REVIEW ARTICLE

The Nordic Nutrition Recommendations 2022 – prioritisation of topics for de novo systematic reviews

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Abstract

Background: As part of the process of updating national dietary reference values (DRVs) and food-based dietary guidelines (FBDGs), the Nordic Nutrition Recommendations 2022 project (NNR2022) will select a limited number of topics for systematic reviews (SRs).

Objective: To develop and transparently describe the results of a procedure for prioritisation of topics that may be submitted for SRs in the NNR2022 project.

Design: In an open call, scientists, health professionals, national food and health authorities, food manufacturers, other stakeholders and the general population in the Nordic and Baltic countries were invited to suggest SR topics. The NNR2022 Committee developed scoping reviews (ScRs) for 51 nutrients and food groups aimed at identifying potential SR topics. These ScRs included the relevant nominations from the open call. SR topics were categorised, ranked and prioritised by the NNR2022 Committee in a modified Delphi process. Existing qualified SRs were identified to omit duplication.

Results: A total of 45 nominations with suggestion for more than 200 exposure–outcome pairs were received in the public call. A number of additional topics were identified in ScRs. In order to omit duplication with recently qualified SRs, we defined criteria and identified 76 qualified SRs. The NNR2022 Committee subsequently shortlisted 52 PI/ECOTSS statements, none of which overlapped with the qualified SRs. The PI/ECOTSS statements were then graded ‘High’ (n = 21), ‘Medium’ (n = 9) or ‘Low’ (n = 22) importance, and the PI/ECOTSS statements with ‘High’ were ranked in a Delphi process. The nine top prioritised PI/ECOTSS included the following exposure–outcome pairs: 1) plant protein intake in children and body growth, 2) pulses/legumes intake, and cardiovascular disease and type 2 diabetes, 3) plant protein intake in adults, and atherosclerotic/cardiovascular disease and type 2 diabetes, 4) fat quality and mental health, 5) vitamin B12 and vitamin B1; 6) intake of white meat (no consumption vs. high consumption and white meat replaced with red meat), and all-cause mortality, type 2 diabetes and risk factors, 7) intake of n-3 LPUFAs from supplements during pregnancy, and asthma and allergies in the offspring, 8) nuts intake and cardiovascular disease (CVD) and type 2 diabetes in adults, 9) dietary fibre intake (high vs. low) in children and bowel function.

Popular scientific summary

• Qualified systematic reviews will be the main foundation for revising dietary reference values and food-based dietary guidelines in the Nordic Nutrition Recommendation 2022.

• This paper describes the results of an open, transparent six-step procedure to identify topics that will be prioritised for de novo systematic reviews by the Nordic Nutrition Recommendation 2022 project.

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Discussion: The selection of topics for de novo SRs is central in the NNR2022 project, as the results of these SRs may cause adjustment of existing DRV and FBDGs. That is why we have developed this extensive process for the prioritisation of SR topics. For transparency, the results of the process are reported in this publication.

Conclusion: The principles and methodologies developed in the NNR2022 project may serve as a framework for national health authorities or organisations when developing national DRV and FBDGs. This collaboration between the food and health authorities in Denmark, Estonia, Finland, Iceland, Latvia, Lithuania, Norway, and Sweden represents an international effort for harmonisation and sharing of resources and competence when developing national DRV and FBDGs.

Keywords: dietary reference values; food-based dietary guidelines; systematic reviews; Nordic countries; the Baltics; national food and health authorities; evidence-based nutrition; nutrient recommendations

To access the supplementary material, please visit the article landing page
September 2019. Deadline for the submission of topics was December 31, 2020. The submitted nominations consisted of three components: 1) a cover letter with a rationale and a description of why a review on a specific topic was warranted and how it related to health issues in Nordic and Baltic populations; 2) a list of references for scientific papers; and 3) a simple ‘PI/ECOTSS’ statement covering the elements ‘population’, ‘intervention/exposure’, ‘outcome’, ‘timing’, ‘setting’ and ‘study design’.

A total of 45 nominations with suggestion for more than 200 exposure–outcome pairs were received. Two nominations were excluded because they were incomplete; they were more like comments (see the complete list at the NNR2022 project website (12)). Forty-three of the nominations fulfilled all elements described earlier. The complete list of nominations, with their rationale and arguments, is available on the NNR2022 project website (12) and as an Electronic Supplementary Table 1. All submissions were considered by the NNR2022 Committee. Several of the nominations were overlapping, and some nominations needed to be interpreted and translated to a scientific question by the NNR2022 Committee. The NNR Committee developed a summary table of the nominations, where overlapping nominations were combined, that represents 43 exposure–outcome pairs (Table 1).

Whilst only a limited number of topics made it through to the final list of SR prioritisations due to limited resources, all public nominations will be evaluated carefully by the NNR2022 Committee and various chapter experts when the DRVs and FBDGs are developed and formulated.

**Step 2. Scoping reviews on all nutrients and food groups considered in NNR2022**

To develop candidate topics for prioritisation of de novo SRs, members of the NNR2022 Committee performed 51 scoping reviews (ScRs), one for each of the nutrients and food group chapters that will be part of the final NNR2022 report. An ScR is a relatively new approach to explore existing evidence (13). It differs from SRs both in its purpose and methodology. The purpose of an ScR is to provide an overview of available research without producing a synthesis and grading of total strength of evidence for a specific research question. An ScR should follow the procedures of the PRISMA Extension for Scoping Reviews (PRISMA-ScR) defined by the Equator Network (13). The methodology is much simpler than the extensive and more costly methodology for qualified SRs.

The objective of the 51 ScRs was to contribute to the shortlisting of topics. The major outcome of the ScRs was the formulation of shortlisted SR topics, formulated as PI/ECOTSS. Forty-nine topics were shortlisted based on the literature search. The literature search for the ScRs is presented in Electronic Supplementary Table 2.

When developing the search strategy for the ScRs, the aim was to identify possible topics that might be chosen for de novo SRs. We assumed that any topic with a significant amount of new data since the last edition of NNR
Table 1. Nomination of topics for systematic reviews from open call

| Topic                                                                 | Population                                                                 | Intervention                                                                                   | Outcome                                                                                           | Timing                      |
|----------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|-----------------------------|
| Obesity                                                              | Adults with body mass index (BMI) > 30                                      | Avoidance obesogenic foods                                                                      | Narrower waist, lower level of triglycerides                                                      | Lifetime                    |
| Plant-based, vegetarian and vegan diets                              | General population                                                         | Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)                 | Heart health and cognitive function                                                               | Years                       |
|                                                                      | General population (all age groups)                                        | Plant-based diet and dietary supplements                                                        | Various health effects (obesity, diabetes, several cancers and heart disease) and vitamin deficiency | Short and long term         |
|                                                                      | Adults                                                                     | Plant protein intake versus animal protein intake                                               | Health effect (total mortality, diabetes type 2, all cancers and cardiovascular disease)           | Weeks                       |
|                                                                      |                                                                            |                                                                                                  |                                                                                                   | Randomized controlled trials (RCTs) and years (cohorts)                                        |
| Healthy children (including infants, babies and toddlers) in the Nordic countries |                                                                            | Vitamin B<sub>12</sub> intake from foods (fortified foods) and supplements up to RDI              | Vitamin B<sub>12</sub> status, cognitive function (growth and development)                         | Years                       |
| Children and women of child-bearing age                              |                                                                            | Intake of plant-based foods                                                                      | Iron status/iron absorption/iron bioavailability                                                 | Short term                  |
| Healthy children and adults                                          |                                                                            | Intake of foods containing plant protein isolates including soy protein isolates                | Blood (plasma) concentrations of amino acids, lipids and glucose/insulin                          | Short term                  |
| Children and pregnant and lactating women                           |                                                                            | Plant-based diet                                                                                 | All possible outcomes, but especially growth, neurological and cognitive developments             | NA                          |
| Detection and correction of vitamin- and mineral deficiencies – biomarkers of intake | Adults                                                                     | Assessment of vitamin and mineral status and need of supplementation                            | Restored adequate vitamin status                                                                | Months                      |
| Sustainability, and environmental and health impacts of foods and diets in the Nordic countries | General population                                                         | Potatoes                                                                                       | General health indicators and sustainability                                                     | Lifetime                    |
|                                                                     | Nordic countries (including all age groups, gender and socio-economic groups) | Dietary patterns and specific food groups                                                        | Environmental impact (e.g. climate impact, eutrophication potential, acidification potential, land use demand, etc.) by using life cycle assessment (health outcomes not stated) | Not stated                  |
|                                                                     | General and healthy populations in the Nordic countries                    | Nordic diet (foods primarily produced in the Nordics) whole food/whole sustainable diet approach | Nutrient intake (protein, vitamin D, calcium, riboflavin, vitamin B<sub>12</sub>, folate, iodine, selenium and zinc), long-term effects on public health and specific health parameters, biological diversity, animal welfare, responsible use of antibiotics in animal food production, carbon sequestration, responsible use of pesticides and use of land and water | >4 weeks                    |
| Inclusion of fruit-juice in FBDG                                     | General population (distinguish in terms of BMI, age and gender)            | Consumption of different volumes of pure fruit juice/compared to placebo/sugar sweetened fruit juice. May be consumed with a meal that induces inflammation | CRP and inflammatory cytokines                                                                  | Short (hours) and long term (weeks)                                                             |
| Vitamin D requirements                                               | Children and adolescents, fair and dark skinned in Nordic countries, including arctic areas | Intake of vitamin D                                                                             | Vitamin D status                                                                                 | Long term                   |
|                                                                     | Prepubertal children with fair and dark skin living in northern Europe     | Vitamin D supplementation                                                                       | Vitamin D status, calcium, PTH, cardiometabolic markers and BMI                                  | >3 months                   |
|                                                                     | Preschool children (1–5 years) with light versus dark skin colour          | Requirement of vitamin D                                                                        | Vitamin D status                                                                                 | Not stated                   |
Table 1. (Continued)

| Topic | Population | Intervention | Outcome | Timing |
|-------|------------|--------------|---------|--------|
| Meal pattern, timing and frequency, and regularity of meals/meal patterns | Children, adults and older adults | Meal pattern | Obesity related, unintentional weight loss/risk for malnutrition | Long term |
| | Children and adults | Timing/frequency/regularity of meals | Cardio metabolic health markers, body weight, obesity, lipid profile, insulin resistance and blood pressure | Not stated |
| Symbiotics in infant formula in treatment of cowmilk allergy | Infants consuming cowmilk formula | Intake of pre- and probiotics | Asthma, gastrointestinal disorders and eczema | Years |
| Degree of processing | General population | Reduction in intake of ultra-processed foods | Prevention of all diet-related Non-communicable diseases (NCDs) | Long term |
| | All population groups | Intake of ultra-processed foods | Diet-related chronic diseases and diet quality | Lifetime |
| Diet in the elderly | Old adults (>75 years) | Weight change | Diabetes mellitus type 2, mortality and sarcopenic obesity | Years |
| | Elderly population, aged 65 years or more | Energy, protein and B12 | Risk of malnutrition, malnutrition, cost of malnutrition or its risk, morbidity, mortality and recovery | Years, lifetime |
| Vitamin K requirements (K1 and K2) | Healthy general population (all ages and different ethnicity) | Intake of vitamin K-rich foods or vitamin K supplement. Vitamin K1 and K2 should be examined separately. Comparators: diets low in total vitamin K/vitamin K1/vitamin K2, and supplements without these vitamins | Different health outcomes of vitamin K1 and K2, for example cardiovascular metabolism, bone health and diabetes | The timing varies |
| | Different populations, but primarily healthy humans, both genders, a broad range of age and ethnicity | Intervention: K2-rich foods or K2 supplement versus placebo, intervention diet versus subjects’ normal diets, lower versus upper percentiles | | A minimum of 4 weeks |
| Milk and dairy products and fat / dairy matrix | General population; different genders, ages, ethnicities, and health status | Intake of different dairy products in various amounts. Comparator(s): lower versus upper quartile | Cardiovascular disease and diabetes type 2 and their risk markers | Depends on study type |
| | Humans, both genders, different ranges of age, ethnicity and cardiovascular health status (not critically ill) | Intake of dairy food groups, different levels, for example: 1) full fat cheese versus low fat cheese, plus control group with no cheese intake; 2) full fat milk versus low fat milk, plus control group with no milk intake; 3) full fat yoghurt versus low fat yoghurt, plus control group with no yoghurt intake | LDL, ox LDL, VLDL, HDL, adiponectin, HbA1c and IL-6 | Minimum 4 weeks |
| | The healthy population — all ages | Dairy fat | Adequate nutrient intake | Lifetime |
| Complementary feeding | 0–2 years age, 3–5 years of age | Intake of different protein sources, sugar and sugary foods, water and other fluids, fruit and vegetables, fish and other sources of omega 3; amount of gluten at introduction and infancy, dose and timing of food allergens, meal order and snacking; effects of different parenting styles and responsive feeding | Overweight/obesity iron deficiency, neurodevelopment, vitamin D status, dental caries and allergies | Years |
| Choline | The Norwegian population, all ages | Intake of choline and all choline forms | Develop dietary recommendations | Years |
Table 1. (Continued)

| Topic                                      | Population                                           | Intervention                                       | Outcome                                                                 | Timing                  |
|--------------------------------------------|------------------------------------------------------|----------------------------------------------------|-------------------------------------------------------------------------|-------------------------|
| Omega-3 fatty acid intake                  | Children, and pregnant and lactating women           | Omega-3 fatty acids                                | All possible health outcomes, growth, neurological and cognitive developments and serum lipids | Lifetime                |
| Intake of whole grains                     | General population, especially in the Nordic countries | Whole grain                                        | Incident of coronary heart disease, stroke, type 2 diabetes, obesity, breast cancer, colorectal cancer, pancreatic cancer, gastric cancer, endometrial cancer, prostate cancer and mortality from all causes, respiratory diseases, infectious diseases and all non-cardiovascular and non-cancer causes | >5 years                |
| Eggs and heart health                      | Adults (18 years of age or older)                    | Intervention: Eggs should be evaluated as a whole-food rather than examining constituents in eggs, such as cholesterol or choline. Comparators: another whole food (e.g. another protein source) | Cardiovascular disease (CVD) as a broad outcome classification coronary heart disease (CHD), coronary artery disease (CAD), ischemic heart disease. Cardiac events, including myocardial infarction. Cerebrovascular disease, including stroke. Both fatal and non-fatal outcomes should be considered | The analysis should be longitudinal in nature |
| Red and processed meat and cancer          | Adults (18 years of age or older), who are free of chronic disease at baseline or study entry | Intervention: Red meat should be evaluated based on unprocessed and processed red meat items, and analyses that focus on this differentiation should be emphasised. Comparator: another whole food (e.g. another protein source) or to varying intake levels of red meat (e.g. daily intake vs. three times per week) | Total cancer incidence and mortality. Specific types of cancer, with an emphasis on colorectal cancer, which has been the most widely evaluated cancer type | The analysis should be longitudinal in nature |
| Gut microbiome                             | Infants in a birth cohort                            | Breast feeding                                     | Composition of the gut microbiome, bodyweight, diabetes type 1 and celiac disease | 5 and 10 years and maybe longer follow-up For 3 months and 1 year Years, lifetime |
|                                            | Adults and children                                  | Plant-based diet                                   | The growth of beneficial bacteria and the reduction of inflammation Gut microbiota, incidence and prevalence of non-communicable diseases | Both short and long term (days/months) |
|                                            | Infants and children under 10 years of age           | Intake of pre-, pro-, syn- and postbiotics         |                                                                          |                         |
|                                            | Healthy adults                                       | Different types of fibres                          | Composition of gut microbiome                                         |                         |
| Neurotoxic pesticide residues              | Children (1–18 years)                                | Intake of common pesticides, including glyphosate and known neurotoxins | Mental health, learning disabilities, intellectual development, brain function, altered gut microbiota, anxiety, depression and child-learning capacity | Intervals from weeks to years |
| Chrono-biology and meal frequency          | General population, adults and teenagers             | Meal-time, meal frequency, temporal distribution and irregular meal patterns | Weight status, adiposity, diet quality and cardiovascular risk factors | Both short mechanistic studies and months/years |
| Vitamin- and mineral requirements during intravenous nutrition supply | Healthy adults | Use of intravenous nutrition (total parenteral nutrition) | Cover nutritional needs of macro- and micronutrients | Days to lifetime |
| Metabolic syndrome                         | Adults                                               | Intake and distribution of macronutrients          | Weight, metabolic syndrome and insulin resistance                      | Lifetime                |
|                                            |                                                      | Intake of ultra-processed foods                    | Cardiovascular disease and hard endpoints                               | Lifetime                |

The NNR2022 Committee formulated scientific questions based on the public call and the principles described in Arnesen et al. (ref 2–3).
would likely have been covered in a recent review article. We selected to set the bar at the level of ‘reviews’, rather than ‘systematic reviews’. By selecting reviews as the bar, we assume that we would pick up research activities that had not yet been dealt with in an SR. Thus, by choosing ‘reviews’, we have had a more open search with lower threshold than if we had selected ‘systematic reviews’.

In the NNR chapters, however, the initial ScR search string will be carefully adjusted and modified (e.g. by including ‘systematic reviews’, ‘meta-analysis’, ‘Mendelian randomisation studies’ and other types of relevant literature) when appropriate.

An evaluation of the results of the open public call (Electronic Supplementary Table 1) was included in each relevant ScR. Each ScR was considered by the NNR2022 Committee. The final version of the ScRs was formulated in a consensus process after several rounds of consultations in the NNR2022 Committee.

The criteria for shortlisting and prioritisation included evidence of significant new and relevant research since the previous edition of NNR (NNR2012) (14) and relevance to current public health concerns in the Nordic or Baltic countries (Box 1).

**Step 3. Identification of qualified SRs to omit duplications**

In order to omit duplication of recent qualified SRs, we established a process to identify relevant qualified SRs.

The definition of a qualified SR was based on the inclusion and exclusion criteria (Box 2) pre-specified by the NNR2022 project (2–4).

The search for qualified SRs was based on searches in PubMed/Medline and inspection of the websites of national and international food and health authorities as described by the Food and Agriculture Organization (FAO) of the United Nations (15). We also contacted the following major national food and health authorities and organisations directly for information on previous or planned SRs:

- National Academy of Sciences, Engineering and Medicine, USA
- Dietary Guidelines Advisory Committee, USA
- World Health Organization (WHO)
- World Cancer Research Fund (WCRF)
- European Food Safety Agency (EFSA)
- Scientific Advisory Committee on Nutrition (SACN), UK
- German Nutrition Society, Germany
- Health Council, The Netherlands
- National Health and Medical Research Council, Australia
- Ministry of Health, New Zealand
- Health Canada, Canada

All identified qualified SRs that fulfilled the inclusion and exclusion criteria are listed in Table 2.

**Box 1. Criteria for shortlisting and prioritisation of topics for de novo SRs.**

- **Relevance**: The topic is within the scope of NNR2022.
- **Within scope (examples)**: Healthy populations/individuals; prevention purposes (e.g. population health topics, clinically oriented topics are not included and people with increased genetic risk for chronic diseases are included); covers different age groups, and pregnant and lactating women; increased requirements during short-term mild infections; etc.
- **Outside scope (examples)**: Long-term infections; malabsorption; various metabolic disturbances; treatment of persons with a sub-optimal nutritional status; clinical guidelines on dietary supplementation.
- **Importance**: The topic has new, relevant and significant data or is an emerging topic in an area of substantial public health interest or concern.
- **Substantial public health concern (examples)**: Overweight, obesity and adiposity-related illness; metabolic syndrome and diabetes mellitus type 2; atherosclerotic cardiovascular diseases; cancer; osteoporosis; neurodegenerative diseases; mental health; oral health; multi-morbidity and mortality; reproductive health; optimal growth.
- **Relevant and significant**: Refers to the overall scientific quality of the evidence, the number of studies, consistency of results and whether new study results appear to expand the DRV- and FBDGs-related information available in the previous edition of NNR.
- **Potential national impact**: The SR may potentially inform national food and health policies and programs. An SR with the specific topic may result in a new or an adjustment of previous DRVs or FBDGs.
- **If the research question is within the scope of NNR2022 and covers an outcome of substantial health concern to the Nordic and Baltic countries, then it has potential national impact. In other words, it may inform DRVs, FBDGs and national food and health policies and programs.**
- **No duplication**: The topic is not currently addressed through other recent qualified SRs.
Step 4: Formulation and shortlisting of PI/ECOTSS statements

All shortlisted topics from the ScRs and the public call were formulated by the NNR2022 Committee as initial PI/ECOTSS statements (2–4). The shortlisted PI/ECOTSS statements were then compared with topics covered in the list of qSRs (Table 2), and overlapping PI/ECOTSS statements, which had not been removed in a previous stage, were excluded from the shortlisting. The initial formulation of PI/ECOTSS statements was adjusted by the NNR2022 Committee during several steps of this process to improve the precision of the scientific question. Consultation with topic experts, the members of the NNR SR Centre and the Scientific Advisory Group was helpful in formulating the final PI/ECOTSS statements. Elimination of PI/ECOTSS statements due to overlap with qSRs was continuously updated in accordance with the ongoing adjustments in PI/ECOTSS statements.

Table 3 presents the 52 PI/ECOTSS statements that were shortlisted.

Step 5. The grading of SR topics into high, medium and low importance

Subsequently, the NNR2022 Committee members graded individually the PI/ECOTSS into ‘High’ (n = 21), ‘Medium’ (n = 9) or ‘Low’ (n = 22) importance (Table 3), based on the criteria described (Box 1). The final grading was then decided in a consensus process. This process took more than 6 months and included careful evaluation of all the 51 ScRs as well as secondary literature- and citation searches.
Table 2. Qualified systematic reviews were identified based on the inclusion and exclusion criteria described in Box 1

| Topic                                      | Year | Authors/organisation (country) | Exposure(s) | Outcome(s)                                                                 | Risk of bias assessment tool | SoE/evidence quality grading |
|--------------------------------------------|------|---------------------------------|-------------|----------------------------------------------------------------------------|------------------------------|------------------------------|
| 1. Sodium and potassium intake             | 2018 | Agency for Health-care Research and Quality (AHRQ) (USA) (22) | Dietary sodium (sodium reduction) and potassium | Blood pressure, risk for cardiovascular diseases, all-cause mortality, renal disease and related risk factors, and adverse events | Cochrane RoB/Newcastle-Ottawa Scale (NOS). Some nutrition-specific items added (e.g. sodium intake assessment) | 'High', 'Moderate', 'Low' or 'Insufficient'. Based on: 1) Study limitations, 2) consistency, 3) directness, 4) precision and 5) reporting bias. Observational studies may be upgraded if very strong effects, a strong dose–response relation or if effects cannot be explained by uncontrolled confounding |
| 2. Vitamin D and calcium                   | 2014 | AHRQ (USA) (23)                | Vitamin D and/or calcium | Bone health, cardiovascular health, cancer, immune function, pregnancy, all-cause mortality and vitamin D status | CONSORT statement for RCTs, own checklist based on STROBE and nutrition-specific items | Grade A–B |
| 3. Omega-3 fatty acids                     | 2016 | AHRQ (USA) (24)                | Omega-3 fatty acids | Cardiovascular disease and risk factors | Cochrane RoB/NOS. Some nutrition-specific items added | 'High', 'Moderate', 'Low' or 'Insufficient'. Based on: 1) Study limitations, 2) consistency, 3) directness, 4) precision, 5) reporting bias and 6) number of studies |
| 4. Omega-3 fatty acids                     | 2016 | AHRQ (USA) (25)                | Omega-3 fatty acids | Maternal and child health: Gestational length, risk for preterm birth, birth weight, risk for low birth weight, risk for peripartum depression, risk for gestational hypertension/preeclampsia, postnatal growth, visual acuity, neurological development, cognitive development, autism spectrum disorder, ADHD, learning disorders, atopic dermatitis, allergies and respiratory disorders and adverse events | Cochrane RoB/NOS. Some nutrition-specific items added | 'High', 'Moderate', 'Low' or 'Insufficient'. Based on: 1) Study limitations, 2) consistency, 3) directness, 4) precision, 5) reporting bias and 6) number of studies |
| 5. Nutrient reference values for sodium    | 2017 | Australian Government Department of Health/New Zealand Ministry of Health (26) | Dietary sodium/sodium reduction | Blood pressure, cholesterol levels, stroke, myocardial infarction and total mortality | Cochrane RoB, modified | Grading of Recommendations Assessment, Development and Evaluation (GRADE) and National Health and Medical Research Council (NHMRC) level of evidence (from I to IV) |
### Table 2. (Continued)

| Topic | Year   | Authors/organisation (country) | Exposure(s)                                      | Outcome(s)                                                                 | Risk of bias assessment tool | SoE/evidence quality grading |
|-------|--------|-------------------------------|-------------------------------------------------|----------------------------------------------------------------------------|------------------------------|------------------------------|
| 6. Dietary patterns | 2020   | DGAC (USA) (27)               | Dietary patterns and macronutrient distribution | Growth, size, body composition, and/or risk of overweight or obesity       | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 7. Dietary patterns (update of 2015 DGAC review) | 2020 | DGAC (USA) (28)               | Dietary patterns                                | Cardiovascular disease, CVD risk factors (blood pressure, blood lipids) | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 8. Dietary patterns and risk of type 2 diabetes (update of 2015 DGAC review) | 2020 | DGAC (USA) (29)               | Dietary patterns                                | Type 2 diabetes               | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 9. Dietary patterns (update of 2015 DGAC review) | 2020 | DGAC (USA) (30)               | Dietary patterns                                | Breast cancer, colorectal cancer, lung cancer and prostate cancer          | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 10. Dietary patterns (update of 2015 DGAC review) | 2020 | DGAC (USA) (31)               | Dietary patterns                                | Bone health, for example, risk of hip fracture and bone mineral density    | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 11. Dietary patterns (update of 2015 DGAC review) | 2020 | DGAC (USA) (32)               | Dietary patterns                                | Neurocognitive health, age-related cognitive impairment and dementia       | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 12. Dietary patterns | 2020 | DGAC (USA) (33)               | Dietary patterns                                | Sarcopenia                    | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 13. Dietary patterns | 2020 | DGAC (USA) (34)               | Dietary patterns                                | Mortality                     | Cochrane RoB 2.0/Rob-Nobs*   | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| Topic                                                                 | Year   | Authors/organisation (country) | Exposure(s)                  | Outcome(s)                                                                 | Risk of bias assessment tool | SoE/evidence quality grading                                                                 |
|----------------------------------------------------------------------|--------|-------------------------------|------------------------------|--------------------------------------------------------------------------|-----------------------------|------------------------------------------------------------------------------------------------|
| 14. Dietary patterns during pregnancy                                | 2020   | DGAC (USA) (35)               | Dietary patterns             | Gestational weight gain                                                  | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 15. Dietary patterns during lactation                                | 2020   | DGAC (USA) (36)               | Dietary patterns             | Human milk composition and quantity                                       | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 16. Folic acid from fortified foods and/or supplements during pregnancy and lactation | 2020   | DGAC (USA) (37)               | Folic acid                   | Micronutrient status, gestational diabetes, hypertensive disorders during pregnancy, human milk composition and developmental milestones in child | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 17. Omega-3 fatty acids from supplements consumed before and during pregnancy and lactation | 2020   | DGAC (USA) (38)               | Omega-3 from supplements     | Risk of child food allergies and atopic allergic disease                  | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 18. Maternal diet during pregnancy and lactation                    | 2020   | DGAC (USA) (39)               | Dietary patterns, food allergen (e.g. cow milk, eggs, fish, soybean, wheat, nuts, etc.) | Risk of child food allergies and atopic allergic diseases (e.g. atopic dermatitis, allergic rhinitis and asthma) | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 19. Exclusive human milk and/or infant formula consumption           | 2020   | DGAC (USA) (40)               | Human milk and/or infant formula | Overweight and obesity                                                    | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 20. Exclusive human milk and/or infant formula consumption           | 2020   | DGAC (USA) (41)               | Human milk and/or infant formula | Nutrient status (e.g. iron, zinc, iodine and vitamin B₁₂ status)          | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 21. Iron from supplements consumed during infancy and toddlerhood    | 2020   | DGAC (USA) (42)               | Iron from supplements         | Growth, size and body composition                                         | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
Table 2. (Continued)

| Topic | Year | Authors/organisation (country) | Exposure(s) | Outcome(s) | Risk of bias assessment tool | SoE/evidence quality grading |
|-------|------|--------------------------------|-------------|------------|----------------------------|-----------------------------|
| 22. Vitamin D from supplements consumed during infancy and toddlerhood | 2020 | DGAC (USA) (43) | Vitamin D from supplements/fortified foods | Bone health (e.g. biomarkers, bone mass, rickets and fracture) up to age 18 years | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 23. Beverage consumption | 2020 | DGAC (USA) (44) | Beverages (milk, juice, sugar-sweetened beverages, low and no-calorie beverages vs. water) | Growth, size, body composition and risk of overweight and obesity | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 24. Beverage consumption during pregnancy | 2020 | DGAC (USA) (45) | Beverages (milk, tea, coffee, sugar-sweetened/low- or no-calorie sweetened beverages and water) | Birth weight | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 25. Alcohol consumption | 2020 | DGAC (USA) (46) | Alcoholic beverages (type and drinking pattern) | Mortality | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 26. Added sugars (update of 2015 DGAC review) | 2020 | DGAC (USA) (47) | Added sugars; sugar-sweetened beverages | Cardiovascular disease, CVD mortality and CVD risk factors | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 27. Types of dietary fat | 2020 | DGAC (USA) (48) | Types of fatty acids, individual fatty acids (e.g. ALA, DHA), dietary cholesterol or food sources of types of fat (e.g. olive oil for MUFA, butter for SFA) | Cardiovascular disease outcomes and intermediate outcomes (blood lipids and blood pressure) | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 28. Seafood consumption during pregnancy and lactation | 2020 | DGAC (USA) (49) | Maternal seafood/fish intake (e.g. fish, salmon, tuna, trout, tilapia; shellfish: shrimp, crab and oysters) | Neurocognitive development (e.g. cognitive and language development; behavioural development; attention deficit disorder; autism spectrum disorder) in the child | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 29. Seafood consumption during childhood and adolescence (up to 18 years of age) | 2020 | DGAC (USA) (50) | Seafood (e.g. fish, salmon, tuna, trout and tilapia; shellfish: shrimp, crab and oysters) | Neurocognitive development (e.g. cognition, depression, dementia, psychomotor performance, behaviour disorders, autism spectrum disorder, mental health … academic achievement) | Cochrane RoB 2.0/Rob-Nobs* | Strength of evidence: 'Strong', 'Moderate', 'Limited' or 'Not Assignable'; based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| Topic                                                                 | Year | Authors/organisation (country) | Exposure(s)                                                                 | Outcome(s)                                                                 | Risk of bias assessment tool | SoE/evidence quality grading |
|----------------------------------------------------------------------|------|-------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------|--------------------------------|
| 30. Seafood consumption during childhood and adolescence (up to 18 years of age) | 2020 | DGAC (USA) (51)               | Seafood (e.g. salmon, tuna, trout and tilapia; shellfish: shrimp, crab and oysters) | Cardiovascular disease (and blood lipids or blood pressure)               | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 31. Frequency of eating                                              | 2020 | DGAC (USA) (52)               | Eating frequency                                                           | Overweight and obesity                                                    | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 32. Frequency of eating                                              | 2020 | DGAC (USA) (53)               | Eating frequency                                                           | Cardiovascular disease                                                    | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 33. Frequency of eating                                              | 2020 | DGAC (USA) (54)               | Eating frequency                                                           | Type 2 diabetes                                                           | Cochrane RoB 2.0/Rob-Nobs*  | Strength of evidence: ‘Strong’, ‘Moderate’, ‘Limited’ or ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) directness, 4) precision and 5) generalisability |
| 34. Dietary patterns and long-term food sustainability and related food security | 2015 | DGAC (USA) (55)               | Dietary patterns                                                           | Environmental impact                                                      | NEL Bias assessment tool    | ‘Strong’, ‘Moderate’, ‘Limited’, ‘Expert opinion only’, ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) quantity, 4) impact and 5) generalisability |
| 35. Sodium intake in children                                        | 2015 | DGAC (USA) (55)               | Dietary sodium                                                             | Blood pressure                                                            | NEL Bias assessment tool    | ‘Strong’, ‘Moderate’, ‘Limited’, ‘Expert opinion only’, ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) quantity, 4) impact and 5) generalisability |
| 36. Sodium intake                                                    | 2015 | DGAC (USA) (55)               | Dietary sodium                                                             | Cardiovascular disease                                                    | NEL Bias assessment tool    | ‘Strong’, ‘Moderate’, ‘Limited’, ‘Expert opinion only’, ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) quantity, 4) impact and 5) generalisability |
| 37. Added sugars and sugar-sweetened beverages                       | 2015 | DGAC (USA) (55)               | Added sugars and sugar-sweetened beverages                                 | CVD, CVD mortality, hypertension, blood pressure, cholesterol and triglycerides | NEL Bias assessment tool    | ‘Strong’, ‘Moderate’, ‘Limited’, ‘Expert opinion only’, ‘Not Assignable’, based on 1) risk of bias, 2) consistency, 3) quantity, 4) impact and 5) generalisability |
Table 2. (Continued)

| Topic | Year | Authors/organisation (country) | Exposure(s) | Outcome(s) | Risk of bias assessment tool | SoE/evidence quality grading |
|-------|------|---------------------------------|-------------|------------|-------------------------------|------------------------------|
| 38. Carbohydrates | 2012 | German Nutrition Society (DGE) (Germany) (56) | Total carbohydrates, sugars, sugar-sweetened beverages, dietary fibre, whole-grain and glycaemic index/ load | Obesity, type 2 diabetes, dyslipidaemia, hyperlipidaemia, blood pressure, cardiovascular diseases, metabolic syndrome and cancer | WHO level of evidence (la-lc, lla-llib) based on study design | WHO/WCRF (convincing, probable, possible and insufficient) / (convincing, probable, limited-suggestive, limited - no conclusion) |
| 39. Fatty acids | 2015 | DGE (Germany) (57) | Dietary fats | Adiposity, type 2 diabetes, dyslipidaemia/hyperlipidaemia, blood pressure, cardiovascular diseases, metabolic syndrome and cancer | WHO level of evidence (la-lc, lla-llib) based on study design | WHO/WCRF (convincing, probable, possible and insufficient) / (convincing, probable, limited-suggestive, limited - no conclusion) |
| 40. Dietary reference values for sodium | 2019 | EFSA (58) | Sodium intake, as 24 h sodium excretion (i.e. not self-reported) | Blood pressure, CVD, bone mineral density, osteoporotic fractures and sodium balance | OHAT/NTP risk of bias tool (based on AHRQ, Cochrane, Clarity, etc.): selection, performance, attrition, detection and selective reporting bias | ‘Uncertainty analysis’ based on consistency, precision, internal and external validities, etc. |
| 41. Dietary reference values for copper | 2012 | EFSA, review by ANSES (France) (59) | Copper | Copper status, bioavailability, cardiac arrhythmia, cancer, arthritis, cognitive function, respiratory disease and cardiovascular mortality | EURRECA system (high, moderate, low or unclear), partly based on Cochrane | Consistency, strength and quality of the studies (see Dhonukshe-Rutten et al. 2013 (60) and EFSA, 2010 (principles) (61)) |
| 42. Dietary reference values for riboflavin | 2014 | EFSA, review by Pallas Health Research (Netherlands) (62) | Riboflavin | Riboflavin status, biomarkers, cancer, mortality, bone health, infant health, etc. | EURRECA system (high, moderate, low or unclear), partly based on Cochrane | Consistency, strength and quality of the studies (see Dhonukshe-Rutten et al. 2013 (60) and EFSA, 2010 (principles) (61)) |
| 43. Dietary reference values for phosphorus, sodium and chloride | 2013 | EFSA, review by Pallas Health Research (Netherlands) (63) | Phosphorus, sodium and chloride | Status, adequacy, health outcomes including cancer, CVD, kidney disease, all-cause and CVD mortality | EURRECA system (high, moderate, low or unclear), partly based on Cochrane | Consistency, strength and quality of the studies (see Dhonukshe-Rutten et al. 2013 (60) and EFSA, 2010 (principles) (61)) |
| 44. Dietary reference values for niacin, biotin and vitamin B6 | 2012 | EFSA, review by Pallas Health Research (Netherlands) (64) | Niacin | Niacin/biotin/vitamin B6, status, adequacy, bioavailability, cancer, CVD, cognitive decline, infant health, all-cause mortality, etc. | EURRECA system (high, moderate, low or unclear), partly based on Cochrane | Consistency, strength and quality of the studies (see Dhonukshe-Rutten et al. 2013 (60) and EFSA, 2010 (principles) (61)) |
| 45. Milk and dairy consumption during pregnancy | 2012 | NNR: Brantsæter et al. (65) | Milk and dairy products | Birth weight, foetal growth, large for gestational age and small for gestational age | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 46. Dietary | 2013 | NNR: Dommelof et al. (66) | Iron intake at different life stages | Requirements for adequate growth, development and maintenance of health (anaemia, cognitive/behavioural function, cancer and cardiovascular disease) | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
### Table 2. (Continued)

| Topic | Year | Authors/organisation (country) | Exposure(s) | Outcome(s) | Risk of bias assessment tool | SoE/evidence quality grading |
|-------|------|--------------------------------|-------------|------------|-------------------------------|-----------------------------|
| 47. Dietary macronutrients | 2012 | NNR: Fogelholm et al. (67) | Dietary macronutrient consumption | Primary prevention of long-term weight gain and body fat changes, or changes after weight loss | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 48. Iodine | 2012 | NNR: Gunnarsdotir et al. (68) | Iodine status | Requirements for adequate growth, development and maintenance of health (pregnancy, childhood development, thyroid function and metabolism) | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 49. Protein intake from 0 to 18 years of age | 2013 | NNR: Hörnell et al. (69) | Protein intake in infancy and childhood | Functional/clinical outcomes and risk factors (including serum lipids, glucose and insulin, blood pressure, body weight and bone health) | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 50. Breastfeeding, introduction of other foods and effects on health | 2013 | NNR: Hörnell et al. (70) | Breastfeeding and introduction of other foods | Growth in infancy, overweight and obesity, atopic disease, asthma, allergy, health and disease outcomes, including infectious disease, cognitive and neurological developments, CVD, cancer, diabetes, blood pressure, glucose tolerance and insulin resistance | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 51. Vitamin D | 2013 | NNR: Lamberg-Allardt et al. (71) | Vitamin D | Dietary reference values, vitamin D status, requirements for adequate growth, development and maintenance of health, upper limits, pregnancy outcomes, bone health, cancer, diabetes, obesity, total mortality, CVD and infections | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 52. Protein intake in elderly populations | 2014 | NNR: Pedersen et al. (72) | Protein intake in elderly populations | Dietary requirements (nitrogen balance), muscle mass, bone health, physical training and potential risks | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 53. Protein intake in adults | 2013 | NNR: Pedersen et al. (73) | Protein intake, protein sources | Dietary requirements, markers of functional or clinical outcomes (including serum lipids, glucose and insulin and blood pressure), pregnancy or birth outcomes, CVD, body weight, cancer, diabetes, fractures, renal function, physical training, muscular strength and mortality | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| Topic                                      | Year | Authors/organisation (country) | Exposure(s) | Outcome(s)                                                                 | Risk of bias assessment tool | SoE/evidence quality grading |
|-------------------------------------------|------|--------------------------------|-------------|-----------------------------------------------------------------------------|------------------------------|------------------------------|
| 54. Dietary fat                           | 2014 | NNR: Schwab et al. (74)        | Types of dietary fat          | Body weight, diabetes, CVD, cancer, all-cause mortality and risk factors (including serum lipids, glucose and insulin, blood pressure and inflammation) | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 55. Sugar consumption                     | 2012 | NNR: Sonestedt et al. (75)     | Sugar intake and sugar-sweetened beverages | Type 2 diabetes, CVD, metabolic risk factors (including glucose tolerance, insulin sensitivity, dyslipidaemia, blood pressure, uric acid and inflammation) and all-cause mortality | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 56. Calcium                               | 2013 | NNR: Uusi-Rasi et al. (76)     | Calcium                  | Calcium requirements, upper intake level, adequate growth, development and maintenance of health, bone health, muscle strength, cancer, autoimmune diseases, diabetes, obesity/weight control, all-cause mortality and CVD | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 57. Health effects associated with foods characteristic of the nordic diet | 2013 | NNR: Åkesson et al. (77)       | Potatoes, berries, whole grains, dairy products and red meat/processed meat | CVD incidence and mortality, Type 2 diabetes, inflammatory factors, colorectal, prostate and breast cancers, bone health and iron status | NNR quality assessment tool (rated A, B or C) | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 58. Carbohydrates                         | 2015 | SACN (UK) (78)                 | Total carbohydrates, sugars, sugar-sweetened food/beverages, starch, starchy foods, dietary fibre and glycaemic index/load | Obesity, cardio-metabolic health, energy intake, colorectal health (cancer, IBS, constipation) and oral health | Cochrane RoB and observational studies: no formal grading, but markers of study quality = cohort size, attrition, follow-up time, sampling method and response rate, participant characteristics and dietary intake assessment | ‘Adequate’, ‘moderate’, ‘limited’ (own grading system based on study quality, study size, methodological considerations and specific criteria to upgrade, for example, dose-response relationship) |
| 59. Alcohol                               | 2018 | WCRF (79)                      | Alcoholic drinks (beer, wine, spirits, fermented milk, mead and cider) | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas and skin) | Cochrane RoB/NOS | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
| 60. Body fatness and weight gain          | 2018 | WCRF (80)                      | Body fatness: BMI, waist circumference, WH ratio, adult weight gain | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS | WCRF (convincing, probable, limited – suggestive, limited – no conclusion) |
Table 2. (Continued)

| Topic                      | Year | Authors/organisation (country) | Exposure(s)                                                                 | Outcome(s)                                                                                           | Risk of bias assessment tool | SoE/evidence quality grading |
|----------------------------|------|--------------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-----------------------------|------------------------------|
| 61. Energy balance         | 2018 | WCRF (81)                      | Dietary patterns, foods, macronutrients, energy density, lactation and physical activity | Weight gain, overweight and obesity                                                                  | From NICE (2014) report (low, moderate and high quality) (ref. obesity: identification, assessment and management of overweight and obesity in) | WCRF                         |
| 62. Height and birthweight | 2018 | WCRF (82)                      | Attained height, growth and birthweight                                      | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
| 63. Lactation              | 2018 | WCRF (83)                      | Lactation                                                                   | Cancer (including of breast, ovary, etc.) in the mother who is breastfeeding                         | Cochrane RoB/NOS            | WCRF                         |
| 64. Meat, fish and dairy   | 2018 | WCRF (84)                      | Meat, fish and dairy products; haem iron; diets high in calcium              | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
| 65. Non-alcoholic drinks   | 2018 | WCRF (85)                      | Non-alcoholic drinks: water/arsenic in drinking water, coffee, tea and mate | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
| 66. Other                  | 2018 | WCRF (86)                      | Dietary patterns, macronutrients, micronutrients in foods or supplements, glycaemic load | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
| 67. Physical activity      | 2018 | WCRF (87)                      | Physical activity, types of physical activity and intensity                  | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
| 68. Preservation and processing | 2018 | WCRF (88)                      | Salting, curing, fermentation, smoking; processed meat and fish              | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS            | WCRF                         |
Table 2. (Continued)

| Topic | Year | Authors/organisation (country) | Exposure(s) | Outcome(s) | Risk of bias assessment tool | SoE/evidence quality grading |
|-------|------|--------------------------------|-------------|------------|------------------------------|----------------------------|
| 69. Wholegrains, fruit and vegetables | 2018 | WCRF (89) | Wholegrains, pulses (legumes), vegetables, fruits, dietary fibre, aflatoxins, beta-carotene, carotenoids, vitamin C and isoflavones | Cancer (including of mouth, pharynx and larynx, oesophagus, liver, colorectal, breast, kidney, stomach, lung, pancreas, gallbladder, ovary, prostate, etc.) | Cochrane RoB/NOS | WCRF |
| 70. Sugars | 2015 | WHO (90) | Total, added or free sugars, sugar-sweetened beverages, fruit juice | Body weight, body fatness and dental caries | Cochrane RoB/cohorts studies: own | GRADE |
| 71. Sodium | 2012 | WHO (91) | Sodium intake/ reduced sodium intake and sodium excretion | Cardiovascular diseases, all-cause mortality, blood pressure, renal function, blood lipids and potential adverse effects | Cochrane RoB | GRADE |
| 72. Potassium | 2012 | WHO (Aburto et al. 2013) (92) | Potassium intake, 24 h urinary potassium excretion | Blood pressure, cardiovascular diseases, all-cause mortality, cholesterol, nor-adrenaline, creatinine and side effects | Cochrane RoB | GRADE |
| 73. Trans-fats | 2016 | WHO (de Souza et al. 2015 (93); Brouwer et al. 2016) (94) | Trans fatty acids | All-cause mortality, cardiovascular disease, type 2 diabetes and blood lipids | Cochrane RoB (for TFA and blood lipids)/NOS | GRADE |
| 74. Saturated fats | 2016 | WHO (Hooper, 2015; Mensink, 2016; Te Morenga 2017) (95–97) | Saturated fat reduction | Cardiovascular disease, mortality, blood lipids, other risk factors and growth (children) | Cochrane RoB, other potential sources of bias, for example, compliance | GRADE |
| 75. Carbohydrate quality | 2019 | WHO (Reynolds et al., Lancet) (98) | Markers of carbohydrate quality, that is, dietary fibre, glycaemic index/load and whole grains | All-cause mortality, coronary heart disease, stroke, type 2 diabetes, colorectal cancer, adiposity-related cancers, adiposity, fasting glucose/insulin/insulin sensitivity/HbA1c, blood lipids and blood pressure | Cochrane RoB/NOS/ROBIS | GRADE |
| 76. Omega-3, omega-6 and polyunsaturated fat | 2020 | Brainard et al. (99) | Higher versus lower omega-3, omega-6 or polyunsaturated fats | New neurocognitive illness, newly impaired cognition and/or continuous measures of cognition | Cochrane RoB | GRADE |

and the main arguments for ranking, is presented in Table 4. The formulation of the PI/ECOTSS was adjusted during the prioritisation process; thus, the formulation of the PI/ECOTSS in Table 4 is more specific compared with Table 3.

The first five top prioritised topics, as well as all relevant background documentation, was submitted to the NNR SR Centre for their comments. In a dialog between the NNR SR Centre and the NNR2022 Committee, the final PI/ECOTSS statements for the five prioritised topics were formulated and agreed on by January 13, 2021 (Table 4). The four remaining PI/ECOTSS statements was agreed on in June 2021. Results from step 1 to 6 in the procedure are summarised in Fig. 2.
Table 3. Shortlisted topics for systematic reviews

| Population          | Intervention or exposure | Comparators                                      | Outcomes                                               | Timing                                      | Setting                                  | Study design                                      | Ranking | Argument for ranking |
|---------------------|---------------------------|--------------------------------------------------|-------------------------------------------------------|--------------------------------------------|------------------------------------------|--------------------------------------------------|---------|-----------------------|
| Adults +40 years    | Iron intake and status    | Several biomarkers of status available for example serum ferritin | Low versus high intake                                | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies | Low     | Public health concern. New evidence unlikely to influence DRV |
| Pregnant women      | Iron intake and status    | Several biomarkers of status available for example serum ferritin | Low versus high intake                                | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Cohort studies | Low     | New evidence unlikely to influence DRV |
| Children First years of life | Iron intake and status    | Several biomarkers of status available for example serum ferritin | Low versus high intake                                | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Cohort studies | Low     | New evidence unlikely to influence DRV |

Magnesium

| Population          | Intervention or exposure | Comparators                                      | Outcomes                                               | Timing                                      | Setting                                  | Study design                                      | Ranking | Argument for ranking |
|---------------------|---------------------------|--------------------------------------------------|-------------------------------------------------------|--------------------------------------------|------------------------------------------|--------------------------------------------------|---------|-----------------------|
| Adults              | Mg intake/ status         | Low versus high dose response to find protective level | Risk of type 2 diabetes and markers of glucose metabolism | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies | Low     | The topic has new, relevant data in an area of substantial public health concern, but no good biomarkers of status. New evidence unlikely to influence DRV |
| Adults              | Mg intake/ status         | Low versus high dose response to find protective level | Risk of CVD and indicators of CVD                    | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies | Low     | The topic has new, relevant data in an area of substantial public health concern, but no good biomarkers of status. New evidence unlikely to influence DRV |
### Table 3. (Continued)

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| Adults     | Plant protein intake     | Animal protein intake | CVD and diabetes in prospective studies. CVD qualified surrogate endpoints and diabetes/insulin resistance/sensitivity in RCTs | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries | RCT and prospective cohorts | High | The topic has new, relevant data in an area of substantial public health concern |
| Adults     | Plant protein intake     | Animal protein intake, different sources | Bone health (to be defined) | Five years for prospective studies and 1 month for RCTs | Relevant for the general population in the Nordic and Baltic countries | RCT and prospective cohorts | Low | The effect of type of protein was not considered a major driver of this public health issue |
| Older adults | Protein intake          | Other macronutrients | Body composition and muscle strength | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs and prospective cohorts | Medium | Total protein intake relevant issue for this age group, sources of protein, much less data. New guidelines, for example, ESPEN, suggest little new data to set recommendations |
| Children   | 1. Total protein intake  | Highest versus lowest protein intakes as defined by, for example, quartiles or risk difference per gram protein from one source relative to other sources | Anthropometry (length in cm and SDS, weight in kg and %), risk of overweight or obesity | Minimum 6 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies (depending on the age of the child) | Relevant for Nordic setting (excludes, for example, populations with high prevalence of childhood malnutrition) | RCT and prospective cohorts | High | The topic has new, relevant data in an area of substantial public health concern |
| Adults     | Protein isolates (dependent on a new search to confirm) | Wholefoods protein | Plasma concentrations of amino acids, lipids, glucose and insulin | Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCT | High | The topic has new, relevant data in an area of substantial public health concern |
### Table 3. (Continued)

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|----------------------|
| Adults +40 years | Zinc intake and status | Low versus high dietary intake of zinc If available, status may be measured as plasma zinc concentration | Type 2 diabetes and markers of diabetes | Minimum 12 months follow-up in cohort studies Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and intervention studies | Medium | Despite public health importance of T2D, the limited evidence available suggests no association between zinc status and T2DM risk Supplemental zinc for the prevention of diabetes has been reviewed in a Cochrane SR |
| Adults +40 years | Zinc intake and status | Low versus high dietary intake of zinc If available, status may be measured as plasma zinc concentration | Cardiovascular disease | Minimum 12 months follow-up in cohort studies Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and intervention studies | Medium | Public health importance of CVD. Zinc has anti-oxidative stress and anti-inflammatory functions. Evidence of association |
| Adults +40 years | Zinc intake and status | Low versus high dietary intake of zinc If available, status may be measured as plasma zinc concentration | Digestive tract cancer | Minimum 12 months follow-up in cohort studies Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and intervention studies | Low | Zinc is not one of the exposures mentioned in the WCRF 3rd expert report as a risk factor for cancer. New evidence unlikely to influence DRV |
| Children first years of life | Zinc intake and status | Low versus high dietary intake of zinc If available, status may be measured as plasma zinc concentration | Growth and cognition | Minimum 12 months follow-up in cohort studies Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Cohort studies | Low | WHO is planning an SRs on zinc for children aged 0–36 months |
## Table 3. (Continued)

| Topic | Dietary fibre |
|-------|---------------|
| **Population** | **Intervention or exposure** | **Comparators** | **Outcomes** | **Timing** | **Setting** | **Study design** | **Ranking** | **Argument for ranking** |
| Children | DF and sub-groups, for example, soluble and in-soluble. Or subgroups related to the fractions in chemical analyses. Or depending on origin gain, pulses and vegetables fruits. | High-low Dose-response | Bowel function* Energy availability Nutrient availability All including risks of high intake. *Specific outcomes have to be identified. | Short time/ few days of follow-up, depending on study design and outcome. | Relevant for the general population in the Nordic and Baltic countries. | Prospective cohort studies, interventions and RCTs. | High | Dietary fibre intake will increase with adherence to a more plant based and environmentally sustainable diet. The effect on children must be considered. |

**Vegetables, fruits and berries**

| Topic | Dietary fibre |
|-------|---------------|
| **Population** | **Intervention or exposure** | **Comparators** | **Outcomes** | **Timing** | **Setting** | **Study design** | **Ranking** | **Argument for ranking** |
| Adults | F&V | No/low consumption and dose-response | T2D and CVD | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries. | Prospective cohort studies and interventions | High | More data since 2012 with potential to influence the quantitative recommendation. |
| Adults | Sub-groups of veggies: dark green leafy and berries | No/low consumption and dose-response | T2D, CVD and bone health | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries. | Prospective cohort studies and interventions | High | Intake will increase with adherence to a more plan-based and environmentally sustainable diet. Health effects must be considered. |
| Adults | F&V | No/low consumption of | Wheezing and asthma | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries. | Prospective cohort studies and interventions | Low | New evidence unlikely to influence DRV. |
| Adults | Potatoes | No/low consumption and dose-response | All-cause mortality, CVD, CHD, stroke, T2D, obesity and hypertension | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | General population | Prospective cohort studies and interventions | Low | Due to limited data. New evidence unlikely to influence DRV. |
| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|--------------|----------|--------|---------|-------------|---------|----------------------|
| Adults (≥ 18 years) | Pulses/legumes (subgroups if possible), exclude peanuts | No/low versus high consumption | Dose-response | CVD and type 2 diabetes in prospective studies. CVD qualified surrogate endpoints and diabetes/insulin resistance/sensitivity in RCTs | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries | High | High priority due to focus on sustainability of diets and not covered by NNR2012 Increasing consumption, greater variety and new studies Important to appraise this association since these foods are important as substitutes for meat |
| Adults | Pulses/legumes | No/low consumption of pulses and sub-groups | Dose-response | Overweight | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries | Low | New evidence unlikely to influence DRV. More studies may be needed |
| Adults | Soy/fermented soy products | No/low consumption soy/fermented soy products | | Alzheimer’s disease/dementia/reproductive health/osteoporosis | Minimum 12 months for prospective studies and 1 month for RCTs, depending on outcome | Relevant for the general population in the Nordic and Baltic countries | Low | New evidence unlikely to influence DRV. More studies may be needed |

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|--------------|----------|--------|---------|-------------|---------|----------------------|
| Elderly 70+ years | Vitamin D | Placebo | Mortality | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case–control studies | Low | New SRs are published, and mortality was included in NNR2012. New evidence unlikely to influence DRV |
| Adults 18–50 years | Vitamin D | Placebo | Cognition | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case–control studies | Low | New SRs are published, but intervention studies are missing. The DO-HEALTH study, however, has included cognition as an outcome. New evidence unlikely to influence DRV |
### Table 3. (Continued)

| Population | Vitamin D | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|-----------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| Elderly, adults, 50+ years | Vitamin D | Placebo | Musculo-skeletal health | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case-control studies | Low | New SRs are published, but bone health/falls/muscle strength and included in NNR2012 |
| Children, adults, 2–18 years | Vitamin D | Placebo | Respiratory infections | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case-control studies | High | New SRs are published, and respiratory infections were not included in NNR2012 |
| Women, 18–45 years | Vitamin D | Placebo | Pregnancy outcomes | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Pregnant and lactating women | RCTs, cohort studies and case-control studies | Low | New SRs are published, and pregnancy outcomes were included in NNR2012 |
| Adults, 18–70+ | Vitamin D | Placebo | Diabetes/metabolic syndrome | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case-control studies | Low | New SRs are published, and diabetes was included in NNR2012 |
| Children, adults and elderly, 2–70+ | Vitamin D | Different doses | Dose-response relations | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case-control studies | High | New SRs are published, and the dose-response relation is fundamental for all outcomes |
| Adults, 18–70+ | Vitamin D | Polymorphism | Vitamin D status | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | | High | New SR is published, and genotypes were not included in NNR2012 |
### Table 3. (Continued)

**Vitamin D**

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| Adults, 18–70+ | Vitamin D | Placebo | Hypertension/blood pressure | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case–control studies | Low | New SR are published, but hypertension/blood pressure was included in NNR2012 |
| Adults | Plasma 25(OH), vitamin D | Dose-response | Vitamin D sufficiency (total mortality and bone health) | Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Interventions and mendelian randomisation studies | High | Appropriate cut-off values for sufficiency essential for setting DRVs. Several new large cohort and clinical studies, including Mendelian randomisation |

**Fat and fatty acids**

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| Adult population | Omega-3 fatty acids | Low versus high | Type 2 diabetes | Minimum of 2 years | Nordic, high-income countries | Controlled trials and cohort studies | High | Important public health issue. New data have emerged |
| Adults and elderly population | Quality of fat | Low versus high | Mental/brain health/cognition | Minimum of 2 years | Nordic, high-income countries | Cohort studies | High | Important public health issue. New data have emerged |

**Sodium**

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| Adults | Sodium intake | Low versus high, dose response to find protective level | Risk of CVD and indicators of CVD | Minimum 4-week intervention in intervention studies, Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and intervention | Low | The topic has been addressed by qSR |

**Ultra-processed foods**

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| All groups: pregnant, children, adolescents and adults | Degree of ultra-processed foods in the diet | No/low intake versus high intake of ultra-processed foods (UPFs) | Noncommunicable diseases (NCDs) Mortality | Minimum 12 months follow-up in cohort studies | Relevant for the general population in the Nordic and Baltic countries | Prospective studies | High | High public interest and media attention |
### Table 3. (Continued)

| Topic | Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|-------|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|----------------------|
| **Meat** | Adult participants in the various cohorts included in the SRs | Meat (processed or unprocessed red meat) White meat | No or low consumption versus high consumption | All-cause mortality CVD and diabetes | Minimum 12 months follow-up in for prospective studies and 1 month for RCTs | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies | High | High public interest and media attention, especially connected to sustainability issues |
| **Fats and oils** | Adults, 18–70+ years | Vegetable oils (olive, sunflower and rapeseeds), and palm and coconut oils | Different consumption levels | Mortality, CVD, T2D and cancer | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs and cohort studies | Medium | Establishing possible benefits of rapeseed oil would be important in the Nordic food environment. However, focusing on fatty acid level might be of greater importance |
| | Children and adults, 1–70+ years | Vegetable oils (olive, sunflower and rapeseeds), and palm and coconut oils | Different consumption levels | Blood lipids | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies, c-c studies and cross-sectional studies | Medium | |
| | Children and adults, 1–70+ years | Vegetable oils (olive, sunflower and rapeseeds), and palm and coconut oils | Different consumption levels | Overweight and obesity | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies, c-c studies and cross-sectional studies | Medium | |
| **Calcium** | Healthy pregnant women and their offspring | Ca exposure: supplement + diet | Different levels of exposures Confounders: supplemental exposure of other nutrients and energy intake | Mother: hypertensive disorders, pre-eclampsia and preterm birth Offspring: birth weight and BP level | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Primary health care | RCTs, cohort studies and c-c studies | High | Common outcome in Nordic countries. Ongoing shift to more plant-based diets might add to the need for supplementation |
| | Adult population/men, 50 years + older | Ca exposure: supplement + diet | Different levels of exposures | Colorectal cancer and prostate cancer | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and c-c studies | Low | The topic is currently addressed through other qSRs |
| Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|--------------------------|-------------|----------|--------|---------|--------------|---------|---------------------|
| Adult population, 50 years + older | Ca exposure: supplement + diet | Different levels of exposures | Injurious falls and fractures | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Low | The topic is currently addressed through other qSRs |
| Healthy pregnant women | B12 exposure: supplement and diet | Different level of exposures | Preterm birth | Primary health care | RCTs, cohort studies and c-c studies | High | B12 insufficiency during pregnancy is common even in non-vegetarian population |
| Elderly, 60 years and older | B12 exposure: supplement and diet | Different level of exposures | Neurological functions: cognitive decline and dementia | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Medium | Findings somewhat conflicting and partly shown only with newer biomarkers |
| Whole population, lifespan approach and all age groups | B12 exposure: supplement and dietary intakes in different diets: vegetarian, vegan and omnivore | Different level of exposures | B12 status in different age groups | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | High | New relevant data available (from RCTs in Nordic countries as well) |
| Children following vegan diet (public call) | B12 exposure: supplement and fortified foods | Different level of exposures | B12 requirement to defend deficiency and to maintain normal function | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | Medium | Important topic. However, the SR may lack well conducted studies to be based on |

| Population | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
|------------|--------------------------|-------------|----------|--------|---------|--------------|---------|---------------------|
| Healthy and pregnant women | Biotin: intake, status propionyl-CoA carboxylase (PCC), pyruvate carboxylase (PC), acetyl-CoA carboxylase (ACC) and deficiency (3HIA and 3 HIA-carnitine) | Different levels of exposures | Clinical abnormalities in offspring: growth, retardation, congenital malformation, neurological disorders, dermatological abnormalities; genome stability (genomic damage in lymphocytes) | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Primary health care | Prospective birth cohorts, RCTs and cross-sectional studies | Low | We need more data in order to do a SR. Not enough literature. New evidence unlikely to influence DRV |

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(page number not for citation purpose)
## Table 3. (Continued)

| Topic                                      | Population                                                                 | Intervention or exposure | Comparators                                                                 | Outcomes                                         | Timing                                                                 | Setting                                                                 | Study design                                                                 | Ranking | Argument for ranking |
|--------------------------------------------|----------------------------------------------------------------------------|--------------------------|-----------------------------------------------------------------------------|-------------------------------------------------|----------------------------------------------------------------------|----------------------------------------------------------------------|--------------------------------------------------------------------------------|---------|----------------------|
| **Fish, fish products and seafood**       | Women and their offspring                                                 | n-3 LPUFAs from fish or supplementation | Supplementation versus placebo (in RCTs) OR above versus below NNR2012 recommendations | Asthma and allergies in the offspring           | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs and observational studies                                                                                           | High    | New relevant data available |
| | Adults, 18–75 years                        | Nuts intake higher than current, for example, 30 g/day                    | High versus low intake   | CVD (or other heart outcome?)                                               | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case–control studies                                                                                           | High    | Very little info on nuts in NNR2012. New relevant data available |
| **Milk and dairy**                         | The general population, adults 18–80 years                                | Full fat dairy           | Low fat dairy                                                               | CVD and blood lipids                           | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | Nordic, other EU or US population                                                                                     | Intervention studies and observational studies                                      | Medium  | Findings published since 2012 provide no consistent evidence that could challenge those previous conclusions on DRVs or FBGDs from NNR 2012 |
| **Micronutrients**                         | Adults                                                                     | Micronutrient status (or intake) | Deficiency, sufficiency and excess                                          | COVID-19 infection and severity                | Minimum 12 months follow-up in cohort studies. Minimum 4-week intervention in intervention studies | General population relevant for Nordic and Baltic countries                                                                 | Prospective cohort studies and interventions                                      | High    | Many nutrients have powerful immunomodulatory actions with the potential to alter susceptibility to COVID-19 infection, progression to symptoms, likelihood of severe disease and survival |

*ROB-Nobs, Risk of bias for nutrition observational studies tool: ’low’, ‘moderate’, ‘serious’, ‘critical’ or ‘no information’.

The table contains all shortlisted topics from the 51 ScRs.
A protocol (17–21) will be developed for all de novo SRs by the SR Centre and published in PROSPERO (https://www.crd.york.ac.uk/prospero). The NNR2022 Committee and the topic experts (i.e. the scientists recruited to author the respective nutrient or food group chapters in NNR2022) will be consulted when finalising the protocols.

Discussion

Given the extent of scientific publications in the field of nutrition and health, and the limited resources available to summarise present research status rigorously and transparently, we have developed a procedure for prioritisation of topics that may be selected for SRs. The selection of topics for de novo SRs is central in the NNR2022 project, as the results of these SRs may cause adjustment of existing DRVs and FBDGs. That is why we have developed this extensive process for prioritisation of SR topics. The current paper describes the results of this procedure used to prioritise topics for de novo SRs in the NNR2022 project. The nine prioritised PI/ECOTSS statements include the following exposure-outcome pairs: 1) plant protein intake in children and growth, 2) pulses/legumes, and cardiovascular disease and type 2 diabetes, 3) plant proteins, and atherosclerotic/cardiovascular disease and type 2 diabetes, 4) fat quality and mental health and 5) vitamin B₁₂ and vitamin B₁₂ status, 6) intake of white meat (no consumption vs. high consumption and white meat replaced with red meat), and all-cause mortality, type 2 diabetes and risk factors, 7) intake of n-3 LPUFAs from supplements during pregnancy and asthma and allergies in the offspring, 8) nuts intake, and CVD and type 2 diabetes in adults, 9) dietary fibre intake (high vs. low) in children and bowel function (Table 4). Small adjustments of the PI/ECOTSS may occur during the development of the protocols. The final wording will be available in the published protocols.

The nine top SR topics are given high priority since significant new evidence within these topics might change the current recommendations. Additionally, increased adherence and more focus on plant-based diets and an environmentally sustainable diet were also important arguments for several of the SR priorities. Health effects of such changes must be considered and evaluated before potentially adjusting DRVs and FBDGs. The topic on vitamin B₁₂ status is also partly due to the aging population and related health consequences. The rational for the prioritisation is given in Table 4.

A delicate balance must be considered when PI/ECOTSS statements are formulated. They may be too narrow to be generalisable. Additionally, it is always tempting to broaden the scope, for example, the exposure, the population or the outcome, but this may massively influence the resources needed for performing the SR. Too broad PI/ECOTSS statements may also be more imprecise and mask specific questions. In this process, we have tried, openly and explicitly, to identify the most relevant PI/ECOTSS for adjusting DRVs and FBDGs in the Nordic and Baltic countries, but, at the same time, use the limited resources available in the most cost-effective manner.

Traditionally, the working group responsible for developing national DRVs and FBDGs select SR topics based on their own scientific knowledge and after consultation with appointed scientists in the field of interest. In the NNR2022 project, we have involved numerous scientists, health professionals, national food and health authorities, food manufacturers, other stakeholders and the general population to generate a large and representative pool of potential SR topics. This pool of topics was valuable when the NNR2022 Committee performed the prioritisation process in the modified Delphi process. Selection of SR topics can never be a fully objective exercise. Some stakeholders may be more proactive than others. The NNR2022 Committee tried to use all available information, independent of subjective engagement by stakeholders. In the end, selection of SR topics was the decision of the NNR2022 Committee.

Although consensus was reached in the NNR2022 Committee, it does not necessarily mean that we have concluded with the ‘correct’ selection. Several other topics might have been considered and prioritised. The question about what is most important in nutritional sciences is large and open. In the present project, we have, however, focused on topics with substantial recent data and public health concern, which is most relevant for setting DRVs and FBDGs in the Nordic and Baltic countries.

A limitation of our study is the literature search (Supplementary Table 2) used to develop the 51 ScRs. We decided initially to limit the search to reviews published in 2011 and later with the filter ‘Humans’. If the search resulted in ≥500 items, we limited the search to papers with the nutrients or food groups in the title. If still ≥500 items, we included the additional requirements: ‘Diet’ OR ‘Dietary’ OR ‘FOOD’ OR ‘Nutrition’ OR ‘Nutritional’. If still ≥500 items, we limited the search to only include ‘Systematic reviews’. The reason why we initially selected to search for reviews published after 2010 is that it is likely that a topic with significant new and relevant data would have been discussed in a review paper published after the search date in the previous edition of NNR. In this type of strategy, we omit all original publications. However, DRVs or FBDGs are seldom, or never, revised based on one or a few original publications. In the present literature search process to identify SR topics, only original study results found important enough to be cited and discussed in review papers are candidate for SR topics.

Additionally, if a large number of reviews were identified for a single nutrient or food group (i.e. ≥500 papers), we added sequentially additional relevant limitations,
### Table 4. Prioritised topics for systematic reviews.

| Topic | Protein |
|-------|---------|
| **Population** | Children (4 months to 5 years) | Adults (≥18 years) |
| **Intervention or exposure** | Total protein intake | Pulses/legumes (subgroups if possible), exclude peanuts |
| **Comparators** | Highest versus lowest protein intakes as defined by, for example, quartiles or risk difference per gram protein from one source relative to other sources. | No/low versus high consumption, Dose-response |
| **Outcomes** | Growth/anthropometric outcomes: weight (kg or z-scores/standard deviation scores (SDS)), length (cm or z-scores/SDS) and BMI (absolute measures or z-scores). Risk of overweight/obesity. Body composition (indices, e.g. fat free mass (FFM), fat mass (FM)). | Athero-sclerotic cardiovascular disease mortality and morbidity (total and subgroups) and type-2 diabetes in prospective studies CVD qualified surrogate endpoints and diabetes/insulin resistance/sensitivity in interventions |
| **Timing** | Minimum 6 months follow-up in cohort studies. Minimum 4 weeks intervention in intervention studies (depending on the age of the child) | Minimum 12 months for prospective studies, 1 month for RCTs, depending on outcome |
| **Setting** | Relevant for Nordic setting (excludes, for example, populations with high prevalence of childhood malnutrition) | Relevant for the general population in the Nordic and Baltic countries |
| **Study design** | Randomised and non-randomised controlled intervention studies. Prospective cohort studies, nested case-control and case-cohort studies | Prospective cohort studies and interventions |
| **Ranking** | 1 | 2 |
| **Argument for ranking** | Several high-quality studies published since NNR2012. Evidence may be stronger than concluded in NNR2012. The reasons why existing SRs produce different results should be explored. More thorough assessment can be made. Many SRs did not include animal versus plant protein | High priority due to focus on sustainability of diets and not covered by NNR2012. Increasing consumption, greater variety and several recent high-quality studies. Important to appraise this association since these foods are important as substitutes for meat. Overview of health effects of different kinds of pulses would be valuable for setting FBDGs |
### Table 4. (Continued)

| Topic | Protein |
| --- | --- |
| **Population** | **Intervention or exposure** | **Comparators** | **Outcomes** | **Timing** | **Setting** | **Study design** | **Ranking** | **Argument for ranking** |
| Adults | Plant protein intake | Animal protein intake | Atherosclerotic, cardiovascular disease, mortality and morbidity (total and subgroups) and type-2 diabetes in prospective studies. CVD qualified surrogate endpoints and diabetes/insulin resistance/sensitivity in RCTs | Minimum 12 months follow-up in cohort studies. Minimum 4 weeks intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCT and prospective cohorts | 3 | Relevant for our encouragement to eat more plant based Important to summarise the new evidence for replacing animal-based protein with plant-based protein in relation to most common chronic diseases in Nordic countries. New RCTs available also from Nordic countries. Relevant for recommendation on protein and on FBDGs. New literature is available. Increasing consumption in Nordic countries. |

| Vitamin B<sub>12</sub> |  |
| --- | --- |
| **Population** | **Intervention or exposure** | **Comparators** | **Outcomes** | **Timing** | **Setting** | **Study design** | **Ranking** | **Argument for ranking** |
| Susceptible groups, that is: 1) children (0–18 years), 2) young adults (18–35 years), 3) pregnant and 4) lactating women, 5) older adults (≥65 years) and 6) vegetarians including vegans | B<sub>12</sub> exposure: supplemental and dietary intake | Different level of exposures | B<sub>12</sub> status: * s/p- B12, *s/p- HOB-LO-TC, *s/p-MMA, *s/p-tHcy, *Combined indicators, *Breastmilk B<sub>12</sub>, (relevant in infants) | Minimum 12 months follow-up in cohort studies. Minimum 4 weeks intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies, case–control studies, cross-sectional studies (the last one relevant for limited periods as pregnancy and lactation) | 4 | High priority due to focus on sustainability of diets and might affect DRVs. In the context of a more plant-based diet, it is important to know how B12 status is impacted in the most vulnerable groups. This SR would identify data that facilitates setting DRVs for vulnerable groups |
### Table 4. (Continued)

| Topic | Fat and fatty acids |
|-------|---------------------|
| **Population** | Quality of fat (e.g. E% from different subtypes, such as saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA) not total amount) | Minimum 5 years follow-up in cohort studies. Minimum 12 months intervention in intervention studies. The duration of follow-up depends on age at inclusion. |
| **Intervention** or exposure | Other level of intake and substitution models | Relevant for the general population in the Nordic and Baltic countries |
| **Comparators** | Outcome: Specific dementias: Alzheimer’s disease (ICD8 290.10 and ICD10 F00 and G30), vascular dementia (ICD10 F01) and unspecified dementia (ICD8 290.18 and ICD10). All-cause dementia. For intervention studies: mild cognitive impairment (G31) and cognitive decline | Prospective cohort studies and intervention studies |
| **Outcomes** | **Timing** | **Setting** | **Study design** | **Ranking** | **Argument for ranking** |
| **Adults (≥50 years)** | Meat and meat products | Prospective cohort studies and RCTs | 6 | High priority due to focus on environmental sustainability and more focus on a plant-based diet. High relevance in the Nordic and Baltic countries. Important to determine the effects of white meat consumption |
| **Meat and meat products** | Adults | White meat | No or low consumption versus high consumption, white meat replaced other red meat | All-cause mortality, CVD and type 2 diabetes and risk factors for the diseases in RCTs | Minimum 12 months follow-up for prospective studies and 1 month for RCTs | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and intervention studies | 5 | High priority due to new evidence on outcome. With ageing population and increasing prevalence of cognitive disorders this is important, health issues and relationship unclear. Increasing elderly population justifies at least one topic on this group |
| **Fish and fish products** | Women and their offspring | n-3 LPUFAs from supplements | Supplementation versus placebo (in RCTs) | Asthma and allergies in the offspring | Minimum 4 weeks intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs | 7 | High priority due to the prevalence of asthma and allergies. Important to document the effect due to in context of recommendations of a more plant-based diet |
Table 4. (Continued)

| Topic | Nuts |
|-------|------|
| **Population** | Intervention or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
| Adults | Nuts intake higher than current, for example, 30 g/day | High versus low intake | CVD and T2D in observational studies AND intermediate endpoints for CVD in RCTs | Minimum 12 months follow-up in cohort studies. Minimum 4 weeks intervention in intervention studies | Relevant for the general population in the Nordic and Baltic countries | RCTs, cohort studies and case-control studies | 8 | High priority due to focus on environmental sustainability and shift towards a more plant-based diet. Evidence needed to establish FBDGs |

| Dietary fibre |
| Population or exposure | Comparators | Outcomes | Timing | Setting | Study design | Ranking | Argument for ranking |
| Children | Dietary fibre and its subgroupings, for example, soluble and in-soluble. Or subgroups related to the fractions in chemical analysis. Or depending on origin (grain, pulses, vegetables and fruits) | High and low dose-response | Bowel function | Relevant for the general population in the Nordic and Baltic countries | Prospective cohort studies and RCTs | 9 | High priority due to relevance for the Nordic and Baltic populations |

simply to reduce the burden of the authors of the 51 ScRs. In total, 13,992 reviews were identified and scrutinised by the ScR authors. Although we do not believe that other topics would have been prioritised with an even more comprehensive search strategy, we cannot rule out the possibility that some important topics have been missed.

It is important to note that the present literature search was only used to select topics for *de novo* SRs. In each of the 51 nutrient and food group chapters that will be part of the final NNR2022 report, a separate literature search will be performed and described.

The organisation, the principles and the methodologies developed in the NNR2022 project build on processes similar to other national authorities or international health organisations. The procedure described in this paper, together with the three previous principle and methodology papers from the NNR2022 project (2–4), may serve as a framework that other national health authorities or organisations can adapt when developing national DRVs and FBDGs. No or few single nations have these qualifications alone. Thus, international collaboration and global harmonisation of methodological approaches are highly needed. The NNR2022 project, which is a collaboration between the food and health authorities in Denmark, Estonia, Finland, Iceland, Latvia, Lithuania, Norway and Sweden, represents such an international effort for harmonisation and sharing of resources and competence.

**Summary and conclusions**

SRs are the preferred method to summarise the causal relationship between nutrient or food group exposure and a health outcome. They are the main fundament for developing DRVs and FBDGs. In this paper, we describe the results of an open, transparent six-step procedure to identify and prioritise topics most appropriate for *de novo* SRs in the NNR2022 project. The nine prioritised PI/ECOTSS include the following exposure–outcome pairs: 1) plant protein intake in children and body growth, 2) pulses/legumes intake, and cardiovascular disease and type 2 diabetes, 3) plant protein intake in adults, and atherosclerotic/cardiovascular disease and type 2 diabetes, 4) fat
quality and mental health, 5) vitamin B<sub>12</sub> and vitamin B<sub>12</sub> status, 6) intake of white meat (no consumption vs. high consumption and white meat replaced with red meat), and all-cause mortality, type 2 diabetes and risk factors, 7) intake of n-3 LPUFAs from supplements during pregnancy and asthma and allergies in the offspring, 8) nuts intake, and CVD and type 2 diabetes in adults, 9) dietary fibre intake (high vs. low) in children and bowel function.

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