

A report on ongoing and planned non-pharmacological intervention studies for the treatment and prevention of malnutrition in elderly a
MaNuEL report



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Geisler, Corinna

Institute of Human Nutrition, Christian-Albrechts-University Kiel, Germany

Correspondence author: cgeisler@nutrition.uni-kiel.de

A report on ongoing and planned non-pharmacological intervention studies for the treatment and prevention of malnutrition in elderly a MaNuEL report

The "Malnutrition in the Elderly Knowledge Hub" (MaNuEL) is an action program as part of the Strategic Research Agenda of the Joint Programming Initiative "A Healthy Diet for a Healthy Life". In the MaNuEL project experts of 22 research groups from 7 countries (Austria, France, Germany, Ireland, Spain, the Netherlands and New Zealand) came together to bundle up all the knowledge on malnutrition.

MaNuEL started on March 1, 2016 and has obtained funding for two years. For further information, please follow <https://www.healthydietforhealthylife.eu/index.php/joint-actions/malnutrition>.

MaNuEL is built on five interconnected malnutrition work packages. All packages cover different domains which are important to improve the knowledge/awareness about malnutrition in older persons e.g. definition, optimal screening, and optimal prevention and treatment, as well as implementation of evidence-based knowledge in clinical practice, policy and education.

One of these work packages is the work package (WP) with the title: Prevention and treatment of malnutrition in older persons (WP 4).

WP 4: Prevention and treatment of malnutrition in older persons.

The subject of WP 4 is the prevention and treatment of malnutrition in older adults. Accordingly, we drafted an overview about ongoing and planned non-pharmacological intervention studies for malnutrition worldwide. Thus, the aim of subtask 4.2 was to search for ongoing and planned non-pharmacological intervention studies.

Main inclusion criteria:

1. **non-pharmacological intervention studies**
2. **nutritional problems and malnutrition**
3. **in healthy older people**
4. **study had not yet been completed**

Main search topics:

1. **>60 years and healthy**
2. **underweight, unattended weight loss**
3. **malnutrition and/or energy-protein malnutrition**
4. **energy and/or protein supply**
5. **additional interventions**

Exclusion criterion: pharmacological interventions patients

Search strategies are listed in table 1 on the next page.

Table 1 Search strategies

clinical register	search strategies	comments/results
EU clinical trials register		free choice of tags
	protein energy malnutrition	
	protein or energy and malnutrition	
	protein or energy or malnutrition	
	under weight or underweight or weight loss	
	under weight protein	results patients only
	underweight protein	
	under weight energy	results patients only
	under weight or underweight or weight loss or weight loss or under fed or underfed or protein energy malnutrition or protein calorie malnutrition or undernourish or under nour or under nutr or undernutr or maln or malnutrition	
	protein energy malnutrition and healthy	
	consmeer	
	risk of malnutrition	EudraCT Number:2007-006153-31
clinicaltrials.gov		
	malnutrition Open Studies Interventional Studies protein Senior Studies that accept healthy volunteers	NCT02683720
	Open Studies Interventional Studies malnutrition protein, energy Senior Studies that accept healthy volunteers	
	under weight or underweight or weight loss Open Studies Interventional Studies malnutrition protein, energy Senior Studies that accept healthy volunteers	
	weight loss	
	underweight	
	low body weight Open Studies Interventional Studies protein Senior Studies that accept healthy volunteers	NCT02912130
	malnutrition Open Studies Interventional Studies energy Senior Studies that accept healthy volunteers	NCT03032237
	malnutrition Open Studies Interventional Studies protein Senior Studies that accept healthy volunteers	

	undernourished; Open Studies; Interventional Studies; protein; Senior; Studies that accept healthy volunteers	
	protein energy malnutrition Open Studies Interventional Studies Senior Studies that accept healthy volunteers	NCT03032237 (s. a.)
	protein calorie malnutrition Open Studies Interventional Studies Senior Studies that accept healthy volunteers	
	under nour Open Studies Interventional Studies protein Senior Studies that accept healthy volunteers	
	under nour Open Studies Interventional Studies energy Senior Studies that accept healthy volunteers	
	under weight or underweight or weight loss or weight loss (MeSH Terms) or under fed or underfed or protein energy malnutrition or protein energy malnutrition (MeSH Terms) or protein calorie malnutrition or undernourish or under nour or under nutr or undernutr or maln or malnutrition (MeSH Terms) not child	
	risk of malnutrition Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Interventional Studies Senior	NCT01057914; NCT02857049; NCT03459001; NCT03417531; NCT03412695; NCT03402061; NCT03073811; NCT01057914
	risk of malnutrition Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Senior Studies that accept healthy volunteers	
	risk of malnutrition Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Interventional Studies Senior Studies that accept healthy volunteers	
	Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Interventional Studies Leucine Senior Studies that accept healthy volunteers	NCT03197402; NCT03281434; NCT02918981; NCT03299972
	Interventional Studies Leucine Senior Studies that accept healthy volunteers	
cc.nih.gov/gov/home/clinicalstudies		currently not available
	protein, healthy	
	protein, energy, healthy	
	protein, energy	
	protein	
	malnutrition	

	risk of malnutrition and senior and leucine and intervention	
researchmatch.org/trials/		
	intervention, 65, healthy, elderly	
	intervention, 65, healthy, protein	
	intervention, 65, healthy, energy	
	risk of malnutrition, healthy, 60+, intervention	
drks-neu.uniklinik-freiburg.de		
	malnutrition, Diät, Nahrungsergänzung und and. Studienthemen	
	malnutrition, protein, Diät, Nahrungsergänzung und and. Studienthemen	
	risk of malnutrition, > 65 Jahre, Interventionell, Diät, Nahrungsergänzungsmittel	
	Leucine, Leucin, Malnutrition, > 65 Jahre, Interventionell, Diät, Nahrungsergänzungsmittel	
isrctn		
	ongoing, nutritional, metabolic, endocrine	
	malnutrition or mal nutrition or undernourished AND (Condition: healthy elderly AND Interventions: energy, protein AND Participant age range: Senior)	
	malnutrition AND (Condition: healthy elderly AND Interventions: energy or protein AND Recruitment Status: Recruiting)	
	malnutrition ongoing, nutritional, metabolic, endocrine AND (Condition: healthy elderly AND Interventions: energy or protein AND Recruitment Status: Recruiting)	
	nutrition AND (Condition: healthy elderly AND Interventions: energy or protein AND Recruitment Status: Recruiting)	
	recruiting, senior, healthy interventions: leucine, gender: both	
	risk of malnutrition, Senior, gender: both,	
	leucine	ISRCTN12419961
eudract.ema.europa.eu		Just registration tool
gsk-clinicalstudyregister.com		
	nutrition protein energy, interventional, recruiting, senior elderly	
	malnourished or undernourished or underfed, interventional, recruiting, elderly	
	healthy, interventional, recruiting,elderly	
	healthy, dietary supplements, interventional, recruiting,elderly	

	risk of malnutrition, interventional, gender: both, Age: 60-100 years	
WHO International clinical trials registry platform		
	nutrition or malnourished and elderly	
	nutrition elderly, young, dietary protein intake, recruiting	NTR6038
	health of the elderly	
	health promotion	
	risk of malnutriton	
anzctr.org		
	weight loss; energy; prevention, Lifestyle, behavior; interventional; healthy volunteers; not yet recruiting, recruiting, active not recruiting;	ACTRN12615001134516
	weight loss; energy; prevention, Lifestyle, behavior, treatment: drugs; interventional; healthy volunteers; condition category: diet and nutrition; not yet recruiting, recruiting, active not recruiting;	
	weight loss, underweight, malnutrition; energy, free amino acids, protein; prevention, Lifestyle, behavior, treatment: drugs; interventional; healthy volunteers; condition category: diet and nutrition; not yet recruiting, recruiting, active not recruiting;	
	weight loss, underweight, malnutrition; energy, free amino acids, protein; prevention, Lifestyle, behavior; treatment: drugs; interventional; healthy volunteers; condition category: public health; not yet recruiting, recruiting, active not recruiting;	
centerwatch.com/clinical-trials/listings/		
	healthy patient studies	
	body composition trials	
	diet and nutrition	
	weight loss	
	weight loss clinical trials, senior oder >60 years	
	leucine	
	risk of malnutrition in elderly	
pubmed		via clinical.trials.gov

Table 2 presented the results of different search strategies. An example of a search is mentioned below:

1. Search terms in ClinicalTrials.gov:

- Condition or disease: **malnutrition**
- **open studies**
- study type: **interventional studies**
- Intervention/treatment: **protein**
- Age Group: **senior (66+)**
- studies that accept **healthy volunteers**

2. Results: 5 studies

3. Selected study:

Increase Protein Intake of Older Meal Service Clients with Readymade Protein-rich Meals and Foods (NCT03032237; ConsuMEER onderzoek)

Table 2 Selected studies

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
1.	Clinical Trials.gov	Evaluating the Efficacy of a Novel Oral Supplement in Tackling Malnutrition in the Elderly (ProMO)	02/12/2016	NCT02683720	Netherlands	82	65 years and older	age 65+; at risk of malnutrition/malnourished	Dietary Supplement: ONS
2.	Clinical Trials.gov	The Multidimensional Effects of Exercise and Nutritional Interventions on Musculoskeletal Functioning, Nutritional Status and Quality of Life in Age-related Sarcopenia	09/12/2016	NCT02912130	UK - Liverpool Hope University	Estimated Enrollment 160	60 - 90 years	Male and Female participants; 60 - 90 years of age; Resident in North West, England, UK; BMI 18,5-30 kg/m ² ; can speak and understand English; willing to consent and follow the study procedures	Protein Supplementation i.e. 1.2-1.5g/kg body weight per day
3.	Clinical Trials.gov	Testing the Effectiveness and Acceptance of Home-delivered Protein-rich Meals and Foods on the Intake of Community-dwelling Older Adults	01/16/2017	NCT03032237	Netherlands - HAN University of Applied Sciences (FrieslandCampina Germany GmbH)	Estimated Enrollment 100	65 years and older	Aged 65 years or over; living at home; be a client of maaltijdservice.nl; being able to eat by themselves; have a microwave to heat meals; live in Nijmegen or Den Bosch area; being able to understand, read and speak Dutch; having signed informed consent	Protein-rich readymade meals and protein-rich dairy products - 1.2 g/kg body weight/d

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
4.	Clinical Trials.gov	Effects of Six Months Treatment With Nutritional Supplements or Dietary Advice, Alone or in Combination on Mortality, Health-related Quality of Life and Health-care Consumption for Elderly Patients at Risk of Malnutrition	01/27/2010	NCT01057914	Sweden, Uppsala University	800	65 years and older	≥ 65 years old; Admitted to one of the participating wards during the recruitment period	<p>1. Dietary supplement: Nutritional supplementation with a liquid formula The patient consumes 400 kcal from a liquid supplementation formula</p> <p>2. Other: Dietary advice The patient receives dietary advice for one hour during the hospital stay</p> <p>3. Other: Combination of supplement and dietary advice The patient receives dietary advice for one hour during the hospital stay and consumes 400 kcal from liquid supplementation formula for six months after discharge</p>

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
5.	Clinical Trials.gov	Effective Consumption of Oral Nutritional Supplements in Geriatrics: A Study Evaluating a Strategy Based on a Preliminary Degustation	07/27/2016	NCT02857049	France, Marseille	220	70 years and older	Patient aged over 70 years, hospitalized in a geriatric service for a short stay; Patient malnourished or at risk of malnutrition, justifying the medical prescription of ONS; Patient agreeing to participate in the study and who signed the informed consent form	Oral nutritional supplements (ONS) degustation
6.	Clinical Trials.gov	Efficacy of a High Quality Protein Leucine-enriched Nutraceutical in Attenuating Inactivity- and Hypo-energetic Diet-induced Muscle Loss in Older Women	06/20/2017	NCT03197402	Canada	20	70 to 75 Years	Females between 70 and 75 years of age (a narrow age range improved homogeneity of the sample for this proof-of-concept trial) with a body mass index (BMI) between 27 and 35, and muscle mass 1 standard deviation below that of sex- and ethnicity-matched 30 years old (note: this has been called 'stage 1 sarcopenia' or 'pre-sarcopenia') will be recruited. In addition, participants will be non-smokers and generally healthy per responses to a standard health screening questionnaire	Dietary supplement: Leucine-enriched protein gel delivery system; Dietary supplement: Milk protein gel delivery system Non-leucine enriched

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
7.	Clinical Trials.gov	The Effects of Whey Versus Collagen Protein Intake on Acute and Longer-term Skeletal Muscle Protein Synthesis in Older Adults	09/11/2017	NCT03281434	Canada	24	60 to 75 years	healthy; ambulatory, and able to perform exercise; active (3500-10000 steps per day)	<p>Dietary supplement: Collagen peptide. Low leucine content protein supplement to be consumed twice daily;</p> <p>Dietary supplement: Whey protein isolate. High quality protein (DIAAS score), high leucine supplement, to be consumed twice daily</p>
8.	Clinical Trials.gov	Nutritional Strategies to Augment the Postprandial Muscle Protein Synthetic Response to the Ingestion of a Low Dose of Protein in Middle-aged Women	09/20/2016	NCT02918981	USA	60	50 to 79 years	BMI<30 kg/m ² ; healthy, sedentary	<p>Behavioral: Resistance Exercise. Unilateral leg extension exercise immediately prior to ingestion of the experimental beverage.</p> <p>Dietary supplement: 14 g Whey protein or: 6.6 g Whey protein + 1.25 g leucine or: 4 g Whey protein + 1.25 g leucine + 2.6 g Whey peptides or: 6.6 g Whey protein + 1.25 g leucine + 0.8 g Citrulline or: other: water (control)</p>

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
9.	Clinical Trials.gov	Effects of 12 Weeks Resistance Exercise and Whey Protein Supplementation on Multiple Indices of Sarcopenia in Older Men	09/11/2017	NCT03299972	USA	52	60 to 80 years	Retired Men aged 60-80 years; Body Mass Index 18.5-30 kg/m ² ; Not participated in resistance exercise within the last 6 months; Free from musculoskeletal injury	Dietary Supplement: Whey Protein 25 g of high leucine whey protein supplementation twice daily (breakfast and lunch) or: Placebo 23.75 g of placebo powder twice daily (breakfast and lunch) or: Resistance Exercise + Whey protein: 60 minutes of resistance exercise twice a week and 25 g of high leucine whey protein twice daily; or: Resistance exercise + Placebo: 60 minutes of resistance exercise twice a week and 23,75 g of placebo powder twice daily
10.	Clinical Trials.gov	Evaluation of a High Calorie, High Protein Tube Feeding Product in an Adult Population with or at Risk of Malnutrition	03/08/2018	NCT03459001	Spain	35	Adults and Seniors	MUST score ≥ 2 ; Under the care of a health care professional for malnutrition or at risk of malnutrition and has been prescribed the study formula; Requires and agrees to be tube fed the enteral feeding product for at least 16 consecutive days as their sole-source of nutritional intake; Free living in the community or is residing in a nursing home and conforms to the requirements set forth on the study product label.	high calorie, high protein tube feed

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
11.	Clinical Trials.gov	Sarcopenia Prevention with a Targeted Exercise and Protein Supplementation Program (STRONG)	0173172018	NCT03417531	Switzerland	800	>75 years	At least 1 of 5 frailty criteria, definition by Linda Fried; low trauma fall in the last 12 months prior to enrollment; Mini Nutritional Assessment (MNA) screening tool (score ≤ 11); Community-dwelling or assisted living	L-leucine-enriched whey protein isolate powder (equivalent to 20 g of Protein); twice daily; all participants will receive a control dose of 24'000 IU vitamin D per month home exercise strength or flexibility (3x30 minutes/week)
12.	Clinical Trials.gov	Development of a Decision Support System to Prevent and Treat Disease-related Malnutrition	01/10/2018	NCT03412695	Norway	100	Adults and Seniors	At nutritional risk, defined as Nutrition Risk Screening (NRS-2002) score >3	nutritional treatment of the patients decision support system "MyFood" are developed in the project with the purpose to prevent and treat disease-related malnutrition.
13.	Clinical Trials.gov	Nutritional Perihabilitation in Older Veterans Undergoing Surgery	03/13/2018	NCT03073811	USA	105	>65 years	Elective abdominal surgery; Referred to the VA Perioperative Optimization of Senior Health Clinic; Able to record dietary intake or has a proxy who can record dietary intake	30 grams of high quality protein (20 grams from Ensure Enlive and 10 grams of whey protein powder) educational on the role of nutrition; Registered Dietitian will instruct participant to follow instruction on handout
14.	Clinical Trials.gov	Nutrition in Disguise: Development and Palatability Testing of Novel Food Products (NiD)	01/17/2018	NCT03402061	Canada	200	>65 years	Older adults living in the community with no food allergies; older adults living in long term care with and without dementia with no food allergies	Dietary Supplement: nutrient enhanced recipes Behavioral interventions
15.	Clinical Trials.gov	Effects of Nutritional Supplementation and Dietary Advice in Elderly Patients After Hospital Discharge.	01/28/2010	NCT01057914	Sweden	800	65 years and older	≥ 65 years old; Admitted to one of the participating wards during the recruitment period	400 kcal from a liquid supplementation formula dietary advice for one hour during the hospital stay

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
16.	WHO int. Clinical trials registry platform	Effectiveness of a combined resistance exercise and nutrition intervention to promote maintenance of physical functioning of community-dwelling elderly in a real-life setting	05.09.16	NTR6038	Netherlands - Wageningen University (WUR); sponsored by: Ministry of Economic Affairs, FrieslandCampina Innopastry	200	65 years or over	Living independently in one of the five selected municipalities; able to understand dutch language; pre-frail or frail according to fried criteria; having signed informed consent	<p>12 weeks intervention:</p> <p>1) Twice weekly 1-Hour progressive resistance-type exercise training, in groups, supervised by physiotherapists</p> <p>2) Increased dietary protein intake during the main meals, using protein-rich products, supervised by a dietitian. 12 weeks maintenance period: participants will be introduced to local exercise and nutrition facilities. Multiple activities will be organized to stimulate participants to maintain the active lifestyle and an adequate protein consumption.</p> <p>The control group receives no treatment in the first 24 weeks, and will receive the maintenance period after 24 weeks</p>

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
17.	WHO int. Clinical trials registry platform	PILOT STUDY 2 i®Prevention Of Malnutrition In Senior Subjects (PROMISS)i™	11/24/2017	NTR6849	Netherlands	100	>70 years	Community-dwelling; Lower protein intake (< 1.0 g/kg/body weight) based on a short food list that is developed and validated using an extended FFQ among Dutch older adults (data available on request); Able to eat independently; Willing to eat our provided products; Able to speak, write and read the Dutch language	Increased dietary protein intake during the main meals, using protein-rich products, supervised by a dietitian yes; 1) replacing habitual products with the newly developed protein rich food products; and 2) consumption of the newly developed protein rich food products in addition to their regular diet in close proximity of regular physical activity.
18.	anzctr	Dietary protein digestion and absorption kinetics and subsequent postprandial muscle protein accretion in healthy older people	09/25/2015	ACTRN12615001134516	Australia - University of Adelaide	20	65 years and older	Male; Body Mass Index (BMI): 22-30 kg/m ² ; Weight stable (<5% fluctuation in body weight in previous 3 months)	Intraduodenal protein infusion; or: intraduodenal administration of milk protein (intrinsically labelled with L-Phenylalanine or L-Leucine or ii) or: amino acid mixture Matching (isocaloric) the milk protein including L-phenylalanine and L-leucine

No.	Register	Study title	Date of submission	ID-Nr.	Country	n	Age	Inclusion criteria	Intervention
19.	EU Clinical Trials Register	Safety and efficacy of subcutaneous (SC) administration of Clinimix N9G15E in elderly patients at risk for malnutrition, at a dose of 1 liter infused over 12 hours for 7 to 10 consecutive days. A prospective, multicentre, randomized, open-label, non-inferiority, controlled phase III B trial carried out in parallel groups: subcutaneous versus peripheral intravenous administration	04/23/2008	EudraCT Number: 2007-006153-31	France	126	Adults, Elderly	<ol style="list-style-type: none"> Both genders Age superior or equal to 65 years Hospitalized and at risk for malnutrition defined by their MNA SF below 12 and GNRI between 83.5 and 97.5. Oral intake <50% of appropriate intake (defined as 30 Kcal/kg/day) for an expected duration of greater than 3 days. Severe dehydrated patients must be rehydrated before enrolling into the trial Dated and signed written informed consent, prior to any study-related procedures, provided by the patient or, according to the law (L. 1122-2), by his legal representative or by a "personne de confiance" if any written designation or, if not, his family member or, if no family member, a close relative Patients in stable condition 	Clinimix N9G15E at a dose of 1 liter infused over 12 hours for 7 to 10 consecutive days
20.	BioMed Central isrctn.com	protein supplementation for preventing bone loss and improving muscle strength in older women: a randomized controlled trial	07/03/2017	ISRCTN12419961	United Kingdom	60	65 years and older	<p>Community-dwelling women aged 65 or over; Not currently engaged in upper body exercise training (within last 6 months); Not using any medications for osteoporosis and not using any medications that can affect bone metabolism; Do not have an underlying disease that impairs bone metabolism, such as hyper/hypoparathyroidism</p>	<p>Group A: Home-based exercise intervention</p> <p>Group B: Home-based exercise intervention and leucine and vitamin D enriched supplement</p> <p>Group C: No intervention (no treatment)</p>

Results

We compiled a list of 20 intervention studies (see table 2 and figure 1). The list contains information about registry name, date of submission, ID-number, country, title, estimated participants, ages, inclusion criteria and types of intervention (energy-/protein intake, behavioral). In a more detailed excel sheet further information are listed e.g. duration, study start and status of recruiting participants. For further information, please contact dliesegang@nutrition.uni-kiel.de.

Most of the studies were found at ClinicalTrials.gov (n=15) but we also found intervention studies at WHO int. Clinical trials registry platform, EU Clinical Trials Register, Australian New Zealand Clinical Trials Registry, and International Standard Randomized Controlled Trial Number Registry.

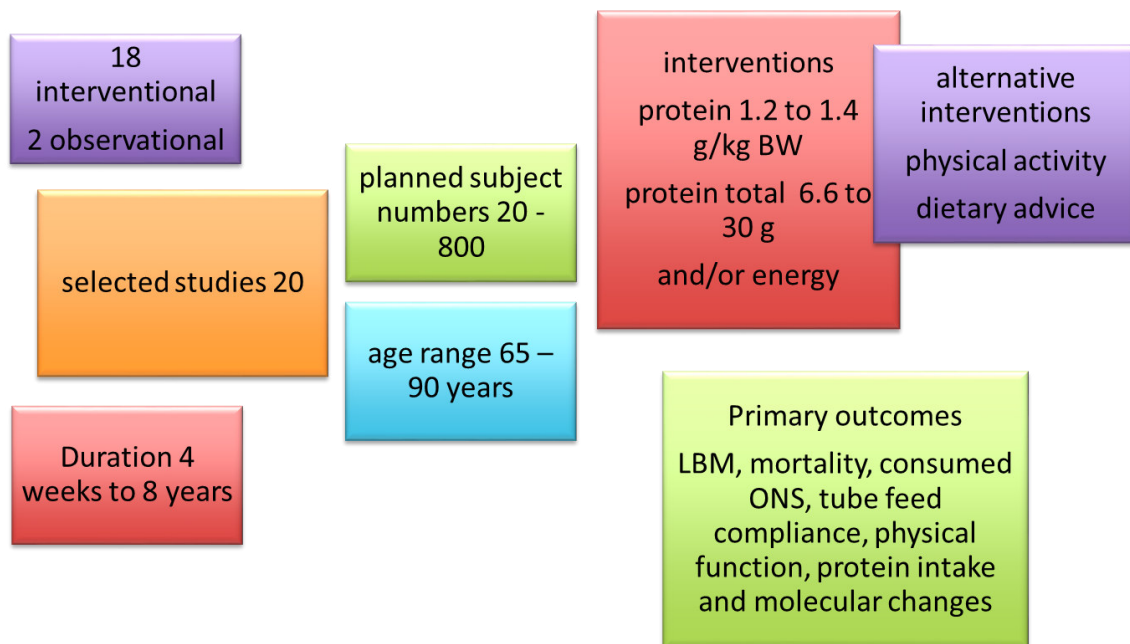


Figure 1 Overview of ongoing and planned non-pharmacological intervention studies

Summary

Most used screening tools in selected studies were:

1. Malnutrition: as inclusion criteria MNA (Mini Nutritional Assessment 2 studies), NRS-2002 (Nutritional Risk Screening 1 study) and ONS prescription (Oral Nutritional Supplements 2 studies)
2. Interventions with ONS: in three studies ONS only and in one plus dietary advice
3. behavioral interventions: in nine studies different behavioral interventions were included e.g. resistance training or dietary advice
4. Primary outcomes: for physical function SPPB (Short Physical Performance Battery 5 studies), SGA (Subjective Global Assessment 3 studies), for nutrition NRS-2002 (1 study), ADL (Activity of Daily Living), TUG (Timed Up and Go), HGS (Hand Grip Strength) and walking/gait speed

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