, and care dependency scale (CDS) sum score.

Results

Patient characteristics

The participants included 3,289 patients from 35 Austrian hospitals, 2,452 patients from 16 Swiss hospitals, and 552 patients from 11 Turkish hospitals. Slightly more than half of the patients (51.5%) in the Austrian hospitals were women, as were 44.7% and 49.8%, respectively, in Swiss and Turkish hospitals. Most patients were admitted to internal medicine (53.4%) and surgical wards (38.2%). The mean patient age was 64.6 years for all three countries combined. In the three countries, the majority of the patients were ≥ 56 years of age; in Turkey and Switzerland, most patients were between 56 and 75 years of age, and in Austria, most patients were older than 75 years. Country - specific differences were found regarding the care dependency of the patients. In Austrian hospitals, 8.5% of the patients were completely or to a great extent care dependent. In Swiss hospitals, this percentage was slightly higher (10.8%), and the percentage of patients who were completely or to a great extent care dependent was highest (14.0%) in Turkish hospitals. Table 1 shows detailed patient characteristics for each country.

Prevalence of malnutrition risk

The prevalence of malnutrition risk was 14.5% in Austrian, 16.5% in Swiss and 33.7% in Turkish hospitalized patients. When adjusting for the patients' sex, age, number of diagnoses and care dependency, the difference observed between the prevalence rates in Austria and Switzerland were not statistically significant ($p = 0.36$). In contrast, the differences noted in the prevalence of malnutrition risk between Austria or Switzerland and Turkey were identified as significant in the multivariable model (table 2).

While the prevalence rates of malnutrition risk were very similar between Austrian and Swiss patients on surgical and intensive care units (ICUs), higher prevalence rates were found for Swiss internal medicine and geriatric patients compared with Austrian internal medicine and geriatric patients. In general, the malnutrition risk prevalence rates were highest in Turkey, with 34.2% of the internal medicine patients and 25.8% of geriatric patients displaying signs of malnutrition. Statistically significant differences in the prevalence of malnutrition risk, based on the respective ward type, among the countries was only found in internal medicine hospital patients ($p < 0.01$). No ICU or surgical patients from Turkish hospitals participated in the study. An overview of the prevalence rates of malnutrition risk by country and ward can be found in figure 1.

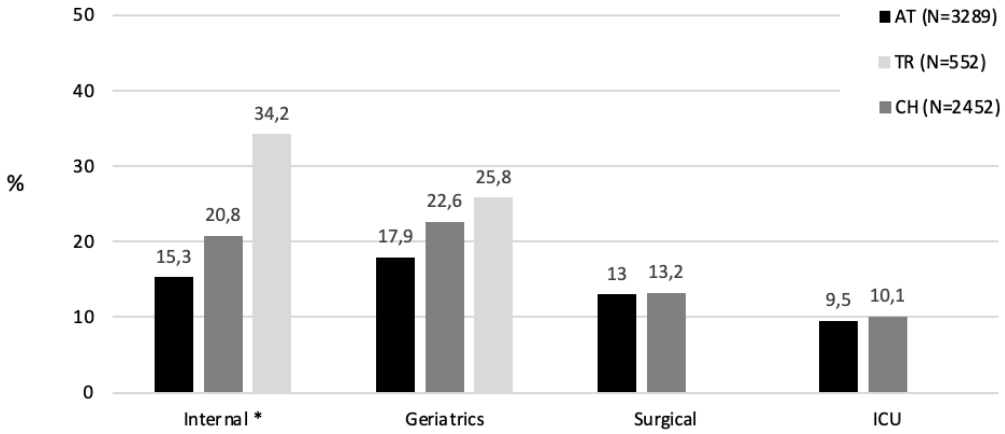

Figure 1. Prevalence of risk of malnutrition by country and type of ward in which the patients were admitted. Abbreviations: *ICU; Intensive Care Unit*

* Statistically significant differences observed among the countries ($p < 0.01$), calculated using χ^2 tests

Nutritional interventions in patients at risk of malnutrition

Standardized screening procedures were applied in 51.3% of Austrian, 53.6% of Swiss, and 38.4% of Turkish patients, using valid and reliable screening tools among all admitted patients. The nutritional interventions applied in patients at risk of malnutrition varied significantly between hospitals in the three countries for all but two interventions (figure 2).

In Austria and Switzerland, the most commonly used interventions for patients at risk of malnutrition were the provision of specific food desired by the patient, the referral to a dietitian and the provision of ONS. Nevertheless, referrals to dietitians were lower in Austria (35.8%) and in Switzerland (37.7%), as compared to the rate of referrals in Turkey (61%); in fact, this was the most frequently conducted intervention in Turkish hospitals. Monitoring of nutritional and fluid intake was higher in Swiss hospitals (25.7% and 19.4%, respectively) compared with those in Austria (9.1% and 8.7%, respectively) and Turkey (7.3% and 11.6%). Turkish patients at risk of malnutrition received ONS, an energy or protein enriched diet, or parenteral nutrition relatively frequently as compared to patients in Austrian or Swiss hospitals. The use of tube feeding was rather infrequent in all three countries, with the highest prevalence rate found in Turkish hospitals (11%). In Austria, 15.3% of patients at risk of malnutrition did not receive any intervention. In Switzerland, this was the case for 11.4% of the patients and, in Turkey, for 5.5% of the patients.

Structural quality indicators

A malnutrition guideline was available in 23 out of 35 (65.7%) Austrian, in 13 out of 16 (81.3%) Swiss, and in 10 out of 11 (90.0%) Turkish hospitals. A multi - disciplinary nutrition support team existed in 77.1% of the Austrian, 75.0% of the Swiss, and 63.6% of the Turkish hospitals. The fulfillment rates of structural quality indicators

on a ward level are shown in table 3. The handover of personalized risk assessment during patient admission, transfer, and discharge was included in standard policy in the majority (≥ 90%) of all participating hospitals. Turkish hospitals scored significantly higher for the quality indicator "participation in refresher courses of all caregivers in the last two years" (92.1%; p = 0.01) compared with Austrian (35.5%) and Swiss (27.6%) hospitals.

Table 1. Characteristics of Austrian, Swiss and Turkish hospitalized participants.
Abbreviations: *CDS; Care Dependency Scale, BMI; body mass index*

	Austria	***Switzerland***	***Turkey***	***P*** [a]
Total population, *n* (%)	3289 (52.3)	2452 (39.0)	552 (8.8)	
Sex (female), *n* (%)	1695 (51.5)	1095 (44.7)	275 (49.8)	< 0.01
CDS, *median (IQR)*	74 (15-75)	71 (15-75)	74.5 (15-75)	< 0.01
Completely dependent	98 (3.0)	86 (3.5)	34 (6.2)	
To a great extent dependent	180 (5.5)	179 (7.3)	43 (7.8)	
Partially dependent	296 (9.0)	297 (12.1)	65 (11.8)	
To a great extent independent	504 (15.3)	515 (21.0)	79 (14.3)	
Completely independent	2211 (67.2)	1375 (56.1)	331 (60.0)	
Age (years), *median (IQR)*	68 (18-99)	67 (18-105)	64 (18-98)	< 0.01
Age (years), *n* (%)	281 (8.5)	180 (7.3)	50 (9.1)	
18 - 35				
36 - 55	602 (18.3)	507 (20.7)	127 (23.0)	
56 - 75	1302 (39.6)	987 (40.3)	256 (46.4)	
≥ 76	1104 (33.6)	778 (31.7)	119 (21.6)	
BMI, *median (IQR)*	25.6 (11.7-58.5)	25.1 (13.0-58.5)	25.9 (13.8-52.9)	< 0.01
Type of ward, *n* (%)				
Medical	1812 (55.1)	1036 (42.3)	511 (92.6)	
Geriatrics	140 (4.3)	90 (3.7)	41 (7.4)	
Surgical	1276 (38.8)	1126 (45.9)	0 (0.0)	
ICU	61 (1.9)	200 (8.2)	0 (0.0)	
Total number of diagnoses, *median (IQR)*	2 (0-11)	3 (0-13)	2 (0-6)	< 0.01
Most frequent medical diagnoses, *n* (%)				
Diseases of the circulatory system	1604 (48.8)	1370 (55.9)	173 (31.3)	
Endocrine, nutritional and metabolic diseases	1043 (31.7)	840 (34.3)	203 (36.8)	
Diseases of the musculoskeletal system and connective tissue	892 (27.1)	754 (30.8)	52 (9.4)	
Diseases of the genitourinary system	730 (22.2)	644 (26.3)	118 (21.4)	
Diseases of the digestive system	682 (20.7)	613 (25.0)	96 (17.4)	
Cancer	578 (17.6)	670 (27.3)	121 (21.9)	

[a] p - values are calculated with the χ^2 test or the Kruskal - Wallis *H* test, depending on the data

Table 2. Univariable and multivariable analyses presenting influencing factors for the prevalence of malnutrition. Abbreviations: *CDS; Care Dependency Scale*

Influencing factors		***Univariable logistic regression***		***Multivariable logistic regression***	
		OR (95% CI)	***P***	***OR (95% CI)***	***P***
Country	Austria (reference)	1	0.00	1	
	Switzerland	1.17 (1.00-1.36)	0.05	1.08 (0.92-1.26)	0.36
	Turkey	2.43 (2.43-3.71)	0.00	3.16 (2.54-3.93)	0.00
Sex	Male (reference)	1		1	
	Female	1.18 (1.02-1.35)	0.02	1.16 (1.01-1.34)	0.04
Number of diagnoses		1.09 (1.06-1.13)	0.00	1.1 (1.05-1.14)	0.00
CDS sum score		0.98 (0.98-0.99)	0.00	099 (0.99-1.00)	0.00
Age		1.00 (1.00-1.01)	0.00	1.00 (1.00-1.00)	0.29

Discussion

The results of the present cross - sectional study provided an extensive overview of prevalence rates of malnutrition risk, concurrently applied interventions, and fulfilled structural quality indicators of nutritional care in hospitals in Austria, Switzerland, and Turkey.

The findings showed that the malnutrition risk is still high in hospital patients in all three countries, especially on the internal medicine and geriatric wards. However, the prevalence rates found in the present study are in line with those cited by other studies [2, 26, 27]. In a recently published systematic review and meta - analysis, Leij - Halfwerk et al. (2019) pooled a broad variety of studies that used different screening tools and found a prevalence rate of protein - energy malnutrition risk of 28% among older patients in European hospitals [27].

The present study findings demonstrated that the prevalence of malnutrition is highest in Turkish hospitals. Patients in Turkish hospitals are three times more likely to be at risk of malnutrition than patients in Austrian and Swiss hospitals. Turkish patients were more care dependent than Austrian and Swiss patients, and previous studies have shown that there is a relationship between the degree of care dependency and the risk of malnutrition [28, 29]. However, the difference in the prevalence rates remained significant, even after adjusting for care dependency. A possible explanation for these findings is that more Turkish patients are at risk of malnutrition by the time they are admitted to the hospital (i.e., they develop the malnutrition risk at home prior to admission). This assumption may be supported by the high prevalence rates of malnutrition or malnutrition risk in community dwelling older adults, which are cited at up to 48% in Turkey [30, 31].

Patients at risk of malnutrition in Turkish hospitals received more interventions, as compared to patients in Austrian and Swiss hospitals. In Turkey, 94.5% of the patients at risk of malnutrition received at least one intervention, whereas only 88.6% of the Swiss patients and 84.7% of the Austrian patients at risk received an intervention. This finding agrees with the results of the NutritionDay survey, which indicated a high malnutrition prevalence rate, as well as a very high rate

of malnourished patients who received nutrition support in Turkish hospitals [32].

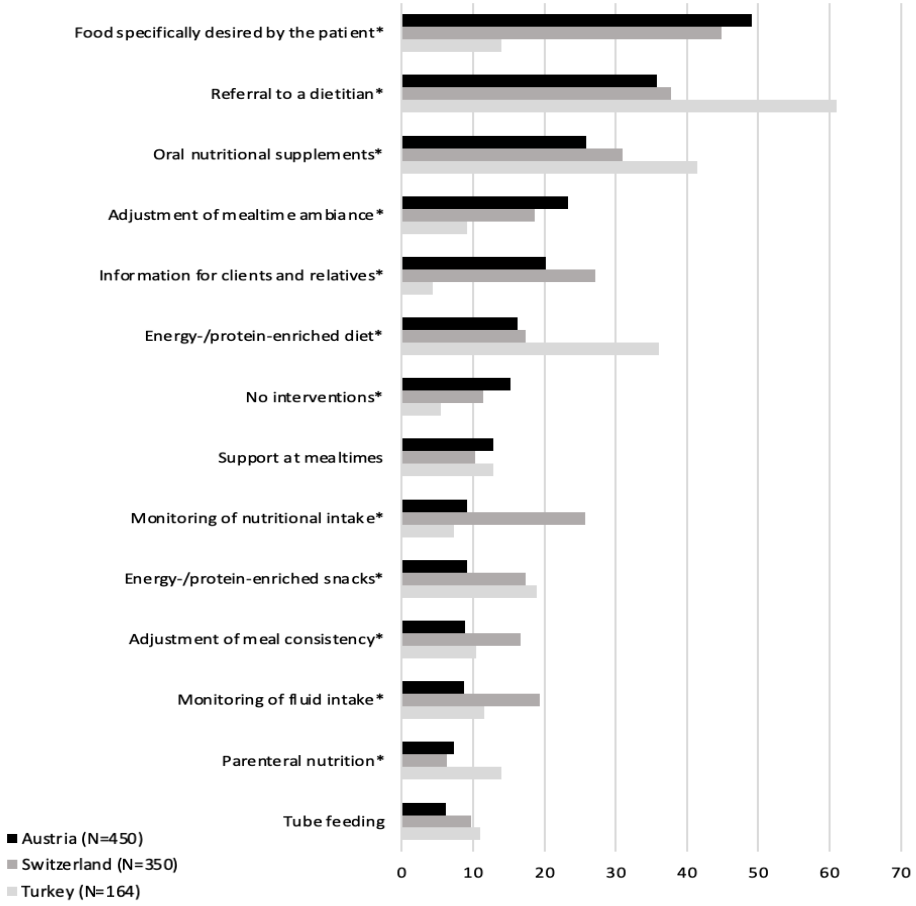

Figure 2. Nutritional interventions performed in patients at risk of malnutrition per country
* Statistical significant differences between the countries ($p < 0.01$), calculated using χ^2 tests

This raises questions about the importance of the type of intervention conducted. For example, Turkish hospital patients were less likely to receive food specifically desired by the patient. Also, the measures of monitoring the patient's nutritional intake and providing the patient or relatives with information or counselling were less commonly performed in Turkish hospitals than in Austrian and Swiss hospitals. On the other hand, Turkish patients received ONS or an energy or protein enriched diet more often than patients in Austrian and Swiss hospitals. This may be due to the fact that most patients in Turkey were referred to a dietitian who may prescribe ONS. Prescribing ONS or an enriched diet is important, but it may be even more important to explain the reason and purpose of these interventions to patients. In this way, long - lasting changes in diet can be ensured.

These results are supported by the findings of a pooled analysis of data from nine RCTs [33]. The energy intake and weight gain of malnourished patients

improved when they consumed ONS and received dietary counseling, but not when they only consumed ONS [33]. Furthermore, the monitoring of nutritional intake checking whether the recommended ONS and / or enriched diet was actually consumed is an often underestimated intervention [1]. On the basis of current guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN), a comprehensive nutritional care plan not only involves nutritional interventions but also provides suggestions for monitoring the efficacy of the plan (e.g., if the calculated requirements for fluid, energy, and protein have been met) [1]. This might be a recommendation for Turkish hospitals.

Table 3. Implementation of structural quality indicators of nutritional care on a ward level per country

	Austria	***Switzerland***	***Turkey***	***P***
Number of wards	220	214	38	
Regular audits are done to ensure compliance with the protocol/guideline. (fill in only if there is a protocol/guideline), *n* (%)	126 (57.3)	122 (57.0)	34 (89.5)	0.40
All clients with a risk are discussed within a multidisciplinary team on the ward, *n* (%)	181 (82.3)	130 (60.7)	28 (73.7)	0.85
Risk assessment is specified for each client in the care file, *n* (%)	200 (90.9)	158 (73.8)	30 (78.9)	0.46
All caregivers have followed a refresher course in the last two years, *n* (%)	78 (35.5)	59 (27.6)	35 (92.1)	0.01
Risk assessment is specified for each client as a standard policy in the hand-off during admission, transfer, and discharge, *n* (%)	201 (91.4)	198 (92.5)	36 (94.7)	0.42

Screening was performed in about half of the patients in Austrian (51.3%) and Swiss hospital patients (53.6%), but the screening rate in Turkish hospitals was lower (38.4%). These numbers are rather low for all three countries when considering the recommendation to screen all patients at hospital admission, regardless of their medical condition. Systematic screening of all hospital patients is strongly recommended in the guidelines [1, 11, 12, 34] but also supported by the findings of the Effect of early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial (EFFORT) [35]. EFFORT showed improved clinical outcomes, such as a lower incidence of adverse clinical outcomes and reduced mortality in patients at risk of malnutrition as a consequence of offering personalized nutritional support, which was initiated in a timely manner after the patient's admission to the hospital, after screening, and after nutritional assessment [35].

The present study's results also revealed differences regarding structural quality indicators among hospitals in the three countries. The use of guidelines was highest in Turkish hospitals, whereas the presence of a multidisciplinary nutrition support team was highest in Austrian hospitals. Although these structural quality indicators clearly provide a basis for adequate nutritional management, studies have shown that it is not enough to only fulfil these indicators. For example, a Swiss study showed that staff

poorly adhere to guidelines, even though they are present in the hospitals [36].

The differences between Austrian and Swiss hospitals were only marginal in terms of the fulfillment of structural quality indicators, patient characteristics and the prevalence of malnutrition. Differences in nutritional care between Austria and Switzerland were only found with regard to the frequency of some interventions in patients at risk of malnutrition. However, the differences were not as striking as those noted between Austria or Switzerland and Turkey, and the frequency of most interventions was similar between Austria and Switzerland.

Strengths and limitations

The LPZ study, the source of the data used in the present cross - sectional study, has the potential to generate a large amount of new data on a broad variety of health topics every year. However, participation in the LPZ study is voluntary for hospitals. If we examine the number of hospitals in each country separately, it is clear that only a small percentage of hospitals participated, which could indicate a selection bias. In Turkey, only a small sample participated in the study. Some participating hospitals may already comply more effectively to good nutritional practices. The prevalence of malnutrition risk in these hospitals is likely to be underestimated, whereas the compliance with structural and process quality indicators may be overestimated. Because informed consent was a requirement it may be possible that either patients (with a poor state of health or highly impaired patients) or their legal representatives declined to participate. These patients are a high - risk group regarding the development of malnutrition, which may have influenced the prevalence rates of malnutrition, as well as interventions against malnutrition. Furthermore, because data were collected at a single time point, the findings cannot be applied to other time points. No statements can be made regarding the causes for the different prevalence rates in the three countries.

Conclusions

This cross - sectional study provided results that showed that a high malnutrition risk among hospital patients is still a concern in Austria, Switzerland, and Turkey; prevalence rates ranged from 14.5% to 33.7%. The findings indicated that significant differences exist in both the prevalence and the identification and treatment of malnutrition, as well as the fulfillment of quality indicators on the ward and institution levels. The study results could be used to discuss these differences and to define, and plan targeted activities in the respective countries. Standards and guidelines need to be developed that can be used by all countries. In future studies, researchers should identify the interventions that are the most effective in preventing and treating malnutrition. The severity of the situation in hospitals with regard to malnutrition should not be underestimated and needs further attention in future management policies.

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Part II

Chapter 3

Impaired nutritional condition after stroke from the hyperacute to the chronic phase: a systematic review and meta-analysis

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Abstract

Introduction Malnutrition is common after stroke and can affect rehabilitation and healthcare costs. A comprehensive overview of stroke patients' nutritional condition from the hyperacute to the chronic phase is lacking. This systematic review aimed to investigate the prevalence of impaired nutritional condition (INC) across the continuum of care in specific phases after stroke.

Methods CAB ABSTRACTS, Embase, and MEDLINE were used to collect studies published between 01 – 01 - 1999 and 26 – 08 - 2020. Primary and secondary outcomes were prevalence of INC and prevalence of malnutrition, respectively. Exploratory outcomes were prevalence of INC at follow - up, nutritional examination methods, prevalence of dysphagia, stroke severity, adverse events, and continent - specific prevalence of INC. A random - effects meta - analysis model was used to estimate the phase - specific pooled prevalence of INC and malnutrition.

Results The dataset consisted of 78 study groups selected over a total of 1,244 identified records. The pooled prevalence of INC and malnutrition were 19% (95% CI: 7 - 31) (N = 4) and 19% (95% CI: 9 - 29) (N = 3), 34% (95% CI: 25 - 43) (N = 34) and 26% (95% CI: 18 - 35) (N = 29), 52% (95% CI: 43 - 61) (N = 34) and 37% (95% CI: 28 - 45) (N = 31), 21% (95% CI: 12 - 31) (N = 3) and 11% (95% CI: 0 - 24) (N = 3) and 72% (95% CI: 41 - 100) (N = 3) and 30% (95% CI: 0 - 76) (N = 2) in the hyperacute, acute, early subacute, late subacute, and chronic phase, respectively.

Conclusion INC and malnutrition are highly prevalent in all stages of stroke care. Since malnutrition has been shown to negatively affect clinical outcomes, mortality, and overall healthcare expenditure in stroke survivors, it is essential to examine and monitor the nutritional status of stroke patients throughout their care journey to guide and plan, timely nutritional support and dietary modification.

Introduction

Malnutrition is common after stroke [1] and relates to poor outcomes as assessed with the modified Ranking Scale, increased prevalence of complications, length of hospital stay, mortality, and hospitalization costs [2, 3]. Several factors that occur after stroke, including dysphagia [4], hemiparesis, decreased mobility, depression [5], and post - stroke dementia [6] compound the risk of malnutrition. Multiple studies in stroke patients have consistently demonstrated that the recommended nutritional intake is not achieved after stroke [7-11].

Over the past decade, stroke patient outcomes have continuously improved through thrombectomy, recombinant tissue plasminogen activator treatments, and case management in stroke units [12]. As stroke mortality declines, the importance of rehabilitation is growing due to high disability rates among survivors, leading to a high overall burden on global healthcare. In Europe, the total cost of stroke was estimated at €60.0 billion in 2017 [13]; almost half of this budget was spent on direct healthcare. The remaining costs were related to informal care, social care systems, non - health or social care areas, and productivity losses. Multidisciplinary and structured stroke rehabilitation reduces disability related to stroke regardless of age, sex, and stroke severity [14]. Combining neurorehabilitation strategies, such as early mobilization and pharmacological intervention [15, 16], also offers the potential to improve outcomes and reduce costs after stroke.

The clinical stroke pathway begins immediately after onset (hyperacute phase), ultimately reaching a chronic phase around six months post - stroke [17]. The optimal time window for rehabilitation therapies is considered to be before the observed peak of recovery, between stroke onset and three months after the stroke event [18]. Stroke care guidelines recommend using a multidisciplinary approach [5, 14] including nutritional screening and treatment of malnutrition [19, 20]. As indicated, malnutrition is common after a stroke. Foley et al. [21] reviewed studies on the prevalence of malnutrition after stroke and possible causes for heterogeneity of its prevalence. They observed a prevalence of malnutrition ranging from 6.1% to 62.0%, but a comprehensive overview of stroke patients' nutritional status from the hyperacute to the chronic phase is lacking. Considering the relevance of nutritional status in the recovery process, this systematic review aimed to investigate the prevalence of impaired nutritional condition (INC), defined as the percentage of not well-nourished patients, across the continuum of care in specific phases after stroke. The term ''nutritional condition'' is used to describe the results of this review.

Materials and methods

Protocol and registration

This systematic review was executed following the Preferred Reporting Items for Systematic Reviews and Meta - Analyses (PRISMA) checklist [22] and registered

in the international Prospective Register of Systematic Reviews (PROSPERO) [23] (registration number: CRD42020205891).

Search strategy

The literature search was performed in ProQuest® by a librarian specialist. ProQuest® was used to inspect three databases (CAB ABSTRACTS, Embase, and MEDLINE) for a conceptual string composed of 'stroke' (OR synonyms) AND 'malnutrition' (OR synonyms). The search was performed for literature published in English between 01 – 01 - 1999 to 26 – 08 - 2020. Document types excluded from the search were conference abstracts, conference papers, conference reviews, case reports, book chapters, short surveys, retracted publications, letters, editorials, clinical trial protocols, and technical reports. The full search strategy is available in the supplemental material (supplemental material, table S1).

Eligibility criteria

Meta - analyses, reviews, intended trials, case reports, pharmaceutical clinical trials, and studies including a re - analysis of a study sample were excluded. The population's inclusion criteria were met if the age was ≥ 18 years and patients were examined for nutritional status within zero hours up to two years after stroke onset. Studies where the nutritional status was used as an eligibility criterion to recruit patients with a specific nutritional status were excluded. Studies were excluded when the entire population was in a comatose / vegetative state or on parenteral nutrition at admission to the study. Selection of the data required that the prevalence of INC was reported in the study as a percentage value or absolute number. The study was excluded if the nutritional status was examined using body mass index (BMI) only. BMI categories might be difficult to interpret considering that both, underweight and obese patients, can be malnourished [24]. Studies where no indications were provided on the method used for the nutritional examination were excluded. Follow - up data were not included when interventions with an impact on the nutritional status were investigated. If a study reported the prevalence of INC or malnutrition in completely independent groups, the data were treated separately. For example, in studies where the study population was separated into two groups that received the nutritional examination in different time periods, the data on prevalence were treated separately.

Study selection and data extraction

Duplicates were removed manually. Screening of titles and abstracts was performed by one reviewer (VH or SG). Two reviewers (VH and SG) performed the screening of full - text articles and data extraction for primary and secondary parameters. A third reviewer (CvdB) was consulted in case of a disagreement. One reviewer performed the data extraction of the exploratory parameters (VH), and, in case of ambiguity, the second reviewer (SG) was consulted. Percentage values were recalculated for accuracy when needed. Reasons for exclusion of the full - text articles were classified according to the Population, Intervention, Comparison, and Outcome

(PICO) framework [25]. The PICO framework can be used to systematically identify and document clinical evidence. Studies were excluded if the inclusion criteria related to the ''population'' (e.g., age) and / or to the ''outcome'' (e.g., missing prevalence data) were not met, or if there was any other reason for exclusion (e.g., language) which was defined ''non - PICO''. The present systematic review does not aim to address research questions related to treatments or differences between intervention and control groups; therefore, the categories ''intervention'' and ''comparison'' were not used.

Outcome parameters

The primary outcome is the prevalence of INC in each phase after stroke by using the definition of timing described by Bernhardt et al. [17] and limiting the chronic phase to two years after stroke: hyperacute (≤ 24 h), acute (> 24 h - ≤ 7 days), early subacute (> 7 days - < 3 months), late subacute (≥ 3 months - < 6 months), and chronic (≥ 6 months - 2 years). Prevalence of INC at baseline was reported for each study included in the analysis and comprised the full dataset. The secondary outcome is the prevalence of malnutrition in the phases mentioned above. A phase - specific pooled prevalence was estimated for the primary and secondary outcomes. Exploratory outcomes are the prevalence of INC at follow - up, methods used for the nutritional examination (percentage of study groups reporting on screening / assessment tools, anthropometrical / biochemical measurements, and description of the methods), the prevalence of dysphagia, stroke severity evaluated with the National Institutes of Health Stroke Scale (NIHSS), adverse events, and continent - specific prevalence of INC.

Criteria used to estimate the prevalence of INC and malnutrition

The prevalence data, as shown in this paper, were based on the method found in the respective study. In case a study reported multiple methods to examine the nutritional status, only one method was selected based on whether it was a method used to generate the primary results or a method largely used in the literature. The methods found in the studies were distinguished in screening / assessment tools or anthropometrical / biochemical measurements. Screening / assessment tools included methods whose outcomes were expressed in pre - defined categories (e.g., no malnutrition, at risk of malnutrition or malnourished). Examples of these tools are, among others, the Malnutrition Universal Screening Tool ('MUST') and the Mini Nutritional Assessment (MNA). Anthropometrical / biochemical measurements included methods that used measurements of anthropometrical or biochemical parameters. Examples of these measurements are bodyweight and serum albumin levels. The extracted data from the nutritional screening / assessment tools needed to be harmonized according to the definition of INC and malnutrition in this systematic review. There was no need to harmonize data from the Global Leadership Initiative on Malnutrition (GLIM) and European Society for Clinical Nutrition and Metabolism (ESPEN) diagnostic criteria of malnutrition because in this case the outcomes are not expressed in pre - defined categories

but rather on the diagnosis of malnutrition after screening. The criteria used for harmonization of data derived from the remaining screening / assessment tools are shown in the supplemental material, table S2.

Criteria used to estimate the time of nutritional examination after stroke

In case the time of nutritional examination after stroke (TNE – S - E) was not reported in the study it was estimated according to the following conditions: (i) time of admission after stroke (TA - S) and time of nutritional examination after admission (TNE - A) were available, (ii) TA - S was missing, but information on the phase after stroke was available. The criteria used for the estimation of TNE – S - E are reported in the supplemental material, figure S1.

Risk of bias

Risk of bias was evaluated for each study using a self - developed checklist including seven questions related to selection, performance, detection, and reporting bias: (1) Is there a reason to believe that the study population is not representative for the stroke population in the assigned phase after stroke? (selection bias). The answer to this question evaluated whether the setting in which the patients were recruited was representative for the phase to which the study group was assigned. All acute care settings were considered representative for study groups assigned to the hyperacute, or acute phase after stroke. Hospitals, rehabilitation centers, long - term care facilities and home (care) were considered representative settings for study groups assigned to the early subacute, late subacute, and chronic phase after stroke; however, in case the study was performed in only one of these settings a risk of bias was detected. (2) Was the stroke diagnosis confirmed using a CT scan / MRI? (performance bias I). (3) Was a validated screening / assessment tool used for nutritional examination? (performance bias II). (4) Was the method used for the nutritional examination clearly defined in the study? (detection bias I). (5) Was the method used for the nutritional examination consistently used in the study? (detection bias II). (6) Where the prevalence data for all stroke patients who received the nutritional examination available in the study? (reporting bias I). (7) Where the prevalence data complete according to the criteria applied to the screening / assessment tools? (reporting bias II). Question 1, 2, 4, 5, and 6 were scored dichotomously (risk of bias / no risk of bias), and question 3 and 7 were scored trichotomously (risk of bias / no risk of bias / not applicable). Question 3 was not applicable in case the nutritional status was examined using anthropometrical / biochemical measurements. Question 7 was not applicable in case the nutritional status was examined using anthropometrical / biochemical measurements or if GLIM or ESPEN criteria were used. A relative risk of bias (relative risk [%]) was calculated as a percentage of the total number of items that were scored.

Statistical analysis

TNE - S - E and TA - S were used as initially reported in the study either as mean (± SD), median (interquartile range [IQR]), or as a value described in the text. When the

mean (± SD) was not available, the median (IQR) was used. This approach is in line with Hozo et al. [26], who showed that, for sample sizes > 25, replacing the sample mean with the reported median is the best estimator for the sample mean. The pooled prevalence of INC and malnutrition was estimated using random - effects (RE) [27] and fixed - effect (FE) [28] meta - analysis models. A RE meta - analysis model was preferred over a FE [29, 30] and used for the interpretation of the results. The between - study variance of the RE model, τ^2, was estimated via the restricted maximum likelihood approach [31]. A meta - analysis of prevalence estimated a weighted average prevalence of the observed proportions, accompanied by a 95% confidence interval (95% CI). NIHSS scores were collected as originally reported in the study, either as a mean or as a median, and used to define the category of stroke severity according to the NIHS Scale. The statistical analyses were carried out in RStudio (R, version 4.0.0; R Project), using the function "rma.uni" from the package *metafor* to pool the raw proportions and package *meta* to create the forest plots.

Results

A total of 1,244 articles were identified through the literature search, of which 99 in CAB ABSTRACTS, 914 in Embase, and 231 in MEDLINE. A total of 233 full - text articles were assessed for eligibility, of which 75 were included in the analysis. In three studies, the nutritional status was evaluated in independent study groups, and this resulted in a total of 78 study groups (figure 1).

General characteristics of the study groups

Study designs were observational and experimental in 68 (87.2%) and 10 (12.8%) study groups, respectively. Fifty - six (71.8%) study groups were performed in hospitals, 17 (21.8%) in rehabilitation facilities, three (3.8%) in nursing homes / care homes / home, and two (2.6%) in a combination of settings. The type of diagnosis reported among the study groups was mainly ischemic and haemorrhagic stroke. TNE - S - E was available and therefore not estimated in 14 (17.9%) out of 78 study groups. The total number of stroke patients who received the nutritional examination was 25,090 ranging from 12 to 4,023 patients per study group. An overview of the general characteristics of the studies is provided in the supplemental material, table S3.

Prevalence of INC

Out of 78 study groups with data on INC, four (5.1%) were conducted in the hyperacute, 34 (43.6%) in the acute, 34 (43.6%) in the early subacute, three (3.8%) in the late subacute, and three (3.8%) in the chronic phase. Overall, the prevalence of INC across phases ranged from 3.8% to 100.0%. Prevalence of INC ranged from 11.1% to 36.3% in the hyperacute phase, 5.0% to 100.0% in the acute phase, 3.8% to 100.0% in the early subacute phase, 12.1% to 27.8% in the late subacute phase,

and 41.0% to 91.4% in the chronic phase (figure 2A). Combining the individual prevalence numbers per phase yielded a pooled prevalence of 19% (95% CI: 7 - 31) based on four study groups in the hyperacute phase, 34% (95% CI: 25 - 43) based on 34 study groups in the acute phase, 52% (95% CI: 43 - 61) based on 34 study groups in the early subacute phase, 21% (95% CI: 12 - 31) based on three study groups in the late subacute phase, and 72% (95% CI: 41 - 100) based on three study groups in the chronic phase (figure 3). In the phases where the pooled prevalence was based on a number of study groups ≤ 5, the results generated with the RE and FE meta - analysis models were overall similar.

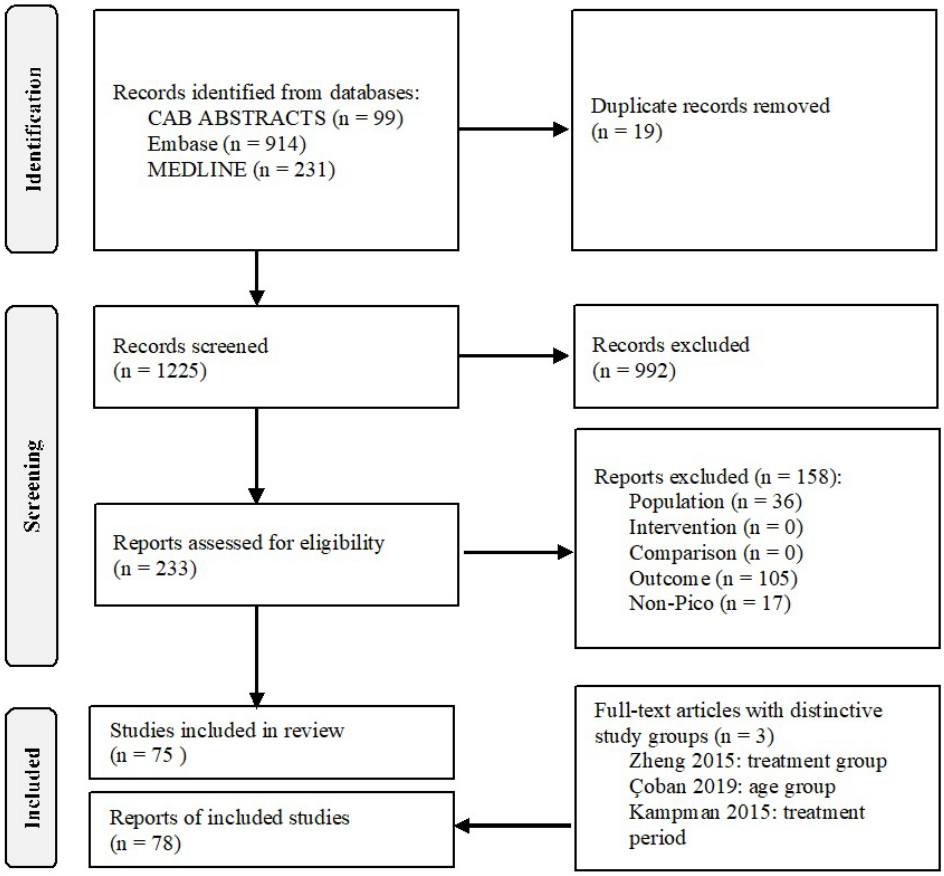
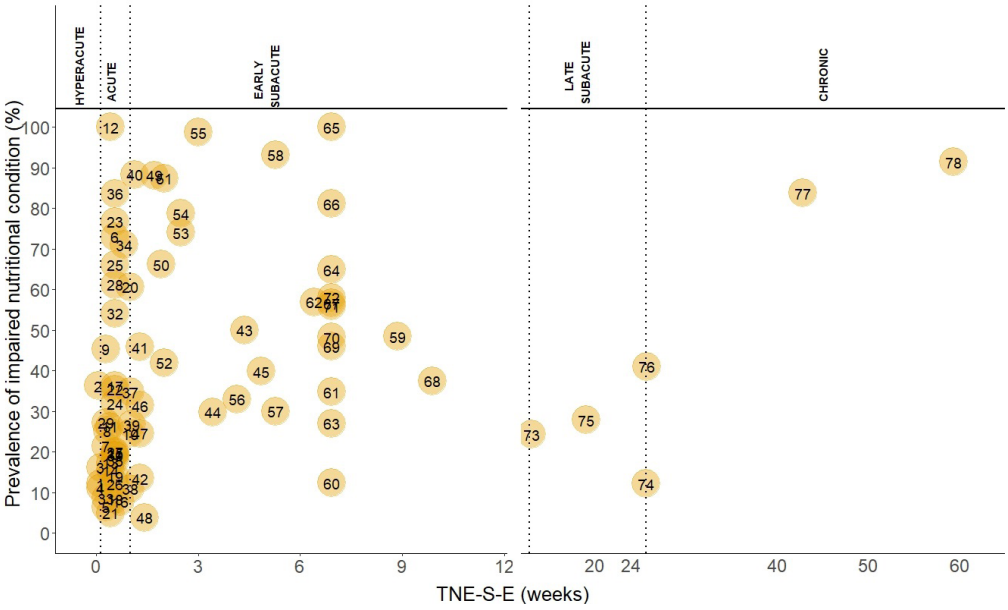
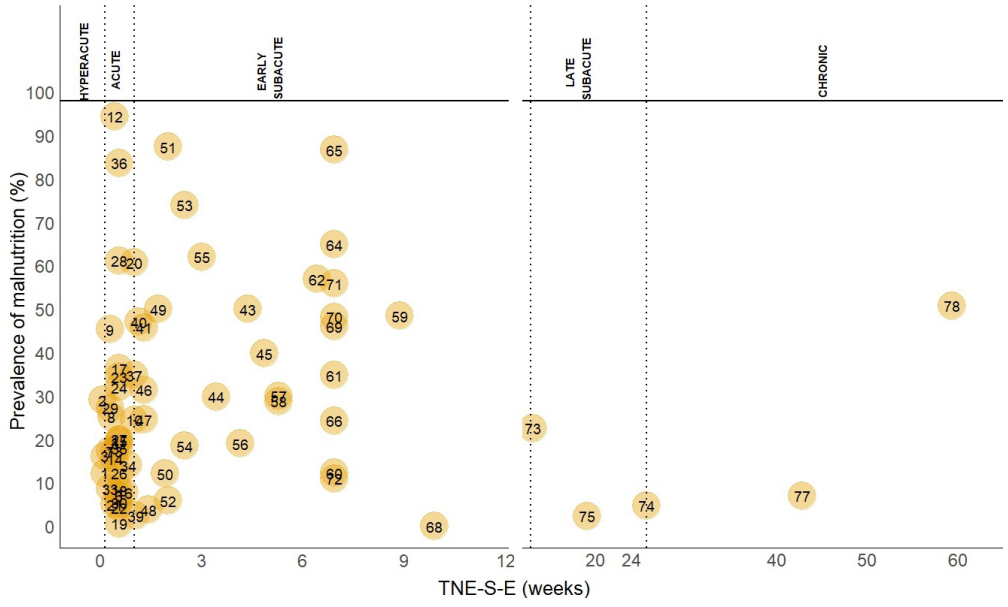


Figure 1. Flowchart. Used under the Creative Commons Attribution License terms, adapted from [22]



A



B

Figure 2. (A) Prevalence of INC in the hyperacute, acute, early subacute, late subacute, and chronic phase after stroke. **(B)** Prevalence of malnutrition in the hyperacute, acute, early subacute, late subacute, and chronic phase after stroke. TNE - S - E is shown in a different scale in the hyperacute, acute, and early subacute phase compared to the late subacute and chronic phase. Numbers in the plots indicate the references to the study groups: 1, Yoo [2]; 2, Gomes [3]; 3, Davis [32]; 4, Kokura [33]; 5, Nozoe [34]; 6, Nip [8]; 7, Sremanakova [35]; 8, Diendéré [36]; 9, Vajpayee [37]; 10, Gandolfo [38]; 11, Crary [39]; 12, NanZhu [40]; 13, Zheng I [41]; 14, Zheng

II [41]; 15, Shen [42]; 16, Food Trial (b) [43]; 17, Xiang [44]; 18, Kokura [45]; 19, Barrio [46]; 20, Otsuki [47]; 21, Robertson [48]; 22, López Espuela [49]; 23, Aliasghari [50]; 24, Crary [51]; 25, Çoban I [52]; 26, Çoban II [52]; 27, Schwarz [53]; 28, Porter [54]; 29, Pandian [55]; 30, Mosselman [56]; 31, Martineau [57]; 32, Ha [58]; 33, Food Trial (a) [59]; 34, Medin [60]; 35, Isono [61]; 36, Far [62]; 37, Brynningsen [63]; 38, Kokura [64]; 39, Kang [65]; 40, Drozdz [66]; 41, Cai [67]; 42, Naito [68]; 43, Hirano [69]; 44, Nishioka (b) [70]; 45, Nishioka (a) [71]; 46, Kampman I [72]; 47, Kampman II [72]; 48, Zhang [73]; 49, Shiraishi [74]; 50, Hsieh [75]; 51. Falsetti [76]; 52, Sato [77]; 53, Lim [78]; 54, James [79]; 55, Nishioka [80]; 56, Aadal [81]; 57, Aquilani [10]; 58, Nishioka [82]; 59, Garbagnati [83]; 60, Westergren [84]; 61, Poels [85]; 62, Hama [86]; 63, Maruyama [87]; 64, Shimizu [88]; 65, Carlsson [89]; 66, Tsai [90]; 67, Kaur [91]; 68, Jung [92]; 69, van Zwienen - Pot [93]; 70, Campillo [94]; 71, Da Silva [95]; 72, Lelli [96]; 73, Scrutinio [97]; 74, Perry [11]; 75, Vilardell [98]; 76, Westergren [99]; 77, Choi [100]; 78, Kim [101]

Prevalence of malnutrition

Of 68 study groups with data on malnutrition, three (4.4%) were conducted in the hyperacute, 29 (42.6%) in the acute, 31 (45.6%) in the early subacute, three (4.4%) in the late subacute, and two (2.9%) in the chronic phase after stroke. Overall, the prevalence of malnutrition across phases ranged from 0.0% to 94.4%. Prevalence of malnutrition ranged from 12.2% to 29.1% in the hyperacute phase, 0.6% to 94.4% in the acute phase, 0.0% to 87.4% in the early subacute phase, 2.7% to 24.3% in the late subacute phase, and 7.7% to 54.3% in the chronic phase (figure 2B). Combining the individual prevalence numbers per phase yielded a pooled prevalence of 19% (95% CI: 9 - 29) based on three study groups in the hyperacute phase, 26% (95% CI: 18 - 35) based on 29 study groups in the acute phase, 37% (95% CI: 28 - 45) based on 31 study groups in the early subacute phase, 11% (95% CI: 0 - 24) based on three study groups in the late subacute phase, and 30% (95% CI: 0 - 76) based on two study groups in the chronic phase (figure 4). In the phases where the pooled prevalence was based on a number of study groups ≤ 5, the results generated with the RE and FE meta - analysis models were overall similar, except for the chronic phase where the FE meta - analysis model showed a pooled prevalence of 10%.

Prevalence of INC at follow - up

Follow - up data on INC at different time points were available in 13 (16.7%) out of the 78 study groups. An increased prevalence of INC occurred in most of these 13 study groups and within three months after stroke (figure 5).

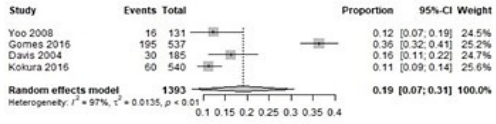
Methods used for the nutritional examination

Screening / assessment tools and anthropometrical / biochemical measurements were used for the nutritional examination in 56 (71.8%) and 19 (24.4%) out of the 78 study groups, respectively, and three (3.8%) reported various methods. Twenty (35.7%) of the 56 study groups used the MNA [102] or the MNA short - form (MNA - sf) [103], eight (14.3%) used the Geriatric Nutritional Risk Index (GNRI) [104], seven (12.5%) used the Subjective Global Assessment (SGA) [105], seven (12.5%) used

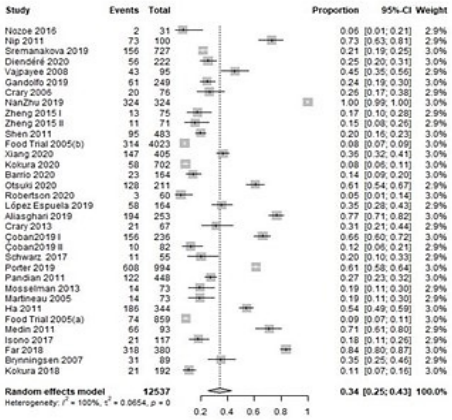
the Nutrition Risk Score (NRS) [106], four (7.1%) used the 'MUST' [107], three (5.4%) used the Patient - Generated Subjective Global Assessment (PG - SGA) [108], two (3.6%) used the Prognostic Nutritional Index (PNI) [109, 110], two (3.6%) used the ESPEN diagnostic criteria of malnutrition [111], one (1.8%) used the Malnutrition Screening Tool (MST) [112], one (1.8%) used the Controlling Nutritional Status score (CONUT) [113], and one (1.8%) used the GLIM criteria [114]. Out of the 19 study groups evaluating the nutritional status with anthropometrical / biochemical measurements, nine (47.4%) used a combination of anthropometrical and biochemical measurements, four (21.1%) used anthropometrical measurements, and six (31.6%) used biochemical measurements only. Anthropometrical measurements included BMI, bodyweight (loss), weight index based on actual bodyweight and reference weight [2, 115], arm muscle circumference, triceps skinfold, and the brachial perimeter. Biochemical measurements included albumin, pre - albumin, transferrin, haemoglobin, total cholesterol, lymphocyte count, ferritin, transthyretin, iron, and urea. In three study groups, a combination of screening / assessment tools and anthropometrical / biochemical measurements was used, and it included either a combination of bedside assessment, bodyweight, height, dietary history, blood test, or 'MUST' and albumin. Figure 6 shows the prevalence of INC examined with different methods and plotted against TNE - S - E.

Prevalence of dysphagia, stroke severity, adverse events, and continent - specific prevalence of INC

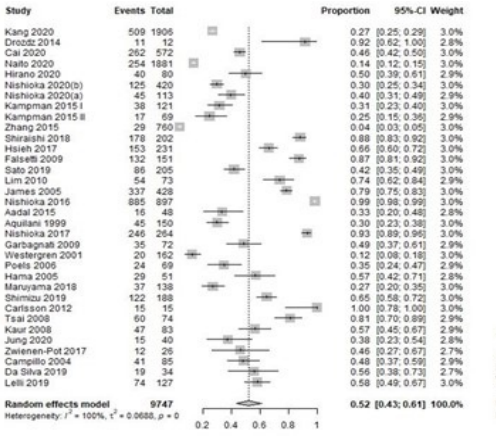
Thirty - two (41.0%) of the 78 study groups reported on the prevalence of dysphagia at baseline in the stroke patients in whom nutritional status was examined. After excluding study groups that used the presence or absence of dysphagia as an eligibility criterion, the prevalence of dysphagia ranged between 6.0% and 87.5%. A wide variety of screening and diagnostic methods were used to assess dysphagia. Out of the 78 study groups, 20 (25.6%) reported NIHSS scores at baseline in the stroke patients who were examined for the nutritional status. Mean / median NIHSS scores ranged from 1.5 to 14.2. Minor (NIHSS scores 1 - 4) and moderate (NIHSS scores 5 - 15) strokes were reported in three (15.0%) and 17 (85.0%) of the 20 study groups, respectively. Poor nutritional status was often linked to adverse events such as post - stroke complications and poor outcomes. Studies reported pressure ulcer development, impaired functional independence, a longer length of hospital stay, hospitalization costs, unfavourable recovery from stroke, and increased mortality. The continent - specific pooled prevalence of INC was 46% (95% CI: 36 - 56) based on 36 (46.2%) study groups in Asia, 37% (95% CI: 28 - 45) based on 29 (37.2%) study groups in Europe, 36% (95% CI: 16 - 56) based on seven (9.0%) study groups in Australia, 46% (95% CI: 13 - 79) based on three (3.8%) study groups in North - America, 74% (95% CI: 39 - 100) based on two (2.6%) study groups in South - America, 25% (95% CI: 30 - 31) based on one (1.3%) study group in Africa, and 42% (95% CI: 36 - 48) based on the total number of 78 study groups (figure S2). In the continents where the pooled prevalence was based on a number of study groups ≤ 5, the results generated with the RE and FE meta - analysis models were overall similar.



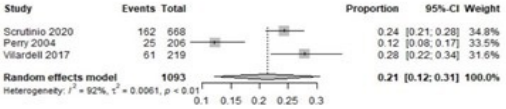
A. Impaired Nutritional Condition – Hyperacute phase



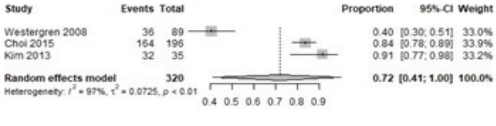
B. Impaired Nutritional Condition – Acute phase



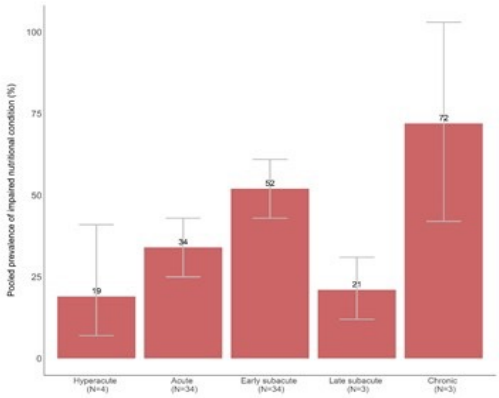
C. Impaired Nutritional Condition – Early subacute phase



D. Impaired Nutritional Condition – Late subacute phase

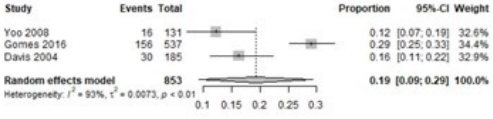


E. Impaired Nutritional Condition – Chronic phase

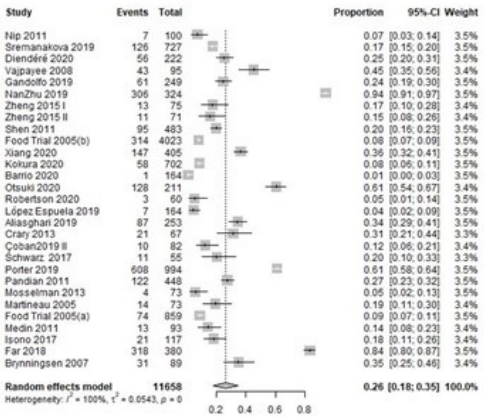


F. Pooled prevalence of INC per phase

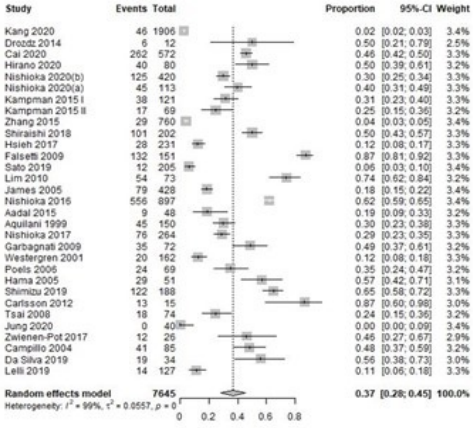
Figure 3. Pooled prevalence of INC in the **(A)** hyperacute phase, **(B)** acute phase, **(C)** early subacute phase, **(D)** late subacute phase, and **(E)** chronic phase. **(F)** Pooled prevalence of INC per phase.



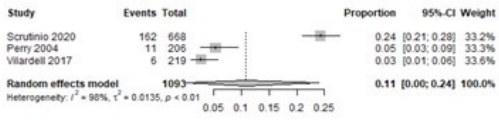
A. Malnutrition – Hyperacute phase



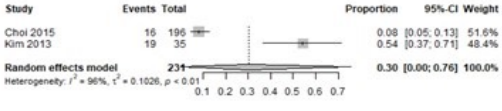
B. Malnutrition – Acute phase



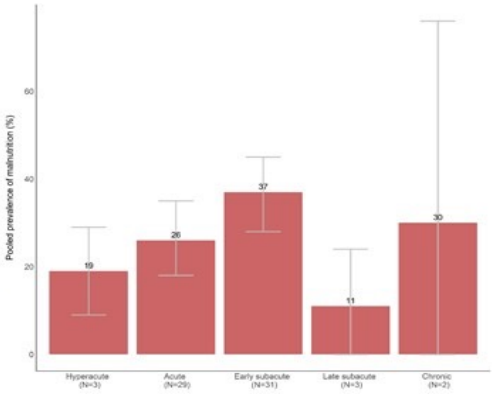
C. Malnutrition – Early subacute phase



D. Malnutrition – Late subacute phase



E. Malnutrition – Chronic phase



F. Pooled prevalence of malnutrition per phase

Figure 4. Pooled prevalence of malnutrition in the **(A)** hyperacute phase, **(B)** acute phase, **(C)** early subacute phase, **(D)** late subacute phase, and **(E)** chronic phase. **(F)** Pooled prevalence of malnutrition per phase.

Risk of bias

A risk of selection bias was found in 38 out of the 78 study groups (48.7%) as the study population was considered not representative for the stroke population in the assigned phase after stroke. A risk of performance bias was found in 53 out of 78 (67.9%) study groups based on methods used for the confirmation of stroke (performance bias I). In these study groups this information was unknown, not reported, or the diagnosis was confirmed differently, e.g., screening by a board certificated neurologists or extraction of data from the patients' medical dossiers. A risk of performance bias based on validity of the screening / assessment tools for nutritional examination (performance bias II) was found in 10 out of the 56 (17.9%) study groups that used screening / assessment tools for the examination of nutritional status. These study groups used e.g., the GNRI or PNI, that have not been validated in specific patient populations. A risk of detection bias was found in two out of 78 (2.6%) study groups as these did not clearly define the methods used to examine the nutritional status (detection bias I). A risk of detection bias was also found in 39 out of 78 (50.0%) study groups as there was no clear indication of consistent performance of methods (detection bias II). In these study groups, it was unclear who performed the evaluation or who collected the data from medical files or a wide variety of assessors was involved. A risk of reporting bias was found in two of the 78 (2.6%) study groups as these study groups included about 99% of confirmed stroke and remaining subjects were diagnosed with "brain tumour" or as "non - stroke" (reporting bias I). In 16 out of 53 (30.2%) study groups that used screening / assessment tools other than GLIM or ESPEN criteria for the examination of nutritional status, reported incomplete prevalence data on INC according to the criteria (supplemental material, table S2) used in this systematic review (reporting bias II). In these cases, data were missing in one or more categories. A summary of the risk of bias is provided in figure 7. The risk of bias and relative risk for each individual study group is provided in the supplemental material, table S4.

Discussion

This systematic review shows the prevalence of INC and malnutrition ranging from 3.8 to 100.0% and from 0.0 to 94.4%, respectively. A high prevalence of INC was reported within three months after stroke. The pooled prevalence of INC was 34% in the acute and 52% in the early subacute phase, respectively. For malnutrition, these numbers were 26% and 37%, respectively. A deterioration of nutritional condition within the first three months was seen from the follow - up data. A poor nutritional condition occurring within three months after stroke parallels the time period associated with the peak of recovery [17, 18]. As poor nutritional status negatively impacts the recovery processes, it is advised to intervene within this time window and to address nutrition as an integral component of rehabilitation therapy.

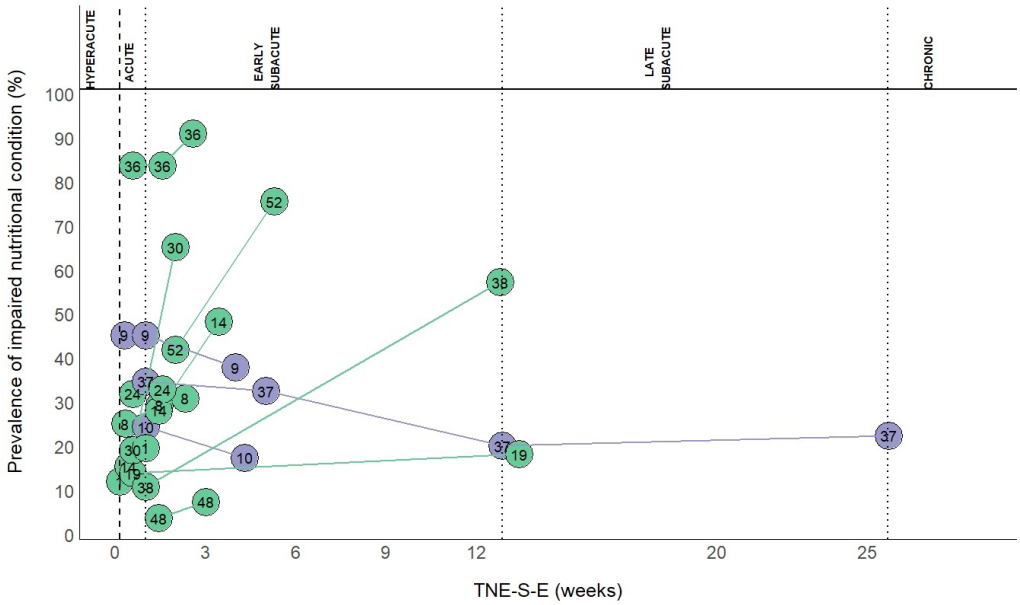


Figure 5. Prevalence of INC at follow - up. Numbers in the plot indicate the references to the study groups: 1, Yoo [2]; 8, Diendéré [36]; 9, Vajpayee [37]; 10, Gandolfo [38]; 14, Zheng II [41]; 19, Barrio [46]; 24, Crary [51]; 30, Mosselman [56]; 36, Far [62]; 37, Brynningsen [63]; 38, Kokura [64]; 48, Zhang [73]; 52, Sato [77]

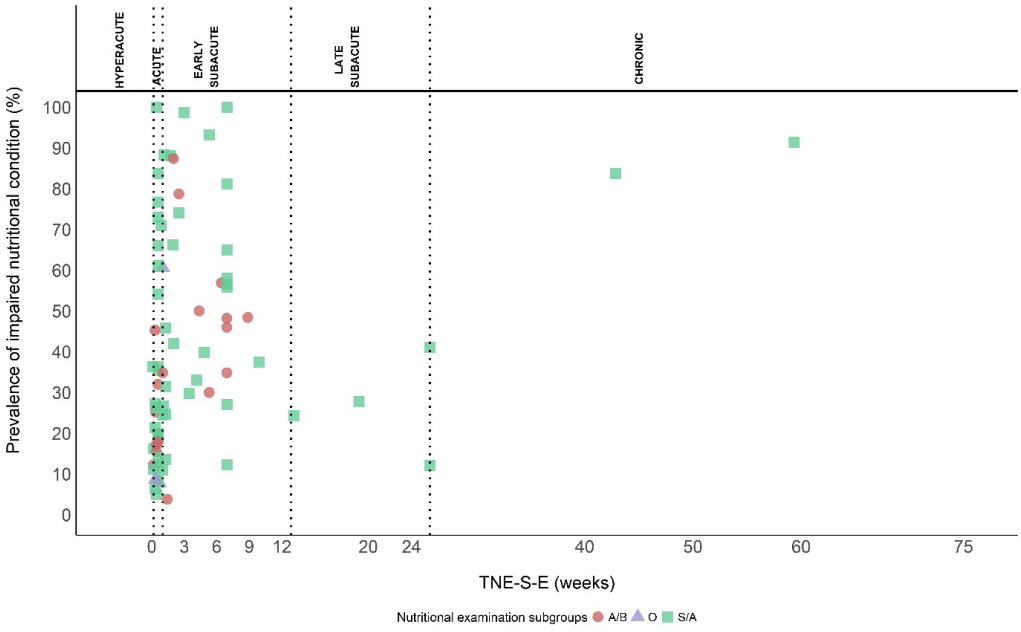


Figure 6. Methods used to examine the prevalence of INC. Screening / assessment tools (S / A) (squares), anthropometrical / biochemical measurements (A / B) (circles), and other (O) (triangles) (combination of S / A tools and A / B measurements).

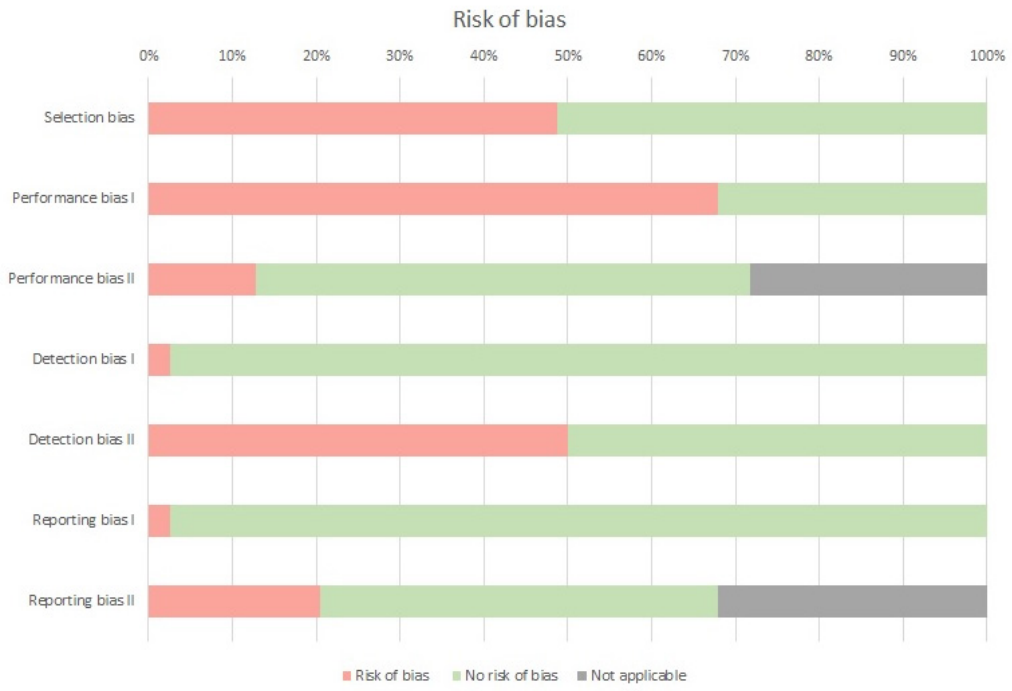


Figure 7. Risk of bias summary

The importance of nutrition in stroke recovery is supported by several studies that demonstrate an association between poor nutritional status and worse stroke outcomes such as disability, complications, extended length of hospital stay, mortality, and costs for hospitalization [2, 3]. Poor nutritional status, inactivity, and immobilization, can lead to muscle loss and sarcopenia and can negatively impact the recovery after stroke [116]. A recent meta - analysis by Su et al. [117] reports that sarcopenia is common after stroke. Furthermore, several studies show that improving the nutritional status of stroke patients using specialized nutritional interventions can significantly improve clinical outcomes. In a randomized controlled trial (RCT) with 102 undernourished stroke patients, intensive nutritional supplementation, including oral nutritional supplements (ONS), improved motor function ($p < 0.002$) [118]. In a rehabilitation center the total Functional Independence Measure (FIM) gain ($p = 0.036$) and efficiency ($p = 0.020$) were improved in cerebrovascular patients (mainly due to stroke) with poor nutritional status and in whom an improvement of the GNRI and energy intake was achieved [119]. A different RCT showed that supplementation of subacute ischemic stroke patients with high protein ONS enhanced the cognitive function evaluated with the Mini - Mental State Examination ($p = 0.01$) [120]. Oral energy and protein - rich (enteral) feeding of acute stroke patients at nutritional risk increased quality of life ($p = 0.009$) and handgrip strength ($p = 0.002$) [121]. A positive effect on energy ($p < 0.0001$) and protein ($p < 0.001$) intake and on albumin ($p = 0.025$) and iron ($p = 0.030$) levels

were observed in acute ischemic stroke patients using ONS providing 600 Kcal and 20 g protein per day in addition to the hospital diet compared to stroke patients randomized to receive only the hospital diet [122]. A recent study investigated the effect of tailored dietary prescription in 454 stroke patients in rehabilitation and reported an inverse correlation between dysphagia and frequency of dietary adjustments in prescriptions ($p = 0.032$) [123]. In addition, more frequent dietary adjustments positively affected FIM motor scores ($p = 0.045$), muscle mass change ($p = 0.028$), and length of hospitalization ($p = 0.019$) [123]. The Feed Or Ordinary Diet (FOOD) trial randomized acute non - dysphagic stroke patients to a control group that received a regular hospital diet or a treatment group that received a regular hospital diet with additional ONS that did not measurably affect mortality or outcome [43]. However, 77.0% of the population in the FOOD Trial was well - nourished at baseline and this may have influenced the effectiveness of ONS. Finally, the importance of examination of nutritional status and dysphagia and an adequate nutritional status in stroke patients is reflected in several (international) stroke guidelines. These guidelines recommend dysphagia screening prior to first oral intake in all stroke patients, screening for malnutrition and the provision of nutritional support, including the use of ONS, in stroke patients with an impaired nutritional status and / or dysphagia [1, 19, 20, 124-127]. These guidelines [1, 19, 126, 127] do not recommend routine administration of ONS in well - nourished stroke patients, in line with the results of the FOOD trial. In these guidelines, also recommendations are given on the use of enteral tube feeding in specific conditions and / or on the route of administration (nasogastric or PEG) [19, 20, 127].

The present systematic review shows variation in the prevalence of INC. This may be attributed to the various methods used to screen or assess the nutritional status. A gold standard method and a recognized definition of malnutrition are lacking [128]. Only recently, the GLIM reached a global consensus on the diagnostic criteria of malnutrition in adults. These GLIM criteria include five key health phenotypic and etiologic health criteria such as involuntary weight loss, BMI, decreased muscle mass, reduced nutritional intake or absorption, and disease - induced burden or inflammation [114]. Foley et al. [21] suggested that a great part of the variation in the estimates of malnutrition in stroke may be attributed to differences in the nutritional examinations. In the present review, 71.8% of the study groups used screening / assessment tools and 24.4% of the study groups used anthropometrical / biochemical measurements. The results showed a higher prevalence of INC when the screening / assessment tools were used, indicating that the prevalence may vary in relation to the methods used for the examination. Additionally, in some cases, the original tools were modified and the adapted versions were used for the examination. The use of one single method might result in significant prevalence variations as well. Geriatric patients showed a prevalence of malnutrition and risk of malnutrition between 3.0% and 58.0% when the nutritional examination was performed with MNA solely [129]. Considerable variation of the prevalence of malnutrition was also observed within patient groups. In cancer patients, the type of cancer was an important determinant [130, 131]. In addition,

the setting in which patients are residing could also play a role. Cereda et al. [132] reported on the nutritional status in older people examined with MNA in various settings. Prevalence rates of malnutrition ranged between 3.1% in the community and 29.4% in rehabilitation / post - acute care. Studies in the present review have also been performed in a variety of healthcare settings. The time of nutritional examination has been suggested to be a reason for the variation of prevalence in stroke patients as well [21]. Although in this systematic review, the timing was taken into account by studying each phase after a stroke, a considerable variation of the prevalence remained. The Stroke Recovery and Rehabilitation Roundtable Taskforce [17] encourages research in the field to provide clear guidance on timing. TNE - S - E was only available in 17.9% of the study groups; the allocation of the remaining studies within a pre - defined phase provides a general indication of the time of nutritional examination after a stroke. The studies included in the analysis were not all explicitly performed to examine the nutritional status in stroke and this might have contributed to the missing data on timing.

When interpreting the data on the prevalence of INC in the hyperacute phase, it is crucial to consider the limited time passed since stroke onset. Data on nutritional status in this phase most likely indicate the state of nutrition before the stroke event rather than an actual stroke - related change in nutritional status. However, some screening / assessment tools determine nutritional risk by allocating a score to reduced or interrupted nutritional intake which would reflect that moment in time. The small number of studies reporting on the nutritional status in the hyperacute phase is likely a result of the significant focus on specific treatments and patient needs within 24 hours after stroke. Lack of data in the late subacute and chronic phase might reflect a reduced number of studies performed at later stages or a lack of attention to the nutritional status over time. Considering the high prevalence of INC occurring within three months after stroke, continuous monitoring of the nutritional status during and beyond this stage of rehabilitation is desirable. The present review shows the prevalence of dysphagia up to 87.5% and Foley et al. [133] reports that dysphagia increases the risk of malnutrition 2.4 fold ($p < 0.008$). This systematic review highlights the need for future research to increase the knowledge on nutritional status after stroke.

To our knowledge, this systematic review has been performed in the most appropriate way to provide a transparent and comprehensive overview of the existing evidence. Nevertheless, this study has some limitations. The screening of titles and abstracts and data extraction of the exploratory parameters was performed by one reviewer, and data on prevalence and timing were harmonized with specific self - developed criteria. One other limitation is that screening and assessment tools were both included, and a differentiation [134] was not performed. Despite this limitation, all eligible literature on nutritional status in stroke was considered valuable and included in the analysis of the review. The risk of bias was evaluated using a self - developed checklist. This checklist included critical questions regarding selection, performance, detection, and reporting bias and provided a comprehensive risk of bias summary. Due to the high heterogeneity

of the data one may not conclude on the exact prevalence of INC; however these results shed light on a problem that is often underestimated.

Summary

In summary, results of the present review indicate that INC and malnutrition occur across the continuum of stroke care, from the hyperacute to the chronic phase. The large prevalence range of INC and malnutrition in the different phases underlines the importance of continuously reviewing the nutritional status in stroke patients to identify and take action to prevent nutritional deterioration. The large prevalence range also indicates heterogeneity in prevalence data amongst different studies. Malnutrition after stroke has been shown to negatively affect clinical outcomes, mortality, and overall healthcare expenditure. This suggests that continuous monitoring of the nutritional status and improved nutritional management within the multidisciplinary context of rehabilitation is warranted, to ensure malnutrition does not go unnoticed, untreated, and impede rehabilitation and recovery after stroke.

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Supplementary material

Table S1. Search strategy

Conceptual String	***Ti,ab(stroke) AND Ti,ab(malnutrition)***
String	Ti,Ab((((cerebrovascular OR cerebral OR brain) n/2 (trauma OR traumas OR injur* OR occlusion OR occlusions OR haemorrhage OR haemorrhages OR hemorrhage OR hemorrhages OR accident OR accidents OR lesion OR lesions OR vasculopathy OR attack OR attacks OR isch*emia OR infarct* OR insult OR insults OR reperfusion OR CVA)) OR (stroke OR strokes))) AND Ti,ab(malnutrition OR malnourish* OR (nutrition* p/0 (status OR intake)) OR undernourish* OR underweight OR (low p/0 body p/0 (mass OR weight)) OR underfed OR underfeeding OR undernutrition OR (nutrition* p/0 (depriv* OR deficien*)))
Databases	CAB ABSTRACTS, Embase, MEDLINE
Publication date	Between 01 – 01 - 1999 and 26 – 08 - 2020
Language	English
Document type exclusions	(Conference Abstract AND Case Reports AND Conference Paper AND Conference paper AND Book chapter AND Short Survey AND Conference Review AND Retracted Publication AND Letter AND Editorial AND Note AND Book AND Chapter AND Comment AND Published Erratum AND Bulletin article AND Clinical Trial Protocol AND Erratum AND Tombstone AND Address AND Technical Report)
# of results	1244

Table S2. Criteria used to estimate the prevalence of INC and malnutrition when examined with screening / assessment tools.

		INC	Malnutrition
Malnourished and at risk of malnutrition*			
MNA	no malnutrition (24-30)		
	at risk of malnutrition (17-23.5)	✓	
	malnourished (<17)	✓	✓
MNA-sf	no malnutrition (12-14)		
	at risk of malnutrition (8-11)	✓	
	malnourished (0-7)	✓	✓
At risk of malnutrition**			
MUST	low risk of malnutrition (0)		
	medium risk of malnutrition (1)	✓	
	high risk of malnutrition (2)	✓	✓
GNRI	no risk of malnutrition (>98)		
	low risk of malnutrition (92-98)	✓	
	moderate risk of malnutrition (82-92)	✓	
	severe risk of malnutrition (<82)	✓	✓
NRS	no risk of malnutrition (0)		
	mild risk of malnutrition (1)	✓	
	moderate risk of malnutrition (2)	✓	
	severe risk of malnutrition (≥3)	✓	✓
MST	no risk of malnutrition (0-1)		
	at risk of malnutrition (≥2)	✓	✓
Severity of malnutrition***			
SGA	no malnutrition (A)		
	moderate/suspected malnutrition (B)	✓	✓
	severe malnutrition (C)	✓	✓
PG-SGA	no malnutrition (A) (0-1)		
	moderate/suspected malnutrition (B)	✓	✓
	severe malnutrition (C) (≥9)	✓	✓
CONUT	no malnutrition (0-1)		
	mild malnutrition (2-4)	✓	✓
	moderate/severe malnutrition (≥5)	✓	✓
PNI	no malnutrition (≥ 50)		
	mild malnutrition (< 50)	✓	✓
	moderate/severe malnutrition (< 45)	✓	✓
	serious malnutrition (< 40)	✓	✓
Malnutrition based on multiple criteria****			
ESPEN criteria	Validated screening tool, BMI, weight loss, fat-free mass index	malnutrition	malnutrition
GLIM criteria	Validated screening tool, phenotypic and etiologic criteria	malnutrition	malnutrition

Table S2. Legend

* The prevalence of INC was defined as the combination of the categories "malnourished" and "at risk of malnutrition" and the prevalence of malnutrition was defined by the category "malnutrition".

** The prevalence of INC was defined as the combination of the categories "medium risk" and "high risk" and the prevalence of malnutrition was defined by the most severe category ("high risk"). The most severe category was used to estimate malnutrition based on the principle that patients who are at high nutritional risk need to be treated, as indicated in the management guidelines of the "MUST".

*** The prevalence of INC and malnutrition were both defined by all the categories of malnutrition. The reason for not differentiating between INC and malnutrition is that in some cases a specific description of the nutritional status was not provided as shown by one of the pre - defined categories of the SGA or PG - SGA that combines both "moderate" and "suspected" malnutrition.

**** The use of pre - defined outcome categories was not applied. Malnutrition was defined based on multiple criteria, and it was not possible to differentiate INC and malnutrition.

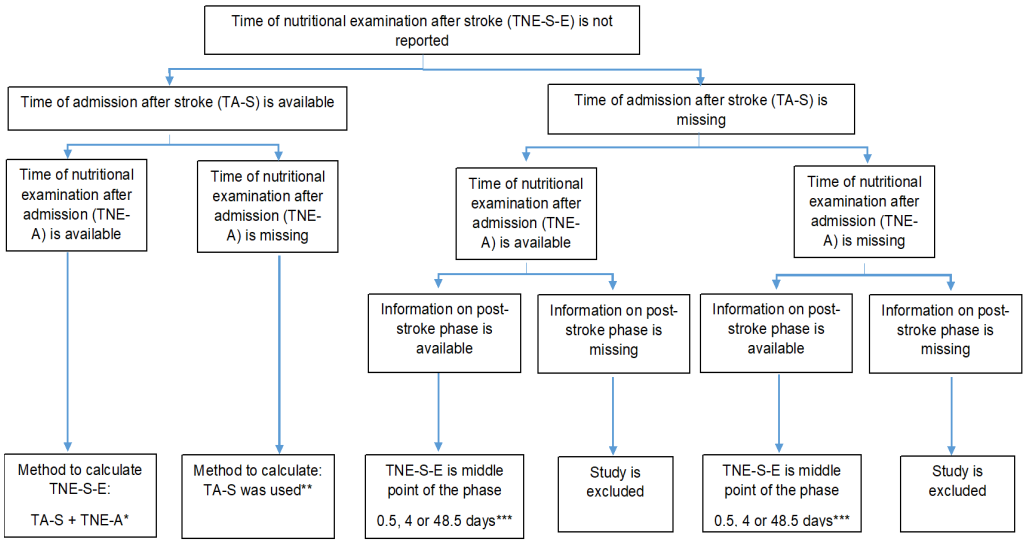


Figure S1. Criteria used to estimate TNE - S - E

Table S1. Legend

* TNE – S - E was estimated using TA - S and TNE - A. For example, in a study where stroke patients were admitted within three days after stroke (TA - S) and nutritional examination was performed within seven days after admission (TNE - A), the TNE – S - E was ten days. TNE - A does not indicate timing after stroke; therefore, it did not affect the estimations except when used combined with TA - S.

** Estimation of TNE – S - E was not needed if TA - S was available and TNE - A was missing. TA - S was considered equal to TNE – S - E since it was assumed that the nutritional

examination was performed soon after the admission.

*** TA - S was missing, but information on the phase was available. In this case, the middle point of the phase was used as guidance: for the hyperacute, acute, and early subacute phase, TNE – S - E was assumed at 0.5, 4, and 48.5 days, respectively. If the study was performed in a rehabilitation setting, it was assumed that the patients were in the early subacute and TNE – S - E was assumed at 48.5 days. If the study was performed with chronic stroke patients, TNE – S - E was not estimated to prevent the inclusion of patients at more than two years after stroke.

In two studies, the criteria used to estimate the time of nutritional examination after stroke were not applicable because the estimations deviated compared to the data reported in the original studies. In both studies only the TNE - A and the indication of the phase were available. According to the criteria, the time of nutritional examination after stroke was 4 [47] and 48 [66] days based on the acute and early subacute phase, respectively. Otsuki et al. [47] reports that the nutritional examination was performed at the 7th day of hospital admission. Similarly, Drodz et al. [66] indicates that the examination was performed on the 8th day of hospital admission. This inconsistency did not affect the allocation of the studies within a specific phase, and indication reported by the authors was used.

Table S3. General characteristics of the study groups

Reference	Corresponding number in Fig 2 and Fig 5	Country	Study Design	Setting	Age (years)[1]	N stroke patients who received the nutritional examination	%INC
Yoo 2008 [2]	1	Korea	Observational	Hospital	64.8 ± 10.3	131	12.20
Gomes 2016 [3]	2	UK	Observational	Hyperacute stroke units in hospital	74.7	537	36.30
Davis 2004 [32]	3	Australia	Observational	Hospital	<75 (n=93), ≥75 (n=92)	185	16.20
Kokura 2016 [33]	4	Japan	Observational	Acute care hospitals: geriatric stroke patients	≥ 75	540	11.10
Nozoe 2016 [34]	5	Japan	Observational	Hospital	70.3 ± 12.8	31	6.50
Nip 2011 [8]	6	Australia	Observational	Hospital	69 ± 15	100	73.00
Sremanakova 2019 [35]	7	UK	Observational	Stroke center	≥ 18 (n=1101)	727	21.40
Diendéré 2020 [36]	8	Burkina Faso	Observational	Hospitals	60.5 ± 14.0	222	25.20
Vajpayee 2008 [37]	9	India	Observational	Hospital	≥ 28	95	45.30
Gandolfo 2019 [38]	10	Italy	Observational	Stroke unit	72.6 ± 15.5	249	24.50
Crary 2006 [39]	11	US	Observational	Stroke unit in tertiary care hospital	66.2 ± 11.8	76	26.30
NanZhu 2019 [40]	12	China	Observational	Stroke unit	77.94 ± 5.55	324	100.00
Zheng 2015 I: (intervention) [41]	13	China	Experimental	Stroke unit	71.4 ± 9.3	75	17.30
Zheng 2015 II: (control) [41]	14	China	Experimental	Ward	71.8 ± 10.1	71	15.50
Shen 2011 [42]	15	Taiwan	Observational	Hospital	70.7 ± 10.3	483	19.70
Food Trial 2005(b) [43]	16	UK	Experimental	Hospital	71±13 (n=2007) and 71±12 (n=2016)	4023	7.80
Xiang 2020 [44]	17	China	Observational	Hospital	66 ± 16	405	36.30
Kokura 2020 [45]	18	Japan	Observational	Acute care hospitals	76.3 ± 12	702	8.30

Table continues

Barrio 2020 [46]	19	Spain	Observational	Hospital neurology department	≥ 34 (n=166)	164	14.00
Otsuki 2020 [47]	20	Japan	Experimental	Hospital	≥ 65	211	60.70
Robertson 2020 [48]	21	Australia	Observational	Acute stroke unit	76±12.8 (n - 30) and 76.7±12.1 (n=30)	60	5.00
López Espuela 2019 [49]	22	Spain	Observational	Hospital neurology unit	77.7 ± 7.0	164	35.40
Aliasghari 2019 [50]	23	Iran	Observational	Hospital neurology units	74.42 ± 7.8	253	76.70
Crary 2013 [51]	24	US	Observational	Joint commission - certified primary stroke center in a tertiary - care academic hospital.	65.7	67	32.00
Çoban 2019 I (age group ≥ 65) [52]	25	Turkey	Observational	Hospital	≥ 65 (n=318)	236	66.10
Çoban 2019 II (age group <65) [52]	26	Turkey	Observational	Hospital	< 65 (n=318)	82	12.20
Schwarz 2017 [53]	27	Australia	Observational	Hospital	≥ 18 (n=83)	55	20.00
Porter 2019 [54]	28	Australia	Observational	Hospital: acute ward and rehabilitation	≥ 18	994	61.20
Pandian 2011 [55]	29	India	Observational	Hospital	58.1 ± 13.7	448	27.20
Mosselman 2013 [56]	30	The Netherlands	Observational	Stroke unit	65 ± 16.7	73	19.20
Martineau 2005 [57]	31	Australia	Observational	Acute stroke unit	72 ± 12.9	73	19.20
Ha 2011 [58]	32	Norway	Experimental	Hospital acute care ward	≥ 65	344	54.10
Food Trial 2005(a) [59]	33	UK	Experimental	Hospital	Adult population (n=1180)	859	8.60
Medin 2011 [60]	34	Sweden	Observational	Acute stroke unit	Adult population (n=104)	93	71.00
Isono 2017 [61]	35	Japan	Observational	Hospital	74.32 ± 0.93	117	17.90

Table continues

Reference	Corresponding number in Fig 2 and Fig 5	Country	Study Design	Setting	Age (years)[1]	N stroke patients who received the nutritional examination	%INC
Far 2018 [62]	36	Iran	Observational	Neurology department	65 ± 10 well -nourished group and 63 ± 12.01 malnourished group	380	83.70
Brynningsen 2007 [63]	37	Denmark	Observational	Hospital acute stroke unit and geriatric stroke rehabilitation unit in hospital	77.9±6.9	89	34.80
Kokura 2018 [64]	38	Japan	Observational	Hospital acute care : geriatric stroke inpatients	79.6 ± 7.6	192	10.90
Kang 2020 [65]	39	Korea	Observational	Hospital	67	1906	26.70
Drozdz 2014 [66]	40	Brasil	Observational	Hospital	≥ 35 (n=18)	12	88.30
Cai 2020 [67]	41	China	Observational	Hospital	67.8	572	45.80
Naito 2020 [68]	42	Japan	Observational	Hospital	Adult population (n=1915)	1881	13.50
Hirano 2020 [69]	43	Japan	Observational	Rehabilitation hospital	62.7 ± 11.6	80	50.00
Nishioka 2020(b) [70]	44	Japan	Observational	Rehabilitation wards in rehabilitation hospital	78.1 ± 7.9	420	29.80
Nishioka 2020(a) [71]	45	Japan	Observational	Rehabilitation wards of rehabilitation hospital	≥ 66	113	39.80
Kampman 2015 I [72]	46	Norway	Experimental	Stroke unit	≥ 20 (n=199)	121	31.40
Kampman 2015 II [72]	47	Norway	Experimental	Stroke unit	≥ 22 (n=86)	69	24.60
Zhang 2015 [73]	48	China	Observational	Hospital	≥ 18	760	3.80

Table continues

Shiraishi 2018 [74]	49	Japan	Observational	Rehabilitation ward in rehabilitation hospital	72.2 ± 12.5	202	88.10
Hsieh 2017 [75]	50	Taiwan	Observational	Hospital	64.3 ± 11.1	231	66.20
Falsetti 2009 [76]	51	Italy	Observational	Neuro rehabilitation unit	79.4 ± 6.2	151	87.40
Sato 2019 [77]	52	Japan	Observational	Stroke care unit and neurology ward in hospital	77 ± 7	205	42.00
Lim 2010 [78]	53	Korea	Observational	University medical center	61.2 ± 12.5 well -nourished, 66.5 ± 11.1 moderately malnourished, 64.7 ± 11.2 severely malnourished	73	74.00
James 2005 [79]	54	US	Observational	Rehabilitation center	≥ 18 (n=919)	428	78.70
Nishioka 2016 [80]	55	Japan	Observational	Rehabilitation ward	71.6 ± 13.3	897	98.70
Aadal 2015 [81]	56	Denmark	Observational	Rehabilitation hospital	≥ 27	48	33.00
Aquilani 1999 [10]	57	Italy	Observational	Rehabilitation center	60 ± 11	150	30.00
Nishioka 2017 [82]	58	Japan	Observational	Rehabilitation ward	78.5 ± 7.5	264	93.20
Garbagnati 2009 [83]	59	Italy	Experimental	Rehabilitation hospital	65.3 ± 12.9	72	48.40
Westergren 2001 [84]	60	Sweden	Observational	Rehabilitation hospital	78.6	162	12.30
Poels 2006 [85]	61	The Netherlands	Observational	Rehabilitation center	56.7 ±11.0	69	34.80
Hama 2005 [86]	62	Japan	Observational	Rehabilitation hospital	66.7 ± 10.2	51	56.90
Maruyama 2018 [87]	63	Japan	Observational	Rehabilitation hospital	63.9 ± 11.0	138	27.00
Shimizu 2019 [88]	64	Japan	Observational	Rehabilitation wards of rehabilitation hospital	78.9 ± 7.7	188	64.90
Carlsson 2012 [89]	65	Sweden	Observational	Stroke unit at hospital, nursing homes and rehabilitation units and a home health service team	83 ± 6.9	15	100.00

Table continues

Reference	Corresponding number in Fig 2 and Fig 5	Country	Study Design	Setting	Age (years)[1]	N stroke patients who received the nutritional examination	%INC
Tsai 2008 [90]	66	Taiwan	Observational	Long term care homes / at home	≥ 40	74	81.10
Kaur 2008 [91]	67	Australia	Observational	Hospital	73	83	56.60
Jung 2020 [92]	68	Korea	Observational	Department of rehabilitation medicine at tertiary hospital	66.8 ± 15.3	40	37.50
Van Zwienen - Pot 2017 [93]	69	The Netherlands	Observational	Nursing home rehabilitation wards	≥ 65 y	26	46.00
Campillo 2004 [94]	70	France	Observational	Rehabilitation care hospital: neuro - disease department	71.0 ± 11.7	85	48.20
Da Silva 2019 [95]	71	Brazil	Observational	Hospital	Adult population	34	55.90
Lelli 2019 [96]	72	Italy and Spain	Observational	Hospital geriatric rehabilitation unit	≥ 65	127	58.00
Scrutinio 2020 [97]	73	Italy	Observational	Inpatient rehabilitation facility	≥ 67	668	24.30
Perry 2004 [11]	74	UK	Observational	Home	71 ± 12.9	206	12.10
Vilardell 2017 [98]	75	Spain	Experimental	Hospital	Adult population (n=225)	219	27.80
Westergren 2008 [99]	76	Sweden	Observational	Home, special accommodation, other settings	77.2 ± 6.6	89	41.00
Choi 2015 [100]	77	Korea	Observational	Medical center	Adult population (n=203)	196	83.70
Kim 2013 [101]	78	Korea	Observational	Hospital rehabilitation department	70.6 ± 7.2	35	91.40

[1] age refers to the number of patients who received the nutritional examination unless otherwise indicated

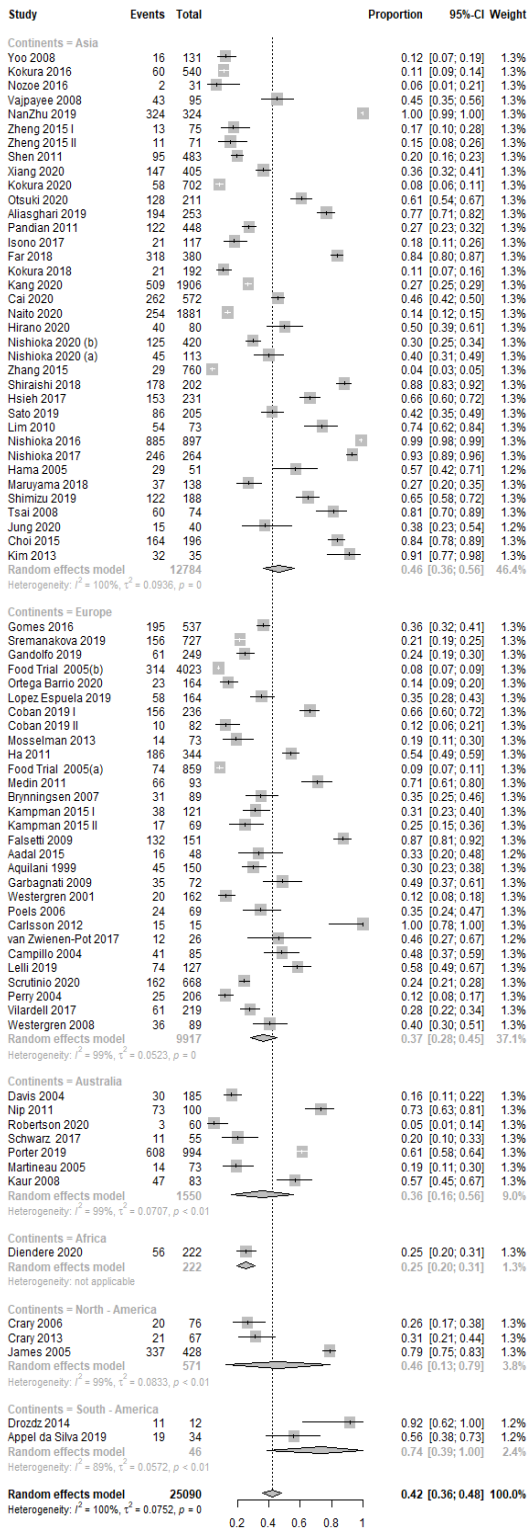
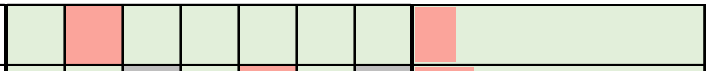
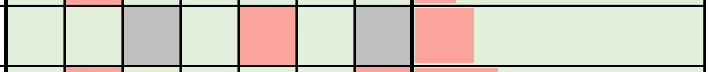
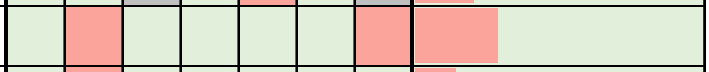
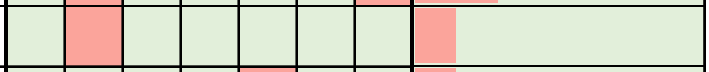
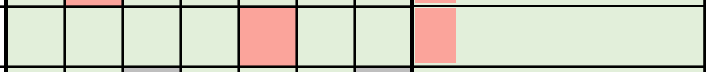
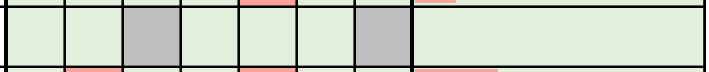
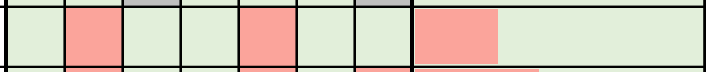
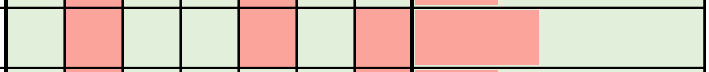
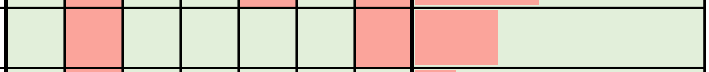
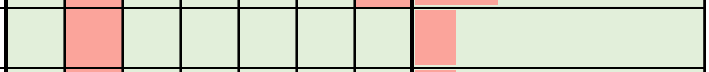
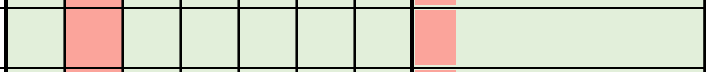
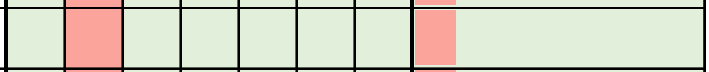
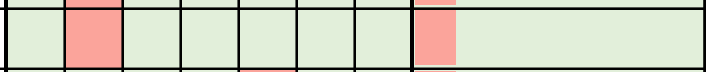
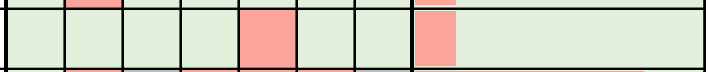
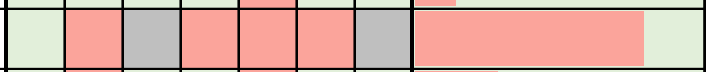
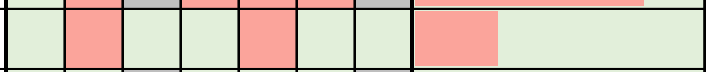
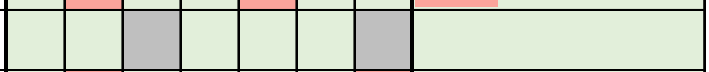
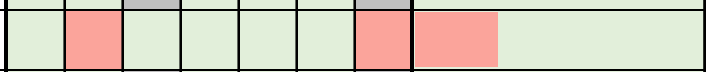


Figure S2. Pooled prevalence of INC per continent

Table S4. Risk of bias per study group

Reference	Corresponding number in Fig 2 and Fig 5	Selection	Performance I	Perfomance II	Detection I	Detection II	Reporting I	Reporting II	Relative risk (%)
Yoo 2008 [2]	1								
Gomes 2016 [3]	2								
Davis 2004 [32]	3								
Kokura 2016 [33]	4								
Nozoe 2016 [34]	5								
Nip 2011 [8]	6								
Sremanakova 2019 [35]	7								
Diendéré 2020 [36]	8								
Vajpayee 2008 [37]	9								
Gandolfo 2019 [38]	10								
Crary 2006 [39]	11								
NanZhu 2019 [40]	12								
Zheng 2015 I: (intervention) [41]	13								
Zheng 2015 II: (control) [41]	14								
Shen 2011 [42]	15								
Food Trial 2005(b) [43]	16								
Xiang 2020 [44]	17								
Kokura 2020 [45]	18								

Table continues

Barrio 2020 [46]	19	
Otsuki 2020 [47]	20	
Robertson 2020 [48]	21	
López Espuela 2019 [49]	22	
Aliasghari 2019 [50]	23	
Crary 2013 [51]	24	
Çoban 2019 I (age group ≥ 65) [52]	25	
Çoban 2019 II (age group <65) [52]	26	
Schwarz 2017 [53]	27	
Porter 2019 [54]	28	
Pandian 2011 [55]	29	
Mosselman 2013 [56]	30	
Martineau 2005 [57]	31	
Ha 2011 [58]	32	
Food Trial 2005(a) [59]	33	
Medin 2011 [60]	34	
Isono 2017 [61]	35	
Far 2018 [62]	36	
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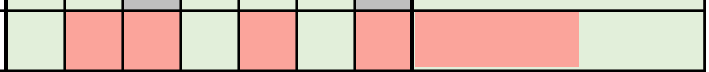
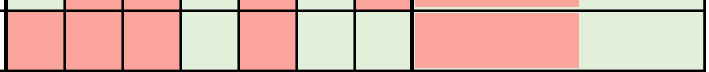
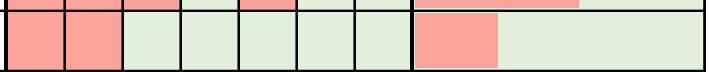
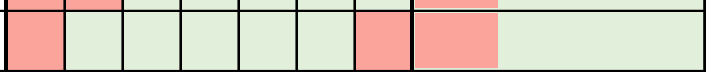
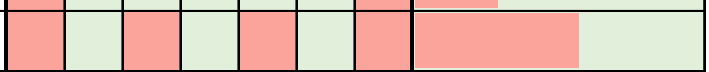
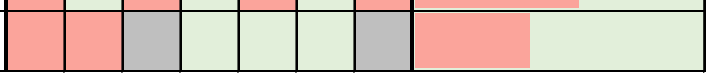
Kokura 2018 [64]	38	
Kang 2020 [65]	39	
Drozdz 2014 [66]	40	
Cai 2020 [67]	41	
Naito 2020 [68]	42	
Hirano 2020 [69]	43	

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Kampman 2015 I [72]	46									
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Zhang 2015 [73]	48									
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Sato 2019 [77]	52									
Lim 2010 [78]	53									
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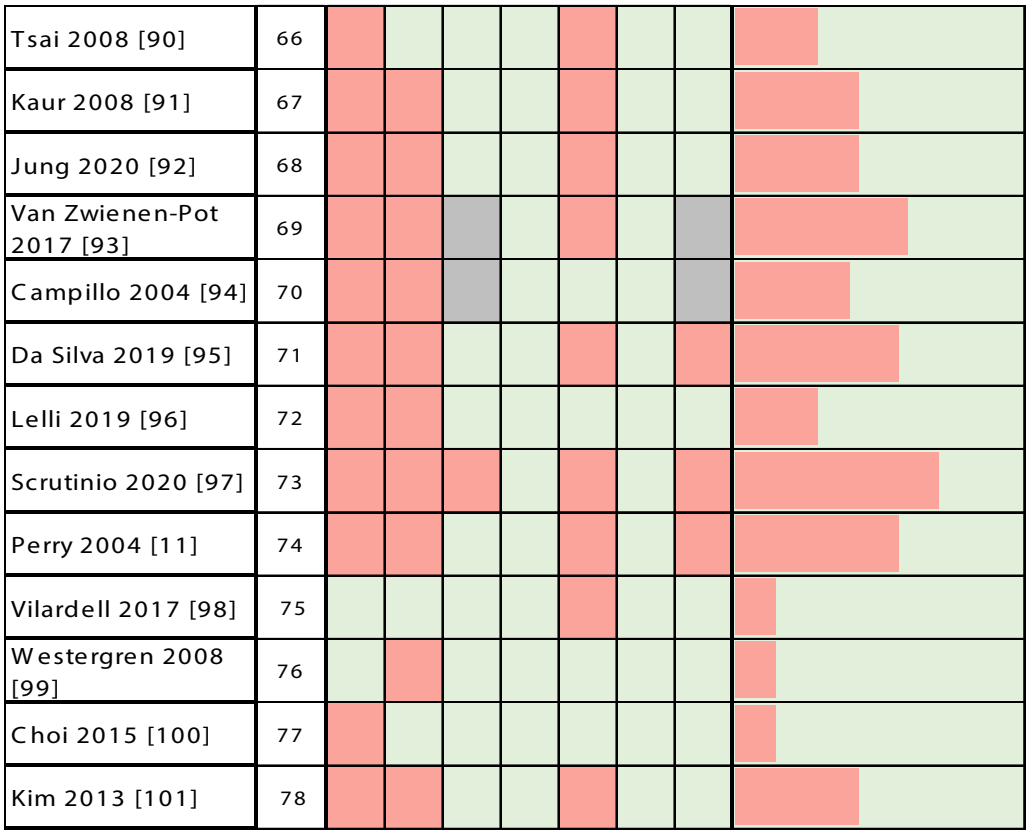

Table S4. Legend

Risk of bias

No risk of bias

Risk of bias is not applicable

Chapter 4

Malnutrition risk and oropharyngeal dysphagia in the chronic post - stroke phase

Viviënne A.L. Huppertz, Walmari Pilz, Gabriela Pilz da Cunha,
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Abstract

Introduction Oropharyngeal dysphagia (OD) and malnutrition are associated with poor clinical outcomes after stroke. The present study evaluated (1) malnutrition risk and OD - related characteristics in patients with chronic post - stroke OD, and (2) the relationship between on the one hand OD severity and on the other hand functional oral intake and dysphagia - specific quality of life.

Methods A cross - sectional study was conducted in a Dutch interdisciplinary outpatient clinic for OD. The standardized examination protocol comprised: clinical ear, nose, and throat examination, body mass index, the short nutritional assessment questionnaire (SNAQ), a standardized fiberoptic endoscopic evaluation of swallowing (FEES), the functional oral intake scale (FOIS), and the MD Anderson dysphagia inventory (MDADI).

Results Forty - two patients with chronic post - stroke OD were included. Mean (± SD) age and BMI of the population were 69.1 (± 8.7) years and 26.8 (± 4.1) kg / m^2 respectively. Seventeen (40.4%) patients presented a moderate to high risk of malnutrition (SNAQ score ≥ 2). The FEES examination showed moderate to severe OD in 28 (66.7%) patients. The severity of OD was significantly related to the FOIS score but not to the MDADI scores.

Conclusion In this specific sample of referred stroke patients, moderate to severe OD and moderate to high risk of malnutrition were common. Despite the use of clinical practice guidelines on stroke and a normal nutritional status at first sight, repeated screening for malnutrition and monitoring the severity and management of OD remain important elements in the care of patients with chronic post - stroke OD.

Introduction

Stroke is ranked within the top ten of diseases that increase the global burden of disease in adults (≥ 25 years) [1]. Current stroke treatments including reperfusion strategies are effective [2, 3], increase the chance of survival, and reduce the rate of disability after stroke [4-6]. Yet, these treatments do not guarantee full recovery after stroke and so the demand for rehabilitation and long - term care rises given the increasing number of stroke survivors. Common detrimental clinical outcomes after stroke are functional and cognitive impairment [7-9], disability [10], malnutrition [11-13], skeletal muscle mass loss [14], oropharyngeal dysphagia (OD), altered systemic immunity, and systemic illnesses such as aspiration pneumonia [15-18].

The extent and pace at which stroke patients recover depend on multiple factors, including nutritional status. Nutritional deficiency is a significant contributing factor to impaired functional outcome [19, 20], post - stroke complications, cognitive impairment, and mortality [21-23]. Malnutrition is a multidimensional concept in stroke care as it can be both, a cause and a consequence of cognitive - and functional problems after stroke. Cognition and functionality of the swallowing mechanism are conjointly important for the intake of nutrition. Swallowing involves multiple muscles and nerves that rely on the central nervous system for sensory feedback, motor programming and execution, and cognitive cortical processing [24-27]. Damaged brain tissue after stroke may result in impaired sensory and motor mechanisms that are essential for swallowing. It is also known that stroke patients often already have a pre - stroke sedentary lifestyle [28], resulting in a higher risk of sarcopenia [29]. Moreover, catabolic pathways of muscle tissue are activated after stroke causing loss of skeletal muscle mass which may affect not only peripheral skeletal muscles, but hypothetically also the muscles involved in swallowing [30-34]. Severe loss of skeletal muscle mass can cause or enhance swallowing difficulties. OD is one of the factors leading to reduced oral food intake in stroke patients [35]. This reduced oral food intake in turn contributes to malnutrition and loss of skeletal muscle mass, thus completing the vicious circle. Swallowing impairment or OD is the difficulty in bolus preparation, airway protection, and / or bolus transport from the mouth to the esophagus. OD may increase the risk of aspiration pneumonia and mortality in stroke patients [36-39]. Adequate intake and absorption of nutrients is important, especially in stroke patients, as these may enhance functional recovery [40, 41], brain tissue repair, prevent cognitive decline, and strengthen the immune system [42, 43]. Stroke patients however are known to have a diminished energy and protein intake [40]. The risk of malnutrition was shown to increase 2.6 - fold in stroke patients with OD [44].

Furthermore, the literature showed that OD may affect patients' health - related quality of life (QoL) and well - being due to dietary modifications, anxiety, tube feeding dependency, fear of choking, and embarrassment to eat in public, etc. [45-49]. The prevalence of OD varied between healthcare settings and was reported in up to 80% of stroke patients across healthcare settings [50]. A few stroke patients developed OD within six months after stroke or suffered from persistent

OD at six months or longer after stroke [50, 51]. A recent cost - of - illness study found that the healthcare costs during hospitalization of dysphagic stroke patients significantly increased as compared to stroke patients without OD. The same study showed that the OD - related complications malnutrition and respiratory tract infections were associated with an exponential increase in healthcare costs within one year after stroke onset. [52]

Stroke care in patients with risk of malnutrition and OD is complicated due to the multidimensional causes and poor clinical outcomes of both conditions. An interdisciplinary clinical approach targeted at the identification, diagnosis, and treatment of malnutrition and OD may improve stroke care and clinical outcomes after stroke.

Research on nutritional and OD - related characteristics of patients with chronic post - stroke OD is needed to increase the body of evidence for best - clinical - practice stroke care and clinical guidelines. Literature reviews on nutritional status in stroke patients across the continuum of care show a lack of studies and also a limited number of studies aiming at both, nutritional status and OD in the late subacute and chronic phase after stroke [53, 54]. In the first place, the present study determined the prevalence and severity of nutritional risk and OD - related characteristics in patients with chronic post - stroke OD using the short nutritional assessment questionnaire (SNAQ) and a fiberoptic endoscopic evaluation of swallowing (FEES). Secondly, the relationship between on the one hand OD severity and on the other hand functional oral intake and dysphagia - specific QoL was explored.

Methods

Study design and study population

This explorative cross - sectional study enrolled patients with chronic post - stroke (≥ 6 months) OD who visited the interdisciplinary outpatient clinic for OD in a tertiary university referral hospital in the Netherlands between 2013 and 2020. Patients with diagnosis other than stroke that could cause OD were excluded, as were patients with a score below 23 on a Mini Mental State Examination [55], and patients who were illiterate or blind.

A standardized examination protocol, used in daily clinical practice at the outpatient clinic, was carried out. The protocol comprised a clinical ear, nose, and throat examination (including cranial nerve function) performed by a laryngologist, determination of body mass index (BMI), the Functional Oral Intake Scale (FOIS) [56], the MD Anderson Dysphagia Inventory (MDADI) [57-59], the SNAQ [60, 61], and a standardized FEES [62-64].

Ethical considerations

The present study was approved by the ethical committee according to the Medical Research Involving Human Subjects Act (Wet Medisch Wetenschappelijk Onderzoek [WMO]) as non - WMO research (METC 2021 - 2519O) [65]. The no - objection system for the use of patient data for scientific research was applied and data were completely pseudonymized.

Data collection

Data were collected in a standardized way by a laryngologist and a speech - and - language therapist as part of regular care. This concerned data on patient demographics (sex, age, BMI), medical history (recurrent stroke, date of last stroke event, speech - and - language therapy), primary objectives (nutritional risk and OD severity), and exploratory objectives (functional oral intake, dysphagia - specific QoL).

Primary objectives

Nutritional risk was examined using the original SNAQ malnutrition questionnaire, a validated screening tool to identify patients at risk of malnutrition in the hospital outpatient setting [60, 61]. The SNAQ is a self - reported questionnaire consisting of three questions on unintended weight loss, decreased appetite, and the use of oral nutritional supplementation or tube feeding. The answers were dichotomous (yes / no) and resulted in a total score indicating the risk of malnutrition. A score below two points indicated a low risk of malnutrition, a score of two points indicated a moderate risk of malnutrition, and a score of three points or more indicated a severe risk of malnutrition. Patients with a SNAQ score of three points or more were referred to a dietitian for a detailed nutritional assessment.

To identify the characteristics and severity of OD, each patient underwent a standardized FEES. The FEES protocol consisted of three trials of thin liquid (3 x 10 ml water), three trials of thick liquid (3 x 10 ml applesauce; One2fruit), and one trial of a bite - sized cracker (Delhaize mini toast 80 gr). To enhance endoscopic visualization of the bolus, water, and applesauce were dyed with 5% methylene blue 10 mg / ml [63, 64]. The viscosities of thin and thick liquid boluses were respectively 1 mPa and 1200 mPa per second measured at 25 degrees Celsius 50 s - 1 of shear rate as recommended by the National Dysphagia Diet [66]. According to the International Dysphagia Diet Standardisation Initiative (IDDSI), thin liquid met the criteria for IDDSI level zero (thin) and thick liquid for level three (moderately thick) [67]. The position of the tip of the flexible endoscope (Pentax FNL - 10RP3, Pentax Canada Inc., Mississauga, Ontario, Canada) allowed observation of the pharyngeal and laryngeal anatomy and physiology during the pharyngeal phase of swallowing. Topical anesthetics were not used as they may affect pharyngolaryngeal sensory function. FEES videos were recorded at 25 frames per second using a Xion SD camera, XionEndoSTROB E camera control unit and Matrix DS data station with DIVAS software (Xion Medical, Berlin, Germany) and the data were stored in a secured drive on the hospital network.

For each bolus swallow, the visuoperceptual variables, penetration - aspiration, pharyngeal residue, and 'other signs' of OD (pre - swallow posterior spill, delayed initiation of the pharyngeal reflex, piecemeal deglutition) were assessed di - or trichotomously by two observers (laryngologist and a speech - and - language therapist) using consensus agreement (table S1) [64, 68, 69]. For the present study, consensus agreement by two experienced observers was chosen, as this method showed a better reproducibility of measurements in terms of observer agreement compared to the independent rating method, as discussion on measurements in a panel improved concordance in previous studies [63, 64, 70].

The severity of OD was evaluated using the Dysphagia Severity Scale (DSS) by Dziewas et al. [71-73]. A DSS score of zero points was defined as the absence of clinically relevant OD. A score of one point indicated mild OD defined by the presence of premature spillage and / or pharyngeal residue, but without penetration - aspiration events. A DSS score of two points indicated moderate OD defined by the presence of penetration - aspiration events with one bolus consistency. A DSS score of three points indicated severe OD defined by the occurrence of penetration - aspiration with two or more bolus consistencies.

Exploratory objectives

To explore the relationship between OD severity and respectively functional oral intake (the level of oral or non - oral intake) and dysphagia - specific QoL, the FOIS [56] and the Dutch version of the MDADI for neurogenic OD were used [57]. The FOIS was completed by the clinician during a structured interview. Patients with a FOIS score of three or lower were completely or partially tube dependent. Patients were completely tube dependent in case oral food intake was not recommended (FOIS 1) or if minimal or inconsistent oral intake was possible (FOIS 2). Patients were partially tube dependent if additional tube supplements were required next to a consistent oral intake of food or liquid (FOIS 3). Patients with a FOIS score above three did not require tube feeding and total oral intake was possible with or without texture modifications and / or thickening of liquids. A patient's diet may have been restricted to a single consistency (FOIS 4) or to multiple consistencies with special preparation (FOIS 5). Diet restrictions may also have been limited to the elimination of specific foods or liquid items only (FOIS 6) or to no restrictions at all (FOIS 7).

The MDADI is a self - reported questionnaire to measure the impact of OD on health - related QoL and the Dutch version has also been validated for patients with neurogenic OD [59]. The MDADI consists of different domains: one global assessment question (MDADI - G) for the effect of OD on overall health - related QoL; the functional scale (MDADI - F) for the impact of OD on daily activities (five questions); the physical scale (MDADI - P) for the physical impact of OD as perceived by the patient (eight questions); and the emotional scale (MDADI - E) for the patient's perceptual response on OD, e.g., self - consciousness, embarrassment, etc. (six questions). The questions were scored on a 5 - point Likert scale (1 = strongly agree / 2 = agree / 3 = no opinion / 4 = disagree / 5 = strongly disagree)

and the MDADI total score (MDADI - T) was based on the sum of all domains (20 questions). The minimum score was 20 representing a poor dysphagia - specific QoL and the maximum possible score is 100 (high dysphagia - specific QoL).

Statistical analyses

Statistical analyses were performed in IBM SPSS statistics 25 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). Normality of continuous variables was determined with QQ - plots and the Shapiro Wilk test. It was checked whether missing data were missing at random. Thereafter, pairwise deletion could be used for the analyses to minimize data loss. Fisher's exact test was conducted to check for differences in categorical variables between groups. For statistical purposes, trichotomous data on penetration - aspiration were dichotomized into zero for the absence of penetration and aspiration, and one for penetration or aspiration. Differences in mean for continuous variables between groups were analyzed using the independent sample t - test. The non - parametric independent Mann - Whitney U test was used to compare median values and non - normally distributed continuous variables. Univariable and multivariable binary logistic regression analyses were performed to assess the relationship between OD severity (DSS) and respectively functional oral intake (FOIS) and patients' dysphagia - specific QoL (MDADI). Independent variables in multivariable regression analyses were limited to two variables per model due to the low number of events per variable [74].

Results

The study sample consisted of 42 patients with chronic post - stroke (≥ 6 months) OD (figure 1). The sample consisted of 32 (76.2%) male patients. Mean (± SD) age and BMI of the total population were 69.1 (± 8.7) years and 26.8 (± 4.1) kg / m^2 respectively. Eleven (26.2%) patients suffered from recurrent stroke and the mean (± SD) time since the last stroke event in the total sample was 39.3 (± 50.8) months. Twenty - seven (64.3%) patients received speech - and - language therapy after the stroke event. Details on patient demographics and medical history can be found in table 1.

Prevalence of nutritional risk

The SNAQ was completed by 41 patients. The SNAQ score of one patient was missing, as this patient was not willing or able to complete the questionnaire. Results of the SNAQ revealed unintentional weight loss > 6 kg in the past six months in eleven (26.2%) patients. Unintentional weight loss of > 3 kg in the past month was present in seven (16.7%) patients. During the month prior to the visit to the outpatient clinic, eleven (26.2%) patients experienced decreased appetite, and fourteen (33.3%) patients used oral nutritional supplements (ONS) or tube feeding. Twenty - four (57.1%) patients presented a low risk of malnutrition, three (7.1%) a moderate risk, and fourteen (33.3%) a high risk. Details on demographics, medical

history, primary and exploratory objectives in patients with low versus moderate or high risk of malnutrition can be found in table 1.

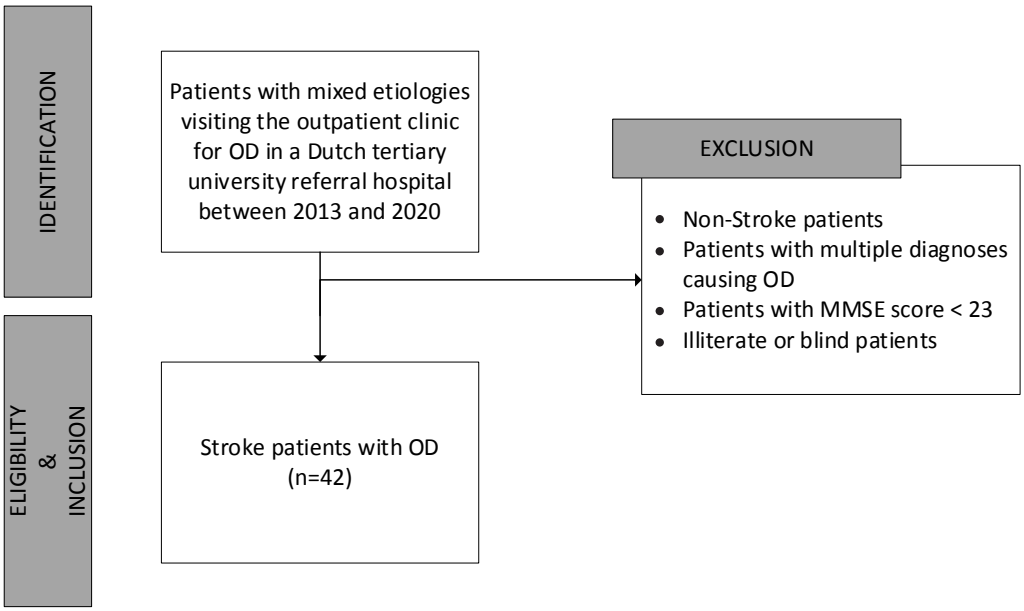

Figure 1. Flow diagram of patients included in the present cross - sectional study

Medical history and patient demographics, except for age ($p = 0.047$), did not significantly differ between the two risk - groups, patients with a low risk versus patients with a moderate or high risk of malnutrition. The prevalence of patients with unintended weight loss of > 6 kg in the last six months or > 3 kg in the last month was significantly different between the nutritional risk groups ($p < 0.001$). The prevalence of patients who experienced a decreased appetite or used ONS or tube feeding did not significantly differ between the nutritional risk groups.

None of the 24 patients with low risk of malnutrition had unintentional weight loss of > 6 kg in six months or > 3 kg in one month. Respectively, eleven (73.3%) and seven (46.7%) patients in the high - risk group had unintentional weight loss of > 6 kg in six months or > 3 kg in one month.

No significant difference in mean BMI was found between patients with versus without decreased appetite ($p = 0.154$), or between patients who used ONS or tube feeding versus patients who did not ($p = 0.129$).

There was no significant difference in the use of ONS or tube feeding between patients with versus without unintentional weight loss ($p = 0.156$ and $p = 0.686$). ONS or tube feeding was used by six (54.5%) out of eleven patients who lost > 6 kg in six months and three (42.9%) out of seven patients who lost > 3 kg in one month.

Characteristics and the prevalence of different OD severity levels

FEES measurements revealed that 29 (69.0%) of the patients presented penetration, eighteen (42.9%) aspiration, 21 (50.0%) pharyngeal residue, and 34 (81.0%) 'other signs' of OD. Penetration and aspiration predominantly occurred during the swallows of thin liquids in fifteen (35.7%) and fourteen (33.3%) patients, respectively. The OD severity was classified in 40 patients based on the FEES results. The OD severity of two patients could not be retrieved of the FEES results. As shown in table 1, nine (21.4%) patients did not have clinically relevant OD, three (7.1%) patients had mild OD, 15 (35.7%) patients had moderate OD, and 13 (31.0%) patients were severely dysphagic according to the DSS. However, four (44.4%) of the nine patients without clinically relevant OD (DSS score of 1) did show 'other signs' of OD in the present study.

Table 1. Patient characteristics of the total population (n = 42) and in patients with low risk of malnutrition versus moderate or high risk of malnutrition according to the SNAQ (n = 41). Abbreviations: *SNAQ; Short Nutritional Assessment Questionnaire, DSS; Dysphagia Severity Scale, FOIS; Functional Oral Intake Scale, MDADI; MD Anderson Dysphagia Inventory*

	Total population (n = 42)	**Low malnutrition risk (n = 24)**	**Moderate/high malnutrition risk (n = 17)**	
Patient demographics	**n (%)**	**n (%)**	**n (%)**	***P***
Sex				
Female	10 (23.8)	5 (20.8)	5 (29.4)	0.714
Male	32 (76.2)	19 (79.2)	12 (70.6)	
Age (years) , *mean (± SD)*	69.1 (±8.7)	70.6 (±8.3)	66.5 (±9.1)	0.047[a]*
Age categories				
< 65 years	14 (33.3)	4 (16.7)	10 (58.8)	0.008
≥ 65 years	28 (66.7)	20 (83.3)	7 (41.2)	
Body mass index (kg / m²), *mean (± SD)*	26.8 (±4.1)	27.0 (±3.7)	26.6 (±4.8)	0.757
Missing value	2	1	1	
Body mass index categories				
< 18.5 kg / m²	0 (0.0)	0 (0.0)	0 (0.0)	1.000
18.5 - 24.9 kg / m²	16 (38.1)	9 (39.1)	6 (37.5)	
25.0 - 29.9 kg / m²	13 (31.0)	8 (34.8)	5 (31.3)	
≥30 kg / m²	11 (26.2)	6 (26.1)	5 (31.3)	
Missing value	2	1	1	
Medical history	**n (%)**	**n (%)**	**n (%)**	***P***
Recurrent stroke				
None	31 (73.8)	20 (83.3)	10 (58.8)	0.241
One	8 (19.0)	3 (12.5)	5 (29.4)	
Two	2 (4.8)	1 (4.2)	1 (5.9)	
Three	0 (0.0)	0 (0.0)	0 (0.0)	
Four	1 (2.4)	0 (0.0)	1 (5.9)	

Table continues

Time (months) since last stroke event, *mean (± SD)*	39.3 (±50.8)	28.7 (±43.0)	52.0 (±60.0)	0.165
Missing value	2	1	1	
Time since last stroke event				
≤ 24 months	22 (52.4)	14 (60.9)	8 (50.0)	0.531
> 24 months	18 (42.9)	9 (39.1)	8 (50.0)	
Missing value	2	1	1	
Speech – and - language therapy				
No	15 (35.7)	9 (37.5)	5 (29.4)	0.742
Yes	27 (64.3)	15 (62.5)	12 (70.6)	
Primary objectives	**n (%)**	**n (%)**	**n (%)**	***P***
Unintended weight loss > 6 kg				
No	28 (66.7)	24 (100.0)	4 (26.7)	<0.001**
Yes	11 (26.2)	0 (0.0)	11 (73.3)	
Missing value	3	0	2	
Unintended weight loss > 3 kg				
No	32 (76.2)	24 (100.0)	8 (53.3)	<0.001**
Yes	7 (16.7)	0 (0.0)	7 (46.7)	
Missing value	3	0	2	
Decreased appetite				
No	28 (66.7)	18 (75.0)	10 (66.7)	0.718
Yes	11 (26.2)	6 (25.0)	5 (33.3)	
Missing value	3	0	2	
Oral nutritional supplement or tube feeding				
No	25 (59.5)	17 (70.8)	8 (53.3)	0.318
Yes	14 (33.3)	7 (29.2)	7 (46.7)	
Missing value	3	0	2	
SNAQ				
Low	24 (57.1)	-	-	
Moderate	3 (7.1)	-	-	
High	14 (33.3)	-	-	
Missing value	1			
Penetration				
No	12 (28.6)	6 (26.1)	5 (29.4)	0.141
Thin	15 (35.7)	11 (47.8)	4 (23.5)	
Thick	1 (2.4)	1 (4.3)	0 (0.0)	
Solid	0 (0.0)	0 (0.0)	0 (0.0)	
Thin + thick	9 (21.4)	5 (21.7)	4 (23.5)	
Thin + solid	1 (2.4)	0 (0.0)	1 (5.9)	
Thick + solid	0 (0.0)	0 (0.0)	0 (0.0)	
Thin + thick + solid	3 (7.1)	0 (0.0)	3 (17.6)	
Missing value	1	1	0	
Aspiration				
No	24 (57.1)	16 (66.7)	7 (41.2)	0.105
Thin	14 (33.3)	7 (29.2)	7 (41.2)	
Thick	1 (2.4)	1 (4.2)	0 (0.0)	
Solid	0 (0.0)	0 (0.0)	0 (0.0)	
Thin + thick	2 (4.8)	0 (0.0)	2 (11.8)	

Table continues

Thin + solid	1 (2.4)	0 (0.0)	1 (5.9)	
Thick + solid	0 (0.0)	0 (0.0)	0 (0.0)	
Thin + thick + solid	0 (0.0)	0 (0.0)	0 (0.0)	
Pharyngeal residue				
No	21 (50.0)	12 (50.0)	8 (47.1)	1.000
Yes	21 (50.0)	12 (50.0)	9 (52.9)	
'Other signs' of oropharyngeal dysphagia				
No	8 (19.0)	6 (25.0)	1 (5.9)	0.207
Yes	34 (81.0)	18 (75.0)	16 (94.1)	
DSS				
No relevant OD	9 (21.4)	4 (18.2)	4 (23.5)	0.325
Mild OD	3 (7.1)	2 (9.1)	1 (5.9)	
Moderate OD	15 (35.7)	11 (50.0)	4 (23.5)	
Severe OD	13 (31.0)	5 (22.7)	8 (47.1)	
Missing value	2	2	0	
Exploratory objectives	**n (%)**	**n (%)**	**n (%)**	***P***
FOIS				
FOIS 1	4 (9.5)	3 (13.0)	1 (6.3)	0.689
FOIS 2	1 (2.4)	0 (0.0)	1 (6.3)	
FOIS 3	0 (0.0)	0 (0.0)	0 (0.0)	
FOIS 4	2 (4.8)	1 (4.3)	1 (6.3)	
FOIS 5	13 (31.0)	6 (26.1)	7 (43.8)	
FOIS 6	7 (16.7)	4 (17.4)	2 (12.5)	
FOIS 7	13 (31.0)	9 (39.1)	4 (25.0)	
Missing value	2	1	1	
Exploratory objectives	**median (25th - 75 th percentile)**	**median (25th - 75 th percentile)**	**median (25th - 75 th percentile)**	***P***
MDADI				
Total	60.0 (53.0-77.0)	61.0 (55.5-78.5)	58.0 (45.0-71.0)	0.499
Missing value	5	3	2	
Global	2.0 (1.0-4.0)	2.5 (1.8-4.0)	2.0 (1.0-4.0)	0.453[a]
Missing value	3	2	1	
Functional	18.0 (14.0-22.0)	18.5 (15.5-22.3)	16.5 (13.3-19.75)	0.664
Missing value	3	1	1	
Physical	23.0 (18.5-28.0)	24.0 (17.0-33.0)	23.0 (19.5-27.0)	0.713
Missing value	1	0	0	
Emotional	19.0 (15.3-22.0)	19.0 (16.0-22.0)	19.0 (13.5-21.8)	0.940
Missing value	2	0	1	

[a] Whitney U - test

*p < 0.05, ** p < 0.001

Significant differences were not found in patient demographics, medical history, or indicators of nutritional risk between patients with no / mild OD versus patients with moderate / severe OD according to the DSS (table 2).

In four (9.5%) patients, the severity of the patients' OD did not allow the testing of all three bolus consistencies during the standardized FEES. In these cases, the swallow of a solid bolus and / or thin liquid was expected to be clinically unsafe with a high risk of very severe aspiration. This expectation was based on the observation of severe aspiration of saliva at the start of the FEES and / or severe aspiration during the thick liquid bolus swallow.

The relationship between on the one hand OD severity and on the other hand functional oral intake and dysphagia - specific QoL

A significant difference in FOIS scores was found between the DSS groups ($p = 0.031$). None of the patients in the no / mild OD group presented a FOIS ≤ 4, one (9.1%) patient of this group presented FOIS 5, and ten patients (91.0%) presented a FOIS ≥ 6. Five (18.5%) patients in the moderate / severe OD group presented a FOIS ≤ 4, twelve (44.4%) patients presented FOIS 5, and ten (37.0%) patients presented a FOIS ≥ 6 (table 2).

For the second aim of this study, univariable regression analysis revealed a significantly increased risk for moderate/severe OD in patients with FOIS 1 - 5 (OR 17.0, 95%CI: 1.885 - 153.273). This increased risk remained significant after correction for age (OR 22.3, 95%CI: 2.138 – 233.346) or BMI (OR 14.126, 95%CI: 1.525 - 130.831) in multivariable regression analysis (table 3).

Median MDADI subdomain scores did not significantly differ between the DSS groups (Table 2). Univariable and multivariable regression analyses did not show a significant relationship between DSS scores and MDADI subdomain scores (table 3).

Table 2. Patient characteristics in patients with no / mild OD severity versus moderate or severe OD according to the DSS (n = 40). Abbreviations: *SNAQ; Short Nutritional Assessment Questionnaire, DSS; Dysphagia Severity Scale, FOIS; Functional Oral Intake Scale, MDADI; MD Anderson Dysphagia Inventory*

	DSS no / mild (n = 12)	**DSS moderate / severe (n = 28)**	
Patient Demographics	**n (%)**	**n (%)**	***P***
Sex			
Female	3 (25.0)	7 (25.0)	1.000
Male	9 (75.0)	21 (75.0)	
Age (years), *mean (± SD)*	69.5 (±7.7)	68.8 (±9.1)	0.814
Age categories			
< 65 years	2 (16.7)	11 (39.3)	0.271
≥ 65 years	10 (83.3)	17 (60.7)	
Body mass index (kg / m²) , *mean (± SD)*	27.8 (±5.1)	26.6 (±3.6)	0.398
Body mass index categories			
< 18.5 kg / m²	0 (0.0)	0 (0)	0.614
18.5 - 24.9 kg / m²	4 (33.3)	11 (42.3)	
25.0 - 29.9 kg / m²	3 (25.0)	9 (34.6)	
≥ 30.0 kg / m²	5 (41.7)	6 (23.1)	
Missing value	0	2	
Medical history	**n (%)**	**n (%)**	***P***
Recurrent stroke			
None	9 (75.0)	20 (71.4)	1.000
One	3 (25.0)	5 (17.9)	
Two	0 (0.0)	2 (7.1)	
Three	0 (0.0)	0 (0.0)	
Four	0 (0.0)	1 (3.6)	
Time (months) since last stroke event, *mean (± SD)*	62.6 (±63.2)	30.6 (±44.7)	0.086
Missing value	1	1	
Time since last stroke event			
≤ 24 months	4 (36.4)	17 (63.0)	0.167
> 24 months	7 (63.6)	10 (37.0)	
Missing value	1	1	
Speech - and - language therapy			
No	7 (58.3)	8 (28.6)	0.091
Yes	5 (41.7)	20 (71.4)	
Primary objectives	**n (%)**	**n (%)**	***P***
Unintended weight loss > 6 kg			
No	6 (60.0)	20 (74.1)	0.442
Yes	4 (40.0)	7 (25.9)	
Missing value	2	1	
Unintended weight loss > 3 kg			
No	7 (70.0)	23 (85.2)	0.360

Table continues

Yes	3 (30.0)	4 (14.8)	
Missing value	2	1	
Decreased appetite			
No	6 (60.0)	20 (74.1)	0.442
Yes	4 (40.0)	7 (25.9)	
Missing value	2	1	
Oral nutritional supplement or tube feeding			
No	7 (70.0)	18 (66.7)	1.000
Yes	3 (30.0)	9 (33.3)	
Missing value	2	1	
SNAQ			
Low	6 (54.5)	16 (57.1)	1.000
Moderate	1 (9.1)	2 (7.1)	
High	4 (36.4)	10 (35.7)	
Missing value	1	0	
Exploratory objectives	**n (%)**	**n (%)**	***P***
FOIS			
FOIS 1	0 (0.0)	2 (7.4)	0.031*
FOIS 2	0 (0.0)	1 (3.7)	
FOIS 3	0 (0.0)	0 (0.0)	
FOIS 4	0 (0.0)	2 (7.4)	
FOIS 5	1 (9.1)	12 (44.4)	
FOIS 6	5 (45.5)	2 (7.4)	
FOIS 7	5 (45.5)	8 (29.6)	
Missing value	1	1	
Exploratory objectives	**median (25th - 75 th percentile)**	**median (25th - 75 th percentile)**	***P***
MDADI			
Total	78.0 (51.5-87.5)	58.0 (53.0-71.0)	0.441
Missing value	3	1	
Global	4.0 (2.0-5.0)	2.0 (1.0-4.0)	0.182[a]
Missing value	1	1	
Functional	21.0 (17.0-25.0)	16.5 (14.0-19.8)	0.133
Missing value	2	0	
Physical	24.5 (16.5-31.8)	23.5 (19.5-27.8)	0.730
Missing value	0	0	
Emotional	22.0 (15.0-24.0)	19.0 (15.3-20.8)	0.310
Missing value	1	0	

[a] Whitney U - test

*p < 0.05, ** p < 0.001

Table 3. Univariable and multivariable regression analyses to assess the relationship between oropharyngeal dysphagia severity (DSS) and respectively functional oral intake (FOIS) and patients' dysphagia - specific QoL (MDADI). Abbreviations: *OD; oropharyngeal Dysphagia, FOIS; Functional Oral Intake Scale, MDADI; MD Anderson Dysphagia Inventory*

UNIVARIABLE ANALYSES										
	n	**OR**	**95% CI**	***P***	**Nagelkerke R^2**					
No relevant OD / mild OD			*Reference*							
Moderate / severe OD										
FOIS 1 - 5	*38*	17.0	(1.885 – 153.276)	0.012*	0.339					
MDADI - Total	*36*	0.956	(0.907 – 1.008)	0.098	0.119					
MDADI - Global	*38*	0.683	(0.395 – 1.182)	0.173	0.071					
MDADI - Functional	*38*	0.839	(0.697 – 1.01)	0.064	0.144					
MDADI - Physical	*40*	0.978	(0.899 – 1.078)	0.653	0.007					
MDADI - Emotional	*39*	0.863	(0.723 – 1.03)	0.103	0.107					
MULTIVARIABLE ANALYSES										
Confounding factor			**Age**				**BMI**			
	n	**OR**	**95% CI**	***P***	**Nagelkerke R^2**	**OR**	**95% CI**	***P***	**Nagelkerke R^2**	
No relevant OD / mild OD			*Reference*				*Reference*			
Moderate / severe OD										
FOIS 1 - 5	*38*	22.334	(2138 – 233.346)	0.009*	0.357	14.126	(1.525 – 130.831)	0.020*	0.355	
MDADI - Total	*36*	0.951	(0.900 – 1.006)	0.079	0.137	0.959	(0.908 – 1.014)	0.143	0.123	
MDADI - Global	*38*	0.679	(0.392 – 1.177)	0.168	0.075	0.732	(0.421 – 1.275)	0.271	0.079	
MDADI - Functional	*38*	0.834	(0.689 – 1.010)	0.063	0.146	0.852	(0.703 – 1.032)	0.102	0.139	
MDADI - Physical	*40*	0.979	(0.887 – 1.081)	0.680	0.008	0.990	(0.896 – 1.095)	0.851	0.029	
MDADI - Emotional	*39*	0.858	(0.717 – 1.028)	0.097	0.111	0.860	(0.716 – 1.032)	0.105	0.144	

*$p < 0.05$, ** $p < 0.001$

Discussion

This explorative cross - sectional study reported specifically on patients with chronic post - stroke OD who were referred to the interdisciplinary outpatient clinic for OD. The patients' risk of malnutrition, the characterization and severity of OD, and dysphagia - specific QoL were the main points of attention. The study revealed that approximately two out of five patients with chronic post - stroke OD who visited the outpatient clinic, had a moderate to high risk of malnutrition. More than half of the patients in the total population were moderately to severely dysphagic. In the high - risk malnutrition group, almost four out of five patients had a moderate to severe degree of OD. These results reinforce the need of screening for the risk of malnutrition in patients with chronic post - stroke OD and vice versa.

Screening and diagnostics of malnutrition and OD and referral to expert healthcare professionals is important in stroke patients. Subsequently, a tailored treatment plan for the identified condition(s) can be developed by an expert healthcare professional. This may prevent poor clinical outcomes related to malnutrition or OD such as skeletal muscle mass loss, nutrient deficiencies, immune deterioration, and aspiration pneumonia. The majority of the patients in the present study were referred by a speech - and - language therapist from the primary healthcare network to the interdisciplinary outpatient clinic for OD. The speech - and - language therapist indicated the referral based on a clinical swallow assessment without having access to imaging techniques such as among others, FEES or videofluoroscopic swallow study. Based on the SNAQ, the standardized screening for malnutrition risk used in the outpatient clinic, the patient could immediately be refered to the dietitian who provided additional information relevant to tailor the treatment for OD.

Interestingly, almost half of the population had a moderate or high risk of malnutrition according to the SNAQ despite the relatively high average BMI values in this population. According to the commonly used cut - off values for BMI, thus in disregard of deviating cut - off values in specific patient populations and in older patients, the present study population could be classified as overweight (mean BMI 26.8 (± 4.1) kg / m^2). Malnutrition in overweight patients can easily be overlooked based solely on appearance or body posture. In the present study, the BMI values did not differ between the patient group with low malnutrition risk versus the patient group with moderate / high malnutrition risk. Similar BMI values were found in the patient group that used ONS and / or tube feeding and in the patient group that did not use ONS and / or tube feeding. European wide, similar BMI values were seen in stroke patients [75]. The mean (± SD) BMI of 198 stroke patients from seven European countries was 26.9 (± 4.9) kg / m^2. These patients were assessed between three and twelve months post - stroke and 19.7% of these patients had a BMI ≥ 30 kg / m^2. Stroke may be associated with a pre - stroke inactive and unhealthy lifestyle [28, 76] affecting the patients' weight prior to the stroke event. BMI values from the present study suggested that patients from the present specific sample of referred stroke patients were not energy deprived.

However, these patients may still be nutrient deficient and compliance of intake requires attention to minimize the risk of qualitative undernutrition. Therefore, repeated screening for malnutrition and monitoring the severity and management of OD remain important.

BMI is sensitive to weight changes and age - related physiological changes and does not provide any information on potential nutritional deficiencies or body composition. Nutritional screening based on a valid comprehensive screening tool such as the SNAQ is recommended as it encompasses multiple indicators of malnutrition besides BMI [77].

A consensus on criteria to screen and assess the patients' nutritional status was lacking until recently. Existing examination tools were not always validated and / or were mistakenly used interchangeable [78]. In 2019, consensus criteria for the diagnosis of malnutrition, the Criteria for the Diagnosis of Malnutrition (GLIM), were published [79, 80]. At that point and during the current study period the outpatient clinic used the SNAQ as part of the standard swallow protocol to screen for malnutrition risk. The SNAQ is a validated, time - efficient, and non - invasive screening tool in the outpatient clinic [61]. The SNAQ score provides an indication of the risk of malnutrition and is useful in the referral of patients to a dietitian. Patients in the present study who scored high on the SNAQ were indeed referred to a dietitian, and it was shown that more than one third of the population received ONS or tube feeding, and more than half of the population was treated for post - stroke OD by the speech - and - language therapist. These results suggested that post - stroke healthcare in the Netherlands is already pro - actively targeting OD rehabilitation and nutritional interventions in these patients, including initiation of ONS or tube feeding. This is in accordance with the ESPEN guidelines for clinical nutrition in neurology [81]. The Netherlands has been top ranked on the Euro Health Consumer Index (EHCI) continuously [82]. Moreover, ONS or tube feeding and / or speech - and - language therapy are reimbursed by the Dutch health insurance system and an extensive primary healthcare network of (allied) health professionals providing nutritional - and OD care, exists [83].

Despite these positive care - related aspects, there was still a high prevalence of patients visiting the outpatient clinic who had a moderate / high risk of malnutrition. The present study showed that the prevalence of patients with unintentional weight loss was higher among patients in the high - risk group as compared to patients in the low - risk of malnutrition group. Almost three out of four patients in the high - risk group experienced unintentionally weight loss > 6 kg in six months.

This raised the question whether these patients were undertreated from a nutritional perspective. Based on the results of the present study this question remained unanswered as specific details on nutritional interventions and OD treatment, e.g., type of intervention, standardization, and duration of treatment, were limited to the use of ONS or tube feeding and the presence or absence of speech - and - language therapy.

As a previous literature review showed some evidence of a relationship between the presence of OD and the risk of malnutrition in stroke patients [84], the present exploratory study aimed to increase the body of evidence on this relationship by investigating a well - defined high - risk patient subgroup with chronic post - stroke OD. The severity of OD did not seem to play a role in the risk of malnutrition in the present study population, as no significant difference in DSS score was found between the low versus high - risk of malnutrition groups.

Additional analyses revealed that the severity of OD was significantly related to the level of functional oral intake in these patients, but the wide confidence intervals indicated that the interpretation of this relationship requires caution. A relationship between OD severity and the patients' dysphagia - specific QoL could not be confirmed in the present small study sample. The chronic state of OD of these patients may have led to an acceptance of function loss or patients may have relatively more severe complaints that affect health - related QoL, such as loss of independence or absent sexual relationships.

Regression analysis did not show a significant relationship between OD severity and the patients' dysphagia - specific QoL. However a significant relationship between the severity of OD and impaired functional oral intake was found.

Considering the available literature on nutritional status in chronic stroke patients and the relationship between nutritional risk and the severity of OD in the present study, it is probably insufficiently known that many chronic stroke patients simultaneously suffer from chronic OD and are at risk of malnutrition. Current (inter)national clinical guidelines for stroke care recommend a screening for OD and malnutrition in the acute phase and proper management of these conditions [81, 85]. There is however a lack of attention for these conditions on the longer term. Future research in this field is recommended as stroke survivors will age and their functionality may deteriorate which makes the implementation of repeated screening for OD and nutritional risk in the chronic phase after stroke an important point of attention. One could think of a long - term surveillance plan which includes repeated screening for OD and nutritional risk at preset time points over the course of five years after stroke, as recommended in head and neck cancer patients [86]. In the Netherlands, this could be integrated in the repeated follow - up for cardiovascular risk management in persons 60+ years of age at the general practitioner [87]. Repeated follow - up visits may also provide insights in the impact of stroke on functionality at older age.

Study limitations

The present study was an explorative cross - sectional study in which valid assessment methods were used to describe nutritional risk and characteristics, and severity of OD in a group of patients with chronic post - stroke OD. Nonetheless, this explorative study design brought along some limitations.

Some statistically significant results were found in the present study, although the sample size was too small to uncover all relevant associations. Wide confidence intervals from regression analyses showed that the interpretation

requires caution. However, the patient population of the present explorative cross - sectional study was a realistic representation of patients with chronic post - stroke OD consulting the interdisciplinary outpatient clinic for OD in a tertiary university referral hospital in the Netherlands.

Furthermore, the interpretation of severity scores for OD such as the DSS requires caution. There is no consensus in the literature on what would be the optimal scale for the classification of the severity of OD. The DSS was based on the presence or absence of premature spillage and / or pharyngeal residue, penetration or aspiration events of one or multiple bolus consistencies, but did not take 'other signs' of OD such as pre - swallow loss of bolus into the pharynx, clearing swallows, etc. into account. The lowest DSS score did not indicate total absence of OD, as 'other signs' of OD may still have been present. Despite these limitations, the DSS was used as OD severity scale for the present study based on the FEES - registry study showing clinical relevance of this scale and a positive correlation with the FOIS in a very large multicenter study including 2,401 patients with neurogenic dysphagia of whom 1,465 had post - stroke OD [73].

Conclusion

This explorative cross - sectional study showed that more than half of the patients from the present specific sample of referred stroke patients had moderate to severe OD and approximately half of this population also had a moderate to high risk of malnutrition. Despite the use of clinical practice guidelines on stroke and a normal nutritional status at first sight, repeated screening for malnutrition and monitoring the severity and management of OD remain important elements in the care of patients with chronic post - stroke OD.

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Supplementary material

Table S1. Description of the fiberoptic endoscopic evaluation of swallowing variables. Abbreviations: *FEES; Fiberoptic endoscopic evaluation of swallowing, OD; Oropharyngeal dysphagia, DSS; Dysphagia Severity Scale*

FEES variable	Description	Scale
Penetration - aspiration	Entry of the bolus into the larynx, remaining on or above the vocal folds (penetration) or below the level of the vocal folds (aspiration). Bolus on the true vocal folds or in the anterior commissure secondarily leaking in the trachea was also classified as aspiration.	Trichotomous scale (range 0 – 2): 0 = no penetration or aspiration 1 = penetration 2 = aspiration
Pharyngeal residue	Bolus remaining in the pharynx after spontaneous clearing swallows. No distinction was made between right - or left - sided residue.	Dichotomous scale (range 0 – 1): 0 = no residue 1 = residue
Other signs of OD	Pre - swallow loss of bolus into the pharynx (pre - swallow posterior spill), delayed initiation of the pharyngeal reflex, and / or clearing or repeated swallows on the same bolus (piecemeal deglutition).	Dichotomous scale (range 0 – 1): 0 = no other signs of OD 1 = other signs of OD
DSS	Severity of OD based on the absence or presence of premature spillage and / or residue, penetration or aspiration events and on the number of consistencies at which the penetration or aspiration events occurred.	4 - point scale (range 0 - 3): 0 = no relevant dysphagia 1 = mild dysphagia (premature spillage and / or residue, but no penetration - aspiration events) 2 = moderate dysphagia (penetration - aspiration events with one consistency) 3 = severe dysphagia (penetration - aspiration events with two or more consistencies)

Part III

Chapter 5

Association between oropharyngeal dysphagia and malnutrition in Dutch nursing home residents: results of the national prevalence measurement of quality of care

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Abstract

Objectives Nursing home residents often have multi - morbidities and geriatric syndromes leading to lower quality of life or mortality. Oropharyngeal dysphagia (OD) and malnutrition are profound conditions in this complex profile of multi - morbidities and are associated with deprived mental and physical health status, e.g., aspiration pneumonia or dehydration. This study aimed to assess the association between OD and malnutrition in Dutch nursing home residents.

Design Data for this cross - sectional study were obtained from the annual National Prevalence Measurement of Quality of Care (LPZ).

Setting The LPZ was conducted in Nursing Homes in The Netherlands.

Participants Participants were nursing home residents age 65 or older and admitted to psychogeriatric or somatic wards.

Measurements The measurements were taken by trained nurses from the participating nursing homes. Anthropometric measurements and unintended weight loss (%) were assessed to determine nutritional status (malnutrition). OD was assessed by means of a standardized questionnaire assessing clinically relevant symptoms of OD such as swallowing problems or sneezing / coughing while swallowing. Cox regression was applied to assess the association between malnutrition and clinically relevant symptoms of OD in older Dutch nursing home residents.

Results Approximately 12% of the residents had swallowing problems and 7% sneezed / coughed while swallowing liquids or solid foods. Approximately 10% of the residents was malnourished. Residents with OD symptoms were more often malnourished compared to residents without OD symptoms. Approximately 17% of the problematic swallowers were concurrently malnourished. Increased risk of malnutrition was found in residents with swallowing problems (PR 1.5, 95% CI: 1.2 - 1.9), as well as in residents who sneezed / coughed while swallowing (PR 1.3, 95% CI: 1.0 - 1.7). Stratification based on wards revealed that problematic swallowers from somatic wards were at a high risk of malnutrition (PR 1.9, 95% CI: 1.3 - 2.8).

Conclusion Clinically relevant symptoms of oropharyngeal dysphagia, such as swallowing problems and sneezing / coughing while swallowing are associated with increased risk of malnutrition in psychogeriatric and somatic Dutch nursing home residents.

Introduction

Oropharyngeal dysphagia (OD) and malnutrition are conditions that result in lower quality of life and that place people at high risk for co - morbidities and mortality. OD is considered a new geriatric syndrome [1] and frequently occurs in nursing home residents [2, 3], especially in residents with stroke [4], dementia [5], or other illnesses or treatments that affect the swallowing mechanism [6]. Furthermore, aging related changes in motor or sensory functions and muscle strength of the oral cavity are shown to affect swallowing capacity and the nutritional status [7, 8]. The integrity of functional swallowing capacity is not only of great importance for safe oral intake of nutrition, but also for a safe oral intake of medication in this multi - morbid population.

OD and malnutrition complicate care in older nursing home residents in view of associated health complications, co - morbidities, and a deprived mental health status. When OD and malnutrition are underestimated, unrecognized (e.g., with silent dysphagia [9, 10]), or left untreated, they may lead to aspiration pneumonia or dehydration respectively [11-14], or to feelings of social isolation [15], anxiety, or even depression [16]. Impaired eating behaviour could also be a consequence of dementia, depression [17, 18], or swallowing capacity, and nutritional status may be influenced by side effects of certain antipsychotic drugs [19, 20].

In order to diagnose OD, the volume - viscosity swallow test (V - VST) is currently recognized as the gold standard [21], however epidemiological studies are often based on the Water Swallow Test (WST) or clinical questionnaires. The use of different assessment methods adds to a wide range of OD prevalence rates in the literature. A cross - country study by Streicher et al. (2017) reported prevalence rates of OD up to 48% using a standardised questionnaire in nursing home residents worldwide [2]. Sarabia - Cobo et al. (2016) found a prevalence rate of almost 70% of OD in nursing home residents when using a mixed - method approach including clinical history, physical examination, the EAT - 10 (Eating Assessment Tool - 10) and the 3 oz - WST [22].

Similar to the diagnosis of OD, a variety of definitions, measurements, and tools to determine nutritional status are applied [18] since there is no gold standard or a universal definition of malnutrition in an older population. As a consequence, the literature contains a wide range of prevalence rates of malnutrition among nursing home residents [23]. Streicher et al. (2017) reported a prevalence of 16% of malnourished nursing home residents based on anthropometric measurements [2], though prevalence rates of malnutrition up to 38% were found based on the mini nutritional assessment (MNA) in institutionalized older people [24].

Treatments in malnourished residents with OD are of compensative or rehabilitative nature and include e.g., diet modifications, nutritional supplementation, oral - motor therapy, postural techniques and / or facilitation techniques [25]. In general, a multidisciplinary approach from an otolaryngologist and / or neurologist and / or gastroenterologist, a clinical geriatrician or elderly care physician, a radiologist, a speech - and - language therapist, a dietitian, and a

nurse and caregiver is recommended for safe and efficient swallowing management [26, 27]. Due to associated health complications and co -morbidities in older nursing home residents, management and care is complicated, even more so in residents with dementia [28]. Therefore, Dutch nursing homes have comprehensive psychogeriatric or somatic wards, tailored to the needs of the residents [29].

Overall, prevalence rates found for OD and malnutrition are inconclusive and there is some evidence that mortality is even more prevalent in coexisting occurrence of OD and malnutrition [30]. However, the association between OD and malnutrition in nursing home residents is still understudied, and especially ward specific literature is lacking. Therefore, this cross - sectional study aimed to delineate associations between OD and malnutrition in Dutch nursing home residents from psychogeriatric and somatic wards.

Methods

Study design

Data were obtained from Dutch nursing home residents who participated in the annual cross - sectional National Prevalence Measurement of Quality of Care (LPZ) measurement rounds of 2016 or 2017. The study population included residents of 65 years or older, living in somatic and psychogeriatric wards of nursing homes across the Netherlands. Data of residents who received palliative care at the day of the measurements were excluded. Detailed information on the study design of the LPZ is available in the study by van Nie - Visser et al. (2013) [31].

Ethical considerations

Approval for the LPZ was given by the Medical Ethical Committee of Maastricht University and the Academic Hospital Maastricht (Maastricht UMC$^+$, The Netherlands). Participation was voluntary and none of the participating residents, nurses, nursing homes, or care institutions received financial compensation.

Data collection

Data on resident characteristics (age, sex, care dependency, and residents' morbidities), and primary outcome measures (nutritional status, clinically relevant symptoms of oropharyngeal dysphagia and nutritional interventions) were collected on a pre - set measurement date. Trained nurses from different wards within the nursing home collected the data and entered and submitted the data electronically [31].

Care dependency

The care dependency scale (CDS) is a validated assessment tool to indicate residents' needs and dependency status. The CDS consists of 15 items, each rated on a five - point Likert - scale. A reduced CDS indicated a higher care dependency of the resident (1 = highly dependent, 5 = almost independent) [32].

Oropharyngeal dysphagia

The standardized questionnaire of the LPZ was established based on literature and consultation of experts (face validity) and included two questions on clinically relevant symptoms of oropharyngeal dysphagia. Questions asked were: *"Does the client have swallowing problems?"* (swallowing problems: 0 = no, 1 = yes) and *"Does the client sneeze or cough while swallowing food or liquids?"* (sneeze / cough while swallowing: 0 = no, 1 = yes).

Nutritional status: malnutrition

Malnutrition in the nursing home residents was indicated based on the operational definition of malnutrition in older people of the European Society for Clinical Nutrition and Metabolism (ESPEN) [33]. Data on anthropometric measurements, weight and height, were collected to determine the Body Mass Index (BMI) for each resident. Residents were considered malnourished with a BMI below 18.5 kg / m^2, or with a reduced BMI (a BMI below 20 kg / m^2 in residents aged 65 - 70 years or a BMI below 22 kg / m^2 in residents age 70 or older) in combination with recent unintended weight loss (> 5% over the past 3 months or > 10% indefinite of time).

Nutritional interventions and referrals

With a multiple - choice question, the nurses could indicate which nutritional interventions the residents received. Nutritional interventions included for example nutritional supplementation and enriched snacks, but also adjustments of food consistency and mealtime - ambiance, or referral to a dietitian. For residents with symptoms of OD, additional questions on meals and beverage consistencies and referral to a speech - and - language therapist were incorporated: *"Does the client receive mashed meals or thickened beverages because of swallowing problems?"* (0 = no, 1 = yes) and *"Is the client supervised by a speech - and - language therapist because of swallowing problems?"* (0 = no, 1 = yes).

Statistical analysis

Statistical analysis was performed in IBM SPSS statistics 24 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). Normality of the data was determined with QQ - plots. Data of residents with missing values for primary outcomes or outliers (residents with a BMI > 70 kg / m^2 or body height < 108 cm) were eliminated. Of residents who participated in both measurement rounds, 2016 and 2017, only the data of 2017 were included. Prior to analysis, numerical data on BMI and weight loss were recoded into a dichotomous variable on malnutrition based on the ESPEN definition of malnutrition. Independent sample t - tests and Chi - square (χ^2) tests were conducted to check for differences between groups. To assess the association between OD and malnutrition in older nursing home residents, the crude and adjusted prevalence ratios (PR) were subtracted from Cox regression to prevent overestimated associations from logistic regression [34, 35]. Confounding factors in the multivariable analysis were based on literature and forward (LR) stepwise regression modelling. The factor 'measurement round' was added to the model to

control for effect modification. P - values below 0.05 were considered statistically significant.

Results

Study population

The study population consisted of 6,349 older residents from Dutch nursing homes. Almost two - thirds (66.0%) were residents from the psychogeriatric wards and the remaining residents (34.0%) were admitted to somatic wards. The majority were women (70.2%) with a mean age of 84.5 (±7.5) years, a mean BMI of 24.8 (± 4.8) kg / m^2, and a mean CDS of 42.4 (± 16.6). Significantly higher mean CDS was found among somatic residents as compared to psychogeriatric residents ($p < 0.001$). No differences were found between the two study rounds for prevalence rates of malnutrition (2016: 10.1% and 2017: 10.5%, $p = 0.584$) or for prevalence rates for sneezing / coughing while swallowing (2016: 7.5% and 2017: 6.3%, $p = 0.064$). The prevalence of residents with swallowing problems was higher ($p=0.017$) in 2016 (13.0%) compared to the prevalence of residents with swallowing problems in 2017 (11.1%).

The prevalence of oropharyngeal dysphagia and malnutrition

Approximately one out of eight residents with swallowing problems (12.1%) and one out of fourteen residents sneezed / coughed while swallowing liquids or solid food (6.9%) (table 1). If somatic ward residents with stroke were excluded, the prevalence of residents with swallowing problems was higher ($p = 0.025$) in psychogeriatric wards (11.3%) compared to somatic wards (9.2%). One out of ten residents was malnourished (10.3%) and malnutrition was more often ($p = 0.002$) seen in psychogeriatric residents (11.1%), as compared to somatic residents (8.7%).

Residents with swallowing problems were more often malnourished compared to residents without swallowing problems, with almost one out of every five problematic swallowers being malnourished (17.2%). Almost half of the problematic swallowers indicated additional problematic sneezing / coughing in the act of swallowing (46.9%). Nearly all residents who indicated sneezing / coughing while swallowing had overall problems swallowing (82.2%). (Table 1)

As shown in table 1, the average CDS was lower ($p < 0.001$), meaning a higher care dependency, in residents with swallowing problems (mean CDS 30.0 ± 14.4) or in residents who sneezed / coughed while swallowing (mean CDS 30.3 ± 14.6) compared to residents without these OD symptoms (respectively mean CDS 44.1 ± 16.2 and mean CDS 43.3 ± 16.4).

Among malnourished residents, approximately one out of five had swallowing problems (20.2%) and one out of ten was sneezing / coughing while swallowing foods or liquid beverages (10.2%).

In comparison to non - malnourished residents (mean CDS 43.0 ± 16.4), the average CDS was lower ($p < 0.001$) in malnourished residents (mean CDS 36.8 ± 34).

Clinical Diagnosis

More than two - thirds of the residents were diagnosed with dementia (65.6%) and nearly half was diagnosed with disease of the circulatory system (44.1%) (Figure 1). Dementia was also the leading clinical diagnosis among residents with clinically relevant symptoms of OD as swallowing problems and sneezed / coughed while swallowing. Furthermore, the residents with swallowing problems had significantly more often diseases of the nervous system (excluding paraplegia) (18.7% vs. 9.0%, $p < 0.001$), stroke (27.7% vs. 16.2%, $p < 0.001$) and disease of the skin and subcutaneous tissue (10.9% vs. 7.9%, $p = 0.004$), as compared to residents without swallowing problems. Residents who sneezed / coughed while swallowing were more often diagnosed with diseases of the nervous system (excluding paraplegia) (19.1% vs. 9.5%, $p < 0.001$) and stroke (31.4% vs. 16.6%, $p < 0.001$), as compared to residents who did not sneeze / cough while swallowing.

Nutritional interventions and referrals

Malnourished residents with clinically relevant symptoms of OD were mostly referred to a dietitian (57.7%), or received energy (E+) and protein (P+) enriched diets (29.2%) and/or snacks (48.5%). (Figure 2)

The majority of the residents with clinically relevant symptoms of OD were referred to a speech - and - language therapist. A 74.6% of the residents with swallowing problems and a 79.2% of the residents who were sneezing / coughing while swallowing were referred to a speech - and - language therapist.

Associations - Univariable

Univariable analysis (table 2) showed an increased risk of malnutrition among nursing home residents with swallowing problems (PR 1.8, 95% CI: 1.5 - 2.2) and among residents who sneezed / coughed while swallowing (PR 1.5, 95% CI: 1.2 - 2.0).

In stratified analysis increased risks of malnutrition amounted to 1.9 (PR 1.9, 95% CI: 1.5 - 2.4) and 1.7 (PR 1.7, 95% CI: 1.2 - 2.4) among residents with swallowing problems at psychogeriatric and somatic wards respectively.

Residents at psychogeriatric wards and with sneezing / coughing while swallowing did also show an increased risk of malnutrition (PR 1.7, 95% CI: 1.3 - 2.3).

Associations - Multivariable

As shown in table 3, an increased risk of malnutrition was found among residents with swallowing problems (PR 1.5, 95% CI: 1.2 - 1.9).

In stratified analysis, increased risks of malnutrition amounted to 1.4 (PR 1.4, 95% CI: 1.1 - 1.8) and 1.9 (PR 1.9, 95% CI: 1.3 - 2.8) among residents with swallowing problems at psychogeriatric and somatic wards respectively.

Table 1. Characteristics and primary outcomes of residents with oropharyngeal dysphagia. Abbreviations: *CDS; care dependency scale*

	Swallowing Problems	**No-Swallowing problems**	***P***	**Sneeze/Cough while swallowing**	**No-Sneeze/Cough while swallowing**	***P***
Total Population, *n (%)*	769 (12.1)	5578 (87.9)		439 (6.9)	5910 (93.1)	
Basic Characteristics						
Female, *n (%)*	499 (64.9)	3955 (70.9)	0.001	265 (60.4)	4189 (70.9)	<0.001
CDS, *mean (± SD)*	30.0 (14.4)	44.1 (16.2)	<0.001	30.3 (14.6)	43.3 (16.4)	<0.001
Age, *mean (± SD)*	83.8 (7.8)	84.6 (7.5)	0.005	83.4 (7.8)	84.6 (7.5)	0.003
BMI, *mean (± SD)*	23.5 (4.3)	25.0 (4.9)	<0.001	24.1 (4.6)	24.9 (4.8)	0.001
Primary Outcomes						
Malnutrition, *n (%)*	132 (17.2)	523 (9.4)	<0.001	67 (15.3)	588 (9.9)	<0.001
Swallowing problems, *n (%)*				361 (82.2)	408 (6.9)	<0.001
Sneeze/Cough while swallowing, *n (%)*	361 (46.9)	78 (1.4)	<0.001			

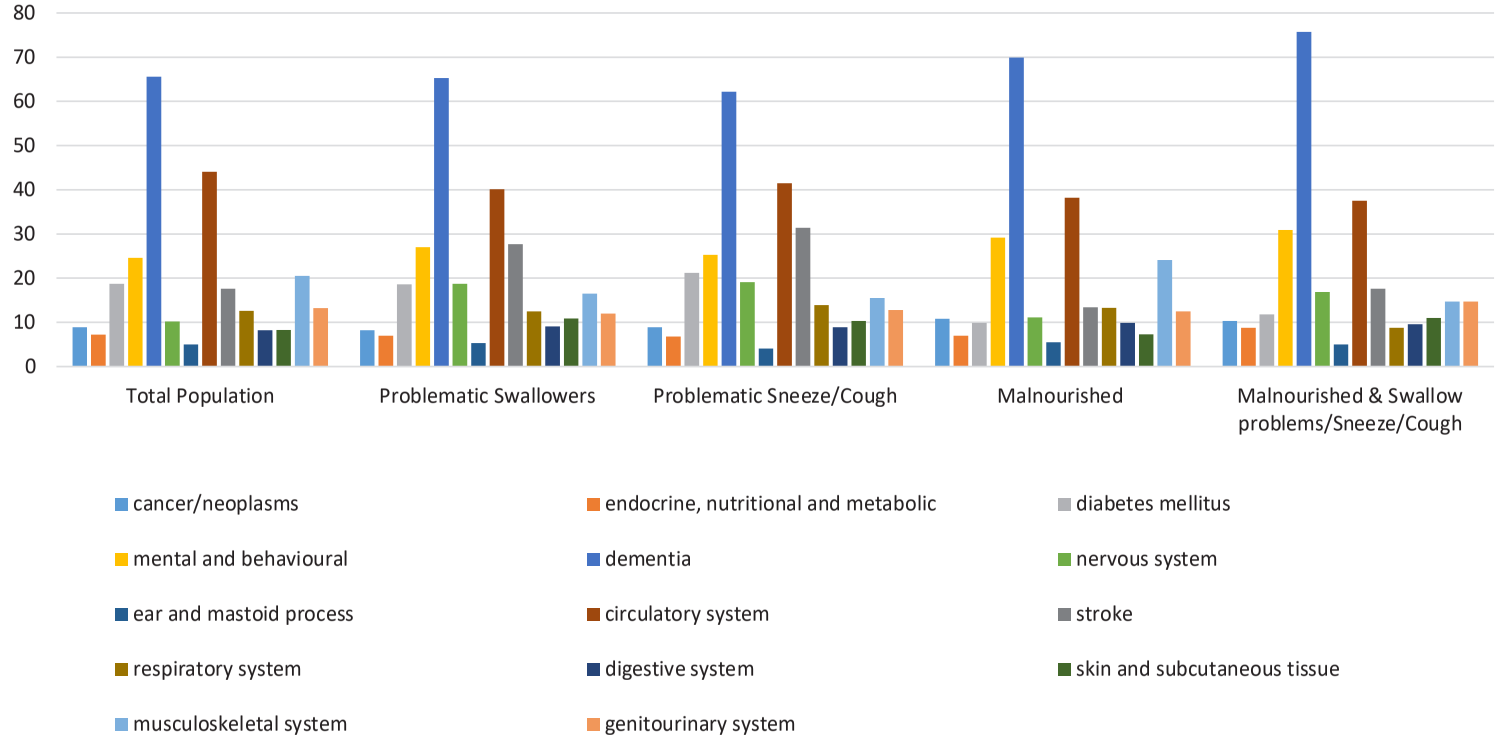

Figure 1. Clinical diagnosis (> 5% in total population) by condition

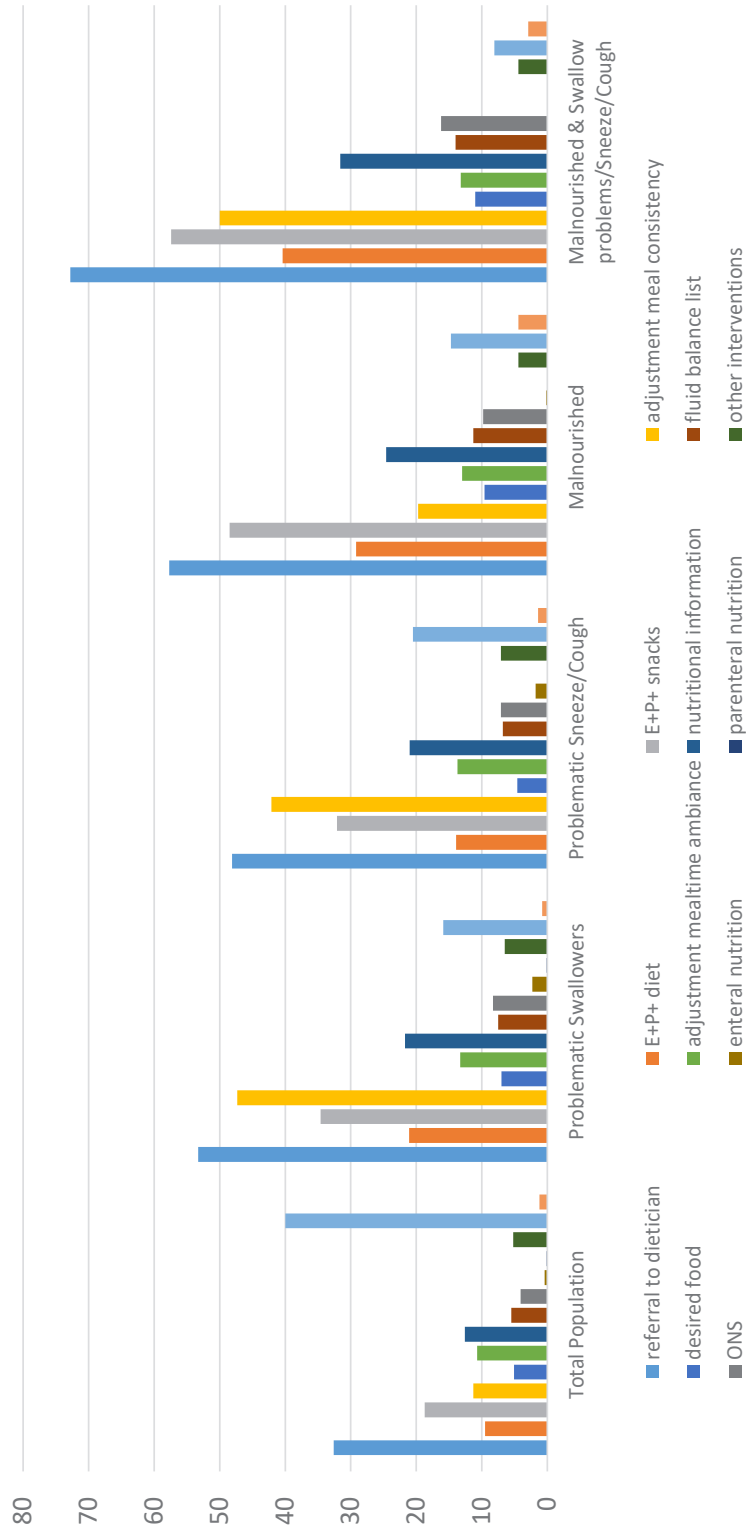

Figure 2. Nutritional interventions applied per condition

Table 2. Univariable prevalence ratios from Cox Regression

Dependent variable	Independent variable	Prevalence ratio	95% CI
Total population (n = 6349)			
malnutrition	swallowing problems	1.8	1.5 - 2.2
malnutrition	sneeze / cough	1.5	1.2 - 2.0
Psychogeriatric ward (n = 4190)			
malnutrition	swallowing problems	1.9	1.5 - 2.4
malnutrition	sneeze / cough	1.7	1.3 - 2.3
Somatic ward (n = 2159)			
malnutrition	swallowing problems	1.7	1.2 - 2.4
malnutrition	sneeze / cough	1.1	0.7 - 1.9

Discussion

This cross - sectional prevalence study showed prevalence figures of oropharyngeal dysphagia and malnutrition among older Dutch nursing home residents and revealed significant associations between oropharyngeal dysphagia and malnutrition among these nursing home residents.

The overall prevalence of OD in this population was lower compared to reported prevalence numbers from previous studies [22, 36]. In the present study, the method of diagnosing OD was of an observational clinical nature while in previous studies instrumental visuo - perceptual assessment methods were applied, which are more likely to identify and physiologically interpret the cases of OD [36-38]. In addition, cases of OD might have been underreported due to the nurses' lack of knowledge about how to judge or interpret OD [39], or the residents' own lack of awareness of their OD [40]. They might assume that swallowing difficulties are natural effects of aging [41].

Nevertheless, even without instrumental visuo - perceptual assessment methods, prevalence rates of OD up to 20.2% were found in the present study among malnourished residents. This finding is in line with the results of a similar study by Poisson et al. (2016) among hospitalized older people [36]. Almost 20.8% of the patients with a reduced BMI had OD. In that population, the prevalence of OD was even higher when nutritional status was assessed with the Mini Nutritional Assessment (MNA) (82.1%) or if it was based on serum albumin levels (70.8%). In addition, Poisson et al. (2016) showed that patients with OD had a significantly lower dietary intake compared to patients without OD.

Table 3. Multivariable prevalence ratios from Cox Regression. Abbreviations: *CDS; care dependency scale*

Dependent variable	Independent variable	Confounders	Prevalence ratio	95% CI
Total population (n = 6349)				
malnutrition	swallowing problems	age, sex, CDS, cancer, diabetes mellitus, mental disorder, circulatory disease (non - stroke), stroke, musculoskeletal system disease	1.5	1.2 - 1.9
malnutrition	sneeze / cough	age, sex, CDS, diabetes mellitus, mental disorder, circulatory disease (non - stroke), stroke, musculoskeletal system disease	1.3	1.0 - 1.7
Psychogeriatric ward (n = 4190)				
malnutrition	swallowing problems	sex, CDS, cancer, metabolic diseases, diabetes mellitus, circulatory disease (non - stroke), musculoskeletal system disease	1.4	1.1 - 1.8
malnutrition	sneeze / cough	sex, CDS, cancer, diabetes mellitus, circulatory disease (non - stroke), musculoskeletal system disease	1.4	1.0 - 1.8
Somatic ward (n = 2159)				
malnutrition	swallowing problems	sex, diabetes mellitus, mental disorder (e.g., depression), stroke	1.9	1.3 - 2.8
malnutrition	sneeze / cough	age, sex, diabetes mellitus, Mental disorder (not dementia), nervous system disease (not paraplegia)	1.2	0.7 - 2.0

The prevalence of malnutrition in this study population is also relatively low as compared to prevalence rates of malnutrition in the literature [23, 24]. However, previous studies were performed in different clinical settings, applied deviant definitions of malnutrition that also included subjects at risk of malnutrition [42] or used methods that tend to over - diagnose malnutrition in this older population [43]. In the present study only those who met the ESPEN criteria were considered as malnourished thus not including those at risk. Furthermore, the problem of malnutrition in frail elderly people has recently received more attention in The

Netherlands, which may be a plausible reason for its relatively low prevalence rate.

Interestingly, Poisson et al. (2016) also found an association between malnutrition and oral self - care dependency. Similar results were found in the present study, where lower average care dependency scores (CDS), meaning higher care dependency, were found in residents with OD and in malnourished residents.

With regard to clinically relevant symptoms of OD, subjective swallowing problems were often accompanied by sneezing / coughing in this study. However, some residents without subjective swallowing problems indicated problems with eating due to sneezing / coughing while swallowing, probably also related to dysphagia as it is known that coughing during oral intake is related to penetration or aspiration [44]. In the present study, adjusted associations between malnutrition and sneezing / coughing while swallowing were found among psychogeriatric residents. Adjusted associations between malnutrition and swallowing problems were significant among both wards, though more pronounced in somatic wards. Differences between wards can be explained by the group of residents with stroke at the somatic wards. According to Foley et al. [45] the chances of malnutrition were more than doubled (OR 2.425, 95% CI: 1.3 - 4.6) among dysphagic residents who had suffered a stroke. Similar results were found in the present study too; residents at the somatic wards had an almost twofold risk of malnutrition (PR 1.9, 95% CI: 1.3 - 2.8) due to swallowing problems.

The group of residents admitted to somatic wards is a relatively small group, approximately one third, of the total population. The majority of residents is admitted to psychogeriatric wards, with dementia as the most frequently occurring clinical diagnosis. A previous study that was conducted in Finnish older nursing home residents revealed two - and three - fold risks of malnutrition due to dementia (OR 2.0, 95% CI: 1.5 - 2.9) and swallowing problems (OR 3.0, 95% CI: 2.1 - 4.4) [46]. Swallowing problems may already develop during the early stages of dementia [47] and develop with impaired cognitive, motor, and sensory mechanisms of swallowing [3].

More specific reference data from the literature on differences between psychogeriatric and somatic wards in nursing homes are lacking at the moment since mainly in Dutch nursing homes these specific distinctions have been made. In addition, to compare the findings of the present study to the literature, take into consideration the difference between varying statistical methodologies to assess associations. Previous studies were based on logistic regression, a commonly used method for the assessment of associations, though known to overestimate associations [34, 35]. Therefore, the alternative Cox regression was applied in the present study to assess the association between malnutrition and OD [34, 35].

In the present study nurses reported clinically observed symptoms or complaints of dysphagia. Another method of swallowing assessment may have produced different results although instrumental swallowing assessments such as video - fluoroscopy are not available in Dutch nursing homes and fiberoptic endoscopic evaluation of swallowing is complicated on such large scale sample sizes of vulnerable nursing home residents.

No conclusion on causality between OD and malnutrition can be drawn from the present cross - sectional study, however the clear evidence of an association between OD and malnutrition shows the need for more research on this issue.

Conclusion

Clinically relevant symptoms of oropharyngeal dysphagia, such as swallowing problems and sneezing / coughing while swallowing are associated with increased risks of malnutrition in psychogeriatric and somatic Dutch nursing home residents. Future research is needed to increase understanding and awareness among affected residents and involved healthcare disciplines to optimize care, tailored to the needs of psychogeriatric and somatic residents with OD and malnutrition in Dutch nursing homes.

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Chapter 6

Association between malnutrition and oral health in Dutch nursing home residents: results of the LPZ study

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Abstract

Introduction According to the World Health Organisation (WHO) and FDI World Dental Federation (FDI), malnutrition and bad oral health are of great concern to global health, especially among the older population. This study aimed to assess the associations between oral health problems ([artificial] teeth problems, chewing problems, and xerostomia) and malnutrition in residents of somatic and psychogeriatric wards in Dutch nursing homes.

Methods Data of the cross - sectional National Prevalence Measurement of Quality of Care study (Landelijke Prevalentiemeting Zorgproblemen [LPZ]) in the Netherlands were used to evaluate nutritional status and oral health of 3,220 residents, aged 65 or older, and living in somatic or psychogeriatric wards in Dutch nursing homes. Cox regression was performed to calculate prevalence ratios (PR) of malnutrition among these residents.

Results Of the total study population, 11.7% were malnourished, 28.6% had xerostomia, 25.6% had chewing problems, and 10.1% experienced problems eating due to (artificial) teeth problems. Within somatic wards, 9.0% were malnourished, where 13.2% of residents in psychogeriatric wards were malnourished. Increased risk of malnutrition was found among psychogeriatric residents who had problems with eating due to (artificial) teeth problems (PR 1.6, 95% CI: 1.1 - 2.3).

Conclusion Poor oral health, mostly problems with eating due to (artificial) teeth problems, was associated with an almost twofold risk of malnutrition in older residents in Dutch nursing homes and even more so in psychogeriatric residents than in somatic residents.

Introduction

Studies on morbidity, mortality, and oral health (care) - related quality of life illustrate an association between poor oral health status and malnutrition [1-7]. The World Health Organization (WHO) [8, 9] and the FDI World Dental Federation (FDI) [10] presented several reports on the global burden of oral health problems and underlined the neglected state of these problems. Prevalence figures of oral health problems differ highly among populations across the world. According to the WHO, one of the population segments that requires special attention is the age group 65+ [8, 9]. Prevalence figures up to 42% for chewing problems [11] and up to 63% for xerostomia [12-14] were found in (malnourished) institutionalized older people. Differences among populations may be the result of the varying causes of oral health problems and confounding effects, methodological differences between studies, and the lack of a uniform definition of oral health [2, 8, 9, 12, 15-17]. Prevalence figures of malnutrition up to 38% were found in institutionalized older people [6, 18, 19]. Thus, along with a deteriorated oral health status, older people are also prone to malnutrition, particularly the ones living in hospitals, residential care homes, and nursing homes [6, 20, 21].

Over the past decades, the WHO and the FDI have emphasized the role of oral health in public health [8-10], and studies among older people in industrialized countries showed decreasing prevalence and incidence of edentulism (tooth loss), while the preservation of functional natural dentition increased simultaneously [15, 22]. Compared with denture wearing residents, dentate residents experienced better oral health outcomes [23]. In addition, maintenance of natural dentition positively influenced the self - image, oral health - related quality of life, as well as general quality of life of older people [24]. Despite these positive results, additional research on oral health in relation to malnutrition remains of great importance, especially among institutionalized older people as oral health conditions are more prone to deteriorate rapidly among these residents [25].

Oral health - related problems commonly reported among older people include halitosis (oral malodour) [26, 27], hyposalivation (objectively measured low saliva secretion) [28], xerostomia (subjective feeling of dry mouth) [12, 13, 29], chewing problems [11], dysphagia (swallowing difficulties) [4], edentulism and dental prostheses [15, 30], (root)caries [25, 31], periodontal disease [32, 33] and poor oral hygiene levels [34]. Studies in dentate and edentate residents illustrate a gender difference: prevalence of xerostomia is higher among women (19.5%) compared to men (11.9%) [35, 36]. Besides, positive associations were found between xerostomia and age [17, 37], presence of systemic non - communicable diseases [9, 35, 38], use of medication [35, 37] and irradiation treatments [39].

Previous studies on oral health in older residents in nursing homes focused mainly on edentulism, visible detrimental oral health indicators such as dental plaque or caries and the influence of impaired mental health and care dependency [25, 40, 41], whereas studies on oral health problems, such as hyposalivation, xerostomia, and chewing problems in this specific population, and even more so in

relation to malnutrition, are limited.

Therefore, the aim of the present cross - sectional study was to assess the association between malnutrition and a range of oral health - related problems among older residents in Dutch nursing homes using data from the National Prevalence Measurement of Care Problems (Landelijke Prevalentiemeting Zorgproblemen [LPZ]) in the Netherlands.

Methods

Study design

The study sample for the present cross - sectional study was derived from a large heterogenous study population of 12,389 residents from Dutch care institutions that participated in the LPZ study rounds of 2013, 2014, and 2015. The annual cross - sectional prevalence measurement of care problems (LPZ study) was initially developed to assess the internal quality of basic care in different healthcare settings, including nursing homes [20, 21, 42, 43]. It consists of the following modules: decubitus, incontinence, malnutrition, falls, use of fixation, chronic wounds, and infections. More detailed information on the study design of the LPZ study is provided by Halfens et al. [21], and van Nie - Visser et al. [43]. Unlike nursing homes elsewhere, Dutch nursing homes comprise of two different types of wards, namely psychogeriatric wards (for residents with a decline in mental ability) and somatic wards (for residents with chronic physical disabilities) [44]. By using standardized measures of oral health, data from the LPZ study allow for between - ward comparisons of the associations between malnutrition and oral health - related problems. In the LPZ study, wards from participating institutions were included only when response rates were above 90% [21, 42]. The sample for the present study consisted of 3,220 nursing home residents who were included if they were 65 years or older, and were admitted to either a somatic ward or psychogeriatric ward within the institutional long - term care sector (*Wonen Zorg Welzijn sector*) in the Netherlands. In case residents participated in more than one study round, the most recent data were used for analysis.

Ethical considerations

All institutions that took part in the LPZ study voluntarily subscribed after a written invitation and there was no financial compensation provided after participation. Measurements were taken after consent of the residents [21]. Approval for the study was given by the Medical Research Ethics Committee of Maastricht University and the Academic Hospital Maastricht (Maastricht UMC+).

Data collection

Per participating institution, one coordinator was assigned to be responsible for the organization of the measurements and for communication with the project team of the LPZ study. In collaboration with the project team, these coordinators trained the

caregivers in correctly carrying out the measurements on the presence, prevention or treatment of malnutrition and oral healthcare related indicators. To improve the reliability of the data that were collected, two different caregivers per resident were involved in the descriptive measurements: one of the caregivers was working at the department where the resident was staying at the time of measurement, the other one came from another department [21].

Assessment of malnutrition

Data on age, Body Mass Index (BMI), and time - specific weight loss (%) were used to assess nutritional status in each LPZ round [21, 45, 46]. Malnutrition was defined as either BMI lower than 18.5 kg / m², or a reduced BMI (< 20 kg / m² in residents younger than 70 years and < 22 kg / m² in residents older than 70 years) in combination with unintentional weight loss (> 5% of habitual weight over past 3 months or > 10% of habitual weight indefinite of time) [45]. Malnutrition was coded dichotomously.

Extreme values for weight, height, and BMI, at both ends of the distribution, were checked case by case, verified, and only one was excluded.

Assessment of oral health

Oral health status was assessed by means of a standardized questionnaire on potential indicators and symptoms of poor oral health that was developed by experts and is annually evaluated and revised when needed [21]. Data were collected on problems with eating due to (artificial) teeth problems, chewing problems and xerostomia, the three main oral health problems assessed in this study.

Residents also indicated whether they had general mouth problems; however, these were not further specified. Response codes were never, sometimes, always, or N / A (unknown). Unknown responses were coded as missing, remaining answers were dichotomized and recoded into no (never) and yes (sometimes / always). The factor (poor) oral health was constructed in which the factors (artificial) teeth problems, chewing problems, and xerostomia were combined to identify residents with at least one of these three major oral health problems.

Statistical Analysis

Statistical analysis has been performed with use of IBM SPSS statistics 22 and IBM SPSS statistics 23 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). Baseline data were, visually and numerically, checked for normal distributions of age and BMI. Descriptive characteristics are presented as means and standard deviations (± SD) for continuous data, while frequencies and percentages are given for categorical data. For analytical purposes, ordinal variables were dichotomized. The χ^2 test was performed to check baseline data for differences between malnourished and non - malnourished residents and between wards. Post hoc analyses were done to check whether participants from the three study rounds differed. To examine associations between malnutrition and oral health factors, crude and adjusted prevalence ratios (PRs) were generated from Cox regression, because odds ratios

from logistic regression may overestimate the prevalence ratios [47, 48]. To confirm this expected overestimation, logistic regression was additionally performed. In regression analysis, listwise deletion was used to deal with missing values. Several multivariable models were used in which oral health factors were either added separately (model 1) or simultaneously (model 2) to control for the effects that oral health factors have on each other. Confounders that were identified from literature and additional statistical analysis within the present study were age, sex, ward type, dysphagia, activities of daily living (ADLs) dependency, oral nutritional supplements (ONS), and diagnosis of disease; diabetes mellitus, psychological disorder, dementia, cardiovascular disease (CVD), cerebrovascular accident (CVA), and kidney / urinary tract / sexual disorder [1, 6, 21, 35, 37, 49]. Stratified analyses were performed to control for interaction and to examine potential differences in PRs between wards. *P* values below 0.05 were considered statistically significant.

Results

Prevalence

As can be seen in table 1, the study population consisted of 3,220 older residents from Dutch nursing homes with a mean age of 84.3 (± 7.4) years, ranging from 65 to 105 years. Most were women (70.2%) and living in psychogeriatric wards (65.2%). BMI (mean 24.2 ± 4.7 kg / m^2) varied greatly among participants, with a minimum of 13 kg / m^2 and a maximum of 51 kg / m^2. The prevalence of malnutrition differed between residents with (n = 2885) and without (n = 335) missing values for oral health factors (p = 0.036), although it did not differ between the residents from different study rounds (p = 0.414), with the percentage of malnutrition in the total study population being 11.7%. The prevalence of oral health problems did differ between study rounds (p < 0.001), albeit without a pattern.

Of the total study population, 28.6% had xerostomia, 25.6% from chewing problems, and 10.1% experienced problems with eating due to (artificial) teeth problems. Poor oral health was seen in 44.5% of the total population and 16.0% complained about general mouth problems that were not further specified. Among the malnourished participants, mean BMI was 17.6 (± 1.7) kg / m^2, 58.5% complained of poor oral health, and 24.3% complained of general mouth problems. More specifically, chewing problems were seen in 40% of the malnourished residents, xerostomia in 33.3%, and (artificial) teeth problems in 20.9%.

Residents were not equally represented between the two types of wards with 65.2% admitted to psychogeriatric wards. Among somatic residents, 9.0% were malnourished, whereas 13.2% of psychogeriatric residents were malnourished. When comparing oral health problems among the wards, the highest prevalence rates were found in psychogeriatric wards, with percentages up to 46.5% for poor oral health. As in the total population, highest prevalence rates were found for xerostomia, followed by chewing problems and eventually (artificial) teeth problems in both types of wards.

The prevalence of (artificial) teeth problems and chewing problems differed between types of wards, with respectively 5.9% and 20.9% in somatic residents and 12.3% and 28.0% in psychogeriatric residents. The prevalence of xerostomia did not differ between somatic wards (27.4%) and psychogeriatric wards (29.2%).

Figure 1 shows that higher percentages of malnourished residents were found among residents who reported oral health problems. Malnutrition was seen in 40.7% of the residents who always had (artificial) teeth problems, whereas this percentage was respectively 22.9% and 10.1% among residents who sometimes or never had (artificial) teeth problems. Among residents who always, sometimes or never had chewing problems, the proportions of malnourished residents were 22.9%, 16.5%, and 8.8%, respectively. Percentages of malnourished residents did not differ between categories of xerostomia.

Associations between malnutrition and oral health problems

Univariable analysis (table 2) showed that older nursing home residents were almost twice as likely to be malnourished with poor oral health (PR 1.8, 95% CI: 1.5 - 2.2) compared with residents who never experienced oral health problems. Residents who experienced problems with eating due to (artificial) teeth problems were almost 2.5 times more likely to be malnourished (PR 2.4, 95% CI: 1.9 - 3.1). Increased PRs were also found for chewing problems (PR 2.1, 95% CI: 1.7 - 2.6) and xerostomia (PR 1.3, 95% CI: 1.0 - 1.6). After adjustment for confounders (model 1), PRs were slightly lower however remained significant, except for xerostomia (table 2). Older nursing home residents with poor oral health were 1.5 times more likely to be malnourished (PR 1.5, 95% CI: 1.2 - 1.9) compared to residents who did not have (artificial) teeth problems, chewing problems, or xerostomia.

Adjusted for other oral health problems (model 2), (artificial) teeth problems remained significant (PR 1.6, 95% CI: 1.2 - 2.1), where chewing problems (PR 1.3, 95% CI: 1.0 - 1.7) now revealed non - significant increased PRs. Stratified analysis showed that residents who did not receive ONS were 1.6 times more likely to be malnourished when experiencing chewing problems (PR 1.6, 95% CI: 1.1 - 2.3) whereas residents who did receive ONS were more likely to be malnourished when they had (artificial) teeth problems (PR 1.9, 95% CI: 1.2 - 3.2).

Residents free from dysphagia were 1.5 times more likely to be malnourished when experiencing (artificial) teeth problems (PR 1.5, 95% CI: 1.1 - 2.2), whereas no significantly increased PRs were found for residents with dysphagia. Among the psychogeriatric residents, a similar trend was found, as seen in the total population; only the PR of (artificial) teeth problems remained significant after additional adjustment for the other oral health problems (PR 1.6, 95% CI: 1.1 - 2.3), whereas at somatic wards no increased risks emerged after additional adjustment for other oral health problems.

Table 1. Characteristics (n [%]) of the total population by nutritional status and ward.
Abbreviations: *ONS; oral nutritional supplements, ADL; activities of daily living, CDS; care dependency scale*

	Total, n = 3220	**Malnourished, n = 378**	**Non-malnourished, n = 2842**		**Somatic, n = 1121**	**Psychogeriatric, n = 2099**	
	n(%)	**n(%)**	**n(%)**	***P***	**n(%)**	**n(%)**	***P***
Malnutrition	378 (11.7)	-	-	-	101 (9)	277 (13.2)	<0.001[a]
(Artificial) teeth problems							
Never	2785 (86.5)	280 (74.1)	2505 (88.1)	<0.001[b]	1022 (91.2)	1763 (84.0)	<0.001[a]
Sometimes	297 (9.2)	68 (18)	229 (8.1)		55 (4.9)	242 (1.5)	
Always	27 (0.8)	11 (2.9)	16 (0.6)		11 (1.0)	16 (0.8)	
Missing value	111						
Chewing problems							
Never	2241 (69.6)	198 (52.4)	2043 (71.9)	<0.001[b]	843 (75.2)	1398 (66.6)	<0.001[a]
Sometimes	587 (18.2)	97 (25.7)	490 (17.2)		172 (15.3)	415 (19.8)	
Always	236 (7.3)	54 (14.3)	182 (6.4)		63 (5.6)	173 (8.2)	
Missing value	156						
Xerostomia							
Never	2093 (65)	229 (60.6)	1864 (65.6)	0.045[b]	733 (70.4)	1360 (64.8)	0.523[a]
Sometimes	880 (27.3)	118 (31.2)	762 (26.8)		292 (26)	588 (28)	
Always	41 (1.3)	8 (2.1)	33 (1.2)		16 (1.4)	25 (1.2)	
Missing value	206						
Poor oral health	1432 (44.5)	221 (58.5)	1211 (42.6)	<0.001[b]	457 (40.8)	975 (46.5)	0.003[a]
Missing value	240						
General mouth problems							
Never	2586 (80.3)	262 (69.3)	2324 (81.8)	<0.001[b]	952 (84.9)	1634 (77.8)	<0.001[a]
Sometimes	310 (9.6)	79 (20.9)	231 (8.1)		85 (7.6)	225 (10.7)	
Always	205 (6.41)	13 (3.4)	192 (6.8)		52 (4.6)	153 (7.3)	
Missing value	119						
Age (years), *mean (± SD)*	84.3 (±7.4)	85.4 (± 7.5)	84.2 (± 7.3)	0.004[c]	84 (±7.7)	84.5 (±7.2)	0.087[c]
Sex (female)	2261 (70.2)	309 (81.7)	1952 (68.7)	<0.001[a]	751 (67)	1510 (71.9)	0.003[a]
BMI (kg/m²), *mean (± SD)*	24.2 (±4.7)	17.6 (±1.7)	25.1 (±4.2)	<0.001[c]	25 (±5.1)	23.7 (±4.4)	<0.001[c]

Table continues

Ward							
Somatic	1121 (34.8)	101 (26.7)	1020 (35.9)	<0.001[a]	-	-	-
Psychogeriatric	2099 (65.2)	277 (73.3)	1822 (64.1)				
Tube Feeding	25 (0.8)	6 (1.6)	19 (0.7)	0.064[b]	14 (1.2)	11 (0.5)	0.026[a]
ONS	428 (13.3)	130 (34.4)	298 (10.5)	<0.001[a]	136 (12.1)	292 (13.9)	0.157[a]
ADL Dependent	3073 (95.4)	370 (97.9)	2703 (95.1)	0.015[a]	1006 (89.7)	2067 (98.5)	<0.001[a]
Eating & Drinking CDS							
Completely dependent	700 (21.7)	141 (37.3)	559 (19.7)	<0.001[a]	96 (8.6)	604 (28.8)	<0.001[a]
To a great extent dependent	771 (23.9)	87 (23)	684 (24.1)		251 (22.4)	520 (24.8)	
Partially dependent	551 (17.1)	51 (13.5)	500 (17.6)		220 (19.6)	331 (15.8)	
To a great extent independent	434 (13.5)	37 (9.8)	397 (14)		220 (19.6)	214 (10.2)	
Completely independent	764 (23.7)	62 (16.4)	702 (24.7)		334 (29.8)	430 (20.5)	
Hygiene CDS							
Completely dependent	1723 (53.5)	262 (69.3)	1461 (51.4)	<0.001[a]	398 (35.5)	1325 (63.1)	<0.001[a]
To a great extent dependent	439 (13.6)	33 (8.7)	406 (14.3)		153 (13.6)	286 (13.6)	
Partially dependent	419 (13)	34 (9)	385 (13.5)		206 (18.4)	213 (10.1)	
To a great extent independent	368 (11.4)	31 (8.2)	337 (11.9)		185 (16.5)	183 (8.7)	
Completely independent	271 (8.4)	18 (4.8)	253 (8.9)		179 (16)	92 (4.4)	
Dysphagia	340 (10.6)	65 (17.2)	275 (9.7)	<0.001[a]	128 (11.4)	212 (10.1)	0.245[a]
Missing value	14						
Diabetes Mellitus	592 (18.4)	45 (11.9)	547 (19.2)	0.001[a]	205 (18.3)	387 (18.4)	0.917[a]
Psychological Disorder	399 (12.4)	64 (16.9)	335 (11.8)	0.004[a]	146 (13)	253 (12.1)	0.426[a]
Dementia	2048 (63.6)	263 (69.6)	1785 (62.8)	0.010[a]	144 (12.8)	1904 (90.7)	<0.001[a]
CVD	1498 (46.5)	149 (39.4)	1349 (47.5)	0.003[a]	640 (57.1)	858 (40.9)	<0.001[a]
CVA/Hemiparesis	692 (21.5)	65 (17.2)	627 (22.1)	0.030[a]	351 (31.3)	341 (16.2)	<0.001[a]
Disorder kidney/Urinary tract/ Sexual organs	437 (13.6)	36 (9.5)	401 (14.1)	0.014[a]	155 (13.8)	282 (13.4)	0.757[a]

[a] Pearson χ^2 test
[b] Fisher exact test
[c] *t* test

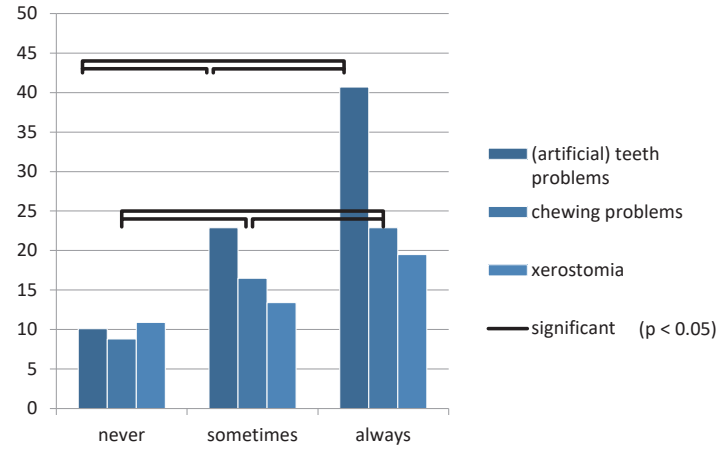

Figure 1. Percentage of malnourished residents among residents who reported oral health problems

Discussion

In studying the prevalence and association of malnutrition and oral health in Dutch nursing homes, this study found positive associations between malnutrition and poor oral health. Specifically, problems with eating due to (artificial) teeth problems were associated with higher malnutrition prevalence rates. This association was more pronounced in residents of psychogeriatric wards than in somatic wards.

The prevalence rates of malnutrition and oral health problems, calculated over the 3 - year period, were lower compared to previous studies [6, 11-13, 18, 19, 50, 51], although percentages of oral health problems, found in the present study with a large sample size were still high; up to 58.5% of malnourished residents with at least one of the major oral health problems. Previous studies were often performed in smaller study populations or did not apply the definition of malnutrition from the European Society for Clinical Nutrition and Metabolism (ESPEN) (2015). Furthermore, in the present study population attention might have been given to residents with specific diseases generally known for their increased risk of malnutrition and different prevalence figures may be due to differences in national income and healthcare systems between the countries in which previous studies were conducted. Moreover, in the present study (poor) oral health was solely measured subjectively by means of a standardized questionnaire, and may have been underestimated, depending on the problem statement in the questionnaire [29].

It appeared that problems with eating due to (artificial) teeth problems and chewing problems are risk factors of malnutrition in the population at large and even more so among specific strata, as, for example, psychogeriatric wards.

Table 2. Prevalence Ratios (Cox) of malnutrition in relation to oral health problems in older residents in Dutch nursing homes.
Abbreviations: *adj.;adjusted, ADL; activities of daily living, ONS; oral nutritional supplements*

	n	No oral health problems	(Artificial) teeth problems, n = 3109	Chewing problems, n = 3064	Xerostomia, n = 3014	Poor oral health, n = 2980
			PR (95%CI)	PR (95%CI)	PR (95%CI)	PR (95%CI)
Total Population	3220					
crude		1.0	2.4 (1.9-3.1)	2.1 (1.7-2.6)	1.3 (1.0-1.6)	1.8 (1.5-2.2)
adjusted model 1[a]		1.0	1.8 (1.4-2.3)	1.6 (1.3-2.0)	1.1 (0.9-1.4)	1.5 (1.2-1.9)
adjusted model 2[ab]		1.0	1.6 (1.2-2.1)	1.3 (1.0-1.7)	1.0 (0.8-1.2)	-
Stratified Analysis						
ONS (non-receiver/receiver)	2792 / 428					
non-receivers adj. model 1[c]		1.0	1.8 (1.2-2.5)	1.9 (1.4-2.4)	1.0 (0.8-1.4)	1.5 (1.2-2.0)
non-receivers adj. model 2[bc]		1.0	1.4 (0.9-2.1)	1.6 (1.1-2.3)	0.9 (0.6-1.2)	-
receivers adj. model 1[c]		1.0	1.8 (1.2-2.7)	1.3 (0.9-1.9)	1.2 (0.9-1.8)	1.4 (1.0-2.1)
receivers adj. model 2[bc]		1.0	1.9 (1.2-3.2)	0.9 (0.6-1.5)	1.2 (0.8-1.7)	-
Dysphagia (dysphagia free/ dyspagia)	2866 / 340					
dysphagia free adj. model 1[d]		1.0	1.9 (1.4-2.6)	1.8 (1.4-2.3)	1.2 (0.9-1.5)	1.5 (1.2-1.9)
dysphagia free adj. model 2[bd]		1.0	1.5 (1.1-2.2)	1.4 (1.0-1.9)	1.0 (0.8-1.3)	-
dysphagia adj. model 1[d]		1.0	1.3 (0.7-2.3)	0.9 (0.5-1.6)	0.9 (0.5-1.6)	1.1 (0.6-2.3)
dysphagia adj. model 2[bd]		1.0	2.0 (1.0-4.0)	0.8 (0.4-1.5)	0.6 (0.3-1.1)	-
Type of ward (somatic/ psychogeriatric)	1121 / 2099					
somatic adj. model 1[e]		1.0	2.2 (1.2-4.2)	1.8 (1.2-2.9)	1.1 (0.7-1.6)	1.4 (0.9-2.1)
somatic adj. model 2[be]		1.0	1.8 (0.9-3.6)	1.5 (0.9-2.5)	0.9 (0.5-1.4)	-
psychogeriatric adj.model 1[e]		1.0	1.8 (1.3-2.3)	1.6 (1.2-2.1)	1.1 (0.9-1.5)	1.6 (1.2-2.0)
psychogeriatric adj.model 2[be]		1.0	1.6 (1.1-2.3)	1.2 (0.9-1.7)	1.0 (0.8-1.3)	-

[a]adjusted for age, sex, type of ward, disease, dysphagia, ADL dependency and ONS
[b]adjustment for other oral health problems
[c]adjusted for age, sex, type of ward, disease, dysphagia and ADL dependency
[d]adjusted for age, sex, type of ward, disease, ADL dependency and ONS
[e]adjusted for age, sex, disease, dysphagia, ADL dependency and ONS

The present study distinguishes itself from previous studies on malnutrition by differentiating between wards in Dutch nursing homes. Unfortunately, these ward - specific PRs from stratified analysis cannot be put into perspective by results of previous studies since this ward - specific division of nursing homes has so far only been seen in the Netherlands. Weak and non - significant associations were found between malnutrition and xerostomia, whereas previous studies did find a significant positive relation between xerostomia, chewing problems, and malnutrition. However, these studies were conducted in different populations, as, for example, Chinese community - dwelling older people [52] or in populations in which xerostomia was identified by objective measurements of saliva flow by means of a Sialometry [53]. Xerostomia and hyposalivation do not have to occur simultaneously per definition [54]. Where dry mouth in terms of hyposalivation can be measured objectively, in this study dry mouth, xerostomia, was solely indicated by the subjective feeling of a dry mouth [29].

Differences in associations also may be explained by the different confounding factors used in previous research. Medication use, especially polypharmacy and medication used in treatment of psychological disorders, is often considered to be a potential confounder because this may have a xerostomic effect [28, 37, 55]. However, a study by Fialová et al. [56] showed that inappropriate medication use was relatively low in western Europe, therefore the lack of information on medication use in this study seems of less concern. Data on whether residents received ONS were available, although not further specified in terms of type or dose, which complicates interpretation of ONS - related associations.

Comparison of the results of the Cox and logistic regression revealed striking higher odds ratios than PRs for strata with a relatively high percentage of malnourished residents, which emphasizes the importance of the predilection of PRs from the Cox or Poisson regression over odds ratios from logistic regression in this study [48].

Data for this study were collected in a representative and large sample of the population under study. Institutions participated voluntary, which may have led to some selection bias. However, average age (> 80 years) and gender distribution (> two – thirds women) were similar to previous studies in institutionalized older people on malnutrition and oral health, and because this study was carried out nationwide and with a large sample size, results of this study are most likely generalizable [18, 57, 58].

This study was furthermore strengthened by the use of valid [46], quick, inexpensive, and noninvasive methods to detect malnutrition and to subjectively asses oral health problems. Whereas other studies used the Mini Nutritional Assessment form, or invasive methods as serum albumin levels to identify malnutrition [1, 3, 4, 6, 18, 58], this study deviates from previous research by applying the most recent ESPEN definition of malnutrition [45]. The ESPEN definition of malnutrition goes beyond the BMI as the sole measure of malnutrition in older people and differentiates between age and gender [45]. It is based on two criteria [45], in which the first criterion focuses only on BMI below the lower

bound of 18.5 kg / m². The second criterion combines unintentional weight loss (%), age - specific BMI, and / or gender - specific Fat Free Mass Index (FFMI) to indicate malnutrition. However, FFMI has not been measured in the LPZ study, and therefore, malnutrition in the present study was based on age - specific BMI and unintentional weight loss (%). Statistical analysis did not show a difference in malnutrition among the three study years, which justifies the pooling of three observation rounds.

Conclusion

Poor oral health, mostly problems with eating due to (artificial) teeth problems, was associated with an almost twofold risk of malnutrition in older residents in Dutch nursing homes. Findings from this study suggest that oral health may play an important role in tackling malnutrition. Future longitudinal research is needed to confirm causation in the relation between malnutrition and oral health.

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Chapter 7

Design of the DYNAMO study: a multicenter randomized controlled trial to investigate the effect of pre-thickened oral nutritional supplements in nursing home residents with dysphagia and malnutrition (risk)

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Abstract

Introduction Oropharyngeal Dysphagia (OD) and malnutrition are frequently reported conditions in nursing home residents and are often interrelated. Best care for dysphagic residents with, or at risk of, malnutrition should target adequate nutritional intake and the safety and efficacy of swallowing. The effect of oral nutritional supplements (ONS) suitable for nursing home residents with concurrent OD and malnutrition (risk) on nutritional status has not been investigated before. The present study aims to investigate the effect of daily use of a range of pre - thickened ONS on the body weight of nursing home residents with OD and malnutrition (risk) compared to standard OD and nutritional care.

Methods / Design The DYNAMO study is a randomized, controlled, multi - center, open label trial with two parallel groups. Study participants will be recruited in nursing homes of several care organizations in the south of the Netherlands. Study duration is twelve weeks. Residents in the control group will receive standard OD and nutritional care, and residents in the test group will receive standard OD and nutritional care with extra daily supplementation of pre - thickened ONS. The main outcome parameter is the difference in body weight change between the control and test groups. An a priori estimation of the required sample size per group (control / test) totals 78. Other outcome parameters are differences in: nutritional intake, health - related quality of life, OD - specific quality of life, activities of daily living, vital signs, and blood nutrient and metabolite levels.

Discussion Regular ONS could address the nutritional needs of nursing home residents with malnutrition (risk), but might be too thin and unsafe for residents with OD. Pre - thickened ONS is suitable for residents with OD. It offers the advantage of being a ready - to - use amylase - resistant product available in several consistencies which are able to increase swallowing efficacy and safety. The DYNAMO study is the first to investigate the effects of pre - thickened ONS on nutritional status in nursing home residents with concurrent OD and malnutrition (risk).

Trial Registration Netherlands Trial Register (NTR): NTR NL7898. Registered 24 July 2019, https://www.trialregister.nl/trial/7898

Introduction

Malnutrition is frequently reported in nursing home populations, although prevalence rates vary considerably between studies, depending on the diagnostic criteria used [1, 2]. A recent study in Dutch nursing homes revealed that 20% of the residents was at risk of malnutrition [3]. A good nutritional status is essential for nursing home residents to maintain overall health, recover from disease, and optimize health - related quality of life (HRQoL) [4, 5]. Conversely, poor nutritional status, e.g., unintentional weight loss, is associated with higher morbidity [6] and mortality rates [7, 8], and lower HRQoL [9].

Nursing home residents are susceptible to malnutrition due to aging - related diseases, physiological changes in body composition and metabolism [10], care dependency [11], and swallowing impairment or eating difficulties [3]. Oropharyngeal dysphagia (OD) affects the efficacy and safety of swallowing as a result of aging - related functional bodily impairment or pathophysiological changes due to dementia, Parkinson's disease, or stroke. A Dutch prevalence study using a standardized questionnaire revealed a prevalence rate of 12% for subjective OD symptoms [12]. Dysphagic residents are at high risk of aspiration (pneumonia), dehydration, malnutrition, and weight loss [13]. A previous study by Carrión et al. [14] described a bidirectional relationship between OD and malnutrition, with 51% of the residents having OD and malnutrition (risk). While OD affects a resident's ability to eat, the consequences of malnutrition affect the ability to swallow; it is a vicious circle.

Nutritional care for dysphagic nursing home residents with malnutrition (risk) should thus simultaneously target adequate nutritional intake and the safety and efficacy of swallowing. Current European and Dutch guidelines for the management of OD and malnutrition suggest food fortification, oral nutritional supplementation (ONS), texture modification of solid food products, and / or thickening of liquids [15-17]. Thick, more viscous fluids tend to flow more slowly, and the assumption is that slower flow improves upper aerodigestive bolus control during swallowing. Studies suggest that increasing fluid thickness, i.e. the viscosity of the fluid, results in increased safety of swallowing, i.e. less aspiration risk [18, 19]. A more severe swallowing impairment often requires higher levels of fluid thickness to prevent aspiration [8].

The thickness of regular ONS is relatively low and is therefore not suitable for the majority of residents with OD and malnutrition (risk). The thickness of regular ONS can be further increased with a thickening powder, which is time consuming and offers an insufficient guarantee of obtaining the desired ONS thickness. Compared to regular ONS, pre - thickened ONS offers the advantage of being a ready – to - use, amylase - resistant product available in several consistencies (from drinkable to spoonable), which are able to increase swallowing efficacy and safety. A recent study showed increased product compliance and user - convenience with pre - thickened ONS compared to manually thickened ONS, with similar gastro - intestinal tolerability [20].

Benefits of ONS on nutritional status in nursing home residents with malnutrition (risk) were described previously [21-24], however no studies exist on the effect of pre - thickened ONS on swallowing in dysphagic nursing home residents. Scientific evidence on the effect of pre - thickened ONS for nutritional care in dysphagic nursing home residents having malnutrition (risk) is needed. The DYNAMO [1] study aims to investigate the effect of daily use of a range of pre - thickened ONS for twelve weeks on the body weight of nursing home residents with OD and malnutrition (risk) compared to standard OD and nutritional care.

Methods and design

Study design

The present study is a randomized, controlled, multi - center, open label (no blinding) trial with two parallel groups. The study duration is twelve weeks, preceded by an enrolment period including pre - screening, informed consent, and definitive screening. A flow diagram of participants is shown in figure 1. If eligible, nursing home residents are randomly allocated into the control or test group directly upon screening (1:1 ratio). Nursing home residents in the control group will receive standard OD and nutritional care, and will be compared to residents in the test group receiving standard OD and nutritional care with extra daily supplementation of the test product. Measurements are performed at baseline (t_1), 6 weeks (t_2), and 12 weeks (t_3). The schedule of enrolment, intervention, and assessments can be found in table 1.

Study population

The study will be carried out in nursing homes of several care organizations in the south of the Netherlands. Participants of the study will be nursing home residents who meet the eligibility criteria (table 2). All eligibility criteria, except for OD and malnutrition (risk), will be verified by the nursing home physician using the electronic patient file.

1 'DYNAMO' is an acronym for this randomized controlled trial (RCT) comprising of Oropharyngeal Dysphagia, Malnutrition, and Nursing and is Greek for life and vital force.

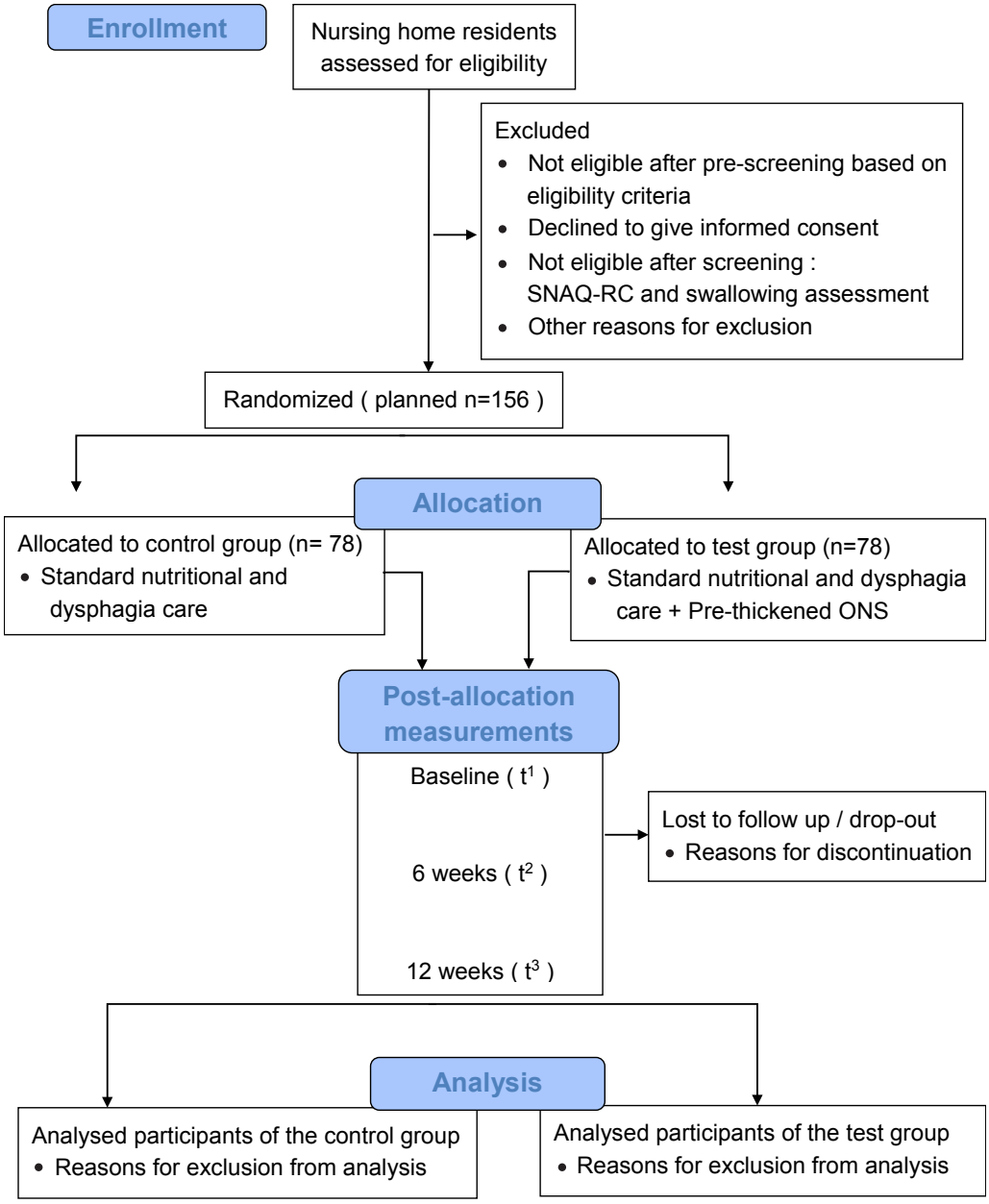

Figure 1. Flow diagram of participants of the DYNAMO study. Abbreviations: *SNAQ - RC; short nutritional assessment questionnaire for residential care.*

Pre - screening and screening

Nursing home residents who meet any of the exclusion criteria (table 2) will be excluded during pre - screening. Pre - screening will be conducted by a member of the trained study team. The validated short nutritional assessment questionnaire for

residential care (SNAQ - RC) [25] will be used as the screening tool for malnutrition (risk). The SNAQ - RC includes body mass index (BMI), unintended body weight loss, care dependency in feeding, and loss of appetite. A swallowing assessment will be carried out by a speech - and - language therapist (SLT) to screen nursing home residents for clinically relevant signs of OD. The swallowing assessment consists of four parts that are illustrated and clarified in table 3. Based on this swallowing assessment, the SLT determines the presence of OD and appropriate thickness of the test product.

Randomization

Eligible nursing home residents will randomly be allocated to the control or test group using the online randomization tool ALEA™ (ALEA Clinical by FormsVision, Abcoude, the Netherlands). Block randomization will be performed with 1:1 allocation based on nursing home (site), type of resident (legally capacitated *vs.* legally incapacitated to act for oneself), and varying block sizes of two and four.

Interventions

Standard OD and nutritional care

Both the control and test group will receive standard OD and nutritional care. Standard nutritional care in the present study is in line with the Dutch guidelines for malnutrition [15] and according to the most recent guideline on nutrition in geriatrics of the European Society for Clinical Nutrition and Metabolism (ESPEN) [17]. The control and test group receive dietary counseling and food fortification with enrichment of meals and provision of snacks in between meals. Regular ONS, possibly manually thickened to a safe thickness level, is provided only to the control group residents if food fortification is not sufficient to increase dietary intake and reach nutritional goals. Standard OD care is defined as the routine practice in each nursing home, with references to the Dutch guidelines for OD [16].

Test product

The test group will receive pre - thickened ONS (the test product) in addition to the standard OD and nutritional care without pre - thickened ONS. The commercially available test product (Nutilis® Complete, Nutricia, Zoetermeer, the Netherlands) is a food for special medical purposes and is provided in 125 mL bottles or 125 gr cups.

It is intended for dietary management of disease - related malnutrition and is a high energy, nutritionally complete pre - thickened supplement suitable for patients with swallowing difficulties. Previously conducted clinical and non - clinical studies did not reveal any safety concerns [26-28].

This ONS is pre - thickened to 4 standardized consistencies (i.e. with increasing thickness) that suits the different severity levels of OD, in accordance with the British Dietetic Association (BDA) guidelines [29]. The target viscosity (i.e. thickness defining its resistance to flow) of the pre - thickened ONS is 65, 450, 1200, and 3000 mPa*s at a shear rate of $50s^{-1}$ and a temperature of 20 °C. Table 4 shows an overview of the available flavors, energy density (kCal / 100 mL or g),

viscosity (mPa.s), BDA stage [29], and corresponding International Dysphagia Diet Standardization Initiative (IDDSI) level for each stage of the pre - thickened ONS [30].

For the test group, a trained SLT and a dietitian will provide a patient - tailored recommendation on the safest thickness level of liquids for swallowing and for the amount of nutritional supplementation (≥ 500 kCal or 2 - 3 units of test product per day).

Table 1. Schedule of enrolment, intervention, and assessments. Abbreviations: *SNAQ - RC; short nutritional assessment questionnaire for residential care, HRQoL; health - related quality of life, OD - specific QoL; oropharyngeal dysphagia - specific quality of life.*

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post - allocation**		
TIME POINT	**$-t_1$**	**0**	**$t_{1\ (baseline)}$**	**$t_{2\ (6\ weeks)}$**	**$t_{3\ (12\ weeks)}$**
ENROLMENT					
Pre – screening Eligibility criteria	X				
Informed consent	X				
Screening malnutrition (risk) SNAQ - RC	X				
Screening oropharyngeal dysphagia Swallowing assessment	X				
Allocation		X			
INTERVENTIONS					
Control group			—	—	—
Test group			—	—	—
ASSESSMENTS					
Body weight			X	X	X
3 - day food diary			X		X
1 - day food diary				X	
Oxygen saturation			X	X	X
3 - day compliance log (test group)				X	X
Product rating questionnaire (test group)				X	
Blood nutrient and hydration markers			X		X
Blood pressure			X		X
Heart - rate			X		X
Upper arm and calf circumference			X		X
Barthel Index			X		X
HRQoL assessment			X		X
OD - specific QoL assessment			X		X
7 - day ActivPAL3™			X	X	X
Activity log			X	X	X
Swallowing assessment					X

Table 2. Eligibility criteria for the DYNAMO study. Abbreviations: *ONS; oral nutritional supplementation*

Inclusion criteria	Exclusion criteria
• Permanent admission to / or living in a somatic or psychogeriatric ward • ≥ 65 years of age • Risk of malnutrition, or malnutrition • Oropharyngeal dysphagia • Informed consent	• Daily use of protein and energy containing ONS over a period of four weeks prior to screening • Daily use of enteral or parenteral nutrition over a period of four weeks prior to screening • Renal disease requiring dialysis • Both lower legs amputated • Known allergy or intolerance to any ingredient of the test product • Participation in any other study within 6 weeks prior to or after randomization • Known cachexia • Uncertainty about the willingness or ability of the resident to comply with the protocol requirements

Table 3. Content of the swallowing assessment. Abbreviations: *3 - OZ WST; 3 ounce water swallow test, WST; Water Swallow Test, MISA; McGill Ingestive Skills Assessment.*

	Assessment	Assessment details
Part I	3 - oz WST [31]	• Resident is asked to drink a glass of 3 oz. of water at room temperature while seated • SLT assesses whether glass is emptied without interruption and without signs of impaired swallowing such as impaired oropharyngeal bolus transit, oral cavity pooling, coughing, drooling, and voice change
Part II	Structured observation of oral intake	• Observation during a meal including solid, as well as liquid products • SLT focuses on maintenance of body posture, self - feed ability, and signs of impaired swallowing, and observations will be documented
Part III	WST with different thickness levels	• Water boluses with different thickness levels are prepared: water + thickening powder • Resident is asked to swallow at least three subsequent sips of the thickened bolus. • SLT determines the appropriate thickening of liquids for safe swallowing, i.e. the thickness at which the resident is able to swallow without showing signs of impaired swallowing
Part IV	Modified version of the MISA [32]	• Evaluation of functional ingestive skills of older persons: maintenance of symmetrical body posture and adequate head position for feeding, ability to grasp and use utensil and cup / glass functionally, appropriately - sized mouthfuls, voice quality after drinking, airway clearance after drinking, quantity of food remaining in mouth after swallowing, location of food remaining in mouth after swallowing, voice quality after earing, airway clearance after solids, ability to eat regular solids, soft solids, puree and pudding, and ability to drink water, thin juices, nectar, honey, and pudding

Blinding
Investigating the effect of the test product on top of standard OD and nutritional care precludes a (iso - caloric) control. Therefore, blinding is not possible and all assessors need to be informed of the intervention plan of the resident. The study coordinator will be involved in the data collection process, as well as in data analysis, which also precludes blinded data analysis.

Study outcomes

The primary outcome of the DYNAMO study is the difference in body weight change between the control and test group from baseline to final measurements after twelve weeks of intervention. Secondary outcomes are changes in nutritional intake, HRQoL, OD - specific QoL, and patient compliance to the test product. In addition, a food diary, oxygen saturation, blood nutrient and hydration markers, blood pressure, heart - rate, upper arm and calf circumference, Barthel Index, 7 - day activPAL3™, activity log, rating of the test product, and dysphagia severity will be assessed. Any (serious) adverse events ([S]AEs) will be monitored, evaluated, and documented. The relation of (S)AEs to the test product will also be evaluated by a medical doctor. Specific safety outcomes of the present study are: respiratory tract infection, urinary tract infection, dehydration, pressure ulcer, fall incident, all - cause hospitalization, and choking. An overview of study outcomes, corresponding instruments, and assessment details can be found in table 5.

Table 4. Overview of the test product range.

Pre - thickened ONS range	Flavors	Energy density *(kCal/100mL or 100g)*	Viscosity *(mPa*s)*	BDA[a] stage	Corresponding IDDSI[b] Level
Drink	vanilla / strawberry	200	65	n / a	2
Drink	vanilla / strawberry / lemon tea / mango passion fruit	245	450	1	3
Crème	vanilla / strawberry / chocolate	245	1200	2	3
Fruit	strawberry / apple	138	3000	3	4

[a] Severity levels of OD in accordance with the British Dietetic Association (BDA) guidelines [29]
[b] Framework of the International Dysphagia Diet Standardization Initiative (IDDSI) [30]

Monitoring and data management

All procedures and persons involved in the collection, handling, and storage of data and documents will be registered in a delegation log. Monitoring will be done by the Clinical Trial Centre Maastricht (CTCM). The data will be handled according to the EU General Data Protection Regulation (GDPR) and the Dutch Act on implementation of the GDPR. Encoded data will be stored in an electronic case report form (eCRF) hosted by an external vendor (Viedoc by PCG Solutions, Uppsala, Sweden).

Power calculation

Previous clinical trials on ONS in nursing home residents with malnutrition risk have shown a significantly increased body weight in residents who received ONS over a period of three to six months compared to residents receiving dietary recommendations or standard OD and nutritional care during this period [21-24]. In a large meta - analysis, Milne et al. (2009) [21] reported a significant weighted mean difference of 2.65% in body weight between patients with mixed geriatric conditions at risk of malnutrition using energy supplementation versus patients without energy supplementation. This equals an effect difference of ~ 1.4 kg for a person weighing 55 kg. This is in line with more recent studies reporting body weight change from baseline of 1.2 (± 2.4) kg [24], 1.22 kg (SEM 0.45) [23], and 1.4 (± 2.4) kg [39] after supplementation with ONS (500 - 600 kilocalories / day) for eight to twelve weeks in nursing home residents with malnutrition risk. Therefore, an increase of 1.4 (± 2.4) kg in body weight is assumed to be a reasonable expected mean outcome for the present test group. The mean body weight change for the control group is conservatively estimated to remain unchanged despite standard OD and nutritional care. Stange et al. (2013) [24] documented fourteen drop - outs from 87 residents (16%) in the test group. For the present study, we estimate a drop out percentage after randomization of 20%. Based on this a priori estimate with an alpha of 0.05 and 0.90 power, of the required sample size per group (control / test) was made and totals 78.

Data analysis

SAS / STAT® Software (by SAS Institute, North Carolina, USA) will be used for analysis of the encrypted data. Descriptive statistics of numerical data will be presented using mean and standard deviation (± SD) or median with interquartile range (IQR), and they will be checked visually for normality using histograms and Q - Q plots. Categorical data will be presented in terms of frequencies or percentages. Numerical data of compliance to the test product will be dichotomized into compliant and not - compliant. Generally, all analyses will be performed according to the intention - to - treat (ITT) principle. Only residents compliant to the intervention will be included in the per protocol analysis, which will be used as a sensitivity analysis for the ITT analyses. Linear mixed models will be performed to check for differences in primary and secondary outcome parameters between the control and the test group at different time - points with correction for baseline differences. A linear mixed model analysis will be used, as this method uses all available data, deals with correlation between repeated measures and assumes missingness to be at random.

Table 5. Overview of study outcomes, instruments, and assessment details. Abbreviations: *EQ - 5D - 5L; EuroQol 5 - dimensions 5 - level, VAS; Visual Analog Scale, EQ - VAS; EUROQoL - VAS, DSS; Dysphagia Severity Scale, DHRQoL; Dysphagia Related HRQoL, DAS; Dysphagia - related Anxiety Scale, 3 - oz WST3 ounce Water Swallow Test, MISA; McGill Ingestive Skills Assessment, (S)AE; (Serious) Adverse Event.*

	Outcome	Instruments	Score	Assessment details
Primary				
	Body Weight	Calibrated lift with integrated scale, mobile chair with integrated scale or wheelchair platform with integrated scale	Body weight weighed to the nearest gram	The resident is in fasting state and preferably dressed in light clothing and without shoes
Secondary				
	Nutritional intake	Standardized three - day food diary and a kitchen scale	Food products weighed to the nearest gram	Food products, leftovers, and napkins with spit out food pieces will be weighed by a member of the trained study team
	HRQoL and OD - specific QoL	Standardized questionnaire EQ - 5D - 5L [33] and VAS: EQ VAS, DSS, DHRQoL [34, 35], and DAS	EQ-5D descriptive system [no problems / slight problems / moderate problems / severe problems / extreme problems] EQ VAS [0 – 100 score], DSS [0 – 10 score], DHRQoL [0 – 10 score], DAS [0 – 10 score]	Self - assessment or proxy - assessment
	Compliance to test product	Standardized compliance log	Amount of product leftover [no leftover / quarter / half / three quarters / complete leftover]	Filled out by nursing staff
Exploratory				
	ADL	Validated Barthel Index (BI) [36]	0 [dependent] - 20 [independent]	Conducted by a member of the trained study team
	Activity	Activity monitor activPAL3™ (PAL Technologies Ltd., Glasgow, UK) [37, 38] with activity log	Steps [count], upright / sitting / lying position [hours], stepping / standing position [hours]	Applied and completed by a member of the trained study team
	Anthropometrics	Measuring tape	Upper - arm and calf - circumference [cm]	Conducted by a member of the trained study team

Table continues

	Blood nutritional - and hydration parameters	Laboratory analysis	Osmolality [mOsmol / kg], sodium [mmol / L], vitamin D [nmol / L], vitamin B12 [pmol / L], folate [nmol / L], magnesium [mmol / L], albumin (g / L), and calcium [mmol / L]	Clinical chemical and hematological laboratory of the Zuyderland Hospital (Heerlen-Sittard, the Netherlands)
	Vital signs	Electronic blood pressure monitor	Heart rate [bpm] and systolic and diastolic blood pressure [mmHg]	Conducted by a member of the trained study team
	Oxygen saturation	Oximeter	Oxygen saturation level [%]	Conducted by a member of the trained study team
	Dysphagia severity: swallowing assessment	3 - oz WST [31], swallow observation, water thickness test, Modified version of the MISA [32]	Swallow of 3 ounce water [positive / negative], descriptive report summary of swallow observation, safest thickness level of liquids for swallowing, completed modified MISA	Conducted by the trained SLT More details in table 3
	Palatability of the test product	Standardized questionnaire	Taste [1 (poor taste) - 10 (very tasty)], viscosity [too thick / good / too thin], sweetness [too sweet / good / not sweet enough], and swallowing ability [1 (very difficult) - 10 (very easy)]	Self - assessment
Safety				
	(S)AEs	(S)AE forms	MedDRA Medical Coding	Coding will be done by the data manager

Discussion

Due to the impairment of oral intake and swallowing, residents with OD are more prone to becoming malnourished [13]. Nutrient density of solid food decreases as water is added to blend the food product, [40] which in turn could increase the feeling of satiety without sufficient caloric intake. In addition, nutrition intake is further hampered because texture modification of solid food products and thickening of liquids with thickening powder may affect appetite and patient compliance [18, 19]. Hence, providing best care for this specific group of patients requires an interdisciplinary approach. The search for available and appropriate nutritional care for dysphagic residents is still ongoing and the need for tailored and practical solutions is becoming even more pressing due to the aging of the population [13].

The results of the DYNAMO study will help to enhance best care for nursing home residents with OD and malnutrition (risk). Best care encompasses the promotion of the safety and efficacy of swallowing and the optimization of the nutritional status. This study is the first study on the effect of pre - thickened ONS on nutritional status in a vulnerable group of nursing home residents with OD and malnutrition (risk).

We hypothesize that the test group will show an improved change of body weight compared to the control group after twelve weeks of intervention, based on results of previous studies with ONS supplementation in nursing home residents [21-24]. The effect is expected within a period of twelve weeks, meaning adjacent policy in care can be determined within this period. An extended study period will lead to unnecessary burden to the participants and a delay of the implementation of the intervention in standard care.

In addition, the previous studies were conducted in nursing home residents who did not specifically have OD and who were supplemented with regular ONS, i.e. not specifically designed and likely not suitable for residents with OD. Providing a pre - thickened ready – to – use, amylase - resistant ONS with a consistency that suits the severity levels of OD could improve swallowing efficacy and safety and oral intake compliance in nursing home residents with OD and malnutrition (risk). This in turn could have positive effects on the nutritional status. The present study therefore also includes QoL, ADL, dietary intake, intake compliance to the test product, and other parameters related to nutritional status. Associations between these parameters will be assessed since improving nutritional status with ONS may further lead to improved QoL and ADL [41].

Practical implementation of the DYNAMO study was closely aligned with nursing home staff and experts in the field of OD and malnutrition. Assessment tools and measurements used in the present study are based on standard OD and nutritional care where possible. For example, SNAQ - RC was used to screen for malnutrition (risk) as this is the standard tool for residential care in the Netherlands. Dutch national OD guidelines recommend bedside screening assessments like a WST and a clinical observation of oral intake [16, 42]. Although the psychometric limitations of these methods are known, instrumental swallowing assessments with a higher sensitivity and specificity, i.e. videofluoroscopy of swallowing (VFS) or fiberoptic / flexible endoscopic

evaluation of swallowing (FEES) [13], have practical limitations and are therefore not part of the standard nursing home care. In the present study, OD screening will be carried out using a combination of existing practice (WST / water thickness test and swallowing observation) and a simplified version of a validated evaluation of functional ingestive skills of older persons (MISA) in order to obtain a patient - tailored recommendation on the safest thickness level for liquids.

Practical implementations and ethical considerations made it impossible to blind participants and assessors in this study. To the best of our knowledge, we have made every effort to limit the effects of this limitation. Participants are randomly allocated to a treatment arm and intervention procedures (apart from the intervention) are standardized for both treatment groups. The primary measure of the study is an objective and valid measure, all measurements are in line with standard care practice and possible effects will be considered in the analysis of the study outcomes.

This pragmatically controlled study closely reflects standard OD and nutritional care and study outcomes therefore have real - life applicability. Execution of standard care in the study design also entails a number of limiting factors. Most importantly, standard care may differ slightly between nursing homes and proper study execution is highly dependent on the engagement of all involved healthcare professionals. Both somatic and psychogeriatric nursing home residents will be included, since OD and malnutrition (risk) are common in both populations. This will result in a highly heterogeneous population, increasing outcome variability. In addition, including incapacitated residents limits some assessments or limits some assessments to be completed by a caretaker. A priori estimation of the inclusion rate is difficult, specifically, the informed consent rate, i.e. the willingness of residents or their legal representatives to participate. Hence, the inclusion rate will be closely monitored.

Dutch nursing homes often comprise of long - term somatic and psychogeriatric wards and short - term rehabilitation wards. Residents at rehabilitation wards follow a rehabilitation trajectory (e.g., after stroke). They are temporarily in need of high intensity care and leave the nursing home after a short period of time. Future studies could also target a group of rehabilitation residents with OD and concurrent malnutrition (risk). In addition, the body of literature on non - institutionalized older populations at risk for OD and malnutrition is poor.

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Chapter 8

General Discussion

In this chapter we discuss the observations and conclusions drawn from this dissertation. In part I of this dissertation, the quality of nutritional care in hospitals was explored as part of an international collaborative project, the National Prevalence Measurement of Quality of Care (Landelijke Prevalentiemeting Zorgkwaliteit [LPZ]) [1], regarding the quality of basic care in hospitals and nursing homes (**part I**). Overall prevalence rates of the risk of malnutrition in Austrian, Swiss, and Turkish adult hospitalized patients were presented along with the differences in quality indicators of nutritional care in these hospitals. In part II and part III, the associations between malnutrition, oropharyngeal dysphagia, and poor oral health were explored in stroke patients (**part II**) and in nursing home residents (**part III**).

Overall, this dissertation endorsed points of attention regarding the performance of nutritional care in European hospitals and the prevalence of malnutrition (risk) in stroke patients and in nursing home residents with oropharyngeal dysphagia and / or poor oral health. We have shown that prevalence rates of malnutrition (risk) are still high, despite the commonly known red flags of health risks in stroke patients and nursing home residents. Our findings may contribute to create more awareness on the importance of nutritional care in these patients, as this is generally under - acknowledged [2-4].

The quality of nutritional care determines the alignment of care with the patient's needs and preferences and contributes to the patient's benefit of care, including the therapy effect of a nutritional intervention, or the extra attention when a dietitian or nutritionist is involved in the patient's care. In the next sections, we first reflect upon our findings regarding the most relevant quality indicators of nutritional care in the hospital setting, including the performance of nutritional screening and nutritional interventions. Thereafter we address meaningful insights for healthcare from our research on components and associations of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents.

Nutritional screening

International and national standards [5-7] recommend timely standard nutritional screening to early identify patients at risk of a condition such as malnutrition [8]. Following nutritional screening, further diagnostic nutritional measurements and tailored treatment determine the actual benefit for the patient at risk of / or with malnutrition, including amongst others, an improved nutritional status, prevention of complications, decreased healthcare costs, and last but not least a better health - related quality of life. In line with the recommendations for standard screening, we found that the prevalence rates of malnutrition risk in various European hospital settings were indeed lower when nutritional screening was common practice (chapter 2). Similar findings were reported in earlier studies in hospitals [9] and long - term care settings [10].

In our cross - sectional study in chapter 2, we showed that nutritional screening was conducted in approximately half or less than half of the adult hospitalized patients in the European countries involved in our study. This may

partially be explained by a lack of resources including the presence of a nutritionist, screening materials, or knowledge of malnutrition [11]. Furthermore, patients may have been too ill to be assessed [12], or other care tasks might be prioritized [13]. Prevalence rates of (the risk of) malnutrition may therefore be an underestimation of the actual severity of the situation. Overall, there is an urge for greater awareness on malnutrition in the hospital [14].

Despite available evidence and national and international clinical guidelines on best practices for nutritional care, we showed that the implementation of nutritional screening in various healthcare settings also leaves much room for improvement considering the high prevalence rates of malnutrition (risk) in stroke patients (chapter 3 and chapter 4) and in nursing home residents (chapter 5 and chapter 6). Meijers et al. (2009) [15] drew similar conclusions from a multicenter study in the Netherlands addressing the quality of nutritional care in various healthcare settings. The seriousness of the situation in various healthcare settings, in respect to the high prevalence rate of malnutrition (risk), has been confirmed by a recent systematic review on malnutrition risk in European older adults; close to half of all European older adults were at risk of malnutrition [16]. Furthermore, up to 28.0% of the hospitalized older adults and 17.5% of older adults in residential care facilities were at high risk of malnutrition [16].

Nutritional interventions

Along with these insights on nutritional screening, in our study in chapter 2 we observed interesting and maybe some paradoxical insights on nutritional interventions, including the provision of nutritional information and oral nutritional supplementation. Prevalence rates of malnutrition risk in the hospitals in our study were lower when nutritional information was provided to patients and their relatives. The provision of patient - tailored nutritional information, e.g., about health risks and the benefits of nutritional treatments, may increase the awareness of patients regarding the risk and negative health consequences of malnutrition. This informative communication and improved awareness may benefit the compliance to treatment [4].

On the contrary and maybe paradoxically, we found the highest prevalence rates of malnutrition risk in the country with the lowest prevalence rate of standard nutritional screening but simultaneously the highest number of referrals to a dietitian, and the highest use of oral nutritional supplementation or parenteral nutrition (chapter 2). More attention for nutrition via the involvement of a dietitian or nutritionist may thus have led to the detection of more cases at risk of malnutrition as the high prevalence rates of referrals to dietitians were accompanied by increased expenditure of oral nutritional supplementation. Similar observations were reported in the nursing home setting by Streicher et al. (2017) [17]. However, also variations in reimbursement regulations [18] or ethical considerations [19] may partially explain the increased use of oral nutritional supplementation in relation to high prevalence rates of malnutrition.

The patient's benefits of nutritional care eventually depend on the alignment of care - to the patient's needs: energy requirements, nutritional status, and eating capabilities and preferences. The provision of nutritional interventions including oral nutritional supplementation should ideally be based upon the results of a comprehensive diagnostic measurement, the above - mentioned needs and preferences of the patients, and on shared decision making by healthcare professionals and patients regarding the actual treatment goals.

In the next two sections, we discuss our findings related to the components and associations of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents. Also the coherence of these health conditions is addressed as previous studies demonstrated an increased risk of malnutrition related to oropharyngeal dysphagia and poor oral health in these populations [20, 21].

Malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients

In line with research from various national and international research groups [20-27], we have shown that the (risk of) malnutrition often occurs in stroke patients with oropharyngeal dysphagia and also in nursing home residents with oropharyngeal dysphagia and / or a compromised oral health status. A number of current clinical practice guidelines in this field already deliberate on the coherence of two or all three components of the triad [28-30]. However, in daily practice, despite efforts made on integration of care, healthcare is often still conducted rather fragmentarily and more targeted at the individual components [31]. In this regard, this dissertation once more draws attention to the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in patients at risk, such as stroke patients and nursing home residents.

Our review in chapter 3 provided a comprehensive overview of pooled prevalence rates of patients with impaired nutritional condition for all phases after stroke. In our study, high prevalence rates of impaired nutritional condition were particularly found in the acute, early subacute, and chronic [32] phase after stroke. Considering the already compromised overall health condition of post - stroke patients, an impaired nutritional condition signifies increased risks of complications of malnutrition or poor clinical outcomes [33, 34].

Subsequently, we conducted a cross - sectional study in a specific sample of referred stroke patients with persistent swallowing problems in a Dutch outpatient clinic for oropharyngeal dysphagia (chapter 4). Almost every second patient in this sample of consecutive patients had a moderate or high risk of malnutrition. Even more increased prevalence rates of the risk of malnutrition were found in the subgroup of patients with worse severity degrees of oropharyngeal dysphagia. Given these findings, it is possible that there are also many hidden cases of patients with risk of malnutrition among stroke patients with less severe or persistent swallowing complaints.

These insights showed us that attention must be paid to stroke patients' nutritional status and swallowing function throughout the entire patients' care trajectory. This also means, monitoring patients, independent of the setting in which they rehabilitate or reside, as is also recommended for patients with head and neck cancer within the first five years after diagnosis [35]. For stroke care, such an approach may require a more intensive multi -, inter -, and transdisciplinary collaboration of healthcare professionals.

Stroke is, along with dementia, the most prevalent diagnosis for nursing home admission [36], emphasizing that acute and long - term care for stroke patients with intensive long - term care needs are also interlinked. Therefore, transdisciplinary care, in various healthcare settings throughout the entire course of the patients' care trajectory is indicated.

Malnutrition, oropharyngeal dysphagia, and poor oral health in nursing home residents

This brings us to our findings in nursing home residents. In the Netherlands, the nursing home population consists of residents often with multimorbidity and handicaps that may affect safe and efficient swallowing and chewing of food. These morbidities and their related handicaps involve amongst others impaired sensory feedback, motor programming and execution, and impaired cognitive processing, and / or years of neglected oral health, decayed dentures, or missing teeth and (pre)molars [37, 38]. Therefore the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health also needs attention in these residents, as the triad is closely related to the residents' overall health and health - related quality of life [39-42].

In our studies, every tenth resident of a large representative sample of Dutch nursing home residents (chapter 5 and chapter 6) was malnourished and an approximately equal amount of residents reported clinically relevant symptoms of oropharyngeal dysphagia. Oral health problems were found in almost half of this population. Our studies also demonstrated an almost twofold risk of malnutrition in residents with oropharyngeal dysphagia or poor oral health as compared to residents without these conditions. Herewith, the findings of national and international researchers regarding the association between these conditions in nursing home residents are confirmed [21, 23, 24].

Apart from the underlying pathophysiology of malnutrition, oropharyngeal dysphagia, and poor oral health in these residents, our findings may partially be explained by barriers in providing and receiving care related to these conditions in the nursing home. Residents with dementia may refuse help with for instance oral hygiene or the applied healthcare routines are not in line with guidelines for these conditions. In recent years substantial work has been done to optimize nutritional care in the nursing home setting [10, 43-45]. However, we should not underestimate that there is still plenty of room for improvement. Improvements were made in the field of modified diets for oropharyngeal dysphagia, e.g., texture modified diets, but the scientific evidence regarding the effectiveness of these

diets is still very limited [46, 47]. Furthermore, standard screening of residents for oropharyngeal dysphagia is rather unusual in nursing homes [47-49]. Screening methods for dysphagia with good psychometric properties are scarce [50], the resources, including time and manpower to screen all residents may be insufficient, the access to speech - language therapy may be difficult, or the use of instrumental swallowing assessments is problematic [48].

There have also been changes in attitudes towards dentition and oral healthcare at old age. Older people more often retain their natural dentition, which brings along new challenges for daily care [51, 52]. Though there are relevant oral healthcare guidelines, such as the Dutch National Guideline for oral care in nursing homes [53], oral healthcare routines in Dutch nursing homes are still incompliant with these guidelines [54, 55]. In many long - term care settings, oral healthcare is still not considered a structural part of daily routine care [54]. Meanwhile, studies have underlined the beneficial effect of improved oral health, e.g., properly fitting dentures and normal saliva secretion, on the swallowing function in an older population [26, 56, 57] and thereby also on the nutritional status.

Finally, it has been noticed that also in nursing home residents, despite existing clinical practice guidelines, the conditions malnutrition, oropharyngeal dysphagia, and poor oral health are still approached in a fragmentary and not in an interdisciplinary way [58, 59]. This may explain that the prevalence rates of malnutrition remain considerably high in patients with oropharyngeal dysphagia and / or poor oral health.

Implications

The findings in this dissertation urge for awareness among healthcare professionals, policymakers, and patients about the negative consequences of malnutrition, oropharyngeal dysphagia, and poor oral health and for the fact that these conditions are associated with each other in stroke patients and nursing home residents.

Awareness of healthcare professionals regarding the negative consequences of malnutrition, oropharyngeal dysphagia, and poor oral health may partially depend on the attention paid to these conditions during their professional education. We recommend the inclusion of our findings regarding the association between malnutrition, oropharyngeal dysphagia, and poor oral health in the education of allied health and medical professionals. In the context of improving quality of care, the competences of healthcare professionals regarding these health conditions may be evaluated and compared between institutions. This evaluation of competences may eventually provide policy makers and educators with insights on areas that deserve more attention, e.g., standard screening, and multi -, inter -, and transdisciplinary collaboration.

Thereupon we recommend to conduct standard nutritional screening in all adult hospitalized patients and more specifically also in stroke patients and nursing home residents to identify patients at risk of malnutrition. A comprehensive diagnostic measurement and clinical reasoning by an expert healthcare professional should follow in patients with an abnormal screening result. This diagnostic

measurement and reasoning determines the underlying causes and potential complications, and tailors the treatment to the needs, preferences, and capabilities of the patient.

This brings us also to the implications of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents. Even though the associations between these conditions are partly acknowledged in some clinical practice guidelines, both the enhancement of guidelines and a better translation of such guidelines into more integrated care remain major points of improvement. With 'integrated care' we refer to models of multi -, inter -, and transdisciplinary care for patients at risk of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health. Promoting care for all three components of the triad concurrently through collaboration of healthcare professionals from different disciplines, the integration of knowledge and practices across disciplines, and the connection of healthcare and service systems.

Guidelines can be underpinned by more integrated research on these intertwined health conditions in stroke patients and nursing home residents. Research may focus on therapy effect studies on all three components, as well as on their combined feasibility, contribution to integrated care, and cost - effectiveness. In this context, also more attention and problem solving strategies for barriers and facilitators of guideline implementation in clinical practice, such as professional training, time constraints, and manpower, are needed.

The DYNAMO study (chapter 7) may provide opportunities for the collection of high - quality evidence regarding the nutritional status of nursing home residents with oropharyngeal dysphagia and the use of pre - thickened oral nutritional supplements in these residents. The protocol of this study encompasses a comprehensive diagnostic swallow examination and nutritional screening. The intervention study is tailored to daily practices in the nursing home to collect reliable data and at the same time limit the burden of residents and healthcare professionals. The study has also been designed to explore changes in the health - related quality of life of these residents during the course of the intervention. Unfortunately, the study already had to be terminated in its earliest phase, due to the COVID - 19 pandemic. We recommend the actual execution of this study in the future as the study can generate interesting data and insights for research, clinical practice, and well - being of the patients.

Methodological reflections

Scientific knowledge, preferably conclusive evidence, is needed to provide strong recommendations to promote integrated care for malnutrition, oropharyngeal dysphagia, and poor oral health in clinical practice guidelines. However, we have come across a number of factors that complicate the generation of conclusive evidence and pooling of findings for a meta - analysis to obtain new insights. In this section, we discuss the problems arising from diversity in examination methods of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and

nursing home residents. Likewise the scarcity of currently available (longitudinal) data in chronic stroke patients is addressed.

For the systematic review and meta - analysis in chapter 3, we had to introduce the term 'impaired nutritional condition' to be able to compare data from the various nutritional screening and diagnostic measurements used to describe the patients' nutritional status in the literature over the past 20 years. Diversity of methods and heterogeneity of patients may lead to poor discrimination of results of nutritional screening and diagnostic measurements [60] which may result in incomparable prevalence data complicating the performance of a meta - analysis. Despite the diversity in screening and diagnostic measurements we were able to compare the data based on a self - developed set of criteria of impaired nutritional condition. A global consensus on diagnostic criteria of malnutrition in adults has been reached recently [61, 62]. The studies in the present dissertation are based on the available knowledge and guidelines at the time of conduction and therefore these recently developed criteria are not included.

Furthermore, the meta - analysis, thus the pooling of data, as described in chapter 3 was also complicated by the lack of (longitudinal) data regarding the nutritional status of stroke patients in the late subacute and chronic phase after stroke. The lack of data in these phases may partially be attributed to a lack of follow - up research in this population. Follow - up of stroke patients may be hampered by the high (~ 60.0%) 5 - year mortality rate of older stroke patients [63], or by the transfer of stroke patients between healthcare settings. To generate scientific evidence for future optimization of clinical practice guidelines, more data about the entire course of the patients' care trajectory are needed.

Concluding remarks

Overall, the findings in this dissertation urge for standard nutritional screening of all adult hospitalized patients and for more awareness regarding the negative consequences and associations of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke and nursing home patients. Though highly prevalent, this triad is under - acknowledged, instigating dormant health risks in these patients. Future research is needed to generate more conclusive evidence to promote integrated care for patients at risk of this dormant triad.

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Summary

This paragraph of the dissertation summarizes its aim and findings, our implications for future research and clinical practice, and starts with a brief introduction on the topic.

The growing population of chronically ill patients and geriatric patients, e.g., stroke patients and nursing home patients, is challenging the current healthcare systems worldwide. A profile of multimorbidity and comorbidity, including malnutrition, oropharyngeal dysphagia, and poor oral health, associated with care dependency and poor clinical outcomes often dominates in these patients. Furthermore, there is evidence of associations within the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in these patients. **(chapter 1)** This dissertation aimed to assess quality indicators of nutritional care in hospitals (part I) and to gain knowledge and reflect on the associations between malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents (part II and part III).

In part I we addressed prevalence rates of the risk of malnutrition in hospitals in Austria, Switzerland, and Turkey and explored differences in quality indicators of nutritional care between these hospitals **(chapter 2)**. Data were collected as part of an international collaborative project (National Prevalence Measurement of Quality of Care [LPZ]). Prevalence rates varied between 14.5% and 33.7% and we found substantial differences in the diagnosis (e.g., the implementation of a standardized nutritional screening) and the treatment (e.g., the provision of oral nutritional supplementation) of malnutrition risk, and regarding the fulfillment of structural quality indicators on ward and institution level (e.g., participation of caregivers in educational refresher courses). We found lower prevalence rates of malnutrition risk when nutritional screening was common practice, though simultaneously we showed that the performance of nutritional screening in the hospital was low despite international and national standards. On the contrary and maybe paradoxically, highest prevalence rates of malnutrition risk were shown when oral nutritional supplementation was provided more often and patients were more often referred to a dietitian. These findings suggest an increased detection rate of cases at risk of malnutrition if extra attention is paid to nutrition via a dietitian or nutritionist. Our findings reinforce the importance of standard nutritional screening to timely identify patients at risk of malnutrition.

Therefore, we recommend standard nutritional screening of all adult hospitalized patients. This may minimize the risk of poor clinical outcomes for patients with abnormal screening results, provided that a comprehensive diagnostic measurement is performed in patients with an abnormal screening result and that the patient is adequately treated and monitored. This process allows shared decision making regarding actual treatment goals, and taking into consideration the patient's needs, capabilities, and preferences.

In stroke patients and in nursing home residents with additional risk of oropharyngeal dysphagia and poor oral health, nutritional treatment may need to be tailored to the patient's swallowing and chewing capabilities. This brings us to part II and

part III of this dissertation in which we addressed the prevalence and associations between malnutrition, oropharyngeal dysphagia and poor oral health in these two patient groups.

In part II we concentrated on the nutritional condition of stroke patients throughout the entire patients' care trajectory **(chapter 3)** and subsequently on a sample of referred stroke patients in an interdisciplinary outpatient clinic for dysphagia **(chapter 4)**.

We first conducted a systematic review of the literature from the past 20 years. Large diversity was found in nutritional screening and diagnostic measurements applied over these years. We therefore introduced the term 'impaired nutritional condition', referring to all not well - nourished patients as supported by a list of criteria. Our pooled prevalence estimates showed high prevalence rates of stroke patients with impaired nutritional condition (not well - nourished) across the continuum of care. Thus despite clinical guidelines, many stroke patients with already a compromised overall health status still have to cope with malnutrition and related complications and poor clinical outcomes in the aftermath of stroke. In addition to the above stressed importance of nutritional screening, we also emphasize the importance of monitoring nutritional status along the entire stroke patients' care trajectory.

In the context of our findings on stroke patients in the chronic phase after stroke, our review also underlined the considerably low number of (longitudinal) studies performed in the late subacute and chronic phase after stroke. To optimize clinical guidelines in the future and improve the care for stroke patients, there is thus an overall need for uniformity in nutritional screening and diagnostic measurements and also for more overall evidence related to the total care trajectory of patients with chronic disorders.

In our study following upon this review, we aimed to describe a specific sample of referred stroke patients with persisted complaints of oropharyngeal dysphagia. We revealed that almost every second patient had moderate or high risk of malnutrition. Even higher prevalence rates of the risk of malnutrition were found in the subgroup of patients with worse severity degrees of oropharyngeal dysphagia.

Therefore, both health conditions, malnutrition and oropharyngeal dysphagia, should receive adequate attention in these stroke patients. On the one hand to improve the overall health and quality of life of the patient and on the other hand to prevent possible hidden cases with risk of malnutrition among stroke patients with less severe or persistent swallowing complaints.

In part III of this dissertation, our research was extended to the nursing home population. This population encompassed residents with various chronic disorders and for many the main diagnoses included stroke and dementia. Prevalence figures and associations of malnutrition risk in relation to clinically relevant symptoms of oropharyngeal dysphagia on the one hand **(chapter 5)** and poor oral health on the other hand **(chapter 6)**, were addressed. Data were collected as part of the Dutch LPZ measurement. We have shown that approximately one out of ten residents was malnourished. Clinically relevant symptoms of oropharyngeal

dysphagia were seen in an equal amount of residents and in almost half of the population the oral health status was poor. Above all, our findings showed that there is a clear association between malnutrition and respectively clinically relevant symptoms of oropharyngeal dysphagia and poor oral health in this population. More specifically, nursing home residents with oropharyngeal dysphagia or poor oral health demonstrated an almost twofold risk of malnutrition as compared to residents without these health conditions. Herewith, we have underpinned findings from previous international research. Malnutrition, oropharyngeal dysphagia and poor oral health are perpetual health conditions in this population despite the substantial work that has been done to optimize care over the past years. National and international colleagues have addressed the poor alignment of oral healthcare with available guidelines and also expressed concerns regarding standard screening for oropharyngeal dysphagia and the poor evidence regarding the effectiveness of dysphagia diets in this population. On top of this, the often fragmented approach in care does not benefit the overall care in this population.

We strongly encourage more awareness regarding the negative consequences and associations of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents. In addition, we encourage the multiplication of conclusive evidence to promote integrated, thus multi -, inter -, and transdisciplinary care across the entire patients' care trajectory.

Our DYNAMO study **(chapter 7)** may be considered as a steppingstone for future, more interdisciplinary research in the field of malnutrition and oropharyngeal dysphagia. The study targets specifically at the rather understudied population of nursing home residents and aims to generate insights on the effect of an innovative nutritional intervention using a pre - thickened oral nutritional supplement in dysphagic nursing home residents with risk of malnutrition. We strongly recommend the actual execution of this study soon, provided that the disturbing effects of the Covid pandemic are no longer of strong concern.

In the final chapter of this dissertation **(chapter 8)** we have discussed our findings in a broad context of national and international research in the field of malnutrition, oropharyngeal dysphagia, and poor oral health in various settings and patient populations.

Overall, our findings reiterate concerns and endorse attention points regarding the performance of nutritional care in European hospitals and the prevalence rates and associations of the health conditions malnutrition (risk), oropharyngeal dysphagia and poor oral health in stroke patients and in nursing home residents. We urge for standard nutritional screening of all adult hospitalized patients and awareness regarding the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents. We strongly encourage improvements in care underpinned by innovative and integrated research on the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health.

Samenvatting

In dit onderdeel van het proefschrift worden de doelen en bevindingen van onze onderzoeken samengevat inclusief de implicaties voor toekomstig onderzoek en de klinische praktijk. De groeiende populatie van chronisch zieke en geriatrische patiënten, waaronder patiënten met een beroerte en verpleeghuisbewoners, is een wereldwijde uitdaging voor de huidige zorgsystemen. Deze patiënten vertonen veelal een profiel van multimorbiditeit en multipele zorgproblemen, zoals ondervoeding, dysfagie en slechte mondgezondheid, geassocieerd met een hoge mate van zorgafhankelijkheid en slechte klinische uitkomsten. In de algemene inleiding wordt ingegaan op de zorgproblemen ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid en ook op de mogelijke associaties tussen deze problemen **(hoofdstuk 1).**

Dit proefschrift had tot doel de kwaliteitsindicatoren van voedingszorg in ziekenhuizen te beoordelen (deel I) en kennis op te doen alsmede te reflecteren op de associaties tussen ondervoeding, orofaryngeale dysfagie en een slechte mondgezondheid bij patiënten met een beroerte en bij verpleeghuisbewoners (deel II en deel III).

In deel I worden prevalentiecijfers van het risico op ondervoeding in ziekenhuizen in Oostenrijk, Zwitserland en Turkije gepresenteerd en worden ook de verschillen in kwaliteitsindicatoren van voedingszorg tussen deze ziekenhuizen onderzocht (**hoofdstuk 2**). De gegevens zijn verzameld in het kader van een internationaal samenwerkingsproject, *The International Prevalence Measurement of Quality of Care (LPZ-International)*, welke gebaseerd is op de Landelijke Prevalentiemeting Zorgkwaliteit [LPZ], die jaarlijks in Nederland verricht wordt vanuit de Universiteit Maastricht.

De prevalentiecijfers van het risico op ondervoeding varieerden tussen 14,5% en 33,7% en er werden substantiële verschillen in de diagnostiek (bijvoorbeeld de implementatie van een gestandaardiseerde voedingsscreening) en de behandeling (bijvoorbeeld het verstrekken van orale voedingssupplementen) van het risico op ondervoeding gevonden. Ook de uitvoering van activiteiten in het kader van structurele kwaliteitsindicatoren op afdelings- en instellingsniveau (bijvoorbeeld deelname van zorgverleners aan opfriscursussen) verschilden.

Lagere prevalentiepercentages van het risico op ondervoeding werden gevonden als er sprake was van een standaard voedingsscreening. Tegelijkertijd toonden we aan dat, ondanks aanbevelingen van gangbare internationale en nationale richtlijnen, standaard voedingsscreening bij patiënten in de ziekenhuizen van deze landen laag was. Daarentegen, en misschien wel paradoxaal, werden de hoogste prevalentiepercentages van het risico op ondervoeding gevonden als orale voedingssuppletie vaker werd gegeven en ook als er vaker werd doorverwezen naar een diëtist. Deze bevindingen suggereren dat meer patiënten met een risico op ondervoeding ontdekt kunnen worden wanneer extra aandacht wordt besteed aan hun voeding via een diëtist of voedingsdeskundige. Deze bevindingen versterken derhalve het belang van de toepassing van een standaard voedingsscreening in

ziekenhuizen om patiënten met een risico op ondervoeding tijdig te identificeren. Daarom ook raden we standaard voedingsscreening aan bij alle volwassen patiënten in het ziekenhuis. Dit kan immers het risico op slechte klinische uitkomsten minimaliseren, op voorwaarde dat een goed diagnostisch en therapeutisch vervolgtraject is ingericht voor patiënten met een abnormaal screeningresultaat.

Bij patiënten met een beroerte en bij verpleeghuisbewoners met verhoogd risico op orofaryngeale dysfagie en een slechte mondgezondheid moet een voedingsbehandeling mogelijk worden aangepast aan het slik- en kauwvermogen van de patiënt. Dit brengt ons bij deel II en deel III van dit proefschrift waarin de prevalentie en associaties tussen ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid bij deze twee patiëntengroepen zijn onderzocht.

In deel II hebben we ons geconcentreerd op de voedingstoestand van patiënten met een beroerte gedurende het gehele zorgtraject van deze patiënten (**hoofdstuk 3**). Vervolgens hebben wij ons onderzoek gericht op een steekproef van doorverwezen patiënten met een beroerte die een interdisciplinaire polikliniek voor dysfagie bezochten (**hoofdstuk 4**).

We hebben eerst een systematische literatuurstudie (literatuur review) uitgevoerd op basis van de literatuur van de afgelopen 20 jaar over een verminderde voedingstoestand na een beroerte, vanaf de acute tot en met de chronische fase. Hierbij werd een grote diversiteit aan screeningsmethoden voor de voedingstoestand en voedinggerelateerde diagnostische metingen gevonden die in de afgelopen jaren zijn toegepast. Om eenduidigheid voor onze reviewstudie te realiseren, introduceerden we de term 'verminderde voedingstoestand', verwijzend naar alle niet goed gevoede patiënten en ondersteund door een lijst met criteria. De gepoolde prevalenties lieten hoge prevalentiecijfers zien van patiënten met een verminderde voedingstoestand over het hele zorgcontinuüm van patiënten met een beroerte.

Geconstateerd werd dat, ondanks diverse klinische richtlijnen, veel patiënten met een beroerte nog steeds te maken hebben met ondervoeding en daaraan gerelateerde complicaties en slechte klinische uitkomsten. Naast het hierboven al genoemde belang van voedingsscreening, benadrukken we derhalve ook het belang van monitoring van de voedingsstatus van patiënten met een beroerte gedurende het hele zorgtraject.

In de context van onze bevindingen, onderstreepte onze review ook het lage aantal (longitudinale) studies dat tot nu toe uitgevoerd is in de chronische fase na een beroerte. Om klinische richtlijnen in de toekomst te optimaliseren en de zorg voor patiënten met een beroerte te verbeteren, is uniformiteit in voedingsscreening en diagnostische metingen nodig en is er ook echt behoefte aan meer wetenschappelijke inzichten met betrekking tot het totale zorgtraject van patiënten met chronische aandoeningen, zoals een beroerte.

In de studie die volgde op deze review, wilden we een specifieke steekproef van

doorverwezen patiënten met een beroerte en met aanhoudende klachten van orofaryngeale dysfagie beschrijven. We vonden dat bijna elke tweede patiënt in deze groep een matig of hoog risico op ondervoeding had. De prevalentiepercentages van het risico op ondervoeding waren het hoogst in de subgroep van patiënten met een ernstige mate van orofaryngeale dysfagie.

Daarom moeten beide gezondheidsproblemen, dus zowel ondervoeding als orofaryngeale dysfagie, voldoende aandacht krijgen in deze groep patiënten met een beroerte. Enerzijds om de algehele gezondheid en kwaliteit van leven van de patiënt te verbeteren en anderzijds om ervoor te zorgen dat mogelijk verborgen casussen van patiënten met risico op ondervoeding en minder ernstige of minder opvallende slikklachten te voorkomen.

In deel III van dit proefschrift werd ons onderzoek uitgebreid naar de verpleeghuispopulatie. Deze populatie omvat verpleeghuisbewoners met verschillende chronische aandoeningen waarbij de belangrijkste hoofdiagnosen vaak een beroerte en dementie zijn. We onderzochten prevalentiecijfers en associaties van risico op ondervoeding in relatie tot klinisch relevante symptomen van orofaryngeale dysfagie enerzijds (**hoofdstuk 5**) en een slechte mondgezondheid anderzijds (**hoofdstuk 6**). Gegevens werden verzameld als onderdeel van de eerdergenoemde Nederlandse LPZ-meting.

We hebben aangetoond dat ongeveer een op de tien verpleeghuisbewoners ondervoed was. Klinisch relevante symptomen van orofaryngeale dysfagie werden gezien bij een even zo grote groep bewoners. We zagen ook dat bij bijna de helft van de verpleeghuisbewoners sprake was van een slechte mondgezondheid. Bovenal lieten onze bevindingen zien dat er een verband bestaat tussen ondervoeding en respectievelijk klinisch relevante symptomen van orofaryngeale dysfagie en een slechte mondgezondheid in deze populatie. Meer specifiek toonden we aan dat zowel verpleeghuisbewoners met orofaryngeale dysfagie als verpleeghuisbewoners met een slechte mondgezondheid een bijna tweevoudig risico op ondervoeding hebben in vergelijking met bewoners zonder deze gezondheidsproblemen. Hiermee hebben we bevindingen uit eerder internationaal onderzoek bekrachtigd.

Ondervoeding, orofaryngeale dysfagie en een slechte mondgezondheid zijn belangrijke zorgproblemen bij deze populatie, ondanks de aanzienlijke hoeveelheid werk dat de afgelopen jaren al is verzet om de zorg met betrekking tot deze drie problemen te optimaliseren. Nationale en internationale collega's werken hier voortdurend aan en blijven wijzen op de noodzaak tot verbetering van de vaak nog sterk gefragmenteerde aanpak van deze zorgproblemen, die de verpleeghuispopulatie niet ten goede komt.

Wij pleiten daarom voor meer bewustzijn omtrent de negatieve gevolgen van de pathofysiologische triade van ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid bij patiënten met een beroerte en bij verpleeghuisbewoners. Daarnaast breken we een lans voor een meer geïntegreerde aanpak van deze problemen.

Onze DYNAMO-studie (**hoofdstuk 7**) kan beschouwd worden als een opstap voor toekomstig, meer interdisciplinair onderzoek op het gebied van ondervoeding en orofaryngeale dysfagie. Deze voorgenomen studie richt zich specifiek op de relatief onderbelichte populatie van verpleeghuisbewoners en heeft tot doel inzicht te verkrijgen in het effect van een innovatieve voedingsinterventie met een voor-verdikte medische bijvoeding bij verpleeghuisbewoners met dysfagie en met een risico op ondervoeding. We raden ten zeerste aan om dit onderzoek alsnog uit te voeren, op voorwaarde dat de effecten van de Covid-pandemie dit toelaten.

In het laatste hoofdstuk van dit proefschrift (**hoofdstuk 8**) worden alle bevindingen nog eens besproken in de bredere context van nationaal en internationaal onderzoek op het gebied van ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid in verschillende settings en patiëntenpopulaties.

Over het algemeen bekrachtigen onze bevindingen het belang van voortdurende verbetering van de voedingszorg in Europese ziekenhuizen, te beginnen met bewustzijn voor het probleem van ondervoeding. Om te beginnen bevelen we dan ook standaard voedingsscreening aan bij alle volwassen ziekenhuispatiënten.

De prevalentiecijfers en associaties van de gezondheidsproblemen (risico op) ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid bij patiënten met een beroerte en bij verpleeghuisbewoners tonen aan dat het hier om hardnekkige problemen gaat bij deze doelgroepen.

Deze problemen vragen nadrukkelijk om een geïntegreerde aanpak, die ook begint met het creëren van bewustzijn met betrekking tot de pathofysiologische triade van ondervoeding, orofaryngeale dysfagie en slechte mondgezondheid.

IMPACT

The percentage of diseased and older people around the globe is rising and the age of the oldest is increasing. Simultaneously, the medical field is developing rapidly, enhancing treatment efficacy, and increasing the chance of survival from severe illness [1]. Surviving severe illness such as stroke does not necessarily result in complete recovery as patients are at risk of poor clinical outcomes including chronic disability and impairments. These patients with poor clinical outcomes are often partially or completely care dependent. These developments are challenging factors for healthcare. Our study findings contribute to the fundaments of these developments in the medical field and improvements in care for adult hospitalized patients, stroke patients, and nursing home residents with malnutrition, oropharyngeal dysphagia, and poor oral health.

In this paragraph we discuss the knowledge utilization of our research on quality of nutritional care in the hospital, and for stroke patients and nursing home residents. We address the scientific relevance of this dissertation, and the impact of our findings for patients and healthcare professionals, educators, management of healthcare institutions, and policy makers in healthcare. Finally, we delineate how we shared our findings to raise awareness on the quality of nutritional care and on the negative consequences of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents.

Aim, most relevant findings, and conclusions of this dissertation

Our overall aim was to gain knowledge and reflect on the quality of nutritional care in hospitals and on malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents, respectively.

We showed that, despite international and national standards, the degree to which standard nutritional screening was performed in the hospitals was low. Nutritional screening is an essential starting point of nutritional care of adult hospitalized patients, as it represents the basis for further comprehensive diagnostic measurements and treatment. Therefore, we encourage standard nutritional screening of all adult hospitalized patients.

Additionally, the insights we gained on the components and associations of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and nursing home residents really urge for more awareness among patients, relatives or informal caregivers, healthcare professionals, educators, and policy makers to improve the care for these patients. An increase in the body of evidence on malnutrition, oropharyngeal dysphagia, and poor oral health and the associations between these conditions may contribute to the enhancement of clinical practice guidelines towards more integrated, thus multi -, inter -, and transdisciplinary care. After dedicated implementation, these developments may structurally contribute to improved care for stroke patients and nursing home residents across the continuum of care.

Scientific relevance

Our findings regarding the suboptimal performance of nutritional screening in hospitals, the alarming prevalence rates of malnutrition, oropharyngeal dysphagia, and poor oral health and the associations between these health conditions in stroke patients and nursing home residents were in line with earlier findings from various national and international research groups. We have stressed the relevance of more awareness and future research on these health conditions despite the already available evidence and national and international clinical guidelines. On top of this, the confirmed associations between malnutrition, oropharyngeal dysphagia, and poor oral health emphasize the importance of more integrated research in this field in stroke patients and in nursing home residents.

The design of our DYNAMO study may be regarded as a stepping stone for future research in the field of malnutrition and oropharyngeal dysphagia and moreover, the study involves a rather understudied population. The study aims to generate insights on the effect of an innovative nutritional intervention (pre - thickened oral nutritional supplementation). It is strongly recommended to actually perform this study in the near future now the disturbing effects of the Covid crisis gradually disappear.

In our studies, we have exposed a number of methodological issues that complicated our research and which are relevant for future research. The most striking issues concerned the present diversity in nutritional screening and diagnostic measurements and the lack of (longitudinal) data in chronic stroke patients, as well as in nursing home residents. These issues must be dealt with in future research in order to enable the generation of more conclusive evidence to promote integrated care for patients at risk of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health. A very significant aspect in this respect involved the operationalization of malnutrition for the pooling of data retrieved from the literature covering the past 20 years, to investigate the prevalence of malnutrition across the continuum of care in stroke patients. To partially deal with the diverse data from the various nutritional screening and diagnostic measurements that were applied in previous studies, we introduced the term 'impaired nutritional condition'. This term refers to all not well - nourished patients, who were discriminated from the well - nourished patients based upon a self - developed set of criteria for impaired nutritional condition. The utilization of uniform language, criteria, and comprehensive methods is very important to enable the comparison of study findings and benchmark future studies in a more reliable way.

In the meantime, progress has already been made with the global consensus on criteria for the diagnosis of malnutrition [2, 3], though based on our findings we concluded that there is still plenty of room for improvement. Also longitudinal research on the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health is indicated as we have shown that the literature on stroke patients in the chronic phase after stroke is still scarce. For nursing home residents it is generally known that this group is complex to study which may in part explain

the fact that this group is understudied.

Therefore we emphasize the necessity to gather relevant and reliable scientific data that covers the total disease trajectory of the patient, including transfers between healthcare settings. This will enable healthcare professionals to tailor treatment and better monitor the course of health conditions, symptoms, and intervention outcomes throughout the entire patients' care trajectory. Given the growing population of chronically ill and ageing patients, including stroke patients and nursing home residents, this is even more important.

Relevance for patients and healthcare professionals

This brings us to the relevance of this dissertation for patients and healthcare professionals. This dissertation has unraveled meaningful insights for better nutritional care for adult hospitalized patients and also for the promotion of integrated care for stroke patients and very frail nursing home residents, as these patients are at high risk of the pathophysiological triad of malnutrition, oropharyngeal dysphagia, and poor oral health.

We strongly encourage standard nutritional screening of all adult hospitalized patients and specifically in stroke patients and nursing home residents. This enables timely identification of patients with risk of malnutrition. Screening may minimize the risk of poor clinical outcomes, provided that the patient with abnormal screening results is subsequently assessed more thoroughly, adequately treated, and monitored.

As shown in this dissertation and confirmed by international literature, oropharyngeal dysphagia and poor oral health may also be the result of malnutrition and vice versa. Considering the still alarmingly high prevalence rates and associations of these health conditions, we urge for more awareness in this respect and recommend the promotion of more integrated care in this context. Awareness may positively affect patients' compliance to treatment and the healthcare professionals' adherence to guidelines. Healthcare professionals, additionally, have an important part to play in creating awareness among patients and the patients' relatives or informal caregivers.

Though not specifically addressed in this dissertation, our findings can also be relevant for other patient groups. For example patients with head and neck cancer [4-7] and patients with other types of neurodegenerative diseases e.g Alzheimer's disease, multiple sclerosis (MS), or amyothropic lateral sclerosis (ALS) as these patients are also at considerable risk of malnutrition, oropharyngeal dysphagia, and poor oral health [8-15].

Furthermore, more awareness and knowledge on symptoms and negative consequences of these health conditions in society in general may also help community dwelling patients and their informal caregivers to signal symptoms and approach a healthcare professional more timely.

The implementation of standardized screening and an increase of awareness may directly influence patient care, though our findings may also have an indirect impact through actions undertaken by healthcare educators, management of

healthcare institutions, and policymakers who are alerted by our findings.

Relevance for healthcare educators, management, and policy makers

The poor performance of nutritional screening in hospitals and the alarmingly high prevalence rates of malnutrition, oropharyngeal dysphagia, and poor oral health in stroke patients and in nursing home residents may encourage healthcare educators, the management of healthcare institutions, and policy makers to review and monitor the competences of healthcare professionals and the quality of care.

In this regard, an additional revenue of our research was a large scale international collaboration to investigate knowledge and knowledge gaps of healthcare professionals regarding malnutrition in geriatric patients. Findings of this study have not been published yet but may provide valuable insights for educative interventions for healthcare professionals. In addition, the management of healthcare institutions may also be triggered to investigate bottlenecks for care according to guidelines, e.g., standard screening in clinical practice. Overall, these actions driven by awareness may lead to a better understanding of our findings in the context of current practices, which is essential for the process towards optimization of care.

Healthcare educators, the management of healthcare institutions, and policymakers partially determine the quality of care as they educate healthcare professionals and decide on the content and structure of care. We therefore aimed to reach a large audience to share our findings.

Knowledge transfer

Results of this dissertation were disseminated through the publication of articles in high impact scientific journals. In addition, findings were communicated through presentations at national and international conferences, webinars, and training programs in the field of malnutrition, poor oral health, and oropharyngeal dysphagia in stroke patients and nursing home residents, e.g., De Geriatriedagen (2020, 's Hertogenbosch, The Netherlands), the congress of the European Society for Swallowing Disorders (ESSD) (2018, Dublin, Ireland), and the International Nursing Home Research Conference (2018, Rome, Italy). These occasions offered the opportunity to easily reach a large and broad target audience and discuss the results and implications of our studies with them. This transparent and continuous transfer of recently gained knowledge and lessons learned may contribute to improvements in the quality of nutritional care and care for stroke patients and nursing home residents with malnutrition, oropharyngeal dysphagia, and poor oral health worldwide.

Findings from this dissertation have also been used in a mini - lecture on the Dutch national television (Slecht gebit, laag gewicht, MAX NPO, 2019) [16] and were communicated via social media channels and websites.

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About the author

Viviënne Huppertz was born on October 2nd, 1992 in Heerlen (the Netherlands). She completed pre-university education with a health track in 2011.
She continued her education at the Wageningen University (the Netherlands) with a bachelor program in International Development Studies and special interest in Communication, Technology and Policy. As part of her bachelor program she also followed a minor program in Nutrition and Dietetics for six - months at the Harokopio University in Athens (Greece).
Back in the Netherlands she started working part-time at 'At Your Request', the meal service center of hospital 'De Gelderse Vallei' in Ede (The Netherlands). After graduating from the bachelor program in 2014, she continued her education at the Wageningen University where she followed a master program in Nutrition and Health. Within this master program she specifically focused on Epidemiology and Public Health and wrote her thesis in this field at the department of Health Services Research at Maastricht University and the department of Human Nutrition and Health at Wageningen University. Within this two – year master program she also completed a six – months internship at Corpoíca in Bogota (Colombia) where she performed a nutritional impact evaluation. In 2017 she started as a full – time PhD student at Maastricht University. This PhD – trajectory was a cooperative project between the School of Nutrition and Translational Research in Metabolism (NUTRIM), Care and Public Health Research Institute (CAPHRI), School for Oncology and Reproduction (GROW) at Maastricht University, Danone Nutricia Research, and the department of Human Nutrition and Health at Wageningen University.
During her PhD trajectory, Viviënne presented her research at national and international conferences. In april 2022 Viviënne started working as a researcher at the department of Health Services Research at Maastricht University.

List of publications

International journals

Huppertz, V.A.L, G.-J. van der Putten, R.J. Halfens, J.M. Schols, and L.C.P.G.M. de Groot. Association Between Malnutrition and Oral Health in Dutch Nursing Home Residents: Results of the LPZ Study. Journal of the American Medical Directors Association. 2017; **18**(11): p. 948-954.

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malnutrition in Dutch nursing home residents: results of the Dutch National Prevalence Measurement of Quality of Care. European Society for Swallowing Disorders Annual Congress. Dublin, Ireland. 2018

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