1. Research Project Version of 28.04.2021 (modified)

Nutrition screening – route to a more practical method

The original (ethically approved) protocol includes several sections where details are given in English and in Estonian. This submission to ClinTrials.gov has had all sections in Estonian removed.

Research Site: Tartu University Hospital Department of Internal Medicine

2. Researchers and Research Centre

2.1.	Lead researcher
Name:	Prof Alastair FORBES
Qualifications:	BSc, MBBS, MD(Res), FRCP
Profession:	Gastroenterologist and Professor of Medicine
Workplace:	Tartu University Hospital Department of Internal Medicine
Workplace address:	Tartu Ülikooli Kliinikum, L-korpus, 6 korrus, Puusepa 8, 50406, Tartu, Estonia
Telephone number:	+372-5883 0422
e-mail:	alastair.forbes@ut.ee
Signature:	Digitally signed

2.2.	Associate Researchers
Name:	Prof Riina Salupere
Qualifications:	MD, PhD
Profession:	Gastroenterologist and Associate Professor of Medicine
Workplace:	Tartu University Hospital Department of Internal Medicine
Workplace address:	Tartu Ülikooli Kliinikum, L-korpus, 9 korrus, Puusepa 8, 50406, Tartu, Estonia
Telephone number:	+372-731 8658, 5331 8658
e-mail:	riina.salupere@kliinikum.ee
Signature:	Digitally signed

Name:	Prof Mai Rosenberg
Qualifications:	MD, PhD
Profession:	Professor of Nephrology
Workplace:	Tartu University Hospital Department of Internal Medicine
Workplace address:	Tartu Ülikooli Kliinikum, L-korpus, 7 korrus, Puusepa 8, 50406, Tartu, Estonia
Telephone number:	+372-731 8276, 5331 8276

e-mail: mai.rosenberg@kliinikum.ee
Signature: Digitally signed

2.3. Head of the Research Institute giving approval to the intended research project:

Name: Prof Margus LEMBER
Role: Dean of the Institute of Clinical Medicine
Workplace: Tartu University Hospital Department of Internal Medicine
Workplace address: Tartu Ülikooli Kliinikum, L-korpus, 6 korrus, Puusepa 8, 50406, Tartu, Estonia
e-mail: margus.lember@ut.ee
Signature: Digitally signed

3. Research Financing

Total cost including any reimbursement of researchers:

The only direct cost of the study is the working time of the researchers, which is included in the calculation of direct working time. The University of Tartu funds Prof. Forbes as a visiting professor. The junior researcher is supported by Professor Forbes' personal research grant. These funds are currently at the University of East Anglia, England, but will be transferred to the University of Tartu.

The patient's measurements (body weight and height) are not associated with any cost, and the patient's blood tests are those already ordered by the patient's doctor on a routine basis.

Patients in the study will not receive any benefits in kind / financial compensation.

4. Brief overview of previous research on the same topic

Malnutrition continues to be a common and important problem in hospitals around the world. Studies have repeatedly shown that more than 30% of hospitalized patients are malnourished or are at a high risk of malnutrition (1). Patients who are malnourished or at significant risk of malnutrition often receive little attention. In-hospital malnutrition is nevertheless associated with a number of significant adverse consequences of hospitalization, including an increased incidence of infections, increased length of hospital stays, and higher mortality. As a result, nutrition screening has been introduced in hospitals in many countries, and is mandatory in some jurisdictions. If nutrition screening indicates malnutrition, it is important to respond actively (2,3). In practice, however, malnutrition is often poorly assessed, and therefore effective or delayed interventions are delayed (4).

The principle that nutrition screening should be simple in nature, and that following a screening strategy, patients recover faster and have a better prognosis, nonetheless remains intact. Better screening is therefore a logical target for research.

Malnutrition cannot be assessed on the basis of a single test, as no single blood test can accurately predict nutritional risk. For example, serum albumin is a marker of disease severity, but this assay result does not correlate with the risk of malnutrition (5). It may

instead be necessary to analyse a number of so-called routine tests (eg haemoglobin, creatinine, albumin, etc.) and to use them in differential nutritional risk assessment scores.
There are numerous risk scores and most are based on body mass index, recent weight loss and the effects of the current disease on diet. The risk scores most commonly used in Europe are NRS 2002 (2) and the universal malnutrition risk score MUST (3). The key disadvantage of their use is that some patients at risk of malnutrition are neglected. As an example, in Denmark, where screening for malnutrition in hospitals is mandatory, only 8% of patients were correctly assessed for their risk of malnutrition (4).
In view of the above, a better solution could be to automatically calculate the risk score for hospitalization, based on clinical data normally collected (for other purposes) during hospitalization.

1. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. *Clin Nutr* 2008; 27(1):5-15.
2. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003; 22(3):321-36.
3. Elia M (editor). Screening for malnutrition: a multidisciplinary responsibility. Development and use of the Malnutrition Universal Screening Tool ('MUST') for adults. Malnutrition Advisory Group (MAG), a Standing Committee of BAPEN. Redditch: Bapen, 2003
4. Geiker NR, Hørup Larsen SM, Stender S, Astrup A. Poor performance of mandatory nutritional screening of in-hospital patients. *Clin Nutr* 2012 ; 31 : 862-7.
5. Bokhorst-de van der Schueren MA, Guaitoli PR, Jansma EP, Vet HC. Nutrition screening tools: does one size fit all? A systematic review of screening tools for the hospital setting. *Clin Nutr* 2014;33 (1):39-58.

5. Purpose, summary and justification of the proposed research

The aim of this research is to assess the nutritional risk in hospitalized patients through nutrition screening and to develop a risk assessment “Tartu Score” while avoiding the addition of additional tasks (surveys, surveys, laboratory analyses) in calculating this new risk score.
The research hypothesis is that a structured combination of clinical data and laboratory tests can provide a nutritional risk assessment score.
The study assumes that several / some of the commonly performed blood tests may be combined to obtain the equivalent of commonly used screening equipment.
The investigators intend that the new nutrition risk assessment “Tartu Score” is as reliable as the best alternatives already in use today. The calculated nutritional risk should therefore be comparable to the results of established scoring systems and be as reliable as the current best alternatives, MUST and NRS 2002.
As a result of the research, nutrition screening should develop into a fully automated risk assessment, during which the laboratory computer program calculates the nutritional risk. The nutritional risk warning could then be displayed automatically by the computer when viewing laboratory tests.

As a result of the nutrition risk screening, the so-called “Tartu score” would then allow for the identification of patients at high risk and the diagnosis of previously undiagnosed malnutrition in hospitals. It could thus be a very valuable tool for doctors.
The advantage of nutritional risk score is its high practical value, simplicity and automaticity. If the nutritional risk score (“Tartu Score”) is successful, the new approach has wide potential for application, and not only in Estonia.

6. Timescale of research

It is planned that the study will run: 01.06.21-31.05.22.

7. Detailed description of the research participants and their recruitment

All patients hospitalized in the internal clinic of the University of Tartu Hospital can potentially be included in the study. The goal is to recruit 300 consecutive eligible adult patients between 01.06.2021 and 31.05.2022. The patient is interviewed only once in the study, and there are no repeated interviews or measurements.

Exclusion criteria are the patient's age <18 years and the patient's state of health and unwillingness or inability to sign an informed consent form. Pregnant and breastfeeding women are not included in the study. Patients who have been hospitalized for more than 72 hours are also excluded. Concerns about infection control during the coronavirus pandemic led to the additional exclusion of patients in isolation for confirmed or suspected viral infection.

The patient is contacted in person and given an information sheet (in Estonian or Russian as appropriate). The patient is fully informed of all risks and benefits, the type of data collection and the design of the study. If the patient agrees to participate, he or she will sign a consent form. Participation in the study is strictly voluntary and takes place only after signing a written consent form. The patient will not be included in the study until he / she has read the information for the patient, thought about it, received answers to all questions of interest and voluntarily signed two copies of the written form of participation in the study, one for the patient and one for retention at the University of Tartu Clinic.

8. Detailed description of the research methodology

The patient will be assessed once during the first 72 hours after admission to the in-patient facility.
The patient is interviewed for changes in body weight in the last three months (<5% weight loss, 5-10% weight loss,> 10% weight loss or weight gain) and food intake in the last week (dietary input 75-100%, 50-75%, 25-50% or less than 25%).

The investigator evaluates the patient's diet, symptoms, and functional status according to the Subjective Global Assessment (SGA) criteria. It takes up to 10 minutes for the researcher and patient to meet the SGA criteria together. The SGA questionnaire itself is completed by the researcher participating in the study.
If height and weight have not yet been recorded by the nurses, they will be measured and recorded. Based on the above, the body mass index (BMI) is calculated.
If the patient is bed-bound, height is estimated (extrapolation of upper limb length) and body weight is also estimated (extrapolation of abdominal circumference).
Age, sex, primary diagnosis, and diagnoses of co-morbidities are found by the investigator in the medical history (eHL). Importantly, many different diagnoses are represented. The researcher codes the current main diagnosis and its severity: we use the World Health Organization's ICD-11 classification (icd.who.int/browse11/l-m/en) and a three-point scale where 1 is mild and 3 is severe. The presence or absence of fluid retention is recorded. The presence or absence of a high metabolic requirement (catabolism) is recorded.
Based on the above, the researcher calculates the MUST (1) and NRS 2002 (2) scores and evaluates the patient's nutrition according to the criteria of the subjective overall assessment (SGA).
Blood tests related to the study, over and above those already arranged by the treating physician, will not be performed and no invasive procedures are planned. Blood test results are obtained from the patient's medical history (eHL), as ordered by the treating physician.
The above activities are planned for a study of 300 patients. As a result of the nutritional risk screening, 200 patients are randomly selected from the 300 patients to generate a risk score.
The study thus creates a new nutritional risk score, which is compared to the widely used nutritional risk scores of MUST and NRS 2002 by analysing data from the remaining 100 patients. Statistical analysis is performed by logistic regression, and is performed by factor analysis. The final formula will be developed by adding proportional weights to the new scores (simplified Baye 's theorem (3)).

1. Elia M (editor). Screening for malnutrition: a multidisciplinary responsibility. Development and use of the Malnutrition Universal Screening Tool ('MUST') for adults. Malnutrition Advisory Group (MAG), a Standing Committee of BAPEN. Redditch: Bapen, 2003

2. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22(3):321-36.

3. Seymour DG, Green M, Vaz FG. Making better decisions: construction of clinical scoring systems by the Spiegelhalter-Knill-Jones approach. Br Med J 1990; 300:223-6).

9. Description of the ethical aspects of the research – Approval PKL-127

The study addresses the issues of confidentiality and protection of personal data.

The consent form does not contain contact information, confidential information, date of birth or ID code.
Sensitive personal data is processed in accordance with the procedure established in the University Hospital of Tartu, which is in accordance with the requirements provided for in the Personal Data Protection Act.
The data obtained after the oral and written consent of the patient and during the collection of the clinical data shall be coded and the coded data shall be further processed and analysed. Personal data is separated from the survey data from the beginning. The link between the personal data collected during the study and the patient's identity is known only to the researcher interviewing the patient. No personally identifiable information will be recorded in the study documentation.
The data shall be stored in digital form in a password-protected folder of the investigator-in-charge, accessible only to the investigator-in-charge. The survey data is stored on the UT clinic server. The data and collected materials related to the research will be stored in the secure archives of the University of Tartu Hospital for 25 years.

10. Information about previous or similar projects undertaken elsewhere
A related pilot study was conducted in the UK and no problems were encountered.

11. Supplementary papers:

11.1 CVs of the Researchers
11.2 Information and consent forms (Estonian and Russian)