

USDA U.S. DEPARTMENT OF AGRICULTURE

DRI-Protein Evidence Scans: Process, Results, and Report

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at the USDA Center for Nutrition Policy and Promotion




Declarations

- None



Agenda

- Define NESR evidence scans
- Overview of protein protocols
- Examples of scan findings
- Report components



NESR is a team of scientists within the USDA Food and Nutrition Service at the Center for Nutrition Policy and Promotion



Systematic Reviews
Rapid Reviews
Evidence Scans

Dietary Guidelines for Americans, Thrifty Food Plan, and other nutrition policy and program efforts

Health and well-being of Americans

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NESR Evidence Scans



Evidence scan

An exploratory evidence description project in which systematic methods are used to search for and describe the volume and characteristics of evidence available on a nutrition question or topic of public health importance. Evidence scans can be either stand-alone projects or the beginning steps of conducting a rapid or systematic review.

Evidence Scan Methodology	
1. Protocol development*	
2. Literature search and screening	
3. Minimal data extraction (No results)	
4. Summarize the volume/characteristics of the evidence, depending on the purpose of the scan (no synthesizing of results or findings)	
5. Develop a report that describes the methods, findings, and considerations	

*Evidence Scan Protocols	
Question development	(NESR + DRI Steering Committee)
Purpose/rationale	(NESR + DRI Steering Committee)
Analytic framework (PICO)	(NESR + DRI Steering Committee, Protein Experts)
Inclusion/exclusion criteria	(NESR + DRI Steering Committee)
Literature search strategy	(NESR)
Methods for screening, minimal data extraction; end-product format	(NESR)



Purpose and rationale for conducting an evidence scan

- Inform protocol development
- Determine if there is enough evidence to conduct a systematic review and/or update an existing review
- Identify questions for subject matter experts
- Estimate resource requirements for future systematic reviews

- Does not answer the research question
- Does not involve risk of bias assessment, synthesis, or grading the strength of the evidence



NESR team works with subject matter experts to develop the evidence scan protocol

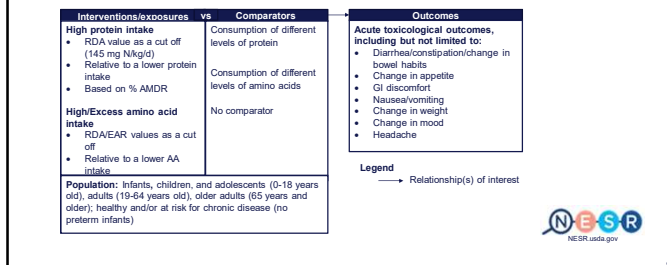
Topic	What is the topic of interest to be addressed in the scan, or closely related series of scans?
Purpose and rationale	What is the purpose of or rationale for the evidence scan? How will the DRI steering committee use the scan to inform future systematic reviews? What DRI value is the scan intended to support development and/or update of?
Question(s)	Draft the questions that the evidence scan(s) will address
Intervention/Exposure and Comparator, and Populations	What is the protein-related intervention or exposure of interest? And what is it being compared to? What sources are being considered (supplements, food-based)?
Population for IVE/C	What populations are of interest for the intervention/exposure in evidence scan? Generally healthy individuals across the entire lifespan, including during pregnancy and lactation? Are there different considerations for different populations (human milk composition, infant formulas, etc)? Or is the population of interest for the scan a certain life stage?
Outcomes	What outcomes of interest should be examined in the evidence scan? Are there key intermediate outcomes or biomarkers of interest? Endpoint health outcomes?
Population for outcomes	What populations are of interest for the outcomes in evidence scan? Generally healthy individuals across the entire lifespan, including during pregnancy and lactation? Are there different outcomes of interest for different populations?
Date range	Is there a date range of interest that you think would capture the most relevant evidence on this topic? (Can be left blank, and NESR can suggest a date or ask a protein expert)
References/Resources	Are there any key references, including existing reviews, related to this topic that represent the type of evidence of interest for the scan? Are there any other countries that have addressed this topic in recent guidance updates? What evidence was considered in the existing DRI report on this topic?

Protein evidence scans conducted to inform future systematic review requirements (October 2021– February 2022)

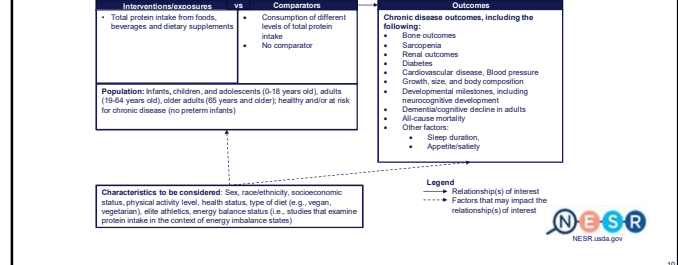
- What is the relationship between high dietary protein intake and risk of acute toxicity?
- What is the relationship between high amino acid intake and risk of acute toxicity?
- What is the relationship between dietary protein intake and risk of chronic disease?
- What is the average daily dietary protein intake requirement of apparently healthy individuals by life stage and sex?
- What is the average daily intake requirement for individual indispensable amino acids of apparently healthy individuals by life stage and sex?



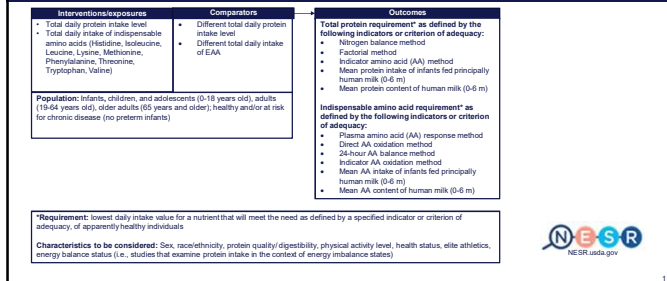
Protein and Amino Acid(s) Upper Level – Analytic Framework



Protein and Chronic Disease Risk– Analytic Framework



Protein/Indispensable Amino Acid Requirements – Analytic Framework



Inclusion/exclusion criteria: Population criteria included participants across the lifespan and those healthy and/or at risk for chronic disease

Category	Inclusion Criteria	Exclusion Criteria
Study participants	- Human participants - Subjects who are pregnant	Non-human participants (e.g., animal studies, in-vitro models)
Age of study participants	- Age at intervention or exposure: - Infants, children, and adolescents (0-18 years) - Adults (19-64 years) - Older adults (65 years and older)	
Health status of study participants	- Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity - Studies that enroll some participants diagnosed with a disease or hospitalized with and illness or injury - Studies that enroll some participants diagnosed with a disease or with the health outcome of interest - Studies which exclusively recruit athletes and/or highly active individuals	- Studies that exclusively enroll participants diagnosed with a disease or hospitalized with an illness or injury (for this criterion, studies that exclusively enroll participants with obesity will not be excluded) - Studies that are to treat participants who have already been diagnosed with the outcome of interest - Studies that exclusively enroll undernourished participants - Studies that exclusively enroll participants with a baseline diet deficient in protein - Studies that exclusively enroll pre-term infants.

Inclusion/exclusion criteria: Publication and study characteristics were tailored by topic

Category	Protein Upper Limit Inclusion Criteria	Protein and Chronic Disease Inclusion Criteria	Protein Requirements Inclusion Criteria
Publication date	- Review Papers 2016 to present	- Review Papers 2016 to present	2000 to present
Publication status	Articles published in peer-reviewed journals	Articles published in peer-reviewed journals	- Reports published by international and government entities - Articles published in peer-reviewed journals
Study design	- Systematic reviews - Meta-analyses - Narrative reviews	- Systematic reviews - Meta-analyses	- Systematic reviews - Meta-analyses - Scoping reviews - Umbrella reviews - Randomized controlled trials - Non-randomized controlled trials, including quasi-experimental and controlled before-and-after studies - Prospective cohort studies - Retrospective cohort studies - Nested case-control studies
Country	Studies conducted in any country	Studies conducted in high or very high HDI countries	Studies conducted in any country
Study duration	- Observational studies: Any duration - Trials: Up to 8 weeks		

Literature search, screening, data extraction, and more

- Literature search strategy
 - Protein upper limit and chronic disease risk scans: Systematic search using PubMed only
 - Protein requirement: Initial searches in PubMed had low precision; therefore, a citation mining strategy was used to identify articles rather than a systematic search
- Dual screening with reconciliation by third party to identify citations meeting inclusion criteria
- Minimal data extraction to describe characteristics of the included studies
- Protein and chronic disease risk scan (for a subset of promising outcomes):
 - AMSTAR 2 (dual assessment) to describe the quality of existing reviews
 - Duplication assessment to identify the number of unique articles included in reviews

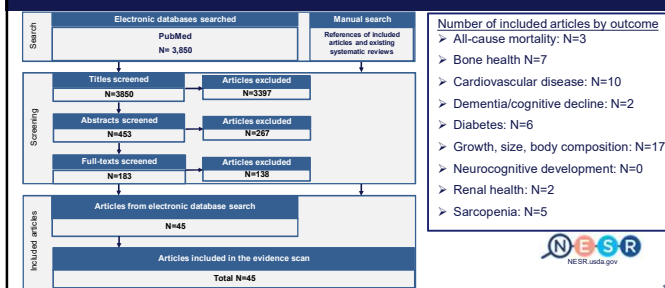


Examples

- Total dietary protein intake and risk of sarcopenia
- Protein requirements



Search Results: Protein Intake and Chronic Disease Risk



Description of the evidence: Sarcopenia

- 5 systematic reviews (3 with meta-analysis) examined protein and sarcopenia outcomes
 - Included a range of 7 to 28 studies (RCTs, PCS, and cross-sectional studies examined most frequently)
 - 3 reviews included studies assessing habitual intake (reported continuously and categorically); 3 reviews included interventions that altered protein intake, and 1 included multi-component interventions that isolated the effect of total protein
 - Population/Life-Stage: All assessed adults 60+ y, with one also assessing adults 19-59 y
- Outcomes Evaluated
 - Muscle strength (4 reviews)
 - All null results across reviews for upper-limb and lower-limb muscle strength aside from a positive relationship in one review for handgrip strength (only when combined with exercise in frail/sarcopenic populations).
 - Muscle mass (4 reviews)
 - Two reviews had trends towards a positive relationship for lean muscle mass gain and for skeletal muscle mass; the other two reviews found only null relationships
 - Sarcopenia overall (1 review)
 - Results mixed/inconclusive



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AMSTAR-2: Sarcopenia

AMSTAR 2

Article	Quality of review (AMSTAR 2)	Funding
Coelho-Junior, 2018	Critically low	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior; Fundação de Amparo à Pesquisa do Estado de São Paulo; CNPq
Kirwan, 2021	Low	Institute for Health Research at Liverpool John Moores University
Lin, 2021	Low	Ministry of Science and Technology, Taiwan
Naseeb, 2017	Critically low	Not reported
Yaegashi, 2021	Critically low	Not reported



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Duplication Assessment: Sarcopenia

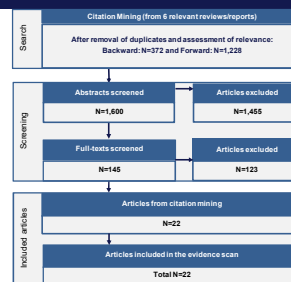
- 72 articles across 5 systematic reviews
 - When divided up by outcome categories (muscle strength, muscle mass, sarcopenia) there was no overlap across reviews
 - Muscle Strength: 35 unique papers
 - Muscle Mass: 63 unique papers
 - Sarcopenia: 2 unique papers
 - Note: Some papers were utilized for one outcome in one review and another outcome in a different review.
- Additional considerations
 - 2 SRs searched 6 databases for observational studies, 2 SRs searched 4 databases for randomized trials; one SR searched 1 database but did not limit study design
 - 1 case-control and 15 cross-sectional studies may be excluded from subsequent reviews



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Search Results: Protein and Indispensable Amino Acid Requirements

- From 6 relevant reviews/reports, the librarian:
 - Extracted all articles cited in these review/reports (backward citation mining)
 - Extracted articles which cited these articles (forward citation mining)
- The librarian removed duplicates and checked articles for relevance
- Analysts dual screened at the abstract and full-text level



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● Description of the evidence: Total Protein Requirements (10 articles)

- **Study designs:**
 - 7 RCTs (1 with MA), 3 SRs (1 with MA)
 - 1 article (Rand, 2003 – SR/MA) included in 2005 IOM report
- **Outcome assessment methods:**
 - Indicator AA oxidation method: 5 RCTs
 - Nitrogen balance method: 3 RCTs, 4 SR and/or MA
 - Factorial method, mean protein content of human milk: 1 SR
- **Populations examined:**
 - All Age Groups: 1 SR (several assessment methods reported)
 - Children (2-12 y): 1 RCT (IAAO)
 - Adults (19-59 y): 2 RCTs (IAAO; MA of nitrogen balance in 1 RCT)
 - Adults (19-59 y) and Older adults (60+ y): 1 RCT and 1 SR/MA (nitrogen balance)
 - Older adults (60+ y): 3 RCTs (IAAO and nitrogen balance), 1 SR (nitrogen balance)
 - Males alone (2 RCTs – 1 in Adults, 1 in Older Adults)
 - Females alone (3 RCTs – 1 in Adults, 2 in Older Adults)



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● Description of the evidence: AA Requirements (12 articles)

- **Study designs:** 11 RCTs, 1 NRCT (6 articles included in 2005 IOM report)
- **Populations examined:** Adults (19-59 y) – 2 mixed population, 1 females alone, 9 males alone
- **AAs and Assessment Methods:**
 - **Not included in 2005 IOM report**
 - Lysine: 1 RCT (IAAO, 24-h indicator AA balance)
 - Methionine: 2 RCTs (IAAO, 24-h indicator AA balance)
 - Valine: 1 RCT (IAAO, 24-h indicator AA balance)
 - Total BCAAs (isoleucine, leucine, valine): 2 RCTs (IAAO)
 - **Included in 2005 IOM report**
 - Leucine: 1 RCT (24-h AA balance, Direct AA oxidation, Nitrogen balance)
 - Lysine: 2 RCTs (IAAO, 24-h indicator AA balance), 1 NRCT (24-h AA balance, Direct AA oxidation)
 - Threonine: 2 RCTs (IAAO, 24-h indicator AA balance)



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● Evidence scan report describes the volume and characteristics of the evidence

Report components

Methodology (Protocol)

Results

Literature search and screening results

Description of the evidence

Considerations for future DRI work

References

Appendices: Abbreviations, literature search strategy, excluded articles (with rationale)

Tables: Inclusion/exclusion criteria, evidence tables

Figures: Analytic framework, literature screening flowchart

Completed reports are available at:
[NESR.usda.gov](https://www.nesr.usda.gov)



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● Strengths and limitations of the approach

- **Strengths**
 - Systematic, iterative, and transparent process
 - Describes the volume and characteristics of existing evidence
 - Provides timely data to aid decision making
- **Limitations**
 - Using reviews and meta-analyses is less direct and sometimes limited data available for extraction
 - Methods used to estimate number of included articles is not tested/validated
 - Information is derived from reference lists of SRs vs original search for primary articles
 - Precision and historical database coverage information



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Volume estimates were interpreted with caution

- Because information was derived from reference lists of SRs (identified from one database) vs an original search for primary articles, all estimates were interpreted with caution
 - Whether an individual article would be included ultimately depends on the requested SR's inclusion/exclusion criteria
 - Duplication assessment may overestimate number of potential includes if the final requested SR is narrower in scope than the source SRs, has stricter inclusion/exclusion criteria
 - Duplication assessment may underestimate number of potential includes if the final requested SR is broader in scope than the source SRs, has looser inclusion/exclusion criteria, or if the source SRs did not search multiple electronic databases
- NESR librarian used an alternate method for estimating volume based on statistics from past NESR reviews and assuming a 20-year publication range (2002-present)



NESR values transparency! The DRI evidence scans are thoroughly documented and accessible online: *NESR.usda.gov*



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