The association between malnutrition and postoperative complications, and the potential for prevention of both

Eli Skeie

Thesis for the degree of Philosophiae Doctor (PhD)
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Scientific environment

This project was conducted from May 2018 to January 2020 at the Centre for Nutrition, Department of Clinical Science, Faculty of Medicine at the University of Bergen, and at the Section for Science and Education, Department for Research and Development at Haukeland University Hospital. The main supervisor was Professor Stig Harthug and the co-supervisors were Dr Randi Julie Tangvik and Dr Anne Mette Koch.

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Eli Skeie
Norheimsund, February 2021

Abstract

Introduction: Poor nutritional status is an established risk factor for suboptimal outcome of hospital stay, including among other things, an increased risk of postoperative complications. Despite the fact that international guidelines for surgery acknowledge this, they do not tell how to identify or prevent and treat malnutrition, and neglected malnutrition at hospitals has been reported for years.

During the past two decades, there has been an increased focus on nutritional care in hospitals as a part of both local and national patient's safety work. In this respect, screening patients for being "at risk of malnutrition" and further assessment of these patient's nutritional status is recommended. Notably, the impacts of the diagnostic criteria on the incidence of postoperative complications, and the effect of implementation of nutritional guidelines on nutritional care at hospitals are scarcely investigated. To explore these relationships, a selection of established quality registers can be used.

Objectives: The overall objective of this thesis was to investigate the association between malnutrition and postoperative complications, and the potential for prevention of both. The specific objectives of the following papers was to investigate:

I. The association between «at risk of malnutrition» and the incidence of surgical site infection in a mixed surgical patient sample at a large university hospital.

II. The prevalence of preoperative malnutrition, and its association with severe postoperative complications and death among patients undergoing gastrointestinal resections at Norwegian hospitals.

III. Whether the increased nutritional policy investment has resulted in changes in the prevalence of patients being «at risk of malnutrition», use of nutritional support and related diagnosis codes during an 11-year period at a large university hospital, and if there remains a further potential to decrease the risk of both malnutrition and postoperative complications.

Methods: To evaluate the prevalence and associations between malnutrition and postoperative complications (Paper I and Paper II), we used data from local and national registry databases: 1) The Malnutrition registry and 2) The local NOIS-POSI database (NOIS, Norwegian Surveillance System for Health Care Associated Infections in Hospitals; POSI, postoperative site infection) at Haukeland University Hospital, and 3) The Norwegian Registry for Gastro Surgery (NoRGast). The Malnutrition registry was also used to evaluate the trends in compliance with nutritional guidelines in the period 2008 - 2018 (Paper III).

Results: We found the incidence of surgical site infections in a large Norwegian university hospital to be positively associated with the prevalence of «at risk of malnutrition» (OR 1.81 (95 % CI: 1.04 - 3.16)) (Paper I). Moreover, we found 35.4 % of patients at Norwegian hospitals having gastrointestinal surgery to be malnourished (Paper II). These patients were 1.29 (95 % CI: 1.13 - 1.47) times more likely to develop severe postoperative complications, and 2.15 (95 % CI: 1.27 - 3.65) times more likely to die within 30 days, as compared to those who were not. We observed no change in the prevalence of «at risk of malnutrition» in the period 2008 – 2018 at a large Norwegian university hospital (Paper III). However, more patients received nutritional support (from 61.6 % in 2008 to 71.9 % in 2018 ($p < 0.001$), with a range from 55.6 to 74.8 %). This trend was seen for both surgical and non-surgical patients ($p < 0.001$). Also, there was an increasing trend of having a dietitian involved in the patient care and using a related diagnosis code for patients “at risk of malnutrition”, despite less common for surgical, as compared to non-surgical patients ($p < 0.001$).

Conclusions: This thesis demonstrated that patients identified to be «at risk of malnutrition» or malnourished by recommended screening tools have an increased risk of postoperative complications as compared to those who are not. Despite a higher percentage of patients “at risk of malnutrition” received nutritional support, each year of the study period, one of four patients «at risk of malnutrition» did not receive nutritional support, and fewer surgical, as compared to non-surgical patients, received support from a dietitian or had a related diagnostic code at admission. This indicates that there is still a potential to reduce the risk of malnutrition on surgical patients, something that should be investigated in well-designed randomized controlled trials in the future.

List of papers

I. Skeie E, Koch AM, Harthug S, Fosse U, Sygnestveit S, Nilsen RM, Tangvik RJ.
A positive association between risk of malnutrition and surgical site infections: A hospital-based register study
PLoS One. 2018 May 15;13(5):e0197344. eCollection 2018.

II. Skeie E, Tangvik RJ, Nymo LS, Harthug S, Lassen K, Viste A.
Weight loss and BMI criteria in GLIM's definition of malnutrition is associated with postoperative complications following abdominal resections – Results from a National Quality Registry
Clin Nutr. 2020 May;39(5):1593-1599. Epub 2019 Jul 20.

III. Skeie E, Sygnestveit K., Nilsen RM, Stig Harthug, Koch AM, Tangvik RJ.
"At risk of malnutrition": Trends in prevalence, nutritional support and medical coding among surgical and non-surgical patients. An 11-year follow-up study
Submitted to Clinical Nutrition December 2020. Revision process ongoing in February 2021.

The published papers (Paper I and Paper II) have open access and are reprinted with permission from publisher. All rights reserved. The unpublished paper (Paper III) is undergoing a revision process with aim of being published in Clinical Nutrition.

Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
ASPEN	American Society for Parenteral and Enteral Nutrition
ASA	American Society of Anesthesiologists physical status classification
BMI	Body mass index
CDC	Centres for Disease Control and Prevention
CI	Confidence intervals
COPD	Chronic obstructive pulmonary disease
CRP	C-Reactive Protein
ECDC	European Centre for Disease Prevention and Control
ECOG	Eastern Cooperative Oncology Group
ESPEN	European Society for Parenteral and Enteral Nutrition and Metabolism
ERAS	Enhanced Recovery After Surgery
GLIM	Global Leadership in Malnutrition
HAI	Healthcare-associated infection
ICD-10	The International Statistical Classification of Diseases and Related Health Problems, 10th version
mE-PASS	Modified Estimation of Physiologic Ability and Surgical Stress
MNA	Mini Nutritional Assessment
MUST	Malnutrition Universal Screening Tool
NOIS	Norwegian Surveillance System for Health Care Associated Infections in Hospitals
NoRGast	Norwegian Registry for Gastrointestinal Surgery

NRS 2002	Nutritional Risk Screening 2002
OR	Odds ratio
PASC	Patient Safety Checklist
POSI	Postoperative site infection
RCT	Randomized controlled trial
SGA	Subjective Global Assessment
SSI	Surgical site infection
WHO	World Health Organization

Contents

1. Introduction

In the past, malnutrition was mainly associated with starvation due to poverty in developing countries or during catastrophes. To investigate how to best refeed after a starvation diet, such as that of the civilians who were starved during the Second World War, the Minnesota Starvation Experiment was conducted in 1944 (1). In the experiment, 36 healthy men volunteered to starve for six months, and afterwards to be refed. The inclusion criteria was, among others, good physical and mental health. Most of the study participants lost more than 25 % of their body weight, and as a consequence, many experienced anaemia, fatigue, apathy, extreme weakness, irritability, neurological deficits and lower extremity edema.

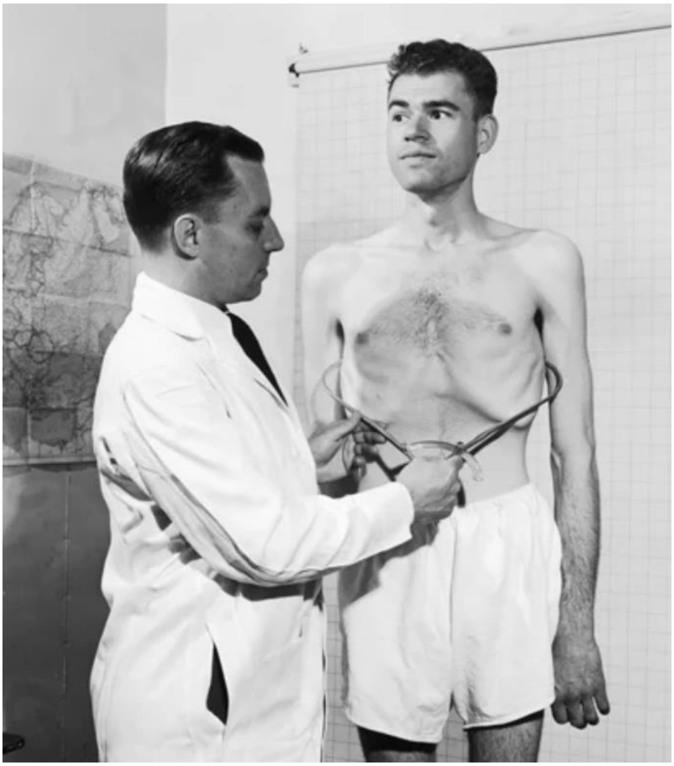

Figure 1: One of the study participants in the Minnesota Starvation Experiment being tested. Photo obtained from the webpage www.refinery29.com/en-us/minnesota-starvation-experiment with following photo credit: Wallance Kirland/The Life Picture Collection/Getty images

We now know that malnutrition also occurs in developed countries. In contrast to the Minnesota Starvation Experiment, many who develop malnutrition are not healthy and young in the first place, but may be ill, old and/or undergoing stress situations such as surgery, and thus may be even more vulnerable.

Surgery is an operative procedure to remove, replace or repair diseased organs or tissue, and is the only curative treatment option for a broad spectrum of diseases (2). Of note, surgery also induces a stress response which is parallel to the scope of the surgery. This leads to hormonal, haematological, metabolic and immunological changes that include mobilization of energy reserves and substrates necessary for the maintenance of the energy processes, the repair of tissues and healing, and for the immune response and survival (3-5). This may further lead to hyperglycaemia and whole-body protein catabolism, which can be clinically manifested by loss of both body fat and lean tissue. To meet the needs of substrates required for the stress response, preoperative energy reserves are required (6). Weight loss results in a reduction in both fat- and fat-free mass, which further leads to decreased muscle strength (7). Reduction of fat-free mass and muscle strength are associated with an increased mortality rate (8). Thus, surgical patients who have low energy reserves are vulnerable under surgery due to their lack of capacity to respond to the increased demands of a surgical intervention (9, 10). Additionally, since several nutrients are needed for the healing process, a low dietary intake or depleted nutrient storage may lead to delayed wound healing (11). In general, consequences of malnutrition include higher morbidity and mortality (12-14), prolonged hospital stays (14), higher readmission rates (14) and increased health care costs (13, 15). Thus, preventing and treating malnutrition is important due to 1) the medical condition itself, and 2) the vulnerability it causes for treatment of other conditions.

The complexity in the relationship between malnutrition and postoperative complications is illustrated in **Figure 2**. In this thesis the focus is on malnutrition as a predictive factor for postoperative complications. If there is a causal relationship, there should be a potential for decreasing the risk of complications by means of detecting the risk of malnutrition before surgery and implementing preventive measures. The relationship between malnutrition and underlying diseases, and surgery as a predictive factor of malnutrition will be referred to in a lesser extent.

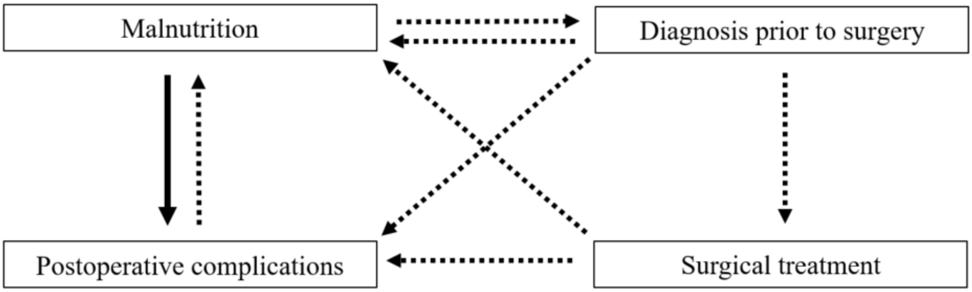

Figure 2: Illustration of the relationship between malnutrition and postoperative complications. In this thesis, the main focus is on malnutrition as a predictive factor of postoperative complications (the widest arrow).

1.1 Malnutrition

1.1.1 Definitions

Undernutrition* and *malnutrition

The World Health Organization (WHO) defines undernutrition as wasting (low weight-for-height), stunting (low height-for-age) and underweight (low weight-for-age), and to be a part of, but not the same as WHO's broader definition of malnutrition: "Deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients" (16). For adults over 20 years, WHO also defines underweight as a body mass index (BMI) of less than 18.5 kg/m^2 (17).

At the same time, undernutrition is often used synonymously with malnutrition (18, 19). European Society for Clinical Nutrition and Metabolism (ESPEN) refers to Sobotka et al.'s definition of malnutrition: "A state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease" (20). This definition is also used by the Norwegian

Directorate of Health (21). Furthermore, ESPEN divides malnutrition into the following subgroups (19):

- Disease-related malnutrition with inflammation
    - *Acute disease or injury-related malnutrition with inflammation* is characterized by a strong inflammatory response. This is relevant for those on the intensive care unit with acute disease or trauma (e.g. major infection, burns, trauma or closed head injury), or those who display specific nutritional challenges due to highly pronounced stress metabolism after major surgical procedures. Here, a combination of high pro-inflammatory cytokine activity, increased corticosteroid and catecholamine release, resistance to insulin and other growth hormones, bed rest and no or reduced food intake rapidly deplete the body 's energy and nutrient store.
    - *Chronic disease related malnutrition with inflammation* is often referred to as cachexia. This occurs frequently in patients with end-stage organ diseases that are complicated by catabolic inflammatory activity, such as cancer and chronic obstructive pulmonary disease. This kind of malnutrition can be characterized by weight loss, low BMI and reduced muscle mass and function in combination with an underlying disease and biochemical indices of either milder ongoing or recurrent inflammation (measured as elevated C-Reactive Protein (CRP) concentrations and/or low albumin in serum).
- Disease-related malnutrition without inflammation is synonymous with non-cachectic disease-related malnutrition. This occurs when malnutrition is combined with a presence of an underlying disease but with no biochemical indices of present or recurrent inflammation. Such malnutrition may occur due to dysphagia, anorexia nervosa and depression, which reduces food intake, or malabsorption.
- Malnutrition without disease is synonymous with non-disease-related malnutrition. This can be related to hunger or socioeconomic or psychological factors.

In this thesis, the focus is on disease-related malnutrition.

"At risk of malnutrition" **and** *At nutritional risk*

Patients with «at risk of malnutrition», also referred to as patients at nutritional risk, are defined as those who are malnourished or at risk of becoming so (19). These patients are identified by a validated malnutrition risk screening tool, which is usually based on information regarding BMI, weight loss, food intake, disease severity and age. ESPEN recommend (22) Nutrition Risk Screening 2002 (NRS 2002) (23) for hospitals, the Malnutrition Universal Screening Tool (MUST) (24) for the community and Mini Nutritional Assessment (MNA) (25) for patients 65 years and older. Another well-known screening tool is Subjective Global Assessment (SGA) (26). These screening tools are also recommended for use in Norwegian hospitals (21), and Haukeland University Hospital uses NRS 2002 as a part of the admission and daily routines. This screening tool is composed by an initial screening and a final screening part. Answering "Yes" to one or more of the following initial screening questions leads to the final screening:

- Is the BMI < 20.5 kg/m^2?
- Has the patient lost weight within the last 3 months?
- Has the patient had a reduced dietary intake the last week?
- Is the patient severely ill?

In addition to the final screening (illustrated in **Table 2**), age ≥ 70 years gives additionally 1 score. A total score ≥ 3 in the final screening classifies as being «at risk of malnutrition». If the answer is "No" to all of the initial screening questions, or the total score < 3, the patients should be screened with weekly intervals to follow up a potential change of the "at risk of malnutrition"-status.

Table 2: The final screening of the NRS 2002, which should be conducted if indicated by the initial screening. In addition to scores in this final screening, age ≥ 70 years gives 1 score. A total score of 3 or more classifies as being «at risk of malnutrition» (23).

Impaired nutritional status		**Severity of disease (≈ stress metabolism)**	
Absent **Score 0**	Normal nutrition status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Weight loss > 5 % in 3 months *OR* food intake 50–75 % of normal needs in preceding week	Mild **Score 1**	Hip fracture Chronic patients, in particular with acute complications, cirrhosis COPD, chronic hemodialysis, diabetes and oncology
Moderate **Score 2**	Weight loss > 5 % in 2 months *OR* BMI 18.5–20.5 kg/m^2 in addition to impaired general condition *OR* food intake 25–50 % of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery, stroke, severe pneumonia, hematologic malignancy
Severe **Score 3**	Weight loss > 5 % in 1 month (≈ > 15 % in 3 months) *OR* BMI < 18.5 kg/m^2 in addition to impaired general condition *OR* food intake 0–25 % of normal requirement in preceding week	Severe **Score 3**	Head injury, bone marrow transplantation and intensive care patients (APACHE >10)

APACHE, Acute Physiology and Chronic Health Evaluation; **COPD**, chronic obstructive pulmonary disease

1.1.2 Clinical diagnosis

Diagnostic coding

The International Statistical Classification of Diseases and Related Health Problems, 10th version, (ICD-10) is recommended for diagnosis coding of conditions related to malnutrition by the Norwegian Ministry of Health (21). ICD-10 codes are used to report diseases and health conditions, are the foundation for the identification of health trends (27) and picture the patient composition of diseases and scope of treatment given at hospitals for the health authorities. There are three main diagnoses related to malnutrition in the ICD-10 system: E46: «at risk of malnutrition», E44: mild to moderate malnutrition, and E43: severe malnutrition. Categorization within the ICD-10 codes in Norway is based on the results of the screening for "at risk of malnutrition", the amount and time period of weight loss, BMI (age adjusted) and amount of recent food intake. The Norwegian criteria (21) for the diagnosis codes are as follows:

- "At risk of malnutrition" (E46) (one of the following):
    - NRS 2002: Score ≥ 3
    - MUST: Score > 2
    - MNA: Score < 11
    - SGA: Grade B

- Mild to moderate malnutrition (E44) (one of the following):
    - Unintended weight loss < 10 % during the last 3 - 6 months, or < 5 % during the last 2 months
    - BMI < 18.5 kg/m^2 (> 70 years: BMI < 20 kg/m^2)
    - BMI < 20 kg/m^2 (> 65 years: BMI < 22 kg/m^2) in addition to unintended weight loss > 5 % last 6 months
    - Food intake < half of estimated needs last week

- Severe malnutrition (E43) (one of the following):
  - Unintended weight loss > 15 % during the last 3 - 6 months, or more than 5 % unintended weight loss the last month
  - BMI < 16 kg/m^2 (> 70 years: BMI < 18.5 kg/m^2)
  - BMI < 18.5 kg/m^2 (> 70 years: BMI < 20 kg/m^2) in addition to unintended weight loss > 5 % last 3 months
  - Food intake < a quarter of estimated needs last week

The Global Leadership in Malnutrition's (GLIM) criteria

Despite the fact that most definitions of malnutrition include the same risk factors (28), there has been a lack of consensus on diagnostic criteria for application in clinical settings. Therefore, the Global Leadership in Malnutrition (GLIM), which represents the four largest clinical nutrition societies (ESPEN, American Society for Parenteral and Enteral Nutrition, Federación Latinomericana de Terapia Nutricional, Nutrición Clinica y Metabolismo and Parenteral and Enteral Nutrition Society of Asia) was constituted to reach a broader consensus on the definition of malnutrition in 2016. These GLIM criteria was launched at the ESPEN conference in 2018 and afterwards published in Clinical Nutrition (29) and the Journal of Parenteral and Enteral Nutrition (30). GLIM encouraged the nutrition community to use the criteria both in prospective and retrospective cohort studies as well as clinical trials in order to validate its relevance for clinical practice (29).

The GLIM criteria for the diagnosis of malnutrition is a two-step approach. First, the patient is identified as being «at risk of malnutrition» by a validated screening tool. Secondly, the patient is assessed for the diagnosis of malnutrition, which requires one phenotypic and one etiologic criterion. These criteria are as following:

- Phenotypic Criteria:
  - Weight loss > 5 % within past 6 months or > 10 % beyond 6 months, *and/or*
  - Low BMI, defined as: < 20 kg/m^2 if < 70 years, or < 22 kg/m^2 if > 70 years (< 18.5 kg/m^2 if < 70 years, or < 20 kg/m^2 if > 70 years for Asia), *and/or*

  - Reduced muscle mass identified by a validated body composition measuring technique

- Etiologic Criteria:
  - Reduced food intake or assimilation, defined as ≤ 50 % of energy requirements > 1 week, *or* any reduction for > 2 weeks, *or* any chronic GI condition that adversely impacts food assimilation or absorption, *and/or*
  - Inflammation. Both acute disease/injury-related and chronic disease-related. CRP may be used as a supportive laboratory measure.

Based on the phenotypic criterion, the severity of malnutrition is defined as moderate or severe, which is described in **Table 3**.

Table 3: Thresholds for the severity grading of the diagnosis of malnutrition (29).

	Phenotypic Criteria *One of the following*			
Malnutrition diagnosis	Weight loss during the past 6 months	BMI among those younger than 70 years	BMI among those older than 70 years	Deficit in muscle mass[1]
Moderate malnutrition	5 - 10 %	18.5 - 20 kg/m^2	20 - 22 kg/m^2	Mild to moderate
Severe malnutrition	> 10 %	< 18.5 kg/m^2	< 20 kg/m^2	Severe

BMI: Body Mass Index; **GLIM**: Global Leadership in Malnutrition

[1] Defined by a validated assessment method, as dual-energy absorptiometry or corresponding standards using other body composition methods like Bioelectrical Impedance Analysis (BIA), or MRI. Physical examination or standard anthropometric measures like mid-arm muscle or calf circumference may be used.

1.1.3 Prevalence of malnutrition

The prevalence of disease-related malnutrition in hospitals is described as varying between patient groups, screening tools used to identify «at risk of malnutrition» and the definitions used to define malnutrition. Searching for the prevalence of malnutrition according to the GLIM criteria among surgical patients resulted in 5 papers, demonstrating a prevalence range between 1.7 % and 42.0 % (Search conducted in PubMed 14 December 2020 using the following search strategy: Search 1: "GLIM criteria" AND surgery (n = 20); Search 2: "GLIM criteria" AND surgical (n = 13); Search 3: "global leadership initiative" AND malnutrition AND surgery (n = 21)). It is worthwhile noting that the paper presenting the prevalence at 1.7 % had modified the GLIM criteria to include two phenotypic criteria (low BMI *and* recent weight loss) in addition to low albumin as an etiologic criterion. A brief overview of these papers can be seen in **Table 4**.

Table 4: Prevalence of malnutrition according to the Global Leadership Initiative for Malnutrition (GLIM) criteria among surgical patients.

First Author, country, year	Study participants	Design	Prevalence of malnutrition (%)	Marks
Kakavas, Greece, 2020 (31)	Cancer patients having major abdominal surgery (n = 218)	Prospective observational study	32.1	
Haines, USA, 2020 (32)	Emergent gastrointestinal surgery (n = 31029)	Retrospective cohort study	1.7	Modified the GLIM criteria to include all the following criteria: low body mass index, recent weight loss and low albumin
Henrique, Brazil, 2020 (33)	Elective gastrointestinal surgery (n = 206)	Prospective cohort study	10.7–41.3	Prevalence depending on the various GLIM combinations
Fiorindi, Italy, 2020 (34)	Surgery of inflammatory bowel disease (n = 53)	Cross sectional study	42.0	
Skeie, Norway, 2020 (35)	Gastrointestinal surgery (n = 6110	Register study	35.4	Only used the second step of the GLIM definition, and did not include muscle mass information

1.1.4 Nutritional guidelines for hospitals

History

"The skeleton in the hospital closet" is a historical article from 1974 by C. E. Butterworth, who criticized hospitals for overlooking malnutrition due to its being a diagnosis that is not "socially acceptable" or "medically acceptable" enough (36). He encouraged the readers to look at the nutritional practices in their institutions and warned that they could find a skeleton behind the first door they opened. Few years later, G. L. Hill et.al described that malnutrition, then defined as anaemia, vitamin deficiency, weight-loss, loss of arm-muscle bulk, and low plasma levels of transferrin and albumin, was almost totally unrecognized at the hospital (37). The persistent trend of neither recognizing, acknowledging nor accepting the problem of malnutrition in association with disease was the reason why the Council of Europe created a network to work systematically with ways by which to integrate nutrition care into patient treatment care in 1999 (38). Later, ESPEN published guidelines regarding screening for «at risk of malnutrition» in 2003 (22). At Haukeland University Hospital, Norway, these actions, together with a request from the Patients' Board regarding integrating nutritional assessment and treatment in the patient care and better hospital food for patients, resulted in a local nutritional strategy in 2006 (39). Haukeland University Hospital is one of the largest hospitals in Norway. In 2019, the hospital had about 945,000 patient meetings and conducted 44,000 surgeries (40).

In 2009 the Norwegian guideline for prevention and treatment of malnutrition was released (21), followed by the more practical handbook for both the primary care and hospitals, called "Kosthåndboken" [Diet Manual] in 2012 (41). To implement the guideline, an overall local nutritional strategy became mandatory for all Norwegian hospitals in 2013 (5). In 2015, malnutrition was made a priority in the national program In Safe Hands (42), a patient safety programme in Norway initiated by the Ministry of Health and Care Services in Norway and operated by the Norwegian Directorate of Health. The same year, malnutrition became a priority in the Western Norway Regional Health Authority's safety programme (43). Patient safety is defined by the WHO as "the absence of preventable harm to a patient during the process of health care and reduction of risk of unnecessary harm associated with health care to an acceptable minimum" (44). The Norwegian Knowledge Centre for Health Services uses the broader definition (45) which also includes the aspect of lack of health services: "patients should not be exposed to unnecessary injury or risk of injury as a result of the health service's efforts and benefits, or lack of the same" (46).

Current guidelines

Due to the tendency of underestimating and undertreating patients «at risk of malnutrition», the Norwegian guidelines for preventing and treating malnutrition aim to ensure that all patients admitted to hospital are screened for being «at risk of malnutrition» at admission, and thereafter weekly (21). The Norwegian guidelines are in accordance with the guidelines from ESPEN (22) and ASPEN (47), and do not differentiate between surgical and non-surgical patients. Patients who are identified with «at risk of malnutrition» should have an individual nutrition care plan that documents nutritional status, nutritional requirements, dietary intake and nutritional support. This should be documented in the electronic patient record and communicated to the next level of care. To convert these guidelines into a more practical design, action plans for hospitals, nursing homes and home care services were developed by the national patient safety programme In Safe Hands (42). The action plan for hospitals is divided into four steps (48):

1) Screen for «at risk of malnutrition»

All patients admitted to hospital should be screened for being "at risk of malnutrition" within 24 hours after admission. Patients who are not identified to be «at risk of malnutrition» at this point should be repeatedly screened with one-week intervals. Validated screening tools as NRS 2002 (23), MNA (25) and MUST (24) are recommended for this step.

2) Assess the nutritional status

Patients who are identified to be "at risk of malnutrition" need a more in-depth evaluation of their nutritional status. This includes determining the extent to which the patient's nutritional requirements, energy and protein in particular, have been covered during a period. To do this, the patient's needs have to be estimated. For the energy requirements, the action plan refers to the "rule of thumb" of 30 kcal/kg body weight per day for adult patients with a low level of activity, but highlights the importance of individual adjustments, particularly for those who are severely undernourished or at risk of refeeding syndrome. In addition, patients with overweight or obesity (BMI ≥ 25 kg/m^2) should have individual adjustments, which is possible by using equations from the Mifflin's formula (49). For others, the Harris-Benedict's formula (50) can be used. Notably, the "gold" standard for measuring energy requirements is by indirect calorimetry (51), but this equipment is not commonly available to clinics. For the protein requirements, the "rule of thumb" is 1 g protein/kg body weight per day (41). More precisely, the needs are estimated to be 0.8–1.0, 1.0–1.5 and 1.5–2.0 g/kg/day for "healthy", "ill" and "critical ill" persons, respectively (41). In energy percent (E %), this should correspond to 10–20 % of the daily energy intake for adults and 15–20 E % for adults 65 years or more (52, 53).

Moreover, the action plan points out that the underlying reasons for reduced dietary intake should be identified (48). This may include reasons related to function level, medical conditions and related treatment, cultural and psychosocial factors, factors related to the environment or aspects of the food (41). The level of severity of the malnutrition should also be assessed. If the malnutrition is considered severe or complex, a dietitian should be involved (48). When this action plan was published in 2016, there was no global agreement on ranking the severity of malnutrition, and cut-offs for this were not presented in the action plan. However, after GLIM released the metrics for grading the severity of malnutrition into moderate and severe in 2018, these should be used (Table 3).

3) Give nutrition support and care

A nutrition care plan for patients "at risk of malnutrition" should be made and implemented as soon as possible and at least within 24 hours after screening. This plan should include a documentation of the nutritional status, aims for the nutritional support (energy, protein, liquid, other), calculated energy needs, information regarding the patient's dietary intake and individualized measures. The types of measures that will be started depend on the nutritional challenges and the aim of the nutritional support (48). In general, it is recommended to start at the lowest step of the "nutrition staircase" (41), which is illustrated in **Figure 3**. However, some cases require starting at a higher level, and/or to include more than one step. The last three steps (oral nutritional supplements, enteral tube feeding and parenteral nutrition) are defined as medical nutrition therapy due to the complexity (19). All measures and aims in the nutritional support plan, and dietary intake and weight change in particular, should be continuous, and at least weekly, measured and evaluated (42).

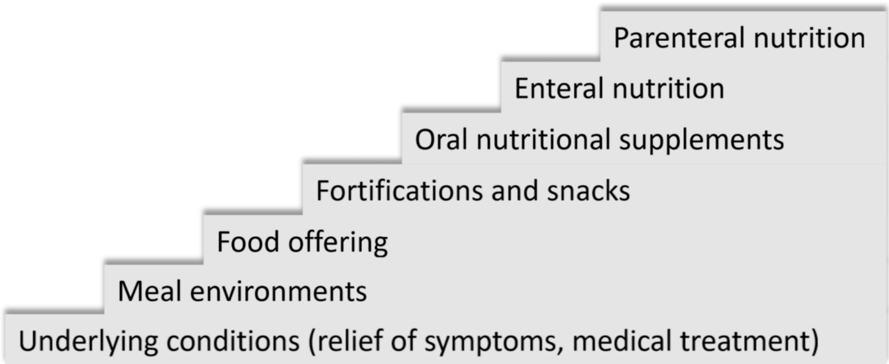

Figure 3: The "nutrition staircase", adapted from the Norwegian Directorate of Health (41). A model demonstrating the complexity of nutrition support to increase with higher steps.

4) Pass on the information

The result from the "at risk of malnutrition" screening, the nutritional status and the nutrition care plan should be documented in the electronic patient record and in the transfer documents (the medical report and the nursing and care report) to the primary caregiver (48). The medical report for those with «at risk of malnutrition» should include an appropriate malnutrition diagnosis code (ICD-10 code E46, E44 or E43). In addition, the action plan emphasizes the importance of informing and including the patients or their next of kind in the plan for treatment and follow-up by sharing assessment results and nutrition plan/protocols.

1.1.5 Nutritional guidelines for surgical patients

Key aspects of perioperative care from a metabolic and nutritional point of view includes avoiding long periods of preoperative fasting and re-establishing oral feeding as early as possible after surgery (3). In a recent review regarding recommendations of perioperative nutrition, ESPEN recommend that the screening for "at risk of malnutrition" should be conducted at least 10 days prior to surgery (54). If it is expected that the patient will be unable to eat or maintain appropriate oral intake for a longer perioperative period, nutrition support is indicated, even if there is no evidence of malnutrition. Also, guidelines regarding prevention of surgical site infections (SSIs) recommend focusing on nutritional counselling if indicated by the preoperative testing (55).

According to the ESPEN guidelines for clinical nutrition in surgery, nutritional care protocols for the surgical patient must include (3):

- a detailed nutritional and medical history that includes body composition assessment
- a nutrition intervention plan
- an amendment of the intervention plan, where appropriate
- clear and accurate documentation assessment of nutritional and clinical outcome

- resistance exercise whenever possible

Thus, the nutritional guidelines for surgical patients are in occurrence with the general ones for hospitals, although formulated in a different way and including resistance exercise in the recommendations. This is explained by the fact that the body needs to both nutritional support/intake and physical exercise to rebuild the peripheral protein mass/body cell mass that is caused by the surgical trauma (3).

Screening for «at risk of malnutrition», as early as possible in the patient's care pathway, and belonging treatment is also recommended by the Enhanced Recovery After Surgery (ERAS), a programme which is designed to achieve early recovery for patients undergoing major surgery through a multimodal perioperative care pathway (56). Moreover, the programme states that nutritional intervention and monitoring of changes should be considered if the surgery can be delayed, and that early resumption of foods should be the standard of care after most types of surgery. The enteral route should always be the first choice, although parenteral nutrition might be indicated in some circumstances.

1.1.6 Implementation of nutritional guidelines

Guidelines aim to improve quality, reduce variation in the health care services, and limit unnecessary or wrong use of resources (57). However, the road from theory to clinical practice may be challenging, random and slow (58). In general, it is well known that the gap between the best available knowledge-based practice and the treatment given from the health care services is too wide (59, 60), a challenge that is recognized as one of the greatest obstacles facing the global health community (61).

To evaluate the degree of implementation success, clinical indicators are needed (62). Therefore, Haukeland University Hospital began to use point-prevalence surveys monitoring the prevalence of patients being «at risk of malnutrition» and the appurtenant treatment strategies. Analysis from the first two years (2008–2009) these surveys were used demonstrated improved screening performance but no change in the percentage of patients “at risk of malnutrition” or number of those who received nutritional support (63).

As a part of the revision of Haukeland University Hospital’s nutritional strategy in 2017, barriers to implementation were hypothesized as the lack of well-suited systems in the electronic patient record for nutrition care, insufficiently clear work tasks and insufficient designation of those responsible to solve the work tasks; in addition, the implementation work did not follow the established leadership structure at the hospital (39). A Norwegian study investigating the nurses’ perspectives concerning barriers to nutritional care for the undernourished hospitalized elderly were 1) loneliness in nutritional care, 2) a need for competence in nutritional care, 3) low flexibility in food service practices, 4) system failure in nutritional care and 5) nutritional care being ignored (64). These assessments demonstrate the complexity of implementation of nutritional guidelines and may be seen in the context of what the European Council of Europe identified as the five important barriers to improving the nutritional care and support of hospitalized patients 20 years ago: 1) a lack of clearly defined responsibilities; 2) a lack of sufficient education; 3) a lack of influence of the patients; 4) a lack of co-operation among all staff groups, and; 5) a lack of involvement from hospital management (6) (38).

Corresponding, the Norwegian Knowledge Centre for the Health Services found the following to be important when aiming to increase the probably of adherence to clinical practice: clinical decision-support systems (including reminders), practice visit and facilitation, audit and feedback, local opinion leaders, tailored interventions, and courses and meetings (57).

The national patient safety programme In Safe Hands recommends the use of dedicated personnel familiar with the Model for Improvement as a framework for testing and implementing the action plan’s measures (42). This framework has three questions to be answered: 1) What are we trying to accomplish?, 2) How will we know that a change is an improvement?, and 3) What changes can we make that will result in improvement? -and then use the Plan-Do-Study-Act cycles for tests (**Figure 4**) (65). In light of this cycle, Paper III in this thesis aims to study the implementation of Haukeland University Hospital's nutritional strategy.

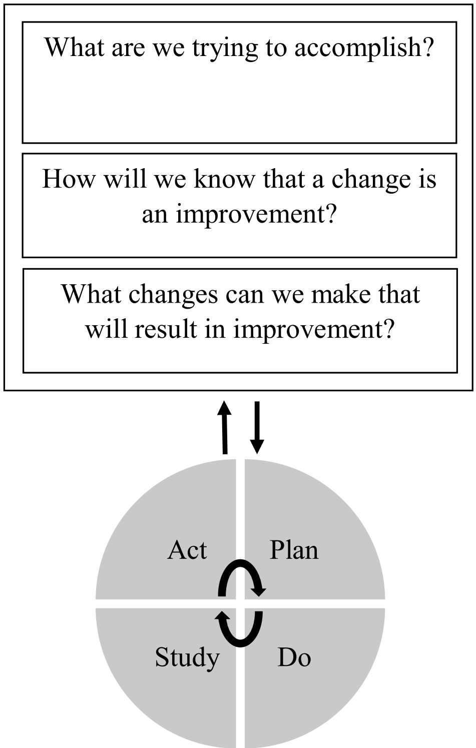

Figure 4: The Model for Improvement framework and the Plan-Do-Study-Act cycle, which is recommended to use for testing and implementing the national patient safety programme In Safe Hands' action plan's measures (42).

1.2 Postoperative complications

Postoperative complications are defined as any deviation from the normal postoperative course, exclusive sequela or failure to cure (66), and are associated with reduced health-related quality of life (67), higher morbidity and mortality (68), and drivers of excessive costs for the health care system (67, 69).

1.2.1 Risk factors

A risk factor may be defined as "a condition, behaviour, or other factor that increases risk" (70). The WHO Guidelines for Safe Surgery state that the patient's characteristics and comorbidity play an important role in determining the likelihood of a postoperative infection (71). The guideline lists the following patient's characteristics as possible risk factors for SSIs: Advanced age, poor nutritional status, diabetes, smoking, obesity, colonization with microorganisms, coexisting infection at a remote body site, altered immune response, preoperative hospitalization. The same risk factors were also listed in the Centres for Disease Control and Prevention (CDC) Guideline of Surgical Site Infections in the 1999 version (72). Interestingly, there was no focus on patient characteristic as a risk factor in the 2017 version of the same guideline (73).

1.2.2 Incidence

The incidence of postoperative complications are related to the specific organ operated on and type of procedure performed. Moreover, it depends on the patient safety focus in the departments, as illustrated by a stepped wedge cluster randomized trial in two hospitals in Western Norway that found a decline of the incidence of complications from 19.9 % to 11.5 % after implementation of the WHO's surgical safety checklist (74). An overview of the incidence of types of postoperative complications, with and without use of WHO's surgical safety checklist can be seen in **Table 5**.

The WHO state that in industrialized countries the rate of major complications has been documented to occur in 3–16 % of inpatient surgical procedures, with a death rate between 0.4 and 0.8 % (2). A recent systematic review and meta-analysis reported the prevalence of preventable patient harm to be 10 % among surgical patients (75).

Table 5: An overview of the incidence of types of postoperative complications, with and without use of the World Health Organization's surgical safety checklists (SSC) at two hospitals in Western Norway (74).

	Control (%)	**SSC (%)**
Respiratory complications	6.4	3.2
Pneumonia	3.7	1.9
Respiratory failure	1.0	0.5
Other[1]	1.8	0.8
Cardiac complications	6.4	4.3
Cardiac arrest	0.5	0.4
Arrhythmia	3.3	2.7
Congestive heart failure	0.7	0.3
Acute myocardial infarction	1.0	0.5
Angina pectoris	0.9	0.4
Infections	6.0	3.4
Sepsis	0.6	0.3
Surgical site	2.2	1.5
Urinary tract	2.8	1.4
Other[2]	0.7	0.3
Surgical wound rupture	1.2	0.3
Nervous system complication	0.5	0.3
Bleedings	2.3	1.2
Embolism	0.5	0.2
Mechanical implant complications	0.1	0.4
Anaesthesia complication	0.3	0.2
Others	2.0	0.7
Death	1.6	1.0

[1] Including asthma, pleura-effusion, and dyspnoea

[2] Including meningitis, peri- and endocarditis, and gastroenteritis

1.2.3 Surgical site infections

As illustrated in Table 5, a large proportion of the postoperative complications is SSI. SSIs can be divided into superficial incisional, deep incisional or organ/space, based on given criteria from the European Centre for Disease Prevention and Control (ECDC) (76). SSIs are also acknowledged as a health care-associated infection (HAI), and defined as “an infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure, or within one year if prosthetic material is implanted at surgery” (77). HAIs may be used synonymously with “nosocomial” or “hospital” infection, and is defined as “an infection occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission” (78).

During the 1990s, several European countries, including Norway, established national surveillance systems for HAIs. The ECDC organizes the protocol for surveillance and sets the definitions. In this way, the incidence of HAIs may be easily compared across borders and diseases. The ECDC’s annual epidemiological surveillance report from 2017 demonstrated the incidence of SSI to vary between 0.5 % (knee prosthesis surgery) to 10.1 % (open large bowel surgery) (79). Depending on the type of surgical procedure, the incidence of in-hospital SSIs per 1,000 post-operative patient-days varied from 0.1 to 5.7 (79). This makes SSIs the second most common HAI in Europe (80). In the USA, it is known to be the most common (81, 82) and most costly (83). In general, low- and middle-income countries have a higher incidence of SSIs as compared to high-income countries (84, 85).

In Norway, it has been mandatory since 2005 to monitor the incidence of SSI for the following five surgery procedures through the NOIS-registry regulation (NOIS; Norwegian Surveillance System for Health Cares Associated Infections in Hospitals) (86): 1) Coronary artery bypass graft; 2) Caesarean section; 3) Hip prosthesis surgery, 4) Cholecystectomy, and 5) Large bowel surgery. The surveillance data is registered in the NOIS-POSI (POSI; postoperative site infection) database, coordinated by the Norwegian Institute of Public Health. The national surveillance data for SSIs in 2018 were derived from 31,937 procedures from 61 hospitals (87). These data demonstrated the incidence of SSIs to be 3.8 %, with a variation between 1.6 % for total hip prosthesis surgery to 13.4 % for open colon surgery (**Table 6)**.

Table 6: The incidence of surgical site infections according to the surgical procedures under mandatory surveillance in Norway, 2018 (87).

Types of surgery	Incidence (%)	95 % CI
Coronary artery bypass graft – sternum	3.8	2.6–4.9
Coronary artery bypass graft – place of harvest	3.7	2.6–4.8
Caesarean section	3.8	3.4–4.2
Hip prosthesis surgery - total	1.6	1.3–1.8
Hip prosthesis surgery - hemi	3.5	2.9–4.0
Cholecystectomy - open	13.0	8.1–18.0
Cholecystectomy – laparoscopic	3.0	2.6–3.5
Colon surgery - open	13.4	11.6–15.1
Colon surgery - laparoscopic	7.7	6.4–8.9

1.2.4 Severity grading

Comparison of complications is often difficult since it depends on type of surgery and diseases, and since methods for reporting such outcomes are not uniform. However, it is possible to use qualitative information regarding the therapy used to treat the complication across different types of surgeries. This is used in the Revised Accordian Classification System (88), which is commonly used internationally and described in **Table 7**.

Table 7: Overview of classifications of postoperative complications according to the definitions of the Revised Accordian Classification System (88).

Revised Accordian Classification System		
Classification	**Grade**	**Definition**
Mild	1	Requiring minor invasive procedures that can be done at the bedside
Moderate	2	Requiring pharmacologic treatment with drugs other than such allowed for minor complications
Severe	3	Requiring a procedure without general anaesthesia
	4	Requiring a procedure with general anaesthesia or resulting in single-system organ failure
	5	Requiring a procedure with general anaesthesia and resulting in a single-system organ failure or resulting in multisystem organ dysfunction
	6	Death

1.3 Surveillance data

Surveillance of diseases, procedures and complications are essential to evaluate the quality of health care services. For this, several types of registers and quality indicators have been developed; they are described in the following subchapters.

1.3.1 National health registries

National health registers contain information from health care services and include consecutively updated information for a defined patient group. These registries are regulated by the law (89), and provides a basis for quality improvement, research and steering. In Norway, there are a total of 17 different health registries (90), and the Norwegian Institute of Public Health has the responsibility to store and disseminate national data according to regulations.

1.3.2 Medical quality registries

Medical quality registries are created to document treatment activity and results for further quality improvement and research (91), and to reduce unwanted variation in health care services and quality (92). To be useful, the results should be available for the general population, health care workers, management and administration, government and researchers. The medical health registries are initiated and established by the professional environment themselves (92).

To qualify as a national medical quality registry, data from all the hospitals in Norway should ideally be included, and it has to be approved by the Norwegian Directorate of Health (92). By the end of 2020, 51 national medical quality registries were established in Norway (93). The institution National Service Environment for Medical Quality Registers is responsible to ensure operation and good utilization of the medical quality registries. This unit has a central part at the Centre for Clinical Documentation and Evaluation together with the Professional Centre for Patient-reported Data at the Northern Regional Health Authority, in addition to regional service centres at the Northern-, Western-, South-Eastern- and Central Norway Regional Health Authority (94).

In addition to the national medical health registry data, the different health trusts may develop their own regional and local quality registries, based on the Health Personnel Act or regulations.

1.3.3 Quality indicators

Quality of care can be defined as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (95). A quality indicator may be defined as a measurable variable that provides information within an area that is hard to measure directly (96). Another definition is that a quality indicator is an indirect measure that says something about the quality of what is measured (97).

A clear understanding of what an improvement should include trends and directions that are prerequisites for quality improvement in the health care services (58). A quality indicator is typically evaluated by its importance, scientific soundness, usability and feasibility (98). Indicators can be used for health policy management, management of the institutions and internal quality improvement, and by the consumers of the health care services to compare the quality among the different providers (97). The quality indicators may be related to structure, process, or outcome of health care (99): "Structure" may describe attributes of the setting, material and human resources or organizational structures (e.g. facilities, financial resources, staffing, tools, standards, guidelines, methods), "process" may describe the series of activities to reach an objective (what is done and how well it is done), and "outcome" may describe the effects of the care provided on the health status or other outcomes (e.g. clinical, economic, patient reported, performance) (100).

Since 2012, the Norwegian Directorate of Health has had the responsibility to develop, convey and maintain national quality indicators for the health care services, which are regulated by the law (101, 102) and based on the framework from the Organisation for Economic Co-operation and Development's Health Care Quality Indicator Project (103).

Nutritional quality indicators

In a recent systematic literature review regarding nutrition care quality indicators in hospitals and nursing homes, 822 quality indicators were categorized into 19 themes and 151 sub-themes (104). Half of the indicators were related to process, a quarter to outcome and a quarter to structure. The authors concluded that these high numbers demonstrated a high interest in and the importance of better nutrition care provisions in institutions. At the same time, it also indicated a low consensus on how to best assess and measure the quality of nutrition care.

At the end of 2019, there were 174 different national quality indicators, of which two concerned nutrition care. Of note, none included nutrition care at hospitals (105). The national quality indicators regarding nutritional care included one for persons 67 years or older living and receiving health care services at home, and one for persons 67 years or older living at nursing homes. Both quality indicators monitor the percentage of persons who have been screened for “at risk of malnutrition” during the last 12 months.

For hospitals, the national patient safety programme In Safe Hands developed four voluntary quality indicators as a part of their action plan for preventing and treating malnutrition (48). Under this recommended action, the hospital wards are encouraged to pick the indicator that is the most suitable for them and use it as a part of their internal improvement work. An overview of these quality indicators can be seen in **Table 8**.

At Haukeland University Hospital, two local process indicators from the mandatory point-prevalence surveys have been used: 1) How many patients (percentage of hospitalized patients) were screened for being “at risk of malnutrition” on the study day, and 2) How many of the patients being “at risk of malnutrition” received nutritional support.

Table 8: Quality indicators monitoring nutrition care at hospitals, as defined by the national patient safety programme In Safe Hands (48).

Type of quality indicator	**Measuring**	**Measured among**
Process indicators		
Screening for «at risk of malnutrition»	Percentage of patients screened for «at risk of malnutrition» within 24 hours after admission	All admissions during the last week
Nutrition care plan	Percentage of patients "at risk of malnutrition" who had a nutrition care plan within 24 hours after screening	Patients "at risk of malnutrition"
Outcome indicators		
Energy needs covered	Percentage of patients having their estimated energy need covered, as defined in the nutrition care plan	Patients «at risk of malnutrition»
Stable body weight	Percentage of patients "at risk of malnutrition" who loss less than 2.5 kg body weight during the hospital stay	Patients "at risk of malnutrition" with a hospital stay longer than 10 days

1.4 Knowledge gaps

A complex relationship between malnutrition and postoperative complications has been described. Despite the fact that international guidelines for surgery acknowledge malnutrition as a risk factor for postoperative complications, particularly infections, they do not tell how to identify nor prevent and treat malnutrition. In general, the definition of malnutrition in the literature has not been consistent, and the potential effect of preventing malnutrition on postoperative complications is poorly investigated. As a step towards filling the knowledge gap, established quality registers can be used to explore the associations between well-defined definitions of malnutrition and postoperative complications.

National and international guidelines for preventing and treating malnutrition recommend screening patients with NRS 2002 to identify those who are “at risk of malnutrition” at hospitals. The extent to which patients who are identified by this tool as being “at risk of malnutrition” have an increased risk of SSI has not been adequately investigated. Therefore, there is a need to investigate the relationship between patients being “at risk of malnutrition” and the risk of developing SSIs.

Patients “at risk of malnutrition” are recommended to have their nutritional status assessed, in addition to nutritional support and care. In light of this, new global criteria for the definition of malnutrition was recently developed (later on known as the GLIM criteria). The nutrition community is encouraged to validate these criteria for relevance in clinical practice. As a part of this, the preoperative prevalence of the new definition of malnutrition, as well as its association with the incidence of severe postoperative complications should be investigated.

During the last two decades, improving nutritional care at hospitals has been assigned enhanced priority in both local and national patient’s safety work. However, the effect of the guidelines, strategies and related action plan on nutritional support and care at hospitals, as well as the potential for further improvement to decrease the risk of postoperative complications remain to be studied.

2. Objectives

The overall objective for this thesis was to investigate the association between malnutrition and postoperative complications, and the potential for prevention of both.

Specific objectives

The specific objectives for the following papers was to investigate:

I. The association between being «at risk of malnutrition» and the incidence of SSI in a larger, mixed surgical patient-sample at a large university hospital (**Paper I**)

II. The prevalence of preoperative malnutrition, and its association with severe postoperative complications and death among patients undergoing gastrointestinal resections at Norwegian hospitals (**Paper II**)

III. Whether the increased nutritional policy investment has resulted in changes in the prevalence of patients being «at risk of malnutrition», use of nutritional support and related diagnosis codes during an 11-year period at a large university hospital, and if there remains a further potential to decrease the risk of both malnutrition and postoperative complications (**Paper III**)

3. Material and methods

3.1 Source populations

The papers included in this thesis are based on the three following registers:

3.1.1 The Malnutrition registry

The Malnutrition registry is based on mandatory point-prevalence surveys measuring the prevalence of being «at risk of malnutrition» at somatic departments at Haukeland University Hospital. Patients under 18 years of age, terminal, pregnant or having bariatric surgery were not included in the surveys.

The point-prevalence surveys were recognized as a local quality improvement project, bringing local nutritional quality indicators, approved by the local privacy representative and the hospital's management, and a part of the hospital's nutritional strategy. The aims of the point-prevalence surveys were to monitor whether the implementation of a new strategy had positive effects on nutritional care in the hospital (63) and to identify in which patient groups/hospital wards screening for patients "at risk of malnutrition" would be of most value (106).

In the period between 31 January 2008 and 13 September 2018, the point-prevalence surveys were repeated annually two to four times, 34 times in total. They were conducted on a predetermined Thursday within each registration period, and the NRS 2002 (23) was used to identify patients "at risk of malnutrition", which is the same screening tool used in the daily practice at Haukeland University Hospital (also known locally as a part of the journal document "BL Trygg pleie"). Regular lectures and computer-based training regarding use of NRS 2002 (= identifying patients "at risk of malnutrition"), and how to give nutritional support (= prevent and treat malnutrition) have been available for the personnel at the hospital, both via interactive electronical lectures and regular meetings. Moreover, tools such as height measurement devices and scales were placed in patient rooms, and scales for patients in wheelchairs and bedridden patients were provided (63). The ward staff were first informed about the surveys two weeks in advance, and then reminded the day prior. The results were reported to the hospital's management; all participating units and the hospital's intranet were posted with information after each survey. Information about the Malnutrition registry is available to the public on the hospital's website (107).

The data is recorded in a data retrieval system developed by Webport (Webport AS, Grimstad, Norway). On the given day for the point-prevalence survey, all hospitalized patients at somatic wards 18 years or older were automatically registered in Webport at 08.00 AM.

Data retrieved from the electronic patient journal (DIPS (108)):

- The patient's name and social security number, and which hospital ward he/she was hospitalized at.

Health personnel collected and filled in the following information:

- Inclusion data: in cases of exclusion, the reason for exclusion related to the NRS 2002 (pregnant, terminal or bariatric surgery). Missing data for exclusion were registered as "not included for unknown reasons".
- Information regarding screening for "at risk of malnutrition": body weight (kg), height (cm), BMI, weight loss, dietary intake and severity of disease/degree of impaired nutritional status.
- Information regarding nutritional support for patients "at risk of malnutrition": no support, menu modification, oral nutrition supplement, enteral nutrition or parenteral nutrition, nutritional support were planned (type not specified), or if it was not intended to give them such. In addition, the question regarding whether a dietitian was involved in the patient care was answered by either "yes" or "no".

Information retrieved from the patient administrative system on request:

- Diagnosis and procedure codes at discharge

A demonstration of the screening process in the point-prevalence surveys can be seen in **Appendix I**.

3.1.2 The local NOIS-POSI registry

The NOIS-POSI registry is a mandatory national health registry for all Norwegian hospitals aiming to monitor the prevalence of SSIs. The registry uses indirectly identifiable health information. Patient's consent is not required since the registry is regulated by the NOIS-regulation (109). This regulation also provides guidelines for the responsibility, collection, collation, storage, use of data, and the submission of data to the Norwegian Institute of Public Health. In addition to the five procedures that are nationally mandatory to report (aortocoronary bypass, caesarean, inserting prosthesis in hip joint (total and hemi prosthesis), colon surgery and cholecystectomy (open and laparoscopic)), Haukeland University Hospital has monitored SSI for several more procedures since 2004 (110). This is registered as a local quality improvement project and is referred to as the local NOIS-POSI database.

This database is also integrated in a professional data retrieval system developed by Webport (Webport AS, Grimstad, Norway) composed of the following:

- Patient administrative data transferred from the electronic patient journal (DIPS (108)): The patient's name and social security number, time of admission, surgery and discharge, diagnostic code and re-admission.
- Surgery data transferred from the surgery planning system (Orbit (111)): surgical procedure, urgency, degree of purity, score from the American Society of Anesthesiologists Physical Status Classification System (ASA-score) (112), antibiotic prophylaxis and reoperation.
- Infection data at discharge: physician fills in the infection form.
- Infection data after admission: a voluntary follow-up mail sent to the patients 25-30 days after surgery. Non-responders are sent reminders and receive telephone follow-up (113).
- Risk index calculated from the ASA-score (112), operation time, degree of purity, and whether the surgery was endoscopic.

The occurrence of SSI is registered within 30 days after surgery (1 year for implants). Superficial SSI is either set by a physician or self-reported via a patient questionnaire

(**Appendix II**). The diagnosis of deep surgical infection and organ/space infection is set by a physician according to standardized criteria from CDC/ECDC (76, 114). The coverages of the local NOIS-POSI database are calculated from the procedures that are registered in the registry, as compared to the patient's administrative data collected by the local data system for surgery at Haukeland University Hospital (Orbit (111)).

3.1.3 The Norwegian Registry for Gastrointestinal Surgery (NoRGast)

NoRGast has collected data prospectively for colorectal, upper gastrointestinal and hepato-pancreato-biliary restrictions in Norway since 2014 and was acknowledged with the status of a National Quality Registry in May 2015 (115). The registry aims to ensure the quality of gastrointestinal surgery at Norwegian hospitals (116) and is created by a working group with representatives from the university clinics and other representative hospitals in Norway. The steering group is responsible for managing the national data, and the professional council has the professional responsibility. The data controller and owner is the CEO at the University Hospital of North Norway.

Data concerning surgical resections in the following organs (procedure code according to the classification of the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCPS) (117)) are mandatory and must be entered in the NoRGast register: colon (JFB 20 - 64 and JFH), rectum (JGB), oesophagus (JCC), gastric (JCD and JDD), liver (JJB), pancreas (JLC) and bile duct (JHC 10 - 99). Small bowel resections, appendectomies, cholecystectomies, stoma surgery without colorectal resection, and hernia repairs are entered in the register on a voluntary basis.

The registry is composed of the following information: gender, age, weight, weight loss, height, BMI, the Eastern Cooperative Oncology Group (ECOG)-score (118), use of anti-diabetic drugs, Glasgow Prognostic Score, the modified Estimation of Physiologic Ability and Surgical Stress (mE-PASS) (119), ASA-score (112) and the existence of severe heart and/or lung disease. Elective surgery is defined as start of anaesthesia between 8 am and 4 pm.

Patients who agree to be included in the registry sign a broad consent (120). This means that the registry is allowed to combine data with other registries, as described in the consent form (**Appendix III**). Coverage (completeness) of the Registry is annually compared to patient administrative data collected by the National Patient Registry (NPR), which is a compulsory registration for all hospitals in order to be eligible for reimbursement for in-hospital patient stays and therapy (115).

3.2 Study design

To meet the aims of the thesis, three observational studies based on established quality registers were performed. Paper I was conducted on a combination of data from the local NOIS-POSI database and the Malnutrition registry, Paper II on data from NoRGast, and Paper III on data from the Malnutrition registry. **Table 9** summarizes key characteristics of the included papers.

Table 9: Key characteristics of the included papers in the thesis.

	Paper I	**Paper II**	**Paper III**
Data sources	The local NOIS-POSI database and the Malnutrition registry	The Norwegian Registry for Gastro Surgery	The Malnutrition registry
Time period	Jan 2008–Dec 2016	May 2005–May 2018	Jan 2008–Sep 2018
Sample size, total	1242	11746	19767
Sample size, papers	1194	6110	18933
Independent variable	«At risk ofmalnutrition»[1]	Malnourished[2]	«At risk of malnutrition»[1], nutritional support and use of related diagnosis codes[3]
Dependent variable	The incidence of surgical site infections within 30 days after surgery	The incidence of severe postoperative complications within 30 days after surgery	Trends during an 11-year period

GLIM: Global Leadership in Malnutrition; **NOIS**: Norwegian Surveillance System for Health Care Associated Infections in Hospitals; **POSI**: postoperative site infection

[1] Defined by Nutritional Risk Screening 2002 (NRS 2002) (23)

[2] Defined by weight and body mass index in the second step of GLIM's criteria for malnutrition (29)

[3] Defined as the ICD-10 codes E46 («at risk of malnutrition»), E44 (mild to moderate malnutrition), and E43 (severe malnutrition)

3.2.1 Paper I

The aim of Paper I was to investigate the association between being «at risk of malnutrition» and the incidence of SSI.

Inclusion criteria for the study populations in Paper I were surgical patients included in both the local NOIS-POSI database and the Malnutrition registry in the period between January 2008 and December 2016. Patients were excluded if the "at risk of malnutrition" screening was conducted more than 30 days before or after surgery, had an unreliably BMI-value, were under the age of 18 or were not screened as warranting the diagnosis «at risk of malnutrition» (**Figure 5**).

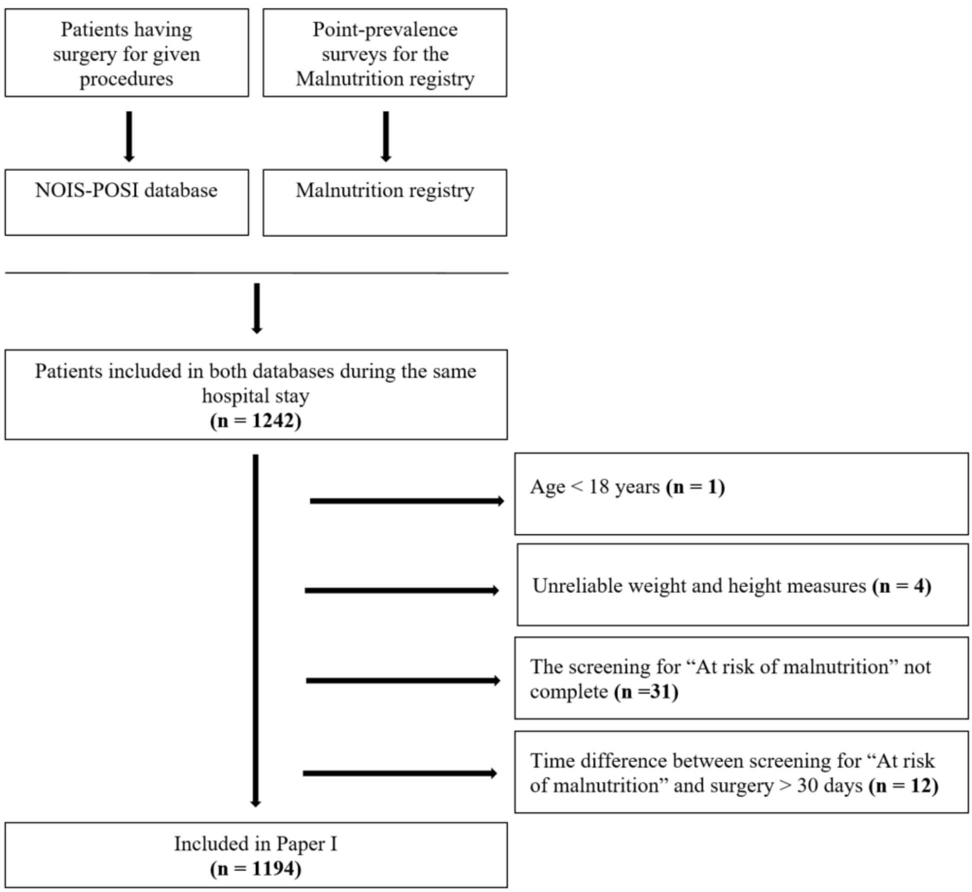

Figure 5: Flowsheet for patients included in Paper I.

3.2.2 Paper II

Paper II aimed to describe the prevalence of preoperative malnutrition among patients undergoing gastrointestinal resection and secondly to explore its association with severe postoperative complications and death.

The study population consisted of surgical patients 18 years or older who were included in the NoRGast database (116) in the period May 2005 to May 2018. Patients who had acute surgery or lacked information regarding weight change or postoperative complications were excluded (**Figure 6**).

Since NoRGast does not include information regarding the "at risk of malnutrition" screening, Paper II only used the second step of GLIM's criteria for the definition of malnutrition (29). All patients included in NoRGast had a need for a major resection and were therefore defined as having a chronic gastrointestinal condition that adversely impacts food assimilation or absorption. This classifies as an aetiologic criterion in the second step of the GLIM's model. GLIM's phenotypic criteria for weight loss and BMI were thus used to diagnose patients with malnutrition and further classify the condition as moderate or severe (Table 4). Severe postoperative complications were defined by the Revised Accordion Classification system grade 3–6 (Table 2) (88).

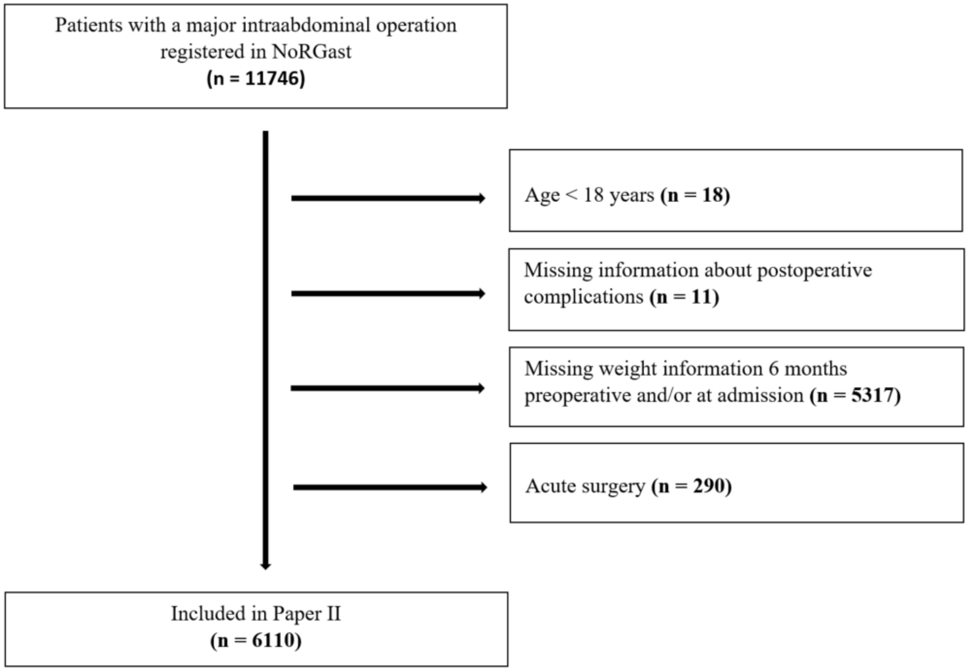

Figure 6: Flow sheet for patients included in Paper II.

3.2.3 Paper III

Paper III aimed to investigate the trends of the prevalence of being «at risk of malnutrition», its corresponding treatment strategies and use of diagnosis coding at discharge during an 11-year period, and if the trends differ between surgical and nonsurgical patients.

Patients 18 years or older who were included in the Malnutrition registry in the period 31 January 2008 to 13 September 2018 were the sample population for Paper III. Patients who were not screened to warrant the diagnosis of "at risk of malnutrition" and patients who were terminal, pregnant or having bariatric surgery were not included in the Malnutrition registry (**Figure 7**).

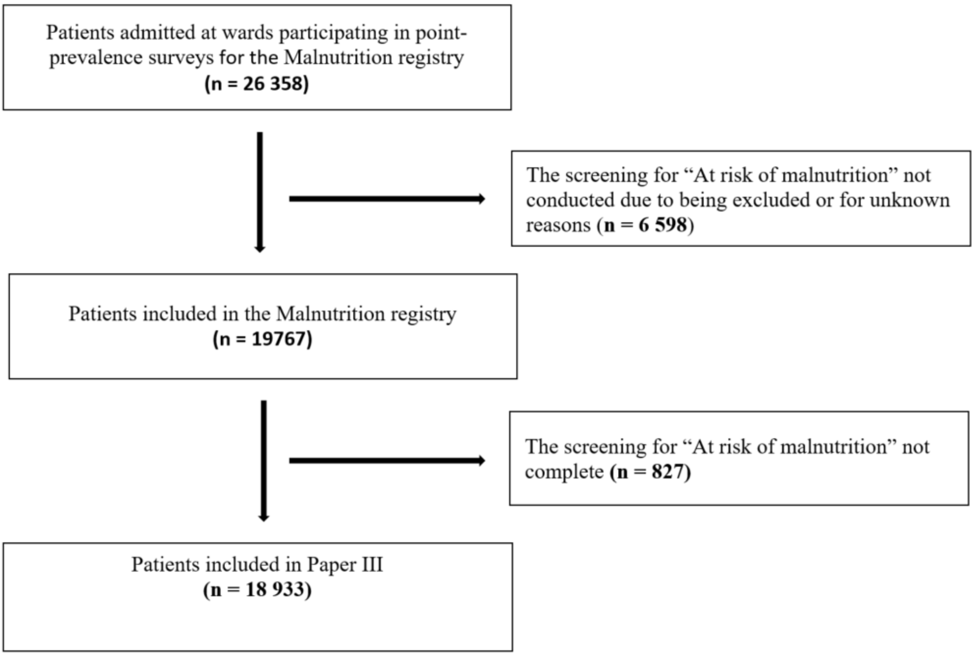

Figure 7: Flowsheet for patients included in Paper III.

3.3 Statistical analysis

3.3.1 Descriptive analysis

We used descriptive statistics to quantify sample characteristics. Continuous variables were reported as medians with 25th and 75th percentiles, whereas categorical variables were reported as counts and percentages. This was done for the total study samples as well as for various sub-groups (Paper I: a) patients «at risk of malnutrition» and those who were not, and b) patients who developed SSI and those who did not; Paper II: the original NoRGast-population and the population included in the paper; Paper III: surgical and non-surgical patients). Data between groups were compared using chi square for categorical data or Mann-Whitney U test for continuous data. All *p* values were 2-sided, and values < 0.05 were considered statistically significant.

3.3.2 Statistical modelling

Regression analysis was used in all papers to investigate the association between risk factors and outcomes. Risk factors included being «at risk of malnutrition» (Paper I), malnutrition (Paper II) and calendar time (Paper III). Outcomes included SSI (Paper I), severe postoperative complications and death (Paper II), and the prevalence of being «at risk of malnutrition» and adherence to nutritional guidelines (Paper III).

Logistic regression was conducted crude and with adjustment for potential confounders (121). The following confounders were evaluated and included in all analyses: age, gender, physical status (Charlson Comorbidity Index (122), ECOG-score (118) and/or ASA-score (112)). In Paper I, we additionally adjusted for surgery emergency (acute or elective). Associations from the logistic regression analysis in Paper I and Paper II were reported as odds ratios (OR) with 95 % confidence intervals (CI).

In paper III, logistic regression was used to investigate time trends in various indicators of the hospital's adherence to nutritional guidelines. In this analysis, calendar year was included in the regression model as a linear term for linear relationship or as a polynomial quadratic term for non-linear relationship. The time trend analyses in Paper III were reported as OR with 95 % CI. In addition, estimated regression lines were presented in graphical format together with the observed percentages.

3.4 Statistical software

IBM SPSS Statistics for Windows, version 23 (123) or higher, was used for statistical analyses inn all papers. R 3.6.2 for Windows (124) was additionally used in Paper III to present the graphical format of time trends.

3.5 Ethics

The studies were performed in accordance with the Helsinki Declaration of 1975, and approved by the Norwegian Regional Committee for Medical and Health Research Ethics (Paper I, 2015/2034; Paper II, 2018/1549; Paper III, 2018/904).

All patient information was anonymized. Signed consent with broad permission was collected for Paper II, but the need for patient consent was waived for the study population in Papers I and III.

4. Summary of main results

4.1 Paper I

In Paper I, the main goal was to investigate the association between the incidence of SSI and being "at risk of malnutrition".

A total of 1,194 patients were included, of which 566 (47.4 %) were men and the median (25th, 75th percentile) for age and BMI were 68 (59, 77) years and 26.0 (23.4, 29.1) kg/m^2, respectively. The incidence of SSIs was 7.7 %, and the study demonstrated that patients "at risk of malnutrition" more often had SSI (11.8 %) as compared to those who were not "at risk of malnutrition" (7.0 %) ($p = 0.047$). There tended to be no differences among patients who developed SSI or not according to age, type of surgery (acute/elective), BMI or ASA-score. The incidence of SSI was positively associated with the prevalence of being «at risk of malnutrition» (OR 1.81 (95 % CI: 1.04 - 3.16)). The NRS 2002's initial questions regarding weight loss and reduced dietary intake during the last weeks were associated with the incidence of SSI (OR 2.15 (95 % CI: 1.23 - 3.76) and OR 2.66 (95 % CI: 1.59 – 4.45), respectively), but not the ones regarding the patients that had a BMI < 20.5 kg/m^2 or were severely ill.

4.2 Paper II

Paper II explored the prevalence of malnutrition according to the BMI and weight loss criteria in the second step of GLIM's definition of malnutrition, and its association with severe postoperative complications among patients undergoing gastrointestinal surgery.

A total of 6,110 patients were included, of which 3,291 (53.9 %) were men and the median (25th, 75th percentile) age and BMI were 68 (58, 75) years and 25.2 (22.5, 28.3) kg/m^2, respectively. Overall, 19 % percent developed severe postoperative complications, and 1 % died within 30 days after surgery. In this study, 2,161 (35.4 %) patients qualified for the diagnosis of malnutrition, of whom 1,206 (19.7 %) were moderately and 955 (15.6 %) were severely malnourished. Malnourished patients were 1.29 (95 % CI: 1.13 - 1.47) times more likely to develop severe postoperative complications, and 2.15 (95 % CI: 1.27 - 3.65) times more likely to die within 30 days, as compared to those who were not. Those who were severely malnourished tended to have a stronger association with severe complications (OR 1.27 (95 % CI: 1.07 - 1.50)), as compared to those who were moderately malnourished (OR 1.17 (95 % CI: 1.00 - 1.37)), indicating that the severity grading in the GLIM criteria is appropriate in the clinical setting.

Almost half of the study population (45.7 %) experienced preoperative weight loss, which alone was associated with increased risk of severe postoperative complications (OR 1.28 (95 % CI: 1.13-1.46)) and death (OR 1.70 (95 % CI: 1.00-2.90)). Those with a weight loss ≥ 5 % had a higher risk of both severe complications and death (OR (95 % CI): 1.27 (1.10 – 1.46) and 2.35 (1.40 – 3.94), respectively). Weight loss was also associated with an increased risk of severe complications when stratifying for patients with obesity (BMI ≥ 30 kg/m^2) (OR (95 % CI): 1.42 (1.04 – 1.94)), but not for death.

We found no association between BMI < 18.5 kg/m^2 and < 20 kg/m^2, which were the cut-offs used in the criteria for moderate and severe malnutrition, respectively, for those under 70 years of age, and the incidence of severe postoperative complications or death. However, the incidence of severe postoperative complications among those 70 years or older were associated with the age-adjusted BMI cut-offs for moderate and severe malnutrition (< 20 kg/m^2 and < 22 kg/m^2, respectively) (OR 1.47 (95 % CI: 1.07-2.03) and OR 1.25 (95 % CI: 1.00-1.57), respectively). Despite the fact that patients 70 years and older with a BMI < 22 kg/m^2 demonstrated no association with death, they had a nearly 2.5-fold increased risk of death when having a BMI < 20 kg/m^2, as compared to those with a higher BMI.

4.3 Paper III

In Paper III, trends concerning being «at risk of malnutrition» and use of nutritional support and diagnosis coding related to malnutrition over an 11-year period with increased nutritional policy were examined, in addition to investigating whether there was a difference in trends between surgical and non-surgical patients.

The number of patients included in the study was 18,933, where 9,866 (52.1 %) were men, and the median (25th, 75th percentile) age and BMI were respectively 65 (51, 76) years and 25.0 (22.1, 28.4) kg/m^2. A total of 5,121 (27 %) patients were identified as «at risk of malnutrition». Fewer surgical patients (21.2 %) were «at risk of malnutrition», as compared to non-surgical patients (30.9 %) ($p < 0.001$), and the prevalence varied between 15.0 % and 27.5 % for surgical patients, and between 26.4 % and 33.9 % among non-surgical patients. No change in the prevalence of «at risk of malnutrition» from 2008 to 2018 was identified. The percentage of patients "at risk of malnutrition" who received nutritional support increased from 61.6 % in 2008 to 71.9 % in 2018 ($p < 0.001$), with a range from 55.6 to 74.8 %. Similarly, dietitians were more involved in the patients' treatment (range: 3.8 – 16.7 %), and there was increased use of ICD-10 codes related to malnutrition during the study period (range: 13.0 - 41.8 %) ($p < 0.001$). The trends for using nutritional support, including a dietitian, and use of ICD-10 codes were seen for both surgical patients and non-surgical patients ($p < 0.001$). However, the use of a dietitian and ICD-10 codes related to malnutrition was less common for surgical patients, as compared to non-surgical patients ($p < 0.001$).

5. Discussion

In this PhD-thesis, «at risk of malnutrition», as defined by the established screening tool NRS 2002 (23), is demonstrated to be associated with an increased risk of SSIs in a general surgical population (Paper I (125)), and that malnutrition, as defined by the cut-off for BMI and weight loss used in the second step of the new GLIM's criteria for malnutrition (29) is associated with severe postoperative complications, including death, among patients having gastrointestinal surgery (Paper II (35)). The association between malnutrition and severe postoperative complications tended to be stronger among those who fulfilled the criteria for severe malnutrition, as compared to those who qualified for moderate malnutrition, indicating a differentiation between severe and moderate malnutrition is appropriate for the clinical setting.

Moreover, the adherence to the nutritional guidelines at Haukeland University Hospital tends to improve during an 11-year period with increasing nutritional policy, monitored by the increased use of nutritional support, involvement of a dietitian and use of a related ICD-10 code for those who are «at risk of malnutrition» (Paper III). Notably, the prevalence of patients "at risk of malnutrition" did not tend to change during the period. All these trends were seen for both surgical and non-surgical patients, despite the fact that use of a dietitian and ICD-10 codes was less common among surgical patients as compared to non-surgical patients.

5.1 Methodological considerations

5.1.1 Study design

Observational data from three different registers have been used in this thesis. In Paper I, incidence data from the NOIS-POSI database was used in combination with point-prevalence data from the Malnutrition registry. Using point-prevalence data gives us snapshots of the prevalence of «at risk of malnutrition» at a given time, and thus we know if the patients were «at risk of malnutrition» on the days the surveys were conducted, but we do not know when it occurred. Therefore, patients who had more than 30 days between the risk screening and surgery were excluded to strengthen the data material's suitability to yield information about the relationship between being «at risk of malnutrition» and the incidence of SSIs. Therefore, we are not able to say whether the status of being «at risk of malnutrition» occurred prior to, or after, the SSI. Because we do not know what occurred first, we do not meet the temporality criterion for evaluating causal relationships, which is one of the nine criteria Bradford Hill developed to strengthen the evidence of a causal relationship in epidemiology (126). Therefore, despite the fact that our hypothesis was that the status «at risk of malnutrition» leads to increased risk of SSIs, it is also possible that SSIs increase the risk of malnutrition due to a decrease in appetite due to pain or illness, and/or that the increased need of nutrients was not achieved. Even so, the study demonstrated NRS 2002 as capable of identifying those who had an increased risk of SSIs, in addition to those who are «at risk of malnutrition». Therefore, these patients should receive special attention regarding prevention and treatment of both malnutrition and SSIs.

In Paper II, postoperative complications were studied in relation to the preoperative GLIM criteria, qualifying for the temporality criterion for causal relationship (126). The temporality criterion was also satisfied in Paper III since we followed the trends for prevalence of patients "at risk of malnutrition" and use of nutritional support and related diagnosis codes by calendar years. However, observational data still only disclose associations, and no causalities. Notably, despite the fact that randomized controlled trial (RCT) is accepted as the gold standard in clinical medical research (127), many questions in human health research can only be answered with observational studies due to ethical or practical reasons (128). Another beneficial part of observational studies it that they often include large study populations, which leads to statistical power to identify and estimate the magnitude of novel relationships (129), which might indicate a possible causality.

5.1.2 Validity

Of note, there are some challenges when using (a combination of) register data regarding the internal validity, meaning that the studies measure what they are intended to measure, in addition to the external validity, meaning that the results of the study can be generalized to the reader's population (130). These methodological issues will be discussed in the following subchapters.

Selection biases

A satisfactory coverage (completeness) in registers reduces the risk of selection bias and is therefore a prerequisite when using the registers for research. Notably, registry data will always have some missing data, but these should be missing at random to reduce the risk of selection bias. Since the local NOIS-POSI database and the NoRGast database were not originally designed for our research questions, we have categorized the register population based on our focus of interest («at risk of malnutrition» or not (Paper I) and degree of weight loss and BMI values (Paper II)). When this is done, the groups may also differ in terms of other relevant prognostic factors, inducing a potential selection bias.

Selection bias may also be induced when investigating subgroups within the registries. In Paper I, we excluded those who were not included in the Malnutrition registry from the local NOIS-POSI database, and also those who had had caesarean section (a procedure with an incidence of SSIs at 3.8 % (87)). Moreover, since the Malnutrition registry is based on point-prevalence surveys, patients with a longer length of stay had a higher chance of being included in this study population, as compared to the "normal" NOIS-POSI database. Thus, these data may have resulted in estimates that are biased (131). A longer length of stay can be associated with a higher morbidity, which may partly explain why we observed a higher incidence of SSIs in this study population (7.7 %) as compared to the national data (3.8 %) (87), where the length of stay does not affect the composition of the study sample. Another explanation for the differences in the incidence of SSIs is that since 2016, the national data for SSIs do not include patient-reported SSIs, a deficiency which reduces the incidence rate in the data before, as compared to after, 2016. In general, the NOIS-POSI must have a coverage above 80 % to be included in the national registry (132). After excluding those who met the exclusion criteria or were not screened for being «at risk of malnutrition» for unknown reasons, 72 % of all patients admitted to the somatic wards were included in the Malnutrition registry (*unpublished data in Paper III*). The rather high coverage may be explained by the fact that the surveys were mandatory and the wards were well-informed and received reminders prior to the surveys.

The coverage of the NoRGast database is calculated from the procedures that are documented in the registry, as compared to the patients' administrative data collected in the National Patient Registry (116, 133). These data have varied from 30 % to 93 % for participating hospitals (115). This variation was demonstrated to be in the implementation phase versus hospitals with a 3-year run-time, but also a variation within participating centres year by year. In 2019, the national coverage in NoRGast was 72 % (134). The limited completeness is mainly due to lack of personnel and logistics at the hospitals, and not due to lack of consent from the patients. In Paper II, nearly fifty percent of the NoRGast population was excluded due to missing weight information 6 months prior to surgery and/or at admission (115). Although the reasons for this are unknown, one might speculate that this is related to the patients' memory (unable to remember previous weight), physical status (unable to stand on weight) or the physicians' focus on weight change as a clinical indicator. This may lead to some biases, but analysis demonstrated no striking differences in morbidity and mortality between the total NoRGast population and the patients included in Paper II.

Potential confounders

To elucidate the true relationship between the exposure status and the outcome of interest, and to reduce the risk of spurious observations, the effects of confounders need to be adjusted for by statistical methods (121, 135). In general, age and gender are recognized as potential confounders, and should therefore be adjusted for (136). In addition, we adjusted for underlying medical conditions and physical status (defined by Charlson Comorbidity Index (122), ECOG- (118) and/or ASA-scores (112)) in all the included papers, since an impaired physical function may increase the risk of both malnutrition and postoperative complications (illustrated for Paper I and Paper II in **Figure 8** and for Paper III in **Figure 9**). Since acute surgery may indicate the severity of the situation, we adjusted for this in Paper I, and in Paper II we excluded those who had acute surgery. Notably, socioeconomic position is also a potential confounder since it is associated with an increased risk of both malnutrition (137) and postoperative complications (138). Unfortunately, we did not have such information.

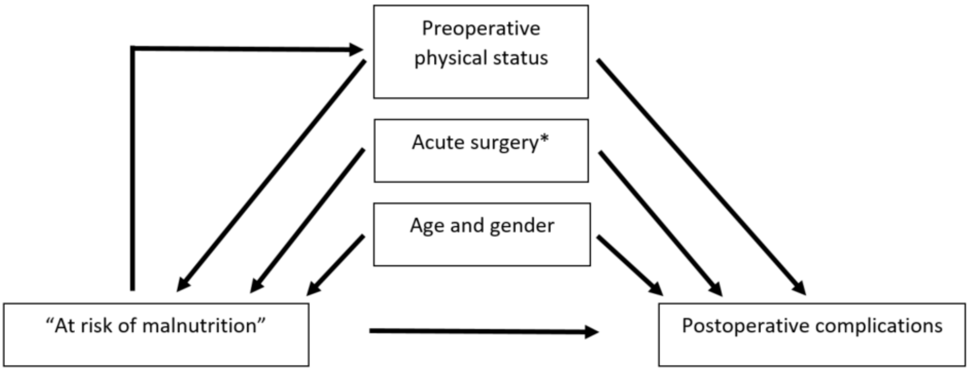

Figure 8: Potential confounders in Paper I and Paper II when investigating the relationship between being "at risk of malnutrition" and postoperative complications. Adjustment for these potential confounders were conducted in Paper I and Paper II. *Those with acute surgery were excluded in Paper II.

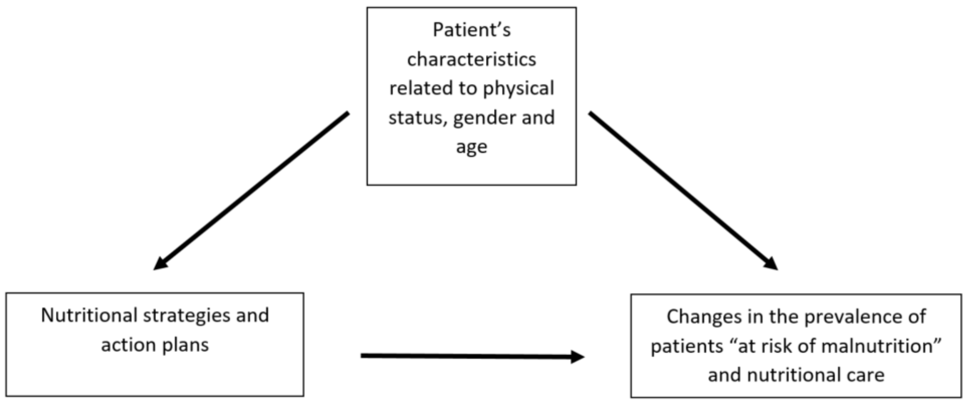

Figure 9: Potential confounders in Paper III when investigating the relationship between calendar years with nutritional strategy and implementation work with indicators of nutritional care and treatment (percentage of patients being "at risk of malnutrition" and the percentage of these who received nutritional support and a related diagnosis code.

Misclassification

"At risk of malnutrition"

Registry data are collected by many people in several different departments and wards over years. NRS 2002, which is used in the Malnutrition registry, is reported to have high practicability (139). The screening tool relies on nutritional parameters that require skilled and trained technicians to measure and control. All wards participating in the Malnutrition registry had access to lectures and computer-based training regarding how to fulfil NRS 2002 and how and to whom give nutritional support. However, we do not know whether the health personnel who actually registered the patients in the database had this training. Notably, since the results were forwarded to the hospital management, the surveys were mandatory, and the wards were well-informed, there is reason to believe that they aimed to conduct registration correctly with well-trained personnel.

It should be mentioned that the Malnutrition registry uses the first translation of NRS 2002 into Norwegian, which was also originally published in the Norwegian guideline for preventing and treating malnutrition. This translation asked for weight loss and reduced dietary intake during the last weeks in the initial screening, and not for weight loss and reduced dietary intake during the last 3 months and the last week, respectively, which is correct according to the original NRS 2002 version. This was first changed in the Norwegian translations in 2014 (21, 140). However, since data had already been collected and entered in the Malnutrition registry for several years using the first translation and changing the questions would make it more complex to investigate changes, the questions were not changed for this database. However, asking about weight loss "during the last weeks" as compared to "during the last 3 months" may not play a big role in the clinical setting. When it comes to reduced dietary intake the "last week" as compared to "the last weeks", this is also not contradictory. Therefore, there is reason to believe that the probability of misclassification of individuals "at risk of malnutrition" in the Malnutrition registry, as compared to whom would be identified by the correct translation of NRS 2002 is very small.

The NRS 2002's sensitivity (correct identification of patients "at risk of malnutrition") and specificity (correct rejection of patients not "at risk of malnutrition") is demonstrated to be higher than other screening tools in a hospital admission setting (141). However, for lack of a "gold standard" to identify patients «at risk of malnutrition», such validation has been conducted by using SGA (26). Notably, a recent systematic review reported that these screening tools in general had moderate validity, agreement, and reliability, and demonstrated variations in individual results using data from a 20-year period (142). Of note, the cut-offs for "low" BMI used in the different screening tools for «at risk of malnutrition» ranges from 18.5 kg/m^2 (24) to 23 kg/m^2 (25). In addition, the BMI variable has some limitations. For example, some patients may be fit and healthy, but have lower weight than is usual for their height (= low BMI). On the other hand, a normal or high BMI does not exclude the presence of malnutrition. This is especially true in populations with a high average age, since older people (often defined as 65 years and older) may have had a height loss, and thus a low BMI is camouflaged (143). With an increasingly aging population, and a strong association between malnutrition and age identifying patients “at risk of malnutrition”, this group is of increasingly clinical and socially importance (144). Thus, it should be noted that NRS 2002, which was used as a screening tool in Paper I and Paper III, gives an extra score for those who are 70 years or older in the final screening, but no age-adjusted questions in the initial screening.

Malnutrition

As previously described, GLIM’s definition of malnutrition is a two-step approach, starting with “at risk of malnutrition” screening. Since the NoRGast database does not include information from “at risk of malnutrition” screening, the definition of malnutrition in Paper II is not in exact agreement with the GLIM criteria (29). Of note, MUST (24), which is an approved screening tool as the first step in the GLIM criteria (29), uses the same cut-offs as the second step in the GLIM criteria (BMI < 20 kg/m^2 and weight loss ≥ 5 %) to identify patients younger than 70 years «at risk of malnutrition». Thus, all these patients could be defined to be at “at risk of malnutrition”, and thus qualify for the GLIM’s definition of malnutrition. Of note, for patients 70 years or more, GLIM uses a higher BMI cut-off (22 kg/m^2) as compared to the MUST (20 kg/m^2). Such lack of age-adjusted BMI cut-off for persons ≥ 70 years also applies for initial screening in NRS 2002 (23), which uses a cut-off at 20.5 kg/m^2 for all age groups. Thus, patients younger than 70 years identified as malnourished in Paper II fulfils the two-step approach of the GLIM criteria, but patients ≥ 70 years with a BMI between 20 kg/m^2 and 22 kg/m^2, without a weight loss ≥ 5 % during the last 3-6 months, would not been identified as «at risk of malnutrition» in GLIM’s first step, and thus not entered the second step to be classified as malnourished. Therefore, some older patients with BMI between 20 and 22 kg/m^2 may be “misclassified” as malnourished in Paper II, since they would not have been identified as “at risk of malnutrition” in GLIM’s first step. A potential consequence of not excluding those who were misdiagnosed with malnutrition is that the associations we observed may be weaker than what they might have been in reality if the two-step approach had been used correctly.

Another limitation in our use of the GLIM definition of malnutrition was lack of information regarding muscle mass, which is one of the potential phenotypic criteria (29). Therefore, patients with no weight loss nor low BMI, but with reduced muscle mass, may be misclassified as not malnourished.

Since GLIM asked the global nutrition community to validate their criteria for the clinical setting, it is of particular importance to be clear about our inclinations. Our one-step approach is simpler than the original two-step approach and is in opposition to the strong GLIM consensus that the first step in the evaluation of nutritional status is the screening for “at risk of malnutrition” with a validated screening tool (29). However, as previously described, the screening is not always a part of the daily routines, and it should be questioned whether it is correct to extend the process to diagnosis malnutrition, instead of simplifying it to more easily implement it in clinical practice.

Surgical site infections

Although the ECDC definitions of SSIs are widely used, many people are involved in the data collection, and different interpretations of these definitions may occur. However, for a hospital setting, a study testing the level of agreement between primary and validation data collectors in a point-prevalence survey of HAIs demonstrated the sensitivity and specificity of SSIs to be very high (98.2 % (95 % CI: 89.2 - 99.9) and 99.9 % (95 % CI: 99.7 – 100), respectively) (145). In the ECDC’s report for 2016, Norway was the only country including the patient-reported data regarding the incidence of SSIs (146). This led to artificially high SSI rates for Norway, as compared to other countries, and have thus not been included in the later ECDC’s reports, as for 2017 (79). In the same way, the patient-reported SSIs are not included in annual report from the Norwegian Institute of Public health from 2018 (87), although they seems to be in the report for 2016 (147). The reason for this not stated but may be due to the fear of misclassification. Of note, the patient-reported SSI only includes superficial SSIs.

To summarize, the incidence data of SSIs in Paper I may be higher than other studies since it included self-reported SSIs. However, there are no grounds for concluding that our study had a higher degree of misclassification than others, since others may be lacking superficial SSIs. Importantly, SSIs are most often identified after hospital discharge (148).

Severe postoperative complications

Moreover, many people contribute in the data collection for the NoRGast database. Of note, the data system used for reporting the data to NoRGast is easy to use regarding classification of complications with the correct Revised Accordian Classification System. Moreover, the Revised Accordian Classification system has been validated by an expert group, demonstrating a correlation of 0.994 with the scores (88). Thus, we believe the chance of misclassification of the definition of “severe postoperative complications” is low in Paper II.

Generalizability

In Paper I, the study population includes a rather general surgical adult population, except missing patients having bariatric surgery or caesarean section. Despite there being a chance of selection bias with more patients with a longer length of stay, as previously described, the point-prevalence surveys mirror the daily situation at a university hospital.

The study population in Paper II included patients having an underlying disease or condition affecting one or more organs important for nutrition – for intake, digestion or assimilation. This qualified for an etiologic GLIM criterion for the whole patient group, indicating that these are basically a group at greater risk than many other patient groups. Therefore, the results from Paper II should only be generalized for patients having elective surgery in the gastrointestinal system.

Although all Norwegian hospitals have the same national nutritional guidelines to follow, which are also in harmony with international guidelines, Haukeland University Hospital, to our knowledge, is the only hospital that has been conducting point-prevalence surveys for being «at risk of malnutrition» and its appurtenant treatment. Performing these surveys two to four times a year, presenting the results to the management and including all departments and wards, the surveys potentially support the implementation process by holding the nutritional focus on the departments, which may lead to improved screening and appurtenant treatment routines. Thus, we are not able to generalize that the improved nutritional support observed in Paper III is true for other hospitals. It should be noted that when evaluating the effect of nutritional support, it is important to differentiate between the intervention (to give nutritional support) and the aim of the intervention (to meet the nutritional needs). In Paper III, we do not have enough information to ascertain whether the nutritional support given was enough to meet the patients' energy and/or protein needs, which was studied in a recent RCT, named EFFORT ("The Effect on early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial") (149). Interestingly, the control group in the EFFORT-study and some other studies included in a systematic review and meta-analysis among medical patients demonstrating a beneficial effect of the nutritional support (150), comprised the patients who had received "normal treatment" at the hospitals. This demonstrates that the "normal treatment" in many hospitals is not enough to meet the patients' energy and/or protein needs.

5.2 Discussion of the main findings

5.2.1 The associations between «at risk of malnutrition» and malnutrition with postoperative complications

The positive association found in Paper I, between "at risk of malnutrition" and SSI is in harmony with statements in international guidelines for prevention of SSIs (71, 72). To our knowledge, the present study is the largest to date demonstrating such an association, applying the internationally recommended screening tool for identifying patients being "at risk of malnutrition" at hospitals, NRS 2002. In addition to our study, a positive association was also demonstrated in a few, rather small studies (conducted in patient groups having surgery for colorectal cancer (n = 352) (151), major laparoscopic abdominal surgery (n = 75) (152) and pancreaticoduodenectomy (n= 64) (*only significant results in the unadjusted analysis*) (153)). The first two of these three studies screened patients for being «at risk of malnutrition» prior to surgery, which strengthens the hypothesis of a causal relationship. The latter one screened after surgery and could therefore not tell whether the patients were «at risk of malnutrition» preoperatively.

The positive association demonstrated between malnutrition and severe postoperative complications in Paper II are in concurrence with a study among cancer patients having major abdominal surgery demonstrating the GLIM criteria to be positively associated with postoperative pulmonary complications and 90-day all-cause mortality (31), and another study from the U.S. National Surgical Quality Improvement Program which demonstrated modified GLIM criteria to be positively associated with both postoperative complications and mortality for colon and small bowel procedures (32). However, since the GLIM criteria were first announced in 2018, and published in 2019, there are still not many studies that have validated them against postoperative outcomes.

Weight loss and postoperative complications

In Paper I and Paper II, we demonstrated that any short-term or long-term weight loss is positively associated with postoperative complications. The adverse effect of preoperative weight loss was first demonstrated among patients with chronic peptic ulcer in 1936, where Studley found a mortality rate at 3.5 % for those who lost less than 20 % prior to surgery, as compared to 33 % for those who lost 20 % or more (154). In Paper I, SSIs was demonstrated to be more than two times more likely if the patient had answered "yes" to the initial NRS 2002's question regarding weight loss during the last weeks. Such a weight loss was seen among 11.6 % of the patients included in the study. In paper II, almost half of the patients (46.0 %) had lost weight during the last 6 months prior to surgery, a fact which alone was associated with an increased risk of both severe complications and death. A weight loss ≥ 5 % during the last 6 months, which classifies for GLIM's weight loss criteria, also demonstrated a clear association with postoperative complications and death. Both in this study and a previous one among patients having upper abdominal surgery (155) demonstrated that the positive association between preoperative weight loss and postoperative mortality is higher among those with a weight loss ≥ 5 % as compared to those with a lesser weight loss. Although these associations have been found consistent in a small number of studies, and even a kind of dose-response relation is demonstrated, none of these studies can confirm the causal relationship. This might be one reason for the relatively weak implementation of preventive measures in this field until now.

The association between preoperative weight loss and postoperative complications was consistent when studying obese patients only (BMI ≥ 30 kg/m^2 (17)), but not for death. The latter may potentially be explained by the fact that most persons with the highest level of weight loss end up with a BMI lower than 30 kg/m^2. Weight loss as a risk factor for postoperative complications is thus not restricted to patients with a lower BMI, which also is reported in previous studies (156, 157). However, despite the fact that preoperative weight loss has been known as a risk factor for postoperative complications for over 80 years (23), the large amount of data missing regarding preoperative weight loss in Paper II illustrates that it is still not recognized as a severe risk factor in all surgical environments.

BMI and postoperative complications

We found no association between the initial NRS 2002's question regarding having a BMI < 20.5 kg/m^2 (23) and the incidence of SSIs, nor a difference of BMI among those who had a SSI and those who did not (Paper I). In Paper II, we found no association between the age–adjusted BMI cut-off for those younger than 70 years (< 20 kg/m^2 and < 18.5 kg/m^2 for moderate and severe malnutrition, respectively) (29)) and the incidence of severe postoperative complications. This is in concurrence with previous studies demonstrating low BMI (defined as < 20 kg/m^2) to not be an independent risk factor for postoperative complications (158). However, patients 70 years or older with a BMI < 20 kg/m^2 and < 22 kg/m^2 (corresponding moderate and severe malnutrition, respectively) had a higher incidence of postoperative complications, as compared to those with a higher BMI. Of note, despite no association between older people with a BMI < 22 kg/m^2 and death, the patients 70 years or older with a BMI of < 20 kg/m^2 had a nearly 2.5-fold increased risk of death, as compared to those with a higher BMI. Based on these results, we find it appropriate to use an age-adjusted BMI cut-off when the patients' current height is used (29). Of note, the cut-off age for corresponding "low" BMI should be further investigated. The age 65 years or older is used in both GLIM and SGA, with increased severity grading starting at < 20 kg/m^2 and < 19 kg/m^2, respectively, whereas NRS 2002 uses 20.5 kg/m^2 irrespective of age at the initial screening but gives an additional score in the final screening to those 70 years or older, and MUST uses no age-adjustment. The different BMI cut-offs used in the different screening tools influence the sensitivity and specificity of the tools (144) and challenge the possibility to compare the results across populations and studies.

Moreover, using BMI as a part of the screening tools is also challenging in populations where the average BMI is high. Many of the tools used to screen for «at risk of malnutrition» were developed two decades or more ago (SGA in 1987 (26), MNA in 1996 (25), NRS 2002 in 2002 (23), and MUST in 2003 (24)), where the average BMI tended to be lower than these days. The prevalence of overweight/pre-obesity (BMI ≥ 25 kg/m^2 – 29.9 kg/m^2 (17)) and obesity (BMI ≥ 30 kg/m^2 (17)) has increased in Norway, as reported from the Trøndelag Health Study, where overweight or obesity were demonstrated among 63.3 % of men 20 years or older in 1995-1997, as compared to 71.0 % in 2006-2008, and among 54.0 % of women 20 years or older in 1995-1997, as compared to 57.7 % in 2006-2008 (159). Also, our study populations demonstrate overweight to be common, with a median (25, 75 percentiles) BMI in Paper I, Paper II and Paper III to be 26.0 (23.4, 29.1), 25.2 (22.5, 28.3) and 25.0 (22.1, 28.4) kg/m^2, respectively. This means that a lower weight loss was needed to meet the BMI criteria when the screening tools were developed, as compared to now. As an example using the average height of men and women at the Norwegian Armed Forces' session, which is 1.74 m (160), the amount of weight loss needed to meet the BMI cut-off used in NRS 2002 (< 20.5 kg/m^2) in Paper I and in the GLIM criteria for those younger than 70 years in Paper II (< 20.0 kg/m^2) is 16.6 kg (21.2 %) and 15.7 kg (20.1 %), respectively. Despite using the average height from the Norwegian Armed Forces' session may be misleading, this still illustrates the large differences of BMI cut-off in the screening and diagnostic tools and the median BMI in the study populations. When such a small part reach the cut-off, the group also loses statistical power to investigate any association. This may explain why we did not find any association between the NRS 2002's initial question regarding the BMI was < 20.5 kg/m^2 and the incidence of SSIs (Paper I) nor between preoperative BMI < 20 kg/m^2 and the incidence of severe postoperative complications for those younger than 70 years (Paper II).

A recent study concluded that screening tools for malnutrition should be regularly re-evaluated to ensure the validation values remain stable due to the rate and magnitude of the population changes observed over recent decades, including age and BMI (144), factors that our findings in Paper I and in Paper II support.

5.2.2 The adherence to the nutritional guidelines

Use of nutritional support and involving a dietitian

We found an increased use of nutritional support and dietitians for those «at risk of malnutrition» during the 11-year period (Paper III). However, on average, statistically more than one of three patients "at risk of malnutrition" over the 11-year period, and at least one of four per year, received no nutritional support. This increasing but unsatisfactory trend is supported by a Swiss study reporting the use of nutritional support (based on documented intervention codes) to patients with documented "at-risk-of-malnutrition" or malnutrition increased considerably after 2010, despite the fact that at least one third had no such documentation in 2014 (161).

There were no overall differences between surgical and non-surgical patients regarding the having nutritional support, but fewer surgical patients tended to have a dietitian involved in their nutritional support as compared to non-surgical patients. The analysis from the first two years of this 11-year period demonstrated no change in the prevalence of patients "at risk of malnutrition" having nutritional support (63). Our results thus indicate that implementation of nutritional guidelines takes time, and may benefit from regional and national campaigns (42, 43).

The EFFORT-study recently demonstrated personalized nutritional support from a dietitian to non-surgical patients «at risk of malnutrition» at hospitals to reduce the rate of readmission, mortality and costs, as compared to hospitalized patients "at risk of malnutrition" receiving treatment as usual (149). This study was included in a recent systematic review and meta-analysis among medical patients that found that nutritional support to patients «at risk of malnutrition» had a greater beneficial effect on important clinical outcomes (improved survival, lower rates of non-elective hospital readmission, higher energy and protein intake and increased body weight) in studies published after 2014 in contrast to earlier. This time difference was thought to be due to a higher quality and lower bias in the newer studies, in addition to the fact that the newer trials used a higher quality of protein and a more individualized, patient-specific approach in their nutritional support (150).

An RCT such as the EFFORT study has so far not been conducted among surgical patients and the evidence for nutritional support in surgical patients is claimed to be of low quality, partly due to the study's not excluding patients who were not "at risk of malnutrition" (3). Thus, ESPEN highlights the need for randomized controlled nutritional intervention studies for surgical patients "at risk of malnutrition" (3). Of note, surgical patients should be evaluated not only by their surgical procedures but should also include medical aspects, including nutritional status and appurtenant support.

Interestingly, we observed that surgical patients received more advanced nutritional support such as enteral and parenteral nutrition, whereas menu modification and oral nutritional supplements were more often used among the non-surgical patients. We do not know whether the advanced type of nutritional support was alone or in addition to oral nutrition. The importance of oral nutrition, when accepted, includes physiological and social functions, enables sensation of taste and flavour and is a part of pleasure and well-being, and should therefore always be included when possible (162).

Use of diagnostic codes for malnutrition

In average, about one of five patients «at risk of malnutrition» were assigned a diagnostic code for malnutrition at discharge. During the 11-year period, we found that the use of diagnosis coding regarding nutritional status increased, both for surgical and non-surgical patients (Paper III). However, fewer surgical patients “at risk of malnutrition” received a related diagnostic code at discharge, as compared to non-surgical patients. The increased lack of coherence between screening for being «at risk of malnutrition» with the use of related diagnostic codes for surgical patients as compared to non-surgical patients was also demonstrated in a Danish registry study where 5.3 % of the patients at surgical departments who had received a diagnostic code for malnutrition had been screened with NRS 2002, as compared to 13.9 % at the medical departments (163). Their results were thought to derive from a higher performance of “at risk of malnutrition” screening in the medical departments. The underlying reasons for this are unknown but may also be seen in conjunction with less involvement of dietitians, and therefore less awareness of the importance. Our results demonstrating an increased use of the “at risk of malnutrition”-related ICD-10 codes is in harmony with a study from Switzerland demonstrating that the prevalence increased from 0.32 % in 1998 to 3.97 % in 2014 (161) and an American study demonstrating the use of diagnostic codes for malnutrition increased almost three-fold in the period from 1993 (1.2 %) to 2010 (3.2 %) (164). Both these studies demonstrated variations within regions, indicating differences in clinical practice.

Since the hospital stay is often of short time (on average, 4.2 days in 2016 in Norway (165)), the importance of passing on the information to the next care giving level is major, and a way of doing this includes use of diagnosis coding. This importance is emphasized by the two national quality indicators regarding nutrition care demonstrating that only 19.3 % (range 5.9 % - 30.6 % across counties) of persons 67 years or older living and receiving healthcare services at home, and only 47.8 % (range 79.5 – 18.9 % across counties) in nursing homes had been screened for «at risk of malnutrition» during the last 12 months (105). Undoubtedly, the coverage of these quality indicators should be improved to increase their value.

5.2.3 Trends in the prevalence of "at risk of malnutrition"

Using NRS 2002, no change in the prevalence of being «at risk of malnutrition» was demonstrated among the total study population, neither for surgical patients nor non-surgical patients in the period 2008 – 2018 (Paper III). Due to the time needed to develop the diagnosis «at risk of malnutrition», in addition to the generally short hospital stay, a change in prevalence of being «at risk of malnutrition» may depend more on factors outside rather than inside the hospital. Moreover, screening for "at risk of malnutrition" distinguishes between those who are "at risk of malnutrition" and those who are not. The use of nutritional support is meant for those who are "at risk of malnutrition" and is not meant to prevent "at risk of malnutrition" but to treat the patients who are at risk. Therefore, it is not surprising that the prevalence of being «at risk of malnutrition» is rather stable, despite the use of nutritional support increases. Of note, there is a potential to detect patients "at risk of malnutrition" at an earlier stage since most patients have one or more meetings as outpatients prior to admission. To screen outpatients with a high risk of malnutrition, in addition to make a dietitian more accessible for these patients, are therefore aims in Haukeland University Hospital's revised nutritional strategy (39).

For surgical patients, the proportion of patients being «at risk of malnutrition» varied between 15.0 % and 27.5 % during the period. This variation may be due to normal variations of the composition of hospitalized patients. To our knowledge, there is no other hospital that has reported trend analysis of the prevalence of malnutrition during a period with the same screening tool in the same departments as we did in Paper III, and it is therefore hard to compare our results with others. However, using data from a systematic review and meta-analysis of NRS 2002 as a predictor of postoperative outcomes in patients undergoing abdominal surgery in the period (166), we can see that there was not a striking change of trend in the prevalence of being «at risk of malnutrition» in the period 2008–2014: **2008**: 14 % (elective gastrointestinal surgery, Switzerland (167)); **2009**: 39.8 % (gastric carcinoma, China (168)); **2010**: 39.3 % (colorectal surgery, Switzerland (169)); **2011**: 30.8 % (colorectal cancer, China (170)); **2012**: 22.4 % (elective abdominal surgery, Germany (171)); **2013**: 34.7 %

(laparoscopic abdominal surgery, China (152)), 68.0 % (pancreaticoduodenectomy, Japan (153)), 41.7 % (gastrointestinal cancers, China (172)); **2014**: 28.1 % (colorectal cancer, Korea (151)). Notably, although these studies use the same screening tool, they differ in type of underlying diseases and demographic factors and are therefore not directly comparable with our study.

6. Conclusion

The overall objective of this thesis was to investigate the association between malnutrition and postoperative complications and the potential for prevention of both.

In Paper I, SSI was demonstrated to occur more often among patients being "at risk of malnutrition" as compared to those who were not.

In Paper II, preoperative malnutrition was demonstrated to be common among patients having abdominal resections and was associated with an increased risk of severe surgical complications.

In Paper III, increasing nutritional policy investment for hospitals demonstrated no change in the prevalence of patients being "at risk of malnutrition" in the period 2008–2018, although there was an increased prevalence of patients "at risk of malnutrition" and receiving nutritional support. Moreover, each year, one of four patients "at risk of malnutrition" received no nutritional support, and the involvement of a dietitian in the patient care and use of related diagnostic codes was less common among surgical patients than among non-surgical patients. This indicates that there is still a potential to reduce the risk of malnutrition in surgical patients.

Despite the indications, there is still a need to investigate the preventive effect of optimal nutritional care on the incidence of both malnutrition and postoperative complications in well-designed RCTs in the future.

7. Future perspectives

Based on the results highlighted in this thesis, the following future perspectives are suggested:

Investigate the effect of adherence to the nutritional guidelines for surgical patients

Patients who are identified as "at risk of malnutrition" should also be recognized as patients with increased risk of postoperative complications. To prevent the potential consequences of malnutrition, the condition should be treated, and the effects investigated. Intervention studies should evaluate the effect of meeting the patients' energy- and protein needs, and not be limited merely to whether or not a nutritional intervention was performed. A promising result here may increase the motivation in the surgical professional environment to implement nutritional guidelines.

Simplify screening and/or diagnostic criteria for malnutrition

To increase the motivation for «at risk of malnutrition» screening and use a related diagnosis code, the nutrition community should strive for simplification. This includes investigating whether the GLIM criteria need to be a two-step approach using some of the variables twice, instead of one step. Moreover, if BMI is still be included as a criterion, the cut-offs should be adjusted to meet the population changes in BMI and age. Moreover, since "at risk of malnutrition" most often occurs and worsens over time, and furthermore needs time to improve, it is rationale to think that the screening and appurtenant treatment should be conducted at an earlier point than at admission for elective surgery. Here, the potential of increased use of user involvement should be investigated.

Develop national quality indicators for nutritional care at hospitals

To date, national quality indicators regarding nutritional care do not include patients in hospital. Quality indicators related to process and results, as described by In Safe Hands (48), should be implemented so that quality of nutritional care in hospitals can be evaluated and compared across hospitals, and actions taken to follow up.

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9efde-3a68-42c2-9613-d7cdebb93a1a:a3ff9539e9401c1a019992645622f23d5c852fcd/Oppretting%20og%20drift%20av%20nasjonale%20medisinske%20kvalitetsregistre%20%E2%80%93%20Veileder.pdf.

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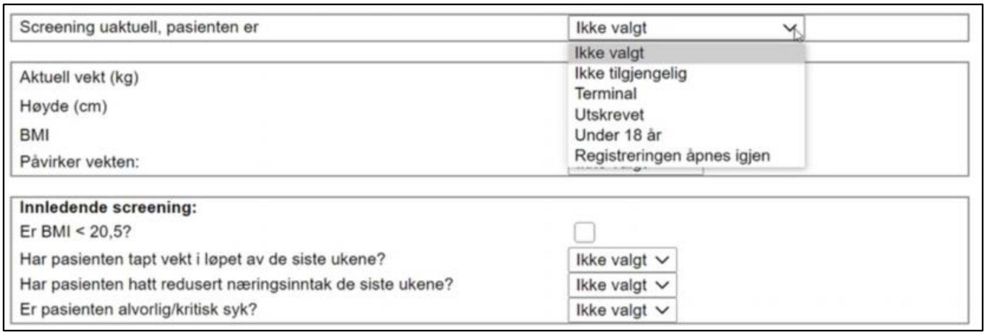
9. Appendices

Appendix I

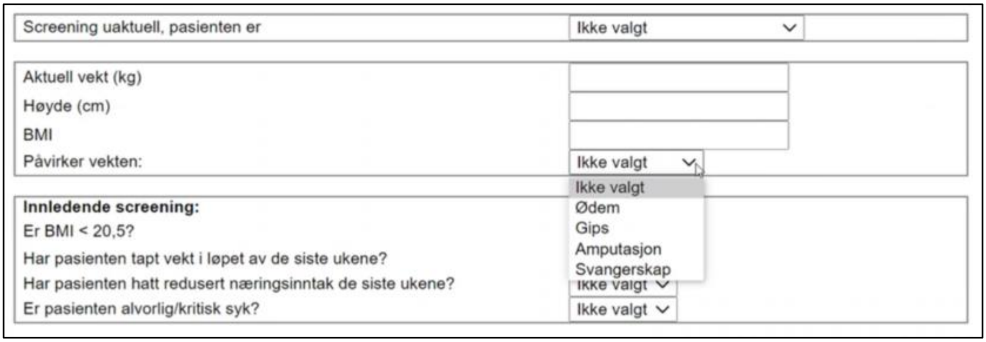
Demonstration of the point-prevalence surveys investigating the prevalence of "at risk of malnutrition" and use of nutritional support among hospitalised patients (using the Webport program).

The initial screening and answer options for why patients cannot be included.



*The initial screening and answer options to **A**) factors affecting weight, **B**) the question regarding weight loss during the last weeks, **C**) the question regarding reduced dietary intake during the last weeks, and **D**) the question regarding critical illness.*

A)



B)

C)

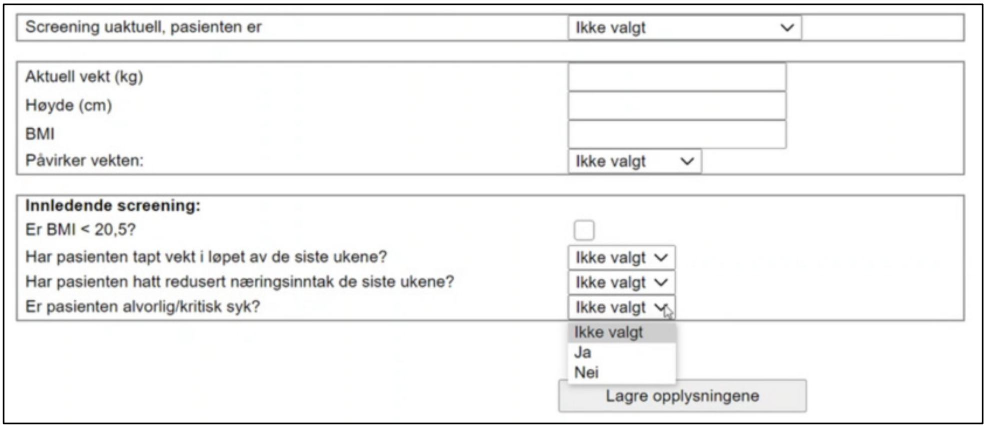
Screening uaktuell, pasienten er — Ikke valgt

Aktuell vekt (kg)
Høyde (cm)
BMI
Påvirker vekten: — Ikke valgt

Innledende screening:
Er BMI < 20,5?
Har pasienten tapt vekt i løpet av de siste ukene? — Ikke valgt
Har pasienten hatt redusert næringsinntak de siste ukene? — Ikke valgt
Er pasienten alvorlig/kritisk syk?

Ikke valgt
Ja
Nei

D)



Screening uaktuell, pasienten er — Ikke valgt

Aktuell vekt (kg)
Høyde (cm)
BMI
Påvirker vekten: — Ikke valgt

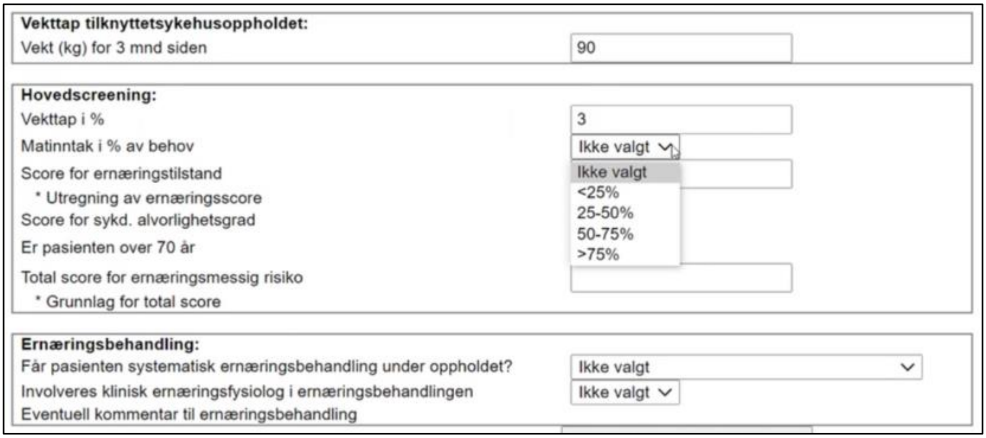
Innledende screening:
Er BMI < 20,5?
Har pasienten tapt vekt i løpet av de siste ukene? — Ikke valgt
Har pasienten hatt redusert næringsinntak de siste ukene? — Ikke valgt
Er pasienten alvorlig/kritisk syk? — Ikke valgt

Ikke valgt
Ja
Nei

Lagre opplysningene

The final screening of NRS 2002 and answer options for ***E)*** *the degree of food intake and* ***F)*** *the score for degree of illness.*

E)

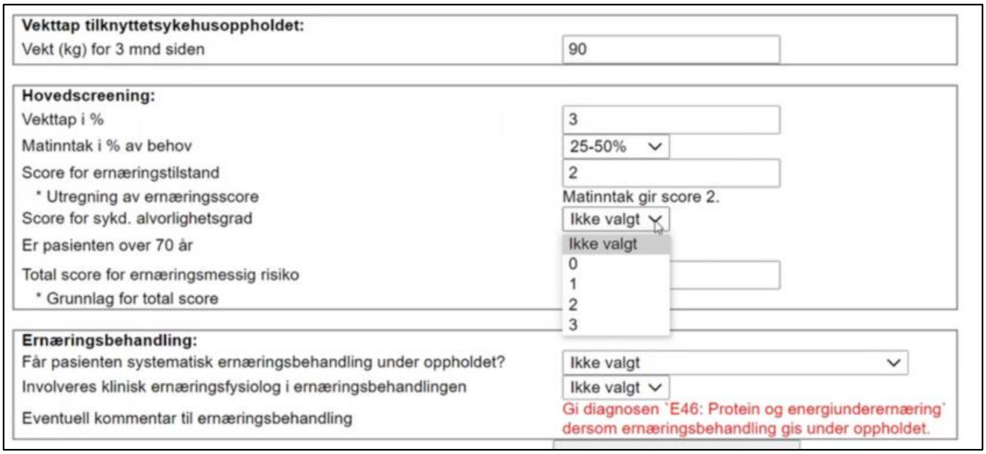


Vekttap tilknyttetsykehusoppholdet:
Vekt (kg) for 3 mnd siden 90

Hovedscreening:
Vekttap i % 3
Matinntak i % av behov Ikke valgt
Ikke valgt
<25%
25-50%
50-75%
>75%
Score for ernæringstilstand
* Utregning av ernæringsscore
Score for sykd. alvorlighetsgrad
Er pasienten over 70 år
Total score for ernæringsmessig risiko
* Grunnlag for total score

Ernæringsbehandling:
Får pasienten systematisk ernæringsbehandling under oppholdet? Ikke valgt
Involveres klinisk ernæringsfysiolog i ernæringsbehandlingen Ikke valgt
Eventuell kommentar til ernæringsbehandling

F)



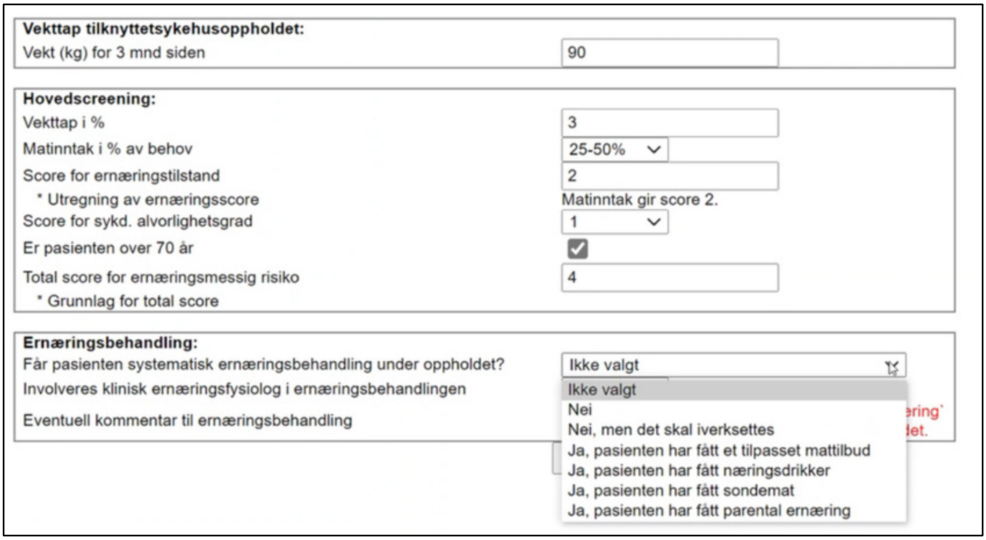
Vekttap tilknyttetsykehusoppholdet:
Vekt (kg) for 3 mnd siden 90

Hovedscreening:
Vekttap i % 3
Matinntak i % av behov 25-50%
Score for ernæringstilstand 2
* Utregning av ernæringsscore Matinntak gir score 2.
Score for sykd. alvorlighetsgrad Ikke valgt
Ikke valgt
0
1
2
3
Er pasienten over 70 år
Total score for ernæringsmessig risiko
* Grunnlag for total score

Ernæringsbehandling:
Får pasienten systematisk ernæringsbehandling under oppholdet? Ikke valgt
Involveres klinisk ernæringsfysiolog i ernæringsbehandlingen Ikke valgt
Eventuell kommentar til ernæringsbehandling
Gi diagnosen `E46: Protein og energiunderernæring` dersom ernæringsbehandling gis under oppholdet.

Follow-up questions with answer options regarding ***G)*** *nutritional support and* ***H)*** *involvement of a dietitian.*

G)



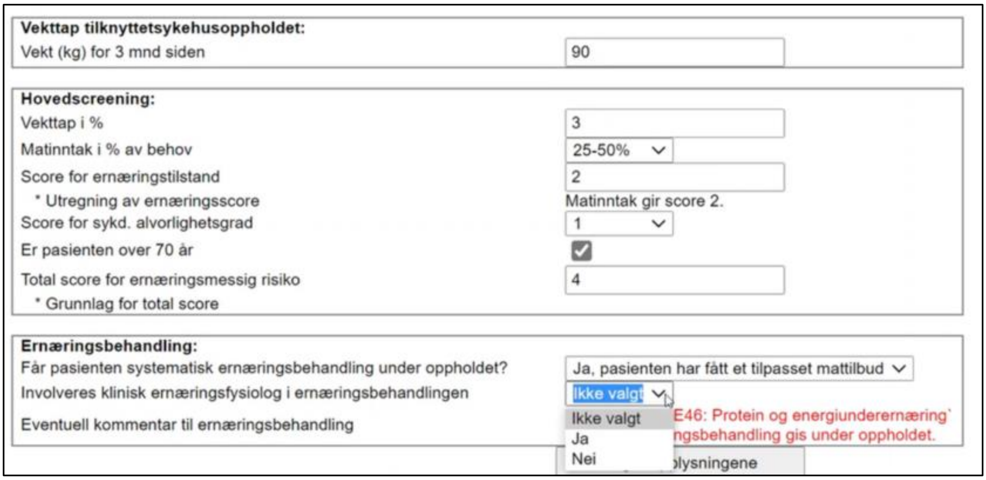
Vekttap tilknyttetsykehusoppholdet:
Vekt (kg) for 3 mnd siden: 90

Hovedscreening:
Vekttap i %: 3
Matinntak i % av behov: 25-50%
Score for ernæringstilstand: 2
* Utregning av ernæringsscore: Matinntak gir score 2.
Score for sykd. alvorlighetsgrad: 1
Er pasienten over 70 år: ☑
Total score for ernæringsmessig risiko: 4
* Grunnlag for total score

Ernæringsbehandling:
Får pasienten systematisk ernæringsbehandling under oppholdet?: Ikke valgt
- Ikke valgt
- Nei
- Nei, men det skal iverksettes
- Ja, pasienten har fått et tilpasset mattilbud
- Ja, pasienten har fått næringsdrikker
- Ja, pasienten har fått sondemat
- Ja, pasienten har fått parental ernæring

Involveres klinisk ernæringsfysiolog i ernæringsbehandlingen
Eventuell kommentar til ernæringsbehandling

H)



Vekttap tilknyttetsykehusoppholdet:
Vekt (kg) for 3 mnd siden: 90

Hovedscreening:
Vekttap i %: 3
Matinntak i % av behov: 25-50%
Score for ernæringstilstand: 2
* Utregning av ernæringsscore: Matinntak gir score 2.
Score for sykd. alvorlighetsgrad: 1
Er pasienten over 70 år: ☑
Total score for ernæringsmessig risiko: 4
* Grunnlag for total score

Ernæringsbehandling:
Får pasienten systematisk ernæringsbehandling under oppholdet?: Ja, pasienten har fått et tilpasset mattilbud
Involveres klinisk ernæringsfysiolog i ernæringsbehandlingen: Ikke valgt
- Ikke valgt
- Ja
- Nei

Eventuell kommentar til ernæringsbehandling
E46: Protein og energiunderernæring
ngsbehandling gis under oppholdet.
ılysningene

Example of a completed form with an automatic feedback regarding use of diagnosis coding related to the «at risk of malnutrition» status.

Screening uaktuell, pasienten er	Ikke valgt
Aktuell vekt (kg)	87
Høyde (cm)	188
BMI	24.6
Påvirker vekten:	Ikke valgt
Innledende screening:	
Er BMI < 20,5?	☐
Har pasienten tapt vekt i løpet av de siste ukene?	Ja
Har pasienten hatt redusert næringsinntak de siste ukene?	Ja
Er pasienten alvorlig/kritisk syk?	Nei
Vekttap tilknyttetsykehusoppholdet:	
Vekt (kg) for 3 mnd siden	90
Hovedscreening:	
Vekttap i %	3
Matinntak i % av behov	25-50%
Score for ernæringstilstand	2
* Utregning av ernæringsscore	Matinntak gir score 2.
Score for sykd. alvorlighetsgrad	1
Er pasienten over 70 år	☑
Total score for ernæringsmessig risiko	4
* Grunnlag for total score	
Ernæringsbehandling:	
Får pasienten systematisk ernæringsbehandling under oppholdet?	Ja, pasienten har fått et tilpasset mattilbud
Involveres klinisk ernæringsfysiolog i ernæringsbehandlingen	Nei
Eventuell kommentar til ernæringsbehandling	Gi diagnosen `E46: Protein og energiunderernæring` dersom ernæringsbehandling gis under oppholdet.
	Lagre opplysningene

Appendix II

Template for follow-up letters to patients

Fornavn/etternavn:
Gateadresse:
Postnr./poststed:

Deres ref.: Vår ref.: Dato:

Har du hatt infeksjon i operasjonssåret?

Sykehuset undersøker rutinemessig hvor mange pasienter som får infeksjon i operasjonssåret etter utskrivelse/behandling ved vårt sykehus. Vi er svært takknemlige hvis du svarer på følgende spørsmål når det har gått 30 dager etter operasjonen. Skjemaet returneres i den vedlagte konvolutten, også om du ikke har hatt tegn til infeksjon.

Har det kommet gulgrønn sårvæske (puss) fra operasjonssåret?	☐ Ja	☐ Nei
Har det vært unormal rødme rundt operasjonssåret (mer enn ½ cm på hver side)?	☐ Ja	☐ Nei
Har lege åpnet operasjonssåret på grunn av infeksjon?	☐ Ja	☐ Nei
Har du fått antibiotika på grunn av betennelse i operasjonssåret?	☐ Ja	☐ Nei
Har du hatt feber (mer enn 38,5 grader) på grunn av betennelse i operasjonssåret?	☐ Ja	☐ Nei

Dato når du evt. oppdaget infeksjonstegn: ____________________

Dato/underskrift ____________________ -- ____________________

Har du svart ”ja” på ett av spørsmålene, tyder det på at du har hatt en infeksjon i operasjonssåret. Vi ber deg da om å kontakte din lege og medbringe dette brevet. Legen skal fylle ut spørsmålene på side 2 før du sender brevet tilbake til oss i den vedlagte konvolutten. Opplysningene vil bli behandlet konfidensielt.

Har du spørsmål knyttet til denne henvendelsen kan du kontakte undertegnede.

Vennlig hilsen

VEND

Utfylles av lege

Pasienten har / har hatt en overflatisk postoperativ sårinfeksjon	☐ Ja	☐ Nei
Pasienten har / har hatt en dyp postoperativ sårinfeksjon	☐ Ja	☐ Nei
Pasienten har / har hatt en postoperativ infeksjon i organ/hulrom	☐ Ja	☐ Nei

Infeksjon ble oppdaget (dato)			
Bakteriologisk prøve:		☐ Ikke tatt	☐ Ingen vekst
Vekst av:		Dato for prøvetaking:	

Evt. klinisk vurdering:

____

____

____

Underskrift, dato og stempel

INFEKSJON I OPERASJONSOMRÅDET

Kasusdefinisjon utarbeidet av European Center for Disease Prevention and Control

Overfladisk postoperativ sårinfeksjon

Infeksjon som oppstår innen 30 dager etter operasjon
OG
infeksjonen omfatter kun hud og subkutant vev omkring snittet
OG
minst ett av de følgende:

- *Purulent sekresjon fra det overflatiske snittet, laboratoriebekreftet eller ikke*
- *Isolering av mikroorganismer ved dyrking av væske eller vev fra det overfladiske snittet, i prøve tatt ved aseptisk teknikk*
- *Minst ett av følgende tegn eller symptomer på infeksjon: smerte eller ømhet, lokal hevelse, rødhet, varme OG det overflatiske snittet med hensikt er åpnet av kirurg, med mindre dyrking fra såret er negativ*
- *En kirurg eller behandlende lege har stilt diagnosen overflatisk postoperativ sårinfeksjon*

Dyp postoperativ sårinfeksjon

Infeksjon som oppstår innen 30 dager etter operasjon uten innsetting av implantat, eller innen 90 dager etter operasjon med innsetting av implantat
OG
infeksjonen synes å være relatert til operasjonen
OG
infeksjonen omfatter dypt bløtvev (for eksempel fascie, muskel) omkring snittet
OG
minst ett av de følgende:

- *Purulent sekresjon fra det dype snittet, men ikke fra organ/hulromdelen av operasjonsområdet*
- *Et dypt snitt åpner seg spontant eller åpnes med hensikt av kirurg når pasienten har minst ett av følgende tegn eller symptomer: feber (>38 ºC), lokal smerte eller ømhet, med mindre snittet er dyrkingsnegativt*
- *En abscess eller andre tegn på infeksjon som omfatter det dype snittet blir påvist ved direkte undersøkelse, under reoperasjon eller ved histopatologisk eller radiologisk undersøkelse*
- *En kirurg eller behandlende lege har stilt diagnosen dyp postoperativ sårinfeksjon*

Postoperativ infeksjon i organ/hulrom

Infeksjon som oppstår innen 30 dager etter operasjon uten innsetting av implantat, eller innen 90 dager etter operasjon med innsetting av implantat
OG
infeksjonen synes å være relatert til operasjonen
OG
infeksjonen omfatter andre deler av kroppen (for eksempel organer og hulrom) enn snittet, som ble åpnet eller manipulert under en operasjon
OG
minst ett av de følgende:

- *Purulent sekresjon fra et dren lagt inn med separat innstikkssted i organet/hulrommet*
- *Isolering av mikroorganismer ved dyrking av væske eller vev fra organet/hulrommet, i prøve tatt ved aseptisk teknikk*
- *En abscess eller andre tegn på infeksjon som omfatter organet/hulrommet blir påvist ved direkte undersøkelse, under reoperasjon eller ved histopatologisk eller radiologisk undersøkelse*
- *En kirurg eller behandlende lege har stilt diagnosen postoperativ infeksjon i organ/hulrom*

Appendix III

Consent for inclusion in NoRGast

NoRGast

Norsk register for Gastrokirurgi

Samtykkeskjema

Informasjon og forespørsel om samtykke til deltakelse i Norsk register for Gastrokirurgi (NoRGast)

Bakgrunn og hensikt

Det nasjonale fagmiljøet har opprettet Norsk kvalitetsregister for Gastrokirurgi – NoRGast. Hensikten er å kartlegge, sikre og forbedre kvaliteten for alle pasienter som får utført operasjon på bukorganer, spiserør eller bukvegg. Databehandlingsansvarlig for registeret er Universitetssykehuset Nord-Norge HF v/administrerende direktør.

Hva skal registreres?

De opplysninger som inngår i registeret er ditt personnummer og navn, hvilken behandling du får i forbindelse med din bukoperasjon, din rekonvalesens og eventuelle komplikasjoner. Det blir ikke tatt noen ekstra prøver eller undersøkelser.

Hvor skal opplysningene i registeret hentes fra?

Din behandlende lege fyller ut et skjema basert på opplysninger som framkommer i forbindelse med innleggelse, behandling og utskrivelse. Opplysninger kan også kan innhentes fra annen helseinstitusjon, fastlege etc., f. eks. ved komplettering av data etter 30 dager. Det skal rutinemessig innhentes supplerende opplysninger fra Norsk Pasientregister og Folkeregisteret som skal inngå i registeret.

Hvem kan få tilgang til opplysningene?

Opplysningene blir lagret i et eget dataregister som er godkjent av Datatilsynet. Alle opplysninger behandles konfidensielt, det vil si at bare personer som jobber med registeret kan lese dem. Alle som har tilgang til registeret har taushetsplikt. Opplysninger vil bli overført fra ditt behandlende sykehus til et nasjonalt register der de lagres i avidentifisert form. Data i registeret vil bli oppbevart så lenge det er gitt konsesjon til registeret. Alle data vil bli slettet dersom konsesjonen opphører.

Forskning og kvalitetssikring

For å kunne kvalitetssikre helsetjenesten ved bruk av registre er det nødvendig å bruke forskningsmetoder for å analysere data. Forskere vil for eksempel kunne bruke registeret til å evaluere hva som har betydning for gode eller dårlige behandlingsresultater, eller hvilken betydning behandlingen har i forhold til sosialmedisinske og helseøkonomiske forhold. For spesielle forskningsprosjekter kan det derfor være aktuelt å knytte sammen informasjon fra registeret med andre offentlige registre (se baksiden av arket). Sammenstilling av data fra andre registre krever forhåndsgodkjenning fra de offentlige instanser loven krever. Ved at andre sykehus i Norge registrerer de samme opplysningene vil det også være mulig å sammenligne resultater, både for kvalitetssikring og i forskning på følger av kirurgisk behandling. Resultater basert på analyser fra registeret vil ikke kunne tilbakeføres til enkeltindivider. Forskningsprosjekter skal godkjennes av Regional komitè for forskningsetikk. Ved å samtykke til å delta i NoRGast aksepterer du at registrerte opplysninger kan benyttes både til kvalitetssikring og forskningsformål, og du samtykker også til at du kan kontaktes på nytt utenom sykehuskontroller.

Rettigheter

Det er frivillig å registrere seg i dette registeret, og for at registrering skal skje må det gis et skriftlig samtykke. Hvis du ikke ønsker å samtykke vil ikke dette ha noen konsekvenser for behandlingen du får på sykehuset. Du har rett til å få vite hva som står om deg i registeret, og du kan kreve at opplysninger som står om deg blir slettet eller rettet på, i henhold til Personopplysningsloven. Mer informasjon om registeret og dine rettigheter finner du på www.kvalitetsregistre.no

Snu arket!

Dekningsgradsanalyser
Opplysningene vil årlig bli sammenstilt med opplysninger fra norsk pasientregister (NPR) for å beregne registerets dekningsgrad.

Det kan være aktuelt å sammenstille informasjon fra registeret med følgende offentlige registre og befolkningsundersøkelser:

Medisinsk fødselsregister
Norsk Pasientregister
Kreftregisteret
Reseptregisteret
Registeret i Statistisk sentralbyrå(FD-Trygd)
Befolkningsundersøkelsene som inngår i Cohort of Norway (Conor)
Norsk intensivregister
Befolkningsundersøkelsene som inngikk i Statens Helseundersøkelser (SHuS)
Skattedirektoratets databaser
Hjerte-/Karregisteret
Folkeregisteret
Dødsårsaksregisteret

Det kan også være aktuelt å bruke opplysninger om deg fra din sykejournal.
Alle slike sammenstillinger krever forhåndsgodkjenning av de offentlige instanser loven krever, for eksempel Personvernombudet, Regional komité for medisinsk forskningsetikk og Datatilsynet.

All informasjon vil bli behandlet med respekt for personvern og privatliv og i samsvar med lover og forskrifter.

Samtykkeerklæring

Jeg samtykker til at mine opplysninger inngår i dette kvalitetsregisteret og at de kan inngå i forsknings-prosjekter innefor formålet til registeret.

Pasientens signatur og dato: ____

Stedfortredende samtykke når berettiget
(Signert av nærstående, dato): ____

Pasient ID/Barkode

Paper I – III

I

PLOS ONE

RESEARCH ARTICLE

A positive association between nutritional risk and the incidence of surgical site infections: A hospital-based register study

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Data Availability Statement: The anonymized data are within the paper and its Supporting Information files. In agreement with the Norwegian Act on medical and health research, the Regional Committee for Medical and Health Research Ethics has approved the full dataset to only be saved in the hospital's own research server. To request access to the full dataset, please contact kkf@helse-bergen.no.

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Abstract

Surgical site infections (SSI) are amongst the most common health care-associated infections and have adverse effects for patient health and for hospital resources. Although surgery guidelines recognize poor nutritional status to be a risk factor for SSI, they do not tell how to identify this condition. The screening tool Nutritional Risk Screening 2002 is commonly used at hospitals to identify patients at nutritional risk. We investigated the association between nutritional risk and the incidence of SSI among 1194 surgical patients at Haukeland University Hospital (Bergen, Norway). This current study combines data from two mandatory hospital-based registers: a) the incidence of SSI within 30 days after surgery, and b) the point-prevalence of patients at nutritional risk. Patients with more than 30 days between surgery and nutritional risk screening were excluded. Associations were assessed using logistic regression, and the adjusted odds ratio included age (continuous), gender (male/female), type of surgery (acute/elective) and score from The American Society of Anesthesiologists Physical Status Classification System. There was a significant higher incidence of SSI among patients at nutritional risk (11.8%), as compared to those who were not (7.0%) ($p = 0.047$). Moreover, the incidence of SSI was positively associated with the prevalence of nutritional risk in both simple (OR 1.76 (95% CI: 1.04, 2.98)) and adjusted (OR 1.81 (95% CI: 1.04, 3.16)) models. Answering "yes" to the screening questions regarding reduced dietary intake and weight loss was significantly associated with the incidence of SSI (respectively OR 2.66 (95% CI: 1.59, 4.45) and OR 2.15 (95% CI: 1.23, 3.76)). In conclusion, we demonstrate SSI to occur more often among patients at nutritional risk as compared to those who are not at nutritional risk. Future studies should investigate interventions to prevent both SSI and nutritional risk among surgical patients.

no). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: ASA, American Society of Anesthesiologists physical status classification system; BMI, Body mass index; NCSP, NOMESCO Classification of Surgical Procedures; NOIS, Norwegian Surveillance System for Health Care Associated Infections in Hospitals; NOMESCO, Nordic Medico-Statistical Committee; NRS-2002, Nutritional risk screening tool (2002); POSI, Postoperative site infection; SSI, Surgical site infection.

Introduction

A surgical site infection (SSI) is defined as an infection that has occurred within 30 days after a surgical procedure in the part of the body where the surgery took place, and is one of the most commonly reported health care-associated infections in both European countries and in the U.S. [1, 2]. Such infections are associated with reduced health-related quality of life [3], higher morbidity and mortality [4], and leads to extreme costs for the health care system [3, 5]. SSI is most often a result of contamination during surgery. However, several patient characteristic affect the risk of developing a SSI, including undernutrition, as described in both WHO Guidelines for Safe Surgery and Centers for Disease Control and Prevention's Guideline for the Prevention of Surgical Site Infection [6, 7].

Although the diagnosis of undernutrition has no commonly accepted definition, the term usually includes conditions associated with low food intake, weight loss and/or low body mass index (BMI) [8]. In the hospital setting, one of the most commonly used screening tools to diagnose patients to be at risk of undernutrition or to already be undernourished is the Nutritional Risk Screening (NRS-2002) [9–11]. In addition to identifying patients to be at nutritional risk, NRS-2002 is able to predict higher treatment costs and one-year mortality in hospitalized patients [12]. Interestingly, only a few and rather small studies (conducted in patient groups having surgery for colorectal cancer (n = 352) [13], major laparoscopic abdominal surgery (n = 75) [14] and pancreaticoduodenectomy (n = 64) (*the latter study only significant results in the unadjusted analysis*) [15]) have demonstrated nutritional risk to be a risk factor for SSI. As NRS-2002 is a well-known, non-invasive and fast screening tool to use in clinical practice, it would be of major interest if it also could identify those with an increased risk of SSI. Thus, we aimed to investigate the association between nutritional risk, as defined by NRS-2002, and the incidence of SSI within 30 days after surgery in a larger, mixed surgical patient-sample.

Materials and methods

Study sample

The present study included 1194 surgical patients from Haukeland University Hospital, which is a combined emergency and referral teaching hospital with 1100 beds in Hordaland County in the western part of Norway. In Norway, monitoring the incidence of SSI after five surgical procedures (aortocoronary bypass, cesarean, inserting prosthesis in hip joint (total and hemi prosthesis), colon surgery and cholecystectomy (open and laparoscopic)) through the NOIS-registry regulation (NOIS; Norwegian Surveillance System for Health Care Associated Infections in Hospitals) has been mandatory since 2005 [16]. The registration is coordinated by the Norwegian Institute of Public Health and registered in the NOIS-POSI (POSI; postoperative site infection) database as previously described [17]. In addition to these nationally mandatory registrations, Haukeland University Hospital has monitored SSI for several more procedures since 2004. This is registered as a local quality improvement project, and is further referred to as the local NOIS-POSI database.

Another quality improvement project conducted at Haukeland University Hospital is the regular prevalence surveys of nutritional risk among hospitalized patients. These point-prevalence registrations have been mandatory for the somatic departments and have annually been repeated three to four times since 2008 among non-terminal, non-pregnant and non-bariatric surgical patients ≥ 18 years [18]. Since then, almost 2000 patients have been evaluated and registered in this Nutritional risk database each year.

The study population includes patients who during the same hospital stay at Haukeland University Hospital, in the period from 2008 and out 2016, were both registered in the local NOIS-POSI database and the Nutritional risk database. The patients were excluded if the

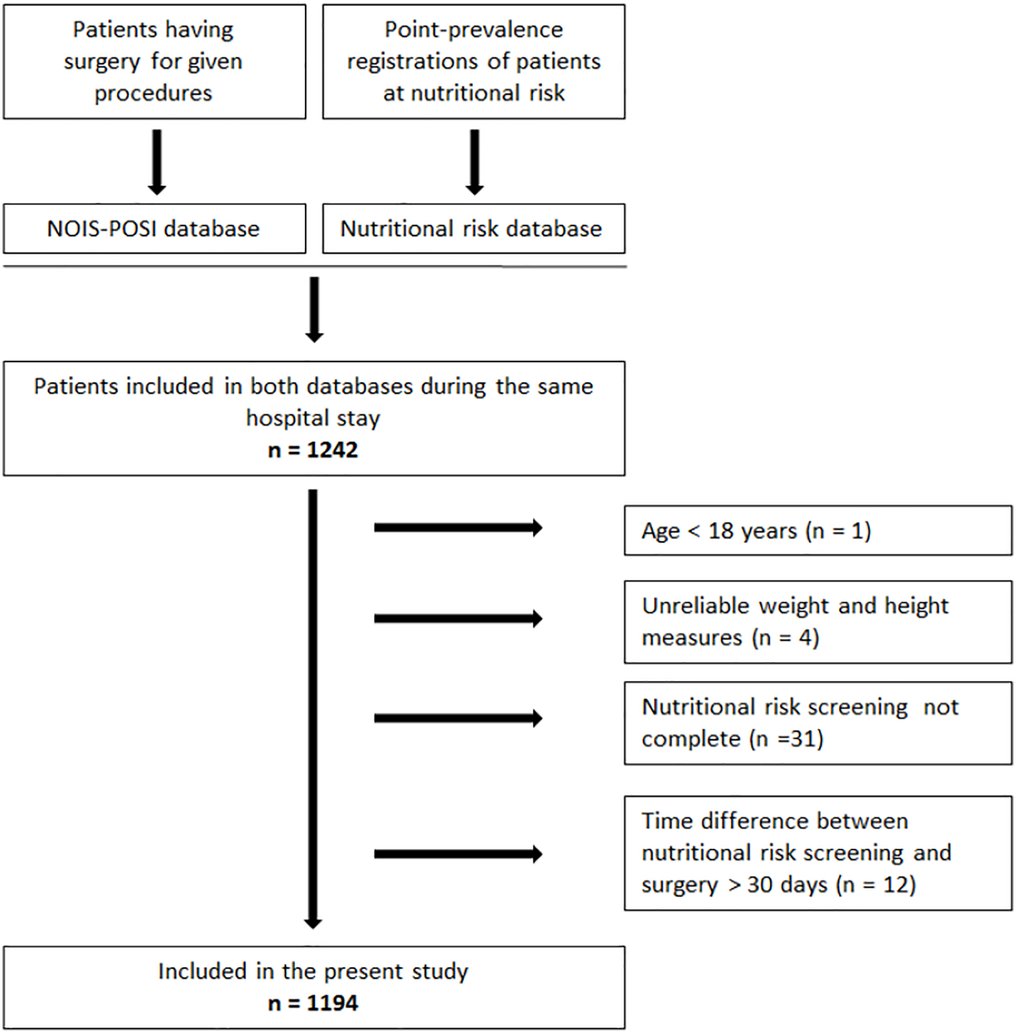

Fig 1. Flow chart of the study sample.

https://doi.org/10.1371/journal.pone.0197344.g001

nutritional risk screening was conducted more than 30 days before or after surgery. Patients with an unreliably BMI-value and patients who were not completely screened to achieve the diagnosis "at nutritional risk" were also excluded (Fig 1).

Ethics

The current study is based on two quality improvement projects that aimed to monitor the incidence of SSI and prevalence of nutritional risk, as well as monitor and improve clinical practice. Such improvement projects do not need to pass Regional Committee for Medical and Health Research Ethics or obtain patient consent according to the Health Research Act, Norway. This current study was approved by the Regional Committee for Medical and Health Research Ethics (2015/2034) before merging data from these two quality improvement projects, and the datasets were anonymized prior to access and analysis. The study is in accordance with the Declaration of Helsinki.

Assessment of clinical data

The incidence of SSI was registered within 30 days after surgery, either at hospital discharge or at voluntary follow-up mail sent to the patients 25–30 days after surgery. The diagnosis of deep surgical infection and organ/space infection was set by a physician after standardized criteria from CDC/ECDC [19, 20], and superficial SSI was either set by a physician or was self-reported by a patient questionnaire. Non-responders were sent reminders and received telephone follow-up as previously described in detail [21].

A nurse or a nurse assistant used the screening tool NRS-2002 to determine whether the patients were at nutritional risk or not. NRS-2002 is based on four introductory questions on low BMI (<20.5 kg/m^2), recent weight loss, recently reduced food intake and critical illness [9]. If one or more of these four questions are answered with "yes", the patient enters the final screening. The final screening gives a total score from 0 to 7 based on more in-depth questions regarding the patient's nutritional status (score 0–3) and the severity of the patient's disease in light of nutritional requirements (score 0–3), in addition to one score if the patient is older than 70 years. A total score of ≥ 3 in the final screening identifies patients to be at nutritional risk.

Both the incidence of SSI and the prevalence of nutritional risk were registered in a professional data retrieval system developed by Webport (Webport AS, Grimstad, Norway). Information about age, gender, type of surgery and score from the American Society of Anesthesiologists Physical Status Classification System (ASA-score), which was used to evaluate the patients' physical status [22], was automatically assigned from the hospital's patient administrative system.

Statistical analysis

Analyses were conducted for the total study sample, as well as separately among patients at nutritional risk and patients that were not, and among patients who developed SSI and patients that did not. Summary measures for continuous variables are reported as medians (25^{th} to 75^{th} percentile), and categorical variables are reported as counts (percentages). The Kolmogorov-Smirnov test was used to assess normality of continuous variables. Mann-Whitney U and chi-square tests were used to compare sub-groups as appropriate. Crude odds ratios with 95% confidence intervals were calculated by logistic regression models, and the adjusted odds ratio included age (continuous), gender (male/female), type of surgery (planed less or more than 24 hours (acute or elective, respectively)) and ASA-score (score 1–4). The statistical package IBM SPSS Statistics was applied. All P-values were two-tailed and values < 0.05 were considered as statistically significant.

Results

Patients' characteristics

In total, 1194 patients were included in the present study (Fig 1), and their general characteristics are described in Table 1. Overall, 47.4% were men and the median (25^{th}, 75^{th} percentile)

Table 1. General characteristics and ASA-score for the study sample and according to patients' nutritional risk status and incidence of surgical site infections[1].

	Study sample	Nutritional risk			Surgical site infections		
		Yes	*No*	P^2	*Yes*	*No*	P^2
	n = 1194	n = 170	n = 1024		n = 92	n = 1102	
General characteristics							
Male, *n (percent)*	566 (47.4)	81 (47.6)	485 (47.4)	1.000	44 (47.8)	522 (47.4)	1.000
Age, *median (25, 75 percentile)*	68 (59, 77)	74 (62, 82)	66 (58, 76)	< 0.001	65 (55, 77)	68 (59, 77)	0.057
Acute surgery, *n (percent)*	205 (17.2)	73 (42.9)	132 (12.9)	< 0.001	18 (19.6)	187 (17.0)	0.624
BMI, *median (25, 75 percentile)*	26.0 (23.4, 29.1)	20.6 (18.6, 25.3)	26.5 (24.0, 29.4)	< 0.001	25.5 (22.8, 29.2)	26.0 (23.4, 29.1)	0.754
ASA-score							
1 or 2, *n (percent)*	719 (60.2)	81 (47.6)	638 (62.3)	< 0.001	56 (60.9)	663 (60.2)	1.000
3 or 4, *n (percent)*	463 (38.8)	88 (51.8)	375 (36.6)	< 0.001	36 (39.1)	427 (38.7)	1.000

[1] Missing data: ASA-score (n = 12); BMI (n = 6)

[2] P-values for differences between patients at nutritional risk or not and patients having an incidence of surgical site infection or not were calculated by using Mann-Whitney U test for continuous variables and chi-square tests for categorical variables

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age and BMI were 68 (59, 77) years and 26.0 (23.4, 29.1) kg/m^2, respectively. The minority of the patients had acute surgery (17.2%). Most patients were operated in the musculoskeletal system (52.5%), the digestive system (22.4%) or the coronary arteries (18.3%). An overview of the different surgeries according to the classification of the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP) [23] are given in Table 2.

The prevalence of nutritional risk and the incidence of SSI

In this study, 170 (14.2%) patients were identified to be at nutritional risk. As compared to patients who were not at nutritional risk, these patients were older, had more often acute surgery, had a lower BMI and tended to have a higher ASA-score (Table 1). Ninety-two (7.7%) patients had an incidence of SSI, whereas most of them (55.4%) were classified as deep according to standardized criteria [19, 20]. There was essentially no difference in age, type of surgery (acute/elective), BMI or ASA-score among those who had SSI and those who did not (Table 1).

Table 2. Overview of the organ system operated in the present study (n = 1194).

Organ system operated[1]	n (%)
Adrenal gland (BC)	9 (0.8)
Palate (EH)	1 (0.1)
Coronary arteries (FN)	218 (18.3)
Diaphragm and gastro-esophageal reflux (JB)	2 (0.2)
Appendix (JE)	7 (0.6)
Intestine (JF)	148 (12.4)
Rectum (JG)	71 (5.9)
Biliary tract (JK)	39 (3.3)
Uterus and uterine ligaments (LC)	70 (5.9)
Vagina (LE)	1 (0.1)
Hip joint and thigh (NF)	474 (39.7)
Knee and lower leg (NG)	153 (12.8)
Trunk (QB)	1 (0.1)

[1] The two first letters of procedure code according to the classification of the Nordic Medico-Statistical Committee Classification of Surgical Procedures [23]

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Table 3. The incidence of surgical site infections (SSI) according to nutritional risk status and contents of the nutritional risk screening tool (NRS-2002) [9][1].

	Study sample[2] (n = 1194)	Incidence of SSI	
		Crude odds ratio (95% CI)[3]	*Adjusted odds ratio (95% CI)*[3,4]
Complete NRS-2002			
Patients at nutritional risk	170 (14.2)	1.76 (1.04, 2.98)	1.81 (1.04, 3.16)
NRS-2002 initial screening			
Four initial questions			
BMI <20.5 kg/m^2? (yes)	92 (7.7)	0.67 (0.26, 1.69)	0.62 (0.24, 1.60)
Has the patient lost weight within the last weeks? (yes)	138 (11.6)	2.14 (1.25, 3.67)	2.15 (1.23, 3.76)
Has the patient had a reduced dietary intake in the last weeks? (yes)	170 (14.2)	2.62 (1.61, 4.26)	2.66 (1.59, 4.45)
Is the patient severely ill? (yes)	151 (12.6)	1.15 (0.62, 2.11)	1.17 (0.59, 2.32)

[1] Missing data for data regarding: BMI (n = 6); weight loss (n = 4); dietary intake (n = 1); severely ill (n = 4)

[2] n (% of the total study sample)

[3] Estimate of odds ratio by logistics regression models. Patients with a positive answer (yes) on a question were compared with those with a negative answer (no) on the same question. One and one question entered into the regression model.

[4] Adjusted for age, gender, acute surgery and ASA-score.

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The association between nutritional risk and SSI

The incidence of SSI was significant higher among patients at nutritional risk (11.8%), as compared to those who were not at nutritional risk (7.0%) ($p = 0.047$). These results were in accordance with the multivariate adjusted analysis, demonstrating patients at nutritional risk to be 1.81 (95% CI: 1.04, 3.16) times more likely to develop SSI as compared to those patients who were not at nutritional risk (Table 3). Furthermore, the initial screening questions about weight loss and reduced dietary intake the last weeks were significantly associated with the incidence of SSI in both crude and adjusted analysis (Table 3). None of the other questions in NRS-2002 demonstrated such associations.

Discussion

Principal findings

In this large cross-sectional study among mixed surgical patients, we demonstrated a positive association between nutritional risk and the incidence of SSI, independent of age, gender, type of surgery (acute/elective) and ASA-score. Among the questions used to define nutritional risk, answering "yes" to the ones regarding reduced dietary intake and weight loss seemed to be strongest associated with SSI.

Clinical relevance

Our results may increase the motivation to systematically identify, prevent and treat undernutrition among surgical patients in accordance with established guidelines [7, 24, 25]. Since both nutritional risk and SSI have adverse effects for the patients' health [3, 4, 12] and the hospital's economics [3, 5, 12], implementing NRS-2002 and treating patients who are at nutritional risk may benefit both patients and hospitals. Moreover, considering both the risk for undernutrition and SSI, as well as the fact that about 75% of the SSIs are first identified after hospital discharge [26], it is of major importance that the result of NRS-2002 is forwarded to the patient and/or the primary care institutions.

Possible mechanisms

A number of factors could underlie the positive association between nutritional risk and SSI. Among the questions used in NRS-2002, "yes" to the one regarding reduced dietary intake the last weeks tended to be strongest associated with the incidence of SSI. This is in accordance with previous studies demonstrating patients answering "yes" to a reduced dietary intake to be more likely for mortality the following year and an increased morbidity, as compared to patients answering "no" to the same question [12]. The reduced dietary intake may be caused by several factors, and the current study did not identify whether the dietary intake decreased prior to or after the incidence of SSI. Regardless timing for the weight loss, key aspects of perioperative care from a metabolic and nutritional point of view includes avoiding long periods of preoperative fasting and re-establishing oral feeding as early as possible after surgery [24]. Moreover, it is recommended to focus on nutritional counseling if indicated by the preoperative testing [25]. A pre- and/or postoperatively low dietary intake or starvation may lead to a delayed wound healing since several nutrients are needed for the healing process [27]. However, another possible explanation of the observed association is that a present SSI decreases the patient's appetite due to pain or illness.

Furthermore, the present study demonstrated weight loss to be of great importance when predicting the incidence of SSI. Weight loss most often occurs due to a reduced dietary intake, but may also be caused by a catabolic state seen during an ongoing or exaggerated stress response after surgery. Such stress is further associated with infection, poor wound healing and impaired immune function [28]. However, previous studies have demonstrated the risk of SSI to increase with both pre- [29] and postoperative [30] weight loss. Of note, NRS-2002 does not divide between wanted or unwanted weight loss. Some patients may be motivated for weight loss prior to surgeries, like elective aortocoronary bypass or inserting prosthesis in hip joint, whereas others may have unwanted weight loss prior to surgery due to reduced general condition or pain, like surgery for acute hip fracture or illness in the digestive system. Interestingly, there was no observed association between BMI less than 20.5 kg/m^2 and SSI, indicating weight loss to be a higher risk factor to SSI than low body weight itself.

As compared to the national NOIS-POSI report from 2014 [31], the incidence of SSI and the median age tends to be higher in the present study (respectively 7.7 vs 4.5% and 68 vs 60 years). This may be seen in context since increasing age is a risk factor for SSI [32]. Interestingly, the current study did not observe a significant association between age and SSI, possibly due to a generally elderly study sample. The higher median age in the current study as compared to the national report may be explained by that it only includes those who were a part of the Nutritional risk database (18 years and older). Moreover, the observed differences may also be explained by the fact that the national NOIS-POSI reports do not include patient-reported SSI and only reports data for one year at a time and only includes the five surgery procedures that are mandatory to report in Norway.

In addition, the present study has a lower percentage of patients being at nutritional risk compared to what is previously reported from the Nutritional database (14.2 vs 29.0%) [12]. This may be explained by only including those who were a part of the NOIS-POSI database. Moreover, the current study has a high amount of elective orthopedic patients who generally have a low prevalence of nutritional risk [33]. It should also be mentioned that the previous report from the Nutritional database is based on data from 2008–2009, and the prevalence of hospitalized patients at nutritional risk may have decreased some during the later years due to the hospital's focus on this area.

Strengths and limitations

Strengths of the current study include the large study sample. The fact that both monitoring the incidence of SSI and the prevalence of nutritional risk are mandatory for the hospital increases the quality of the study. According to this, the NOIS-POSI database reports over 90% complete follow-up after discharge [26]. Other strengths with the study includes that the staff were trained to conduct the monitors and that the ASA-score was used to adjust for physical status when investigating the association between the nutritional risk status and SSI.

There are some limitations in the current study. First of all, the data material is a selection of two different register databases: There is a selection of the original Nutritional risk database since the current study includes only surgical patients, and there is a selection of the original local NOIS-POSI database since NRS-2002 is not validated for patients being less than 18 years, terminal or pregnant. Despite NRS-2002 is a validated screening tool that in a fast way identifies patients to be at nutritional risk or not [9], it does unfortunately not give any detailed information about the patients' nutritional status. Moreover, the observed association between nutritional risk and SSI could be partially explained by socioeconomic factors or other variables related to both nutritional risk and SSI. Unfortunately, as the current data material is a combined selection of two different surveillance databases with only a few available variables, we did not have information to evaluate potential confounding by other variables than age, gender, type of surgery (acute/elective) and ASA-score. When using point-prevalence data, the probability of including patients with longer length of stay increases (i.e., length bias). Thus, this may have led to a more ill study population, which can be reflected in the higher number of incidence of SSI, as compared to previously reported. Further, the present study design is not able to describe the causality between nutritional risk and SSI, and could not identify whether the patients were at nutritional risk prior to or after the surgery.

Conclusions

In conclusion, we demonstrate SSI to occur more often among patients being at nutritional risk as compared to those who are not at nutritional risk. Future studies should investigate interventions to prevent both SSI and nutritional risk among surgical patients.

Supporting information

S1 File. Anonymized data set. The data set is anonymized and has grouped the age and type of surgery variables. Replicated results may thus in some degree differ from what is reported in the manuscript.
(XLS)

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Original article

Weight loss and BMI criteria in GLIM's definition of malnutrition is associated with postoperative complications following abdominal resections – Results from a National Quality Registry

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SUMMARY

Background & aims: Although malnutrition is thought to be common among patients with intra-abdominal diseases and is recognized as a risk factor for postoperative complications, diagnostic criteria for malnutrition have not been consistent. Thus, the Global Leadership Initiative in Malnutrition (GLIM) has recently published new criteria for malnutrition. The aims of this study were to investigate the prevalence of malnutrition according to weight loss and BMI criteria in GLIM's second step for the diagnosis and their association with severe postoperative complications in patients undergoing gastro-intestinal resections.

Method: The current study includes adult patients who were prospectively included in the Norwegian Registry for Gastrointestinal Surgery in the period between 2015 and 2018. Exclusion criteria were acute surgery and lack of information regarding preoperative weight and/or postoperative complications. Severe surgical complications were classified according to the Revised Accordion Classification system and malnutrition with the GLIM criteria. Associations were assessed by logistic regression analyses, and the adjusted odds ratio included age (continuous), gender (male/female) and scores from the American Society of Anesthesiologists Physical Status Classification System and the Eastern Cooperative Oncology Group.

Results: Out of 6110 patients, 2161 (35.4%) were classified as with malnutrition, 1206 (19.7%) with moderate and 955 (15.6%) with severe malnutrition. Malnourished patients were 1.29 (95% CI: 1.13–1.47) times more likely to develop severe surgical complications, and 2.15 (95% CI: 1.27–3.65) times more likely to die within 30 days, as compared to those who were not.

Conclusion: Preoperative malnutrition is common among patients having gastrointestinal resections and is associated with an increased risk of severe surgical complications.

1. Introduction

Surgery is the only curative treatment option for a broad spectrum of intraabdominal diseases. Even in the era of modern surgery and perioperative care, a significant proportion of patients experience severe postoperative complications, even mortality. The incidence of severe complications following intraabdominal resection surgery is related to the specific organ operated on and type of procedure performed. However, comparison of the severity

Abbreviations: ASA, American Society of Anesthesiologists Physical Status Classification System; BMI, Body Mass Index; ECOG, Eastern Cooperative Oncology Group; GLIM, Global Leadership Initiative in Malnutrition; NCPS, Nordic Medico-Statistical Committee Classification of Surgical Procedures (NCPS); NOMESCO, Nordic Medico-Statistical Committee; NoRGast, Norwegian Registry for Gastrointestinal Surgery; NPR, National Patient Registry; mE-PASS, modified Estimation of Physiologic Ability and Surgical Stress; WHO, World Health Organization.

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of complications is often difficult since methods for reporting such outcomes are not always uniform [1].

Risk factors for postoperative complications include preoperative weight loss and malnutrition [2–7]. Despite most definitions of malnutrition include the same risk factors [8], there has been a lack of consensus on diagnostic criteria for application in clinical settings. Therefore, the Global Leadership Initiative in Malnutrition (GLIM) recently published new definitions of malnutrition for adults, based on a two-step model for risk screening and diagnosis assessment [9]. The definitions are based on both phenotypic criteria (weight loss, low body mass index (BMI) and reduced muscle mass), and etiologic criteria (reduced food intake or assimilation and inflammation). Although such conditions are thought to be prevalent among patients with gastrointestinal diseases, the frequency and severity of malnutrition among gastrointestinal patients are not well described. Moreover, the GLIM encourages the nutrition community to use the criteria both in prospective and retrospective cohort studies as well as clinical trials in order to validate its relevance for clinical practice [9].

The main purpose of this study was to describe the prevalence of preoperative malnutrition among patients undergoing gastrointestinal resections, and secondly to explore the association between nutrition status and severe postoperative complications and death.

2. Material and methods

2.1. Study sample

The present retrospective study includes 6110 patients from the Norwegian Registry for Gastrointestinal Surgery (NoRGast). NoRGast has collected data prospectively for colorectal, upper gastrointestinal and hepato-pancreato-biliary restrictions in Norway since 2014, and was acknowledged with the status of a National Quality Registry in May 2015 [10]. It is mandatory to enter data in the NoRGast register for resections in the following organs (procedure code according to the classification of the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCPS) [11]): colon (JFB 20–64 and JFH), rectum (JGB), esophagus (JCC), gastric (JCD and JDD), liver (JJB), pancreas (JLC) and bile duct (JHC 10–99). Small bowel resections, appendectomies, cholecystectomies, stoma surgery without colorectal resection, and hernia repairs are entered in the register on a voluntary basis. By the end of 2015, nine hospitals entered data into the registry, whereas 29 out of the 32 hospitals performing more than 20 gastrointestinal resections per year participated by the end of May 2018. Since 2014, more than 13500 operations have been entered into the database. Among the formal resections are some 3900 colonic, 1500 rectal, 850 liver, 300 gastric, 200 esophageal and 390 pancreatoduodenectomies [10]. The current study includes data for adult patients (≥18 years) with a major intraabdominal operation, here defined as a surgery that included total or partly resection of the colon, rectum, esophagus, gastric, liver, pancreas or bile duct, registered in NoRGast in the period from May 2015 to May 2018 [12]. Patients were excluded if information regarding weight at admission and/or 6 months prior to surgery were not available.

Coverage (completeness) of the Registry was compared to administrative data collected by the National Patient Registry (NPR), which is a compulsory registration for all hospitals in order to be reimbursed for in-hospital patient stays and therapy [10]. Compared to NPR, completeness of the NoRGast varied from 30% to 93% for participating hospitals, mainly due to time-lag in the implementation phase. There was a variation in completeness between hospitals in the implementation phase versus hospitals with a 3-year run-time, but also a variation somewhat within participating centers year by year. Missing values ranged from zero for several variables and up to 52% for preoperative weight changes in colonic resections [10].

2.2. Ethics

All patients included in NoRGast signed a written consent and data were stored in a non-identifiable way in the NoRGast database. The current study was approved by the Regional Committee for Medical and Health Research Ethics (2018/1549) and is in accordance with the Declaration of Helsinki.

2.3. Clinical data

The patient's weight six months prior to surgery was self-reported or retrieved from patient files when available, whereas current weight at admission was scaled by health professionals. Weight changes are reported as percentages. The GLIM criteria for the diagnosis of malnutrition uses a two-step-model for risk screening and diagnosis assessment, where the first step is to identify patients who are at nutritional risk with a validated screening tool [9]. Secondly, patients who meet at least one of the phenotypic and one of the etiologic criteria of malnutrition are identified. Since NoRGast does not include all the information needed in the first step of the GLIM's model to identify malnutrition, the current study only uses the second step. Based on their need for a formal, major resection, all NoRGast-patients were a priori defined as having a chronic gastrointestinal condition that adversely impacts food assimilation or absorption, which is one of the etiologic criteria in the second step of the model. The GLIM's phenotypic criteria for weight loss or BMI were used to diagnose patients with malnutrition and further classify the condition as moderate or severe (Table 1). Underweight was defined according to World Health Organization (WHO)'s cut offs criteria (BMI < 18.5 kg/m^2) [13] and is thus also included in the GLIM criteria of severe malnutrition.

Postoperative complications within 30 days following surgery were scored using the Revised Accordion Classification system [1]. Complications are grouped in four levels: mild (grade 1), moderate (grade 2), severe (grade 3–5) and death (grade 6). Severe complications (grade 3–5) are divided into the following groups: severe complication requiring a procedure without general anesthesia (grade 3), severe complications requiring a procedure with general anesthesia or resulting in single-system organ failure (grade 4), and severe complication requiring a procedure with general anesthesia and resulting in a single-system organ failure or resulting in multisystem organ dysfunction (grade 5) [1]. Accordion grade 6 denotes death.

The American Society of Anesthesiologists Physical Status Classification System (ASA-score) [14], the Eastern Cooperative Oncology Group (ECOG)-score [15] and the modified Estimation of Physiologic Ability and Surgical Stress (mE-PASS) [16] were used to evaluate the patients' physical status prior to surgery. In order to obtain an exact and standardized definition in all operating departments and avoid any personal opinion of this matter, elective surgery was defined as start of anesthesia between 8 am and 4 pm. All relevant data were extracted directly from the NoRGast database.

2.4. Statistical analysis

Analyses were conducted for the total study sample as a whole, with separate analysis for the different nutritional characteristics and specific organ operated upon. Summary measures for continuous variables are reported as medians and range (25th to 75th

Table 1
Weight loss and BMI criteria in GLIM's second step for the diagnosis of malnutrition.

Malnutrition diagnosis	Criteria *(at least one of the following)*		
	Weight loss during the past 6 months	BMI among those younger than 70 years	BMI among those older than 70 years
Malnutrition	>5%	<20 kg/m^2	<22 kg/m^2
Moderate malnutrition	5–10%	18.5–20 kg/m^2	20–22 kg/m^2
Severe malnutrition	>10%	<18.5 kg/m^2	<20 kg/m^2

BMI: Body Mass Index; **GLIM**: Global Leadership in Malnutrition.

percentile), and categorical variables are reported as counts (percentages).

Multivariate logistic regressions for severe complications and death were constructed to investigate the association between nutritional characteristics (underweight, malnutrition and weight changes) and these outcomes, with adjustment for age (continuous), gender (male/female), ASA-score (score 1–5) and ECOG (score 0–4). The statistical package IBM SPSS Statistics was applied. All p-values were two-tailed and values less than 0.05 were considered statistically significant.

3. Results

3.1. Patients' characteristics

In total, 6110 patients were included in the present study (Fig. 1), and their general and nutritional characteristics are described in Tables 2 and 3, respectively. Overall, 3291 (53.9%) were men and the median (25th, 75th percentile) age and BMI were 68 (58, 75) years and 25.2 (22.5, 28.3) kg/m^2. The majority of the study sample, 4494 (73.6%) patients, had a malignant tumor. Severe complications, excluding death, occurred in 1188 (19.4%) patients, and 61 (1.0%) died within 30 days following surgery.

As compared to the total group of patients registered in NoRGast (n = 11746), patients included in the present study tended to have a higher frequency of surgery due to tumor and neoadjuvant treatment with chemotherapy (Table 2). The prevalence and distribution of severe postoperative complications tended to be similar in both groups, except for a higher mortality-rate among the total NoRGast group.

3.2. The prevalence of malnutrition and underweight

At the time of surgery, 2161 patients (35.4%) suffered from malnutrition, of whom 1206 (19.7%) were moderately malnourished and 955 (15.6%) were severely malnourished. Underweight was observed in 216 (3.5%) patients (Table 3).

The distribution of resected organ in the study sample and their nutritional characteristics are described in Table 4. In general, patients who had pancreatic, esophageal or gastric surgery tended to be more often malnourished (356 (52.9%), 87 (44.6%) and 100 (37.3%) patients, respectively), as compared to those having surgery in other gastrointestinal organs.

3.3. Nutritional status and severe surgical complications/mortality

3.3.1. Malnutrition and underweight

Patients with malnutrition at time of surgery were more likely to develop severe surgical complications and to die within 30 days, as compared to those who were not (OR (95% CI): 1.29 (1.13, 1.47) and 2.15 (1.27, 3.65), respectively) (Table 5). These results were not noteworthy altered when adjusting for specific organs operated on or when grade 3 were excluded from the definition of severe surgical complications (data not shown).

When investigating the different nutritional categories separately, the multivariate analysis demonstrated that both patients

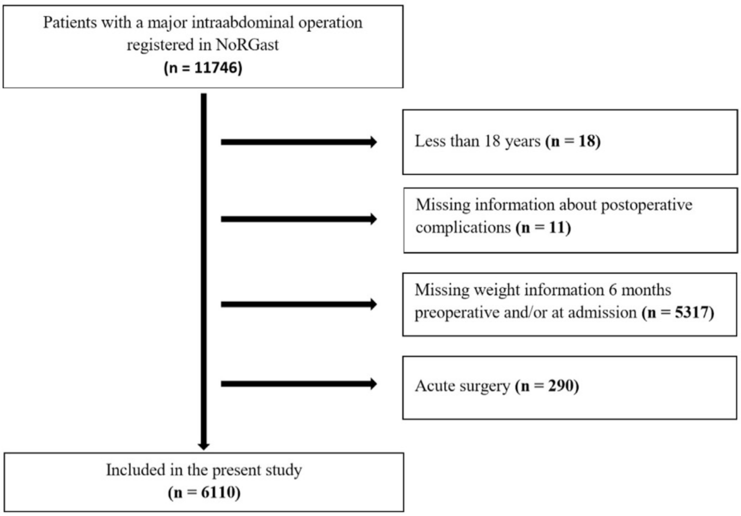

Fig. 1. Flow chart of the study sample.

Table 2
General characteristics and postoperative complications among patients included in the study sample and in NoRGast.

	Study sample	NoRGast
	n = 6110	n = 11746
General characteristics		
Male[a]	3291 (53.9)	6156 (52.4)
Age[b]	68.0 (58.0, 75.0)	68.0 (58.0, 76.0)
Age ≥ 70 years	2626 (43.3)	5321 (45.3)
BMI[b]	25.2 (22.5, 28.3)	25.2 (22.6, 28.4)
Surgery due to tumor[a]	4494 (73.6)	7932 (67.5)
Chemotherapy[a]	572 (9.4)	811 (6.9)
Radiotherapy[a]	98 (1.6)	175 (1.5)
Chemo- and radiotherapy[a]	418 (6.8)	610 (5.2)
mE-PASS[b]	0.35 (0.28, 0.50)	0.36 (0.29, 0.53)
ASA-score[a]		
1	311 (5.1)	693 (5.9)
2	3516 (57.5)	6531 (55.6)
3	2162 (35.4)	4115 (35.0)
4	118 (1.9)	377 (3.2)
5	3 (0.0)	20 (0.2)
ECOG-score[a]		
0	4306 (70.5)	7858 (66.9)
1	1298 (21.2)	2524 (21.5)
2	381 (6.2)	843 (7.2)
3	92 (1.5)	252 (2.1)
4	15 (0.2)	87 (0.7)
Classification of postoperative complications[a, c]		
None, mild or moderate (grade < 3)	4861 (79.6)	9228 (78.6)
Severe, excluding death (grade 3–5)	1188 (19.4)	2298 (19.6)
Death (grade 6)	61 (1.0)	198 (1.7)

ASA-score, American Society of Anesthesiologists Physical Status Classification System; **BMI**, Body Mass Index; **CRP**, C-reactive protein; **ECOG**, Eastern Cooperative Oncology Group score; **mE-PASS,** modified Estimation of Physiologic Ability and Surgical Stress; **NoRGast**: Norwegian Registry for Gastrointestinal Surgery. Missing information for BMI (n = 34), ECOG-score (n = 19) and ASA-score (n = 1) in the study sample.
[a] n (percent).
[b] Median (25, 75 percentile).
[c] Postoperative complications according to the Accordion classification scale [1].

with moderate and severe malnutrition had an increased risk for severe surgical complications (OR (95% CI): 1.17 (1.00–1.37) and 1.27 (1.07–1.50), respectively), whereas the association with death alone was significant for patients with severe malnutrition (OR (95% CI): 2.16 (1.25–3.73)) only. Patients with underweight had a 2.68 (95% CI: 1.11–6.46) higher risk dying, as compared to those who were not underweight. There were no statistically significant differences in the incidence of severe surgical complications between these two groups.

Table 3
Nutritional characteristics in the study sample (n = 6110).

Nutritional characteristics	n (%)
Categories of preoperative weight loss (%)	
≤0	3320 (54.3)
0.1–4.9	1116 (18.3)
5–9.9	949 (15.5)
10–14.9	467 (7.6)
≥15	258 (4.2)
Categories of BMI (kg/m^2)	
<18.5 (underweight)	216 (3.5)
18.5–24.9 (normal weight)	2709 (44.3)
25–29.9 (pre-obesity)	2176 (35.6)
≥30 (obesity)	974 (15.9)
Diagnosis of malnutrition	
Malnutrition[a]	2161 (35.4)
Moderate malnutrition[b]	1206 (19.7)
Severe malnutrition[c]	955 (15.6)

BMI, Body Mass Index. Missing information for BMI (n = 35).
[a] Malnutrition: weight loss ≥5% within the past 6 months, BMI <20 kg/m^2 (<70 years) and/or BMI < 22 kg/m^2 (≥70 years).
[b] Moderate malnutrition: weight loss 5–10% within the past 6 months, BMI 18.5–20 m/kg^2 (age < 70 years) and/or BMI < 22 m/kg^2 (≥70 years).
[c] Severe malnutrition: weight loss >10% within the past 6 months, BMI <18.5 m/kg^2 (<70 years) and/or BMI < 20 m/kg^2 (≥70 years).

3.3.2. *Categories for age and BMI*

Stratifying for age, we found no significant relationship between BMI <18.5 kg/m^2 and <20 kg/m^2 (cut offs used in the criteria of the diagnosis of moderate and severe malnutrition, respectively), and the incidence of severe surgical complications and death for patients younger than 70 years. However, for those aged 70 years or more, the BMI categories used in the criteria of moderate and severe malnutrition (<20 kg/m^2 and <22 kg/m^2, respectively) demonstrated increased risks for severe surgical complications (OR (95% CI): 1.47 (1.07, 2.03) and 1.25 (1.00, 1.57), respectively). Moreover, the older patients with BMI <20 kg/m^2 had a nearly 2.5-fold increased risk for death (OR (95% CI): 2.46 (1.09, 5.55)), as compared to those with a higher BMI. There was no significant relationship between BMI <22 kg/m^2 and death for older patients with (data not shown).

3.3.3. *Weight change*

Two thousand, seven hundred and ninety patients (45.7%) experienced weight loss during the 6 months prior to surgery. This was significantly associated with both severe complications and death (OR (95% CI): 1.28 (1.13–1.46) and 1.70 (1.00–2.90), respectively). Patients with a weight loss ≥5% demonstrated a higher risk for both severe complications and death (OR (95% CI): 1.27 (1.10–1.46) and 2.35 (1.40–3.94), respectively), whereas those with weight loss > 10% only demonstrated a significant increased risk for death (OR (95% CI): 2.23 (1.30–4.18)) (Table 5), as compared to those with a lower weight loss.

Stratified analysis for obese patients (BMI ≥ 30 kg/m^2) revealed that those with preoperatively weight loss had an increased risk for severe surgical complications, as compared to those who did not lose weight (OR (95% CI): 1.42 (1.04–1.94)). Preoperative weight loss did not increase the risk of death for this patient group as it did for the total population.

As compared to patients having weight loss or weight gain, patients who had a stable weight prior to surgery demonstrated a decreased risk for severe surgical complications and death in the crude analysis (OR (95% CI): 0.68 (0.60–0.78) and 0.46 (0.25–0.84), respectively), but only statistically significant in the adjusted analysis for severe surgical complications (OR (95% CI): 0.75 (0.65–0.85)). There was no significant association between gaining weight and severe surgical complications or death (Table 5).

4. Discussion

The present study demonstrates that even if only 3.5% of the patients undergoing gastrointestinal resections met the WHO's criteria for underweight, over a third (35.4%) of the patients met the weight loss and BMI criteria in GLIM's second step for the diagnosis of malnutrition at time of surgery. In total, patients with malnutrition were near thirty percent more likely to develop severe surgical complications and over two times more likely to die within 30 days postoperatively, as compared to those who did not have malnutrition according to the selected GLIM-criteria. Moreover, almost half of the patients had lost weight prior to surgery, which by itself was significantly associated with increased risk for both severe complications and death.

The prevalence of underweight among patients having gastrointestinal surgery is reported to be higher in Eastern than in Western countries [6,17], probably due to a generally lower BMI in Asian populations. Even though, studies from both Japan [5] and

Table 4
Distribution of organ system operated on and prevalence of malnutrition and/or underweight.

Organ system operated	Study sample[a]	Malnutrition[a,b]	Moderate malnutrition[a,c]	Severe malnutrition[a,d]	Underweight[a,e]
Total	6110 (100)	2161 (35.4)	1206 (19.7)	955 (15.6)	216 (3.5)
Esophagus	195 (3.2)	87 (44.6)	49 (25.1)	38 (19.5)	10 (5.1)
Stomach	267 (4.4)	100 (37.3)	62 (23.2)	38 (14.2)	5 (1.9)
Small bowel	254 (4.2)	79 (31.1)	44 (17.3)	35 (13.8)	12 (4.7)
Colon	2360 (38.6)	789 (33.4)	458 (19.4)	331 (14.0)	93 (3.9)
Rectum	1371 (22.4)	411 (30.0)	237 (17.3)	174 (12.7)	41 (3.0)
Liver	953 (15.6)	329 (34.5)	182 (19.1)	147 (15.4)	27 (2.8)
Pancreas	673 (11.0)	356 (52.9)	169 (25.1)	187 (27.8)	25 (3.7)
Spleen	37 (0.6)	10 (27.0)	5 (13.5)	5 (13.5)	3 (8.1)

[a] n (%).
[b] Malnutrition: weight loss ≥5% within the past 6 months, BMI <20 kg/m^2 (<70 years) and/or BMI < 22 kg/m^2 (≥70 years).
[c] Moderate malnutrition: weight loss 5–10% within the past 6 months, BMI 18.5–20 m/kg^2 (age < 70 years) and/or BMI < 22 m/kg^2 (≥70 years).
[d] Severe malnutrition: weight loss >10% within the past 6 months, BMI <18.5 m/kg^2 (<70 years) and/or BMI < 20 m/kg^2 (≥70 years).
[e] Underweight: Body Mass Index <18.5 kg/m^2.

Table 5
The association between nutritional characteristics and the incidence of severe surgical complications[a] and death within 30 days after surgery.

Nutritional characteristics	Study sample (n = 6110)	Severe surgical complications, including death[a] (n = 1249)		Death (n = 61)	
	n (%)	Crude OR (95% CI)[f]	Adjusted OR (95% CI)[f,g]	Crude OR (95% CI)[f]	Adjusted OR (95% CI)[f,g]
Malnutrition[b]	2161 (35.3)	1.33 (1.17, 1.52)	1.29 (1.13, 1.47)	2.84 (1.69, 4.76)	2.15 (1.27, 3.65)
Moderate malnutrition[c]	1206 (19.7)	1.17 (1.00, 1.36)	1.17 (1.00, 1.37)	1.45 (0.82, 2.57)	1.23 (0.69, 2.21)
Severe malnutrition[d]	955 (15.6)	1.35 (1.15, 1,59)	1.27 (1.07, 1.50)	2.86 (1.68, 4.88)	2.16 (1.25, 3.73)
Underweight[e]	216 (3.5)	1.31 (0.96, 1.80)	1.34 (0.97, 1.85)	3.02 (1.29, 7.09)	2.68 (1.11, 6.46)
Weight loss > 0%	2790 (45.7)	1.36 (1.20, 1.54)	1.28 (1.13, 1.46)	2.13 (1.26, 3.59)	1.70 (1.00, 2.90)
Weight loss ≥ 5%	1674 (27.4)	1.37 (1.19, 1.56)	1.27 (1.10, 1.46)	2.96 (1.79, 4.91)	2.35 (1.40, 3.94)
Weight loss > 10%	701 (11.5)	1.33 (1.11, 1.60)	1.19 (0.98, 1.43)	3.03 (1.72, 5.33)	2.33 (1.30, 4.18)
Stable weight	2388 (39.1)	0.68 (0.60, 0.78)	0.75 (0.65, 0,85)	0.46 (0.25, 0.84)	0.57 (0.31, 1.04)
Increased weight	932 (15.3)	1.09 (0.92, 1.29)	1.04 (0.88, 1.24)	0.84 (0.40, 1.77)	0.90 (0.42, 1.92)

[a] Severe surgical complications are defined as grade 3–6 in the Revised Accordion Scale.
[b] Malnutrition: weight loss ≥5% within the past 6 months, *or* a BMI <20 kg/m^2 if age <70 years *or* BMI <22 kg/m^2 if age ≥70 years).
[c] Moderate malnutrition: weight loss 5–10%, *or* BMI <20 m/kg^2 if younger than 70 years *or* BMI <22 m/kg^2 if age ≥70 years.
[d] Severe malnutrition: weight loss >10%, *or* BMI <18.5 m/kg^2 if younger than 70 years *or* BMI <20 m/kg^2 if age ≥70 years.
[e] Body mass index <18.5 kg/m^2.
[f] Estimate of odds ratio by logistics regression models. Patients who met the criteria for the different nutritional characteristics were compared with those who were not.
[g] Adjusted for age, gender, American Society of Anesthesiologists Physical Status Classification System score (ASA-score) and Eastern Cooperative Oncology Group score (ECOG-score).

USA [6] demonstrates that patients with underweight are more likely to have postoperative complications, which is in accordance with our findings. However, the strength in this relationship tends to be stronger in the American population [6], as compared to both the Japanese [5] and the Norwegian population (the current study), possible due to a shift towards a higher BMI in the general population.

In the current study, half of the patients were overweight or obese. The experience from the North-American population, where overweight or obesity is prevalent, is that patients need to lose substantial weight before the definition of underweight occurs [9]. Thus, it is important to emphasize that BMI by itself is not adequate to identify all those who have nutritional challenges, and especially not in populations where BMI tends to increase. For example, BMI may remain relatively unchanged despite the patient's muscle mass decreases and visceral fat increases, leading to sarcopenic obesity [18]. Sarcopenia is recognized to have high personal, social and economic burdens when untreated [19]. Thus, the European Working Group on Sarcopenia in Older People 2 recently published new recommendations with the aim to increase the awareness of sarcopenia and its risk [20]. Despite sarcopenia can occur earlier in life, it is most common among older people. Moreover, also older people may be a vulnerable group for the BMI definitions of underweight since their current height may have decreased due to fractures and thus camouflages a low BMI [21]. The current study observed that among patients 70 years or more, a BMI <22 kg/m^2 was associated with an increased risk of severe surgical complications, and that a BMI <20 kg/m^2 was associated with both an increased risk for severe surgical complications and death alone, as compared to those with a higher BMI. Therefore, we find it appropriate that the new malnutrition criteria use an age-adjusted BMI cut off for those 70 years or more when the patients' current height is used [9].

Hospitalized patients with weight loss have previously been demonstrated to have an increased risk for both morbidity and mortality the following year [1,3,4,7,22], as compared to patients not having weight loss. In the present study, any preoperative weight loss had a statistically significant association with severe surgical complications, whereas the WHO's definition of underweight did not. Reporting weight loss as a stronger predictor of complications than underweight has been shown in some published studies [23], whereas others do not confirm this [17,24]. Interestingly, stratified analysis among patients with obesity (BMI ≥ 30 kg/m^2) in the current study population demonstrated that weight loss increased the risk of severe surgical complications also in this group. Thus, weight loss as a risk factor is not restricted to patients with a lower BMI. This is supported in results from previous studies [25,26], and underlines the importance of also evaluating sarcopenia, weight loss and malnutrition among patients with a normal or high BMI.

Weight loss leads to a reduction in both fat-free mass and fat mass, which further results in decreased muscle strength [27].

Reduction of fat-free mass and muscle strength are associated with an increased mortality rate [28]. Reduction of fat mass, which is not only a lipid storage depot, but also a nutritional reserve that influence the inflammatory and immune response, may decrease the patients ability to handle the stress of surgery [29]. Additionally, a low dietary intake or depleted nutrient storage may lead to a delayed wound healing since several nutrients are needed for the healing process [30]. In summary, a low BMI and/or weight loss may lead to ill-prepared patients regarding the stress of surgery through a complexity of pathways, and thus increase the risk for adverse outcomes. Unfortunately, information regarding preoperative weight loss often tends to be missing in the clinic, as demonstrated in NoRGast where only 48% of the patients undergoing resections of the large bowel had this information. This indicates that information about weight loss is still not recognized as relevant in all surgical environments.

4.1. Clinical relevance

Preventing severe surgical complications are of major interest for patients, health professionals and hospital administration, due to the impact on the patients' health and the health care system's costs. Guidelines recommend focusing on nutritional counseling if indicated by the preoperative testing [31,32]. Our study points towards WHO's definition of underweight and GLIM criteria for weight loss and low BMI being such indicators. Thus, patients with these conditions should receive nutritional counseling in order to stop the development of malnutrition. Moreover, the current study indicates that the severity grading in the GLIM criteria (moderate and severe malnutrition) is appropriate in the clinical setting since the criteria for severe malnutrition tends to be more strongly associated with severe postoperative complications, as compared to the criteria for moderate malnutrition. Of note, since gaining weight prior to surgery have demonstrated limited results on the outcome, it may be more important to prevent weight loss and malnutrition. This may be especially challenging in the current patient group due to underlying gastrointestinal diseases in a major part of the study population, but possibly all the more important. These topics should further be evaluated in prospective studies.

4.2. Strengths and limitations

The current study analyses a large, nationwide study sample and the use of standardized definitions of postoperative complications. Moreover, the diagnostic criteria for underweight and malnutrition are well-defined and are collected prior to surgery.

Analyses based on registry data might always inherit some biases. Many people are involved in the registration, and since the completeness of the registry is limited, selection biases might be introduced. However, the limited completeness is mainly due to lack of personnel and logistics at the hospitals, and not due to lack of consent from the patients. Although we did not observe any striking differences in morbidity and mortality between the total NoRGast population and the patients included in the current study, some biases might occur. Potentially, this could be related to weight information since nearly fifty percent of the NoRGast population was excluded due to missing weight information 6 months prior to surgery and/or at admission. Moreover, the current study were not able to exclude those who were not at nutritional risk according to first step of the GLIM criteria. Thus, the observed associations between weight loss and BMI criteria in GLIM's second step for the diagnosis of malnutrition may even be stronger than reported here. It should also be mentioned that we only disclosed associations and no causalities.

5. Conclusions

Our study demonstrates that preoperative weight loss and malnutrition are common among patients having colorectal, upper gastrointestinal or hepato-pancreato-biliary restrictions, and that these conditions are associated with an increased risk of severe surgical complications.

Statement of authorship

Eli Skeie: methodology, formal analysis, writing – original draft, review & editing, visualization. **Randi Julie Tangvik**: writing – review & editing, supervision. **Linn Såve Nymo**: investigation, writing – review & editing, project administration. **Kristoffer Lassen**: investigation, writing – review & editing, project administration. **Stig Harthug**: writing – review & editing, supervision. **Asgaut Viste**: conceptualization, investigation, supervision, writing – review & editing. All authors gave final approval of the version to be submitted.

Conflict of interest

The authors declare that they do not have any conflict of interest.

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IV

Errata

Page 19	Wrong symbol: “(< 70 years: < 20 kg/m^2)” changed to “(> 70 years: < 18.5 kg/m^2)”
Page 19	Wrong symbol: “(...) weight loss < 5 % last 6 months” changed to “(...) weight loss > 5 % last 6 months”
Page 20	Wrong symbol: “Weight loss < 5 %” changed to “Weight loss > 5 %”
Page 28	Missing explanation of abbreviation: “(…) prevention of SSIs recommend” changed to “(…) prevention of surgical site infections (SSIs) recommend”
Page 32	Unnecessary explanation of abbreviation: “(...) surgical site infections (SSIs)” changed to “(…) SSIs”
Page 38	Missing quotation marks: “(...) and outcome may describe” changed to “(...) and “outcome” may describe”
Page 39	Wrong number: “(...) In Safe Hands developed two voluntary quality indicators” changed to “(...) In Safe Hands developed four voluntary quality indicators”
Page 43	Missing word: “(...) nutritional care in the hospital (63), to identify” changed to “(...) nutritional care in the hospital (63) and to identify”
Page 55	Wrong number: “(p < 000.1)” changed to “(p = 0.047)”
Page 57	Wrong number: “(range 3.0 – 41.8 %)” changed to “(range 13.0 – 41.8 %)”
Page 65	Wrong word: “(…) “misclassified” as being “at risk of malnutrition” in Paper II” changed to “(…) “misclassified” as malnourished in Paper II”
Page 70	Missing and wrong words: “(…) demonstrating low BMI (defined as < 20 kg/m^2) as an independent risk factor” changed to “(…) demonstrating low BMI (defined as < 20 kg/m^2) to not be an independent risk factor”

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