# APPENDIX 1

## Recommendations 1-7

**A1.a. Macro and micronutrient requirements from 6 to 24 months.**

### Key Questions

- ***Does an energy intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?***

- ***Does a carbohydrate intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?***

- ***Does a protein intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?***

- ***Does a lipid intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?***

**a**.
**P** In the healthy infant, in the period 6-24 months,
**I** an energy intake above the recommended levels for age
**C** compared with an intake corresponding to recommended levels
**O** results in different short- and long-term nutritional and metabolic outcomes?

**b.**
**P** In the healthy infant, in the period 6-24 months,
**I** a carbohydrate intake above the recommended levels for age
**C** compared with an intake corresponding to recommended levels
**O** results in different short- and long-term nutritional and metabolic outcomes?

**c.**
**P** In the healthy infant, in the period 6-24 months,
**I** a protein intake above the recommended levels for age
**C** compared with an intake corresponding to recommended levels
**O** results in different short- and long-term nutritional and metabolic outcomes?

d
**P** In the healthy infant, in the period 6-24 months,
**I** a lipid intake above the recommended levels for age
**C** compared with an intake corresponding to recommended levels
**O** results in different short- and long-term nutritional and metabolic outcomes?

**KEYWORDS**

**Population**

A. Infant
B. Child
C. Adolescent
D. Young adult

**Exposure Factors / Comparison**

MeSH Terms/ Text word: weaning; wean*; diet; food; beverages; infant nutritional physiological phenomena; meals; food and beverages; infant food; eating; diet; diets; supplementary feeding Solid food

A. Complementary feeding
B. "Proteins" OR proteins[Text Word]
C. "lipids" OR lipids[Text Word]
D. "sugars" OR sugars[Text Word]
E. "carbohydrates" OR Carbohydrates[Text Word]
F. "Dietary Carbohydrates"[Mesh]
G. "dietary fats" OR dietary fats[Text Word]
H. "dietary proteins" OR dietary proteins[Text Word]
I. "Energy Intake"[Mesh]

**Outcomes**

A. Overnutrition
B. Obesity
C. Growth
D. Body Size
E. Body Height
F. Diabetes Mellitus (diabetic patient)
G. Noncommunicable Diseases
H. Nutritional and Metabolic Diseases (metabolic disorder)
I. Pediatric Obesity (childhood obesity)
J. Overweight
K. Body Mass Index (Z-Score)
L. Body Weight Changes
M. Body Weight
N. Body Composition
O. Nutritional Status
P. Growth and Development ('growth, development and aging')
Q. Fat body (Fat pad)
R. Adipose tissue
S. Body fat
T. Adiposity rebound

## Guidelines Research

*Temporal limitation: 2015-2021.*

**PUBMED https://www.ncbi.nlm.nih.gov/pubmed/**

#1

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena" OR weaning OR (Solid food*) OR solids OR “infant food” OR infant feed*) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake"[Mesh]) AND ("Obesity" OR "Pediatric Obesity" OR "Overweight" OR "Body Mass Index" OR "Body Weight Changes" OR "Body Weight" OR "Body Composition" OR "Nutritional Status" OR "Growth and Development" OR "Growth" OR "fat body" OR "adipose tissue" OR body fat OR “adiposity rebound” OR "Diabetes Mellitus" OR "Nutritional and Metabolic Diseases" OR "Noncommunicable Diseases"[Mesh]) AND "2015/03/07"[PDat]:"2021/03/14"[PDat] AND ("infant" OR "Child" OR "Adolescent" OR "Young Adult"[Mesh])

Filters applied: Guideline, Practice Guideline, in the last 5 years. Clear all

**EMBASE https://www.embase.com**

#1

Query

('overnutrition'/exp OR 'growth, development and aging'/exp OR 'obesity'/exp OR 'childhood obesity'/exp OR 'body size'/exp OR 'body weight'/exp OR 'body height'/exp OR 'body mass'/exp OR 'body mass index z score'/exp OR 'body weight change'/exp OR 'body composition'/exp OR 'nutritional status'/exp OR 'adipose tissue'/exp OR 'adiposity rebound'/exp OR 'diabetic patient'/exp OR 'non communicable disease'/exp OR 'metabolic disorder'/exp) AND ('weaning'/exp OR 'wean*' OR 'complementary feeding'/exp OR 'supplementary feeding'/exp OR 'solid food'/exp OR 'dietary intake'/exp OR 'caloric intake'/exp OR 'protein intake'/exp OR 'amino acid intake'/exp OR 'carbohydrate intake'/exp OR 'sugar intake'/exp OR 'fat intake'/exp OR 'lipid intake') AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim) AND 'practice guideline'/de AND [2015-2021]/py

**UPTODATE https://www.uptodate.com/home**

Society Guideline Links: *complementary feeding*

**SOCIETY GUIDELINE LINKS: *Complementary feeding, Weaning, Alimentary – nutrition,***

National Guideline Clearinghouse (NGC) https://www.ahrq.gov/gam/index.html

Canadians Medical Association (CMA) https://www.cma.ca/clinicalresources/practiceguidelines

National Guideline Centre (NGC) - National Institute of Health and Care Excellence (NICE) https://www.rcplondon.ac.uk/about-us/what-we-do/national-guideline-centre-ngc

Scottish Intercollegiate Guidelines Network (SIGN) https://www.sign.ac.uk/our-guidelines.html

Australian Clinical Practice Guidelines (ACPG) https://www.clinicalguidelines.gov.au/

New Zealand Guidelines Group (NZGG) https://www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group

American Academy of Pediatrics (AAP) https://www.aap.org/en-us/Pages/Default.aspx
*DateRange (01/01/2013-03/19/2019) AND ((complementary feeding) OR (weaning)) AND (Guideline)*
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) https://www.naspghan.org/

European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) http://www.espghan.org/

Geneva Foundation for Medical Education and Research (GFMER) https://www.gfmer.ch/Guidelines/Allattamento_it/Allattamento_alimentazione_complementare.htm

Società Italiana di Nutrizione Umana (SINU) http://www.sinu.it

Società Italiana di Pediatria (SIP) http://www-sip.it/

Società Italiana di Pediatria Preventiva e Sociale (SIPPS) https://www.sipps.it/

Società Italiana di Nutrizione Pediatrica (SINUPE) https://www.sip.it/2017/09/21/sinupe-societa-italiana-di-nutrizione-pediatrica/

Società Italiana di Endocrinologia e Diabetologia Pediatrica (SIEDP) http://www.siedp.it/pagina/84/linee+guida%2C+raccomandazioni+e+consensus

## Sysitematic Review Research

*Temporal Limitation: 2011/15-2021*

**PUBMED**

#1

systematic[sb] AND ((((((("Infant Nutritional Physiological Phenomena"[Mesh]) AND "Overnutrition"[Mesh]) OR "Growth"[Mesh]) OR "Diabetes Mellitus"[Mesh]) OR "Nutritional and Metabolic Diseases"[Mesh]) OR "Noncommunicable Diseases"[Mesh])

*Filters applied: Meta-Analysis, Systematic Reviews, in the last 5 years, Child: birth-18 years.*

#2

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena" OR weaning OR (Solid food*) OR solids OR “infant food” OR infant feed*) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake"[Mesh]) AND ("Obesity" OR "Pediatric Obesity" OR "Overweight" OR "Body Mass Index" OR "Body Weight Changes" OR "Body Weight" OR "Body Composition" OR "Nutritional Status" OR "Growth and Development" OR "Growth" OR "fat body" OR "adipose tissue" OR body fat OR “adiposity rebound” OR "Diabetes

Mellitus" OR "Nutritional and Metabolic Diseases" OR "Noncommunicable Diseases"[Mesh]) AND "2015/03/07"[PDat]:"2021/03/14"[PDat] AND ("infant" OR "Child" OR "Adolescent" OR "Young Adult"[Mesh])

*Filters activated: Meta-Analysis, Systematic Reviews, published in the last 5 years*

#3

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena"[ MeSH Terms] OR weaning OR ((Solid food*) OR solids)) OR “infant food” OR infant feed*) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake"[MeSH Terms]) AND ((((((((((("Obesity" OR "Pediatric Obesity"[MeSH Terms]) OR "Overweight"[MeSH Terms]) OR "Body Mass Index"[MeSH Terms]) OR "Body Weight Changes"[MeSH Terms]) OR "Body Weight"[MeSH Terms]) OR "Body Composition"[MeSH Terms]) OR "Nutritional Status"[MeSH Terms]) OR "Growth and Development"[MeSH Terms]) OR "Growth"[MeSH Terms]) OR "fat body"[MeSH Terms]) OR "adipose tissue"[MeSH Terms]) OR body fat[Text Word]) OR “adiposity rebound” OR "Diabetes Mellitus"[MeSH Terms]) OR "Nutritional and Metabolic Diseases"[MeSH Terms]) OR "Noncommunicable Diseases"[MeSH Terms]) AND "2015/06/13"[PDat]: "2021/03/14"[PDat] AND ("infant" OR "Child" OR "Adolescent" OR "Young Adult"[Mesh])

*Filters activated: Systematic Reviews, Meta-Analysis, published in the last 5 years*

**EMBASE**

#1

Query

('overnutrition'/exp OR 'growth, development and aging'/exp OR 'obesity'/exp OR 'childhood obesity'/exp OR 'body size'/exp OR 'body weight'/exp OR 'body height'/exp OR 'body mass'/exp OR 'body mass index z score'/exp OR 'body weight change'/exp OR 'body composition'/exp OR 'nutritional status'/exp OR 'adipose tissue'/exp OR 'adiposity rebound'/exp OR 'diabetic patient'/exp OR 'non communicable disease'/exp OR 'metabolic disorder'/exp) AND ('weaning'/exp OR 'wean*' OR 'complementary feeding'/exp OR 'supplementary feeding'/exp OR 'solid food'/exp OR 'dietary intake'/exp OR 'caloric intake'/exp OR 'protein intake'/exp OR 'amino acid intake'/exp OR 'carbohydrate intake'/exp OR 'sugar intake'/exp OR 'fat intake'/exp OR 'lipid intake') AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim) AND ('meta analysis'/de OR 'systematic review'/de) AND [2015-2021]/py

**COCHRANE LIBRARY**

#1

MeSH descriptor - Infant Nutritional Physiological Phenomena- Infant Nutritional Physiological Phenomena in Title Abstract Keyword - with Cochrane Library publication date Between Jan 2010 and March 2021, in Cochrane Reviews (Word variations have been searched)

#2

Weaning OR "Complementary feeding" in Title Abstract Keyword - with Cochrane Library publication date Between Jan 2010 and March 2021, in Cochrane Reviews (Word variations have been searched)

#3

(Infant Nutritional Physiological Phenomena OR complementary feeding) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake") AND ("Obesity" OR "Pediatric Obesity" OR "Overweight" OR "Body Mass Index" OR "Body Weight Changes" OR "Body Weight" OR "Body Composition" OR "Nutritional Status" OR "Growth and Development" OR "Growth" OR "fat body" OR "adipose tissue" OR body fat OR "adiposity rebound" OR "Diabetes Mellitus" OR "Nutritional and Metabolic Diseases" OR "Noncommunicable Diseases")" with Publication Year from 2012 to 2021, with Cochrane Library publication date Between Jan 2012 and March 2021, in Trials (Word variations have been searched)

## Studies Research

**PUBMED**

#1

((((((("Infant Nutritional Physiological Phenomena"[Mesh]) AND "Overnutrition"[Mesh]) OR "Growth"[Mesh]) OR "Diabetes Mellitus"[Mesh]) OR "Nutritional and Metabolic Diseases"[Mesh]) OR "Noncommunicable Diseases"[Mesh])

*Filters applied: Clinical Trial, Multicenter Study, Observational Study, Randomized Controlled Trial, in the last 5 years, Infant: birth-23 months*

#2

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena" OR weaning OR (Solid food*) OR solids OR "infant food" OR infant feed*) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake"[Mesh]) AND ("Obesity" OR "Pediatric Obesity" OR "Overweight" OR "Body Mass Index" OR "Body Weight Changes" OR "Body Weight" OR "Body Composition" OR "Nutritional Status" OR "Growth and Development" OR "Growth" OR "fat body" OR "adipose tissue" OR body fat OR "adiposity rebound" OR "Diabetes Mellitus" OR "Nutritional and Metabolic Diseases" OR "Noncommunicable Diseases"[Mesh]) AND

"2015/03/07"[PDat]:"2021/03/15"[PDat] AND ("infant" OR "Child" OR "Adolescent" OR "Young Adult"[Mesh])
*Filters applied: Clinical Trial, Multicenter Study, Observational Study, Randomized Controlled Trial, from 2013/3/7 - 2021/3/15.*

#3

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena"[ MeSH Terms] OR weaning OR ((Solid food*) OR solids)) OR “infant food” OR infant feed*) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake"[MeSH Terms]) AND ((((((((((("Obesity" OR "Pediatric Obesity"[MeSH Terms]) OR "Overweight"[MeSH Terms]) OR "Body Mass Index"[MeSH Terms]) OR "Body Weight Changes"[MeSH Terms]) OR "Body Weight"[MeSH Terms]) OR "Body Composition"[MeSH Terms]) OR "Nutritional Status"[MeSH Terms]) OR "Growth and Development"[MeSH Terms]) OR "Growth"[MeSH Terms]) OR "fat body"[MeSH Terms]) OR "adipose tissue"[MeSH Terms]) OR body fat[Text Word]) OR “adiposity rebound” OR "Diabetes Mellitus"[MeSH Terms]) OR "Nutritional and Metabolic Diseases"[MeSH Terms]) OR "Noncommunicable Diseases"[MeSH Terms]) AND "2013/03/13"[PDat]: "2021/03/15"[PDat] AND ("infant" OR "Child" OR "Adolescent" OR "Young Adult"[Mesh])

*Filters applied: Clinical Trial, Multicenter Study, Observational Study, Randomized Controlled Trial, Infant: birth-23 months, from 2013/3/7 - 2021/3/15.*

**EMBASE**

('overnutrition'/exp OR 'growth, development and aging'/exp OR 'obesity'/exp OR 'childhood obesity'/exp OR 'body size'/exp OR 'body weight'/exp OR 'body height'/exp OR 'body mass'/exp OR 'body mass index z score'/exp OR 'body weight change'/exp OR 'body composition'/exp OR 'nutritional status'/exp OR 'adipose tissue'/exp OR 'adiposity rebound'/exp OR 'diabetic patient'/exp OR 'non communicable disease'/exp OR 'metabolic disorder'/exp) AND ('weaning'/exp OR 'wean*' OR 'complementary feeding'/exp OR 'supplementary feeding'/exp OR 'solid food'/exp OR 'dietary intake'/exp OR 'caloric intake'/exp OR 'protein intake'/exp OR 'amino acid intake'/exp OR 'carbohydrate intake'/exp OR 'sugar intake'/exp OR 'fat intake'/exp OR 'lipid intake') AND [2010-2021]/py AND ('case control study'/de OR 'cohort analysis'/de OR 'controlled study'/de OR 'cross sectional study'/de OR 'intervention study'/de OR 'major clinical study'/de OR 'observational study'/de OR 'prospective study'/de OR 'randomized controlled trial'/de) AND ('article'/it OR 'article in press'/it) AND ('body composition analyzer'/dv OR 'body weight scale'/dv OR 'growth chart'/dv OR 'sphygmomanometer'/dv OR 'x ray bone densitometer'/dv) AND ('clinical trial'/lnk OR 'clinicaltrials gov'/lnk OR 'disease management'/lnk OR 'epidemiology'/lnk OR 'etiology'/lnk OR 'prevention'/lnk OR 'therapy'/lnk) AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim)

**COCHRANE LIBRARY**

#1

535 Trials matching "#1 - (Infant Nutritional Physiological Phenomena OR complementary feeding) AND ("Proteins" OR proteins OR "lipids" OR lipids OR "sugars" OR sugars OR "carbohydrates" OR

Carbohydrates OR "Dietary Carbohydrates" OR "dietary fats" OR dietary fats OR "dietary proteins" OR dietary proteins OR "Energy Intake") AND ("Obesity" OR "Pediatric Obesity" OR "Overweight" OR "Body Mass Index" OR "Body Weight Changes" OR "Body Weight" OR "Body Composition" OR "Nutritional Status" OR "Growth and Development" OR "Growth" OR "fat body" OR "adipose tissue" OR body fat OR "adiposity rebound" OR "Diabetes Mellitus" OR "Nutritional and Metabolic Diseases" OR "Noncommunicable Diseases")" with Publication Year from 2012 to 2021, with Cochrane Library publication date Between Jan 2012 and March 2021, in Trials (Word variations have been searched)

**Figure a1.1. Guidelines search flow diagram.**

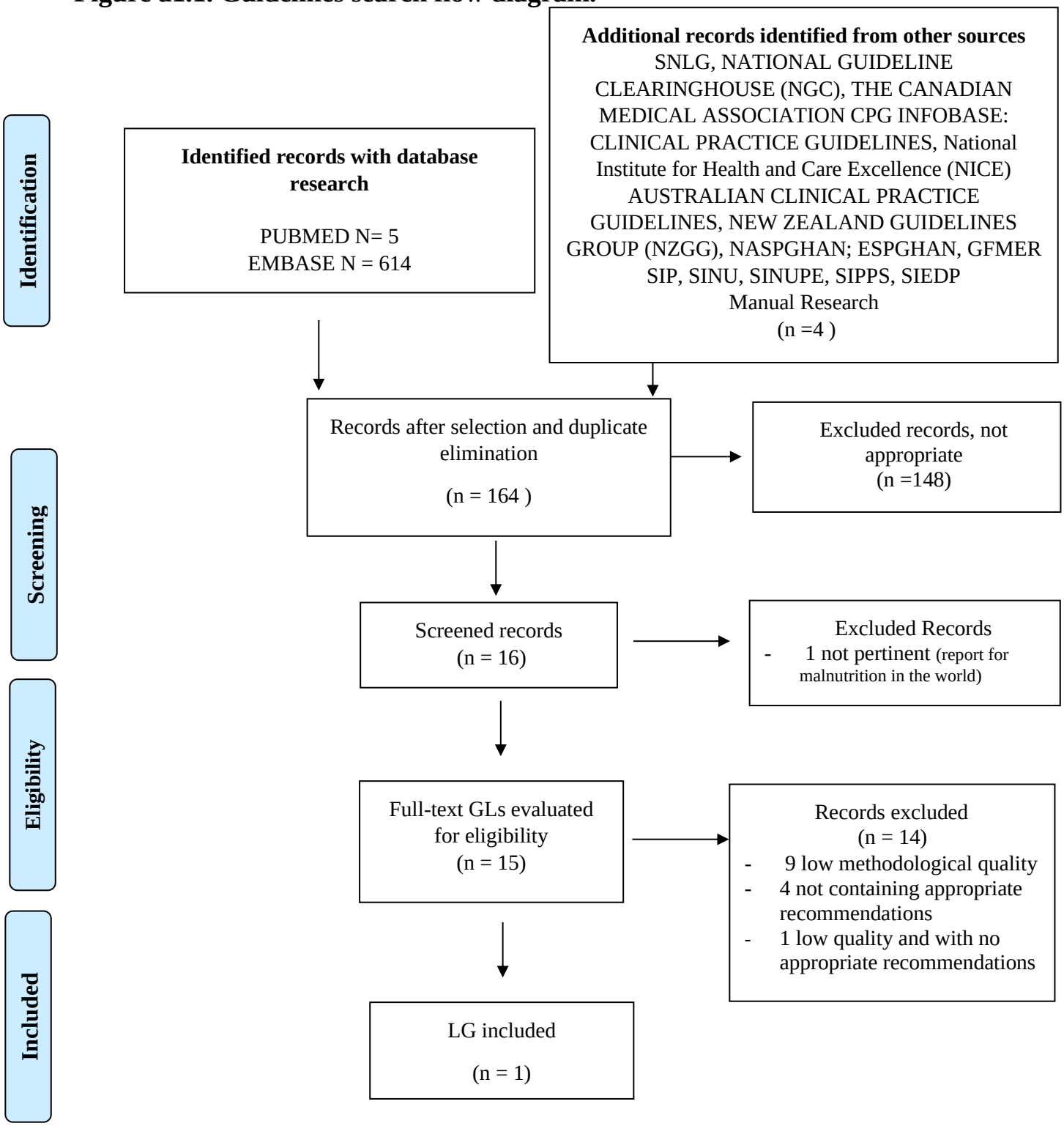


**Figure a1.2. SRs search flow diagram**

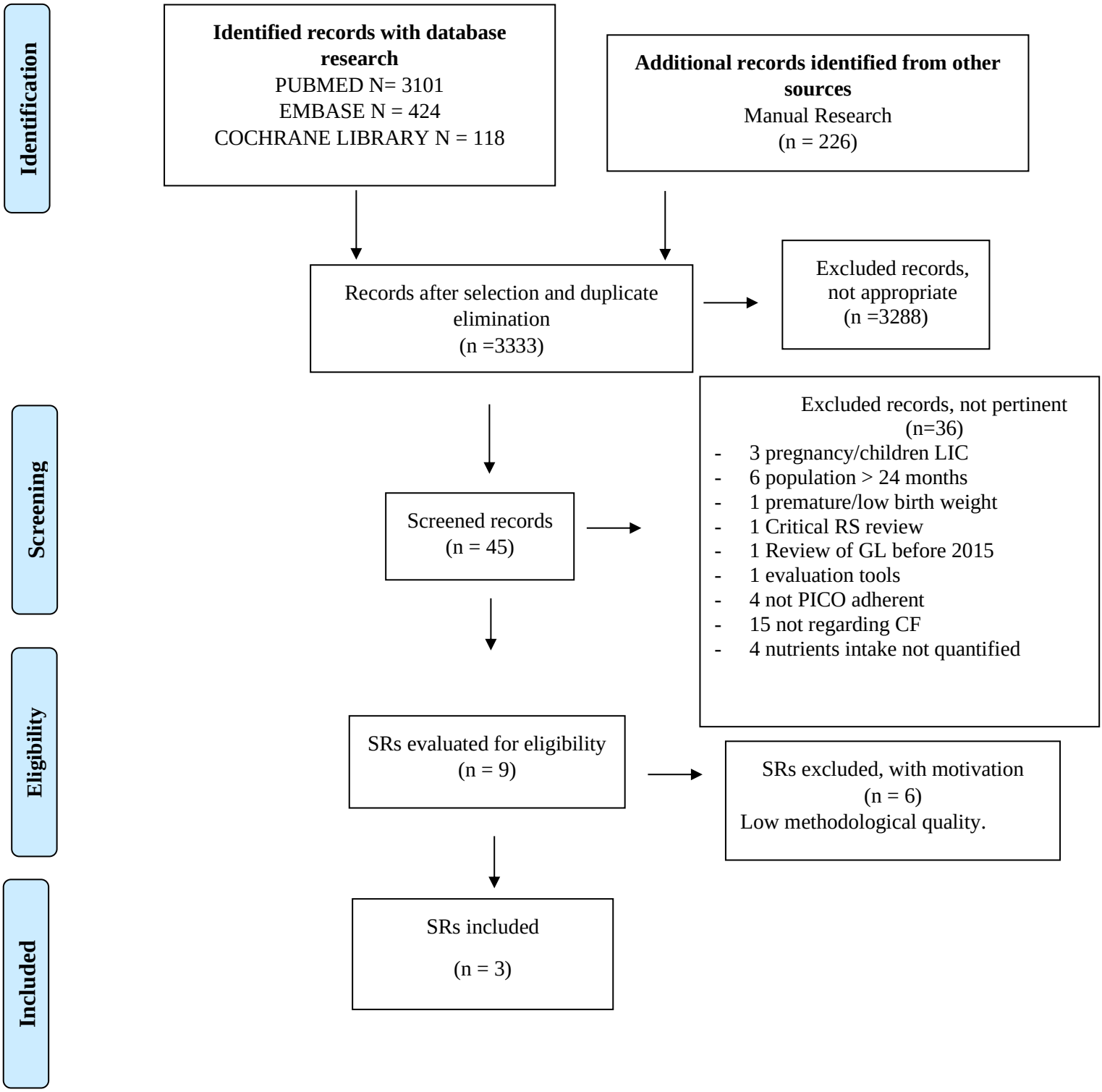
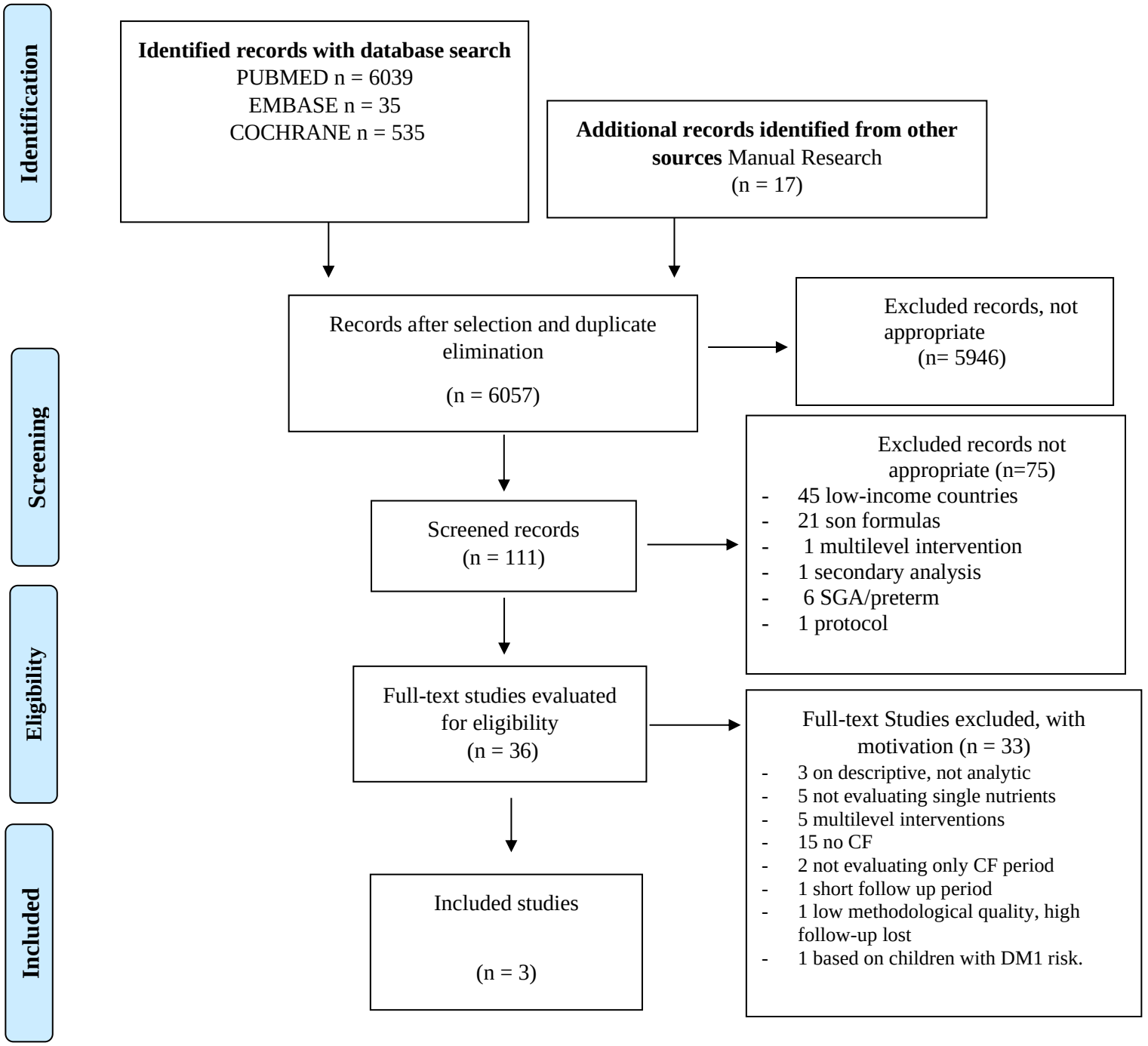


**Figure a1.3. Studies search flow diagram.**



## A1.a. METHODOLOGICAL EVALUATION

**Table a1.1. Appraisal of the Clinical Guidelines and Documents**

| Guidelines and Clinical Documents | Methodological Evaluation | | | |
|---|---|---|---|---|
| | **Multidisciplinary panel** | **Systematic evidence research** | **Grading of recommendations** | **GL overall assessment** |
| SIEDP-SIP 2018 [1] | Yes | No, only MEDLINE | Yes | Moderate methodological quality |

**Table a1.2. Clinical Guidelines and Documents excluded.**

| GL Excluded | Multidisciplinary panel | Systematic evidence research | Grading of recommendations | Reason for exclusion |
|---|---|---|---|---|
| Alvisi et al. 2015 [2] | Limited to Pediatricians and Nutritionists. | No | No | Review document, with recommendations for clinical guidance.<br>Low methodological quality. |
| Canada's Dietary Guidelines 2018 [3] | Limited to Nutritionists and Public Health Experts. | No | No | Low methodological quality.<br>No relevant recommendations. |
| Dereń et al. 2019. EAP ECOG [4] | No | No | No | Low methodological quality. |
| EFSA 2013<br>Scientific opinion [5] | No | No | No | Low methodological quality regarding response to questions. |
| Fewtrell et al. 2017. ESPGHAN Complementary feeding [6] | No | Declared but not published | No | Low methodological quality. |
| Fidler Mis ESPGHAN 2017 Sugar in Infants, Children, and Adolescents [7] | No | Declared but not published | No | Low methodological quality. |
| WHO 2015 Sugar intake [8] | Yes | Yes | Yes | No appropriate Recommendations. |

| | | | | |
|---|---|---|---|---|
| Heyman et al. 2017 AAP - Fruit Juice [9] | No | No | No | Low methodological quality. |
| Kastorini et al. 2019 – Greece GL [10] | Yes | Declared but not published | Declared but not published | Low methodological quality.<br>No appropriate recommendations. |
| Koletzko et al. 2019 The Early Nutrition Project Recommendations [11] | Yes | Yes but not explicated (Previously Published RS used: For the Questions in this Consensus Patro-Golab Et Al. 2016) | No Consent Vote | Low methodological quality. |
| NICE 2015 Preventing excess weight gain [12] | === | ==== | === | Interventions Following the CF Period. |
| Romero-Velardea et al. 2016. Alimentation complementaria [13] | Limited to Pediatrician and nutrition Experts | No | No | Low methodological quality. |
| Schwarzenberg et al. 2018. AAP Policy Statement [14] | No | No | No | Low methodological quality. |
| USDA 2015-2020 [15] | Yes | Yes | Related to quality of Evidence | No appropriate recommendations. |

**Table a1.3. Appraisal of the Systematic Reviews**

| **AMSTAR 2** | Hörnell et al. 2013 [16] | Pearce et al. 2013 [17] | Ferrè et al. 2021 [18] |
|---|---|---|---|
| **1. Did the research questions and inclusion criteria for the review include the components of PICO?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **2. Did the report of the review contain an explicit statement that the review methods were established before the conduct of the review and did the report justify any significant deviations from the protocol?**<br>**(Yes/Partial Yes/No)** | Yes | No | Partial Yes |
| **3. Did the review authors explain their selection of the study designs for inclusion in the review?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **4. Did the review authors use a comprehensive literature search strategy?**<br>**(Yes/Partial Yes/No)** | Partial Yes | Partial Yes | Partial Yes |
| **5. Did the review authors perform study selection in duplicate?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **6. Did the review authors perform data extraction in duplicate?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **7. Did the review authors provide a list of excluded studies and justify the exclusions?**<br>**(Yes/Partial Yes/No)** | Yes | No | Yes |
| **8. Did the review authors describe the included studies in adequate detail?** | Yes | Partial Yes | Partial Yes |

| | | | |
|---|---|---|---|
| **(Yes/Partial Yes/No)** | | | |
| **9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?**<br>**(Yes/Partial Yes/No/Includes only NRSI-RCT)** | RCT - Partial Yes<br>NRSI - Yes | NRSI - Yes | RCT - Partial Yes<br>NRSI - Partial Yes |
| **10. Did the review authors report on the sources of funding for the studies included in the review?**<br>**(Yes/No)** | No | No | No |
| **11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?**<br>**(Yes / No / No meta-analysis conducted)** | No meta-analysis conducted. | No meta-analysis conducted. | No meta-analysis conducted. |
| **12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?**<br>**(Yes / No / No meta-analysis conducted)** | No meta-analysis conducted | No meta-analysis conducted | No meta-analysis conducted |
| **13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?**<br>**(Yes / No / No meta-analysis conducted)** | No meta-analysis conducted | No meta-analysis conducted | No meta-analysis conducted |

| | | | |
|---|---|---|---|
| **16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?**<br>**(Yes/No)** | Yes | Yes | Yes |
| **OVERALL EVALUATION** | **Moderate quality.** | **Moderate quality.** | **Moderate quality.** |

**Table a1.4. Appraisal of the SR's Overview**

| **COCHRANE TOOL FOR REVIEW OVERVIEWS.** | | Patro-Gołąb et al. 2016 [19] |
|---|---|---|
| Objectives | To summarize evidence from systematic reviews of the effects of interventions. | Appropriate |
| Selection Criteria | Describe inclusion and exclusion criteria for reviews. | Appropriate |
| Research | Typically search for only relevant (Cochrane) Intervention reviews. | Appropriate (RCT and Observational Studies) |
| Data Collection | From included systematic reviews. | Not Appropriate (Narrative reports of outcomes and inclusion error for RS by Hooper et al. 2015 - age > 24 months) |
| Limits evaluation | For included systematic reviews. | Appropriate |
| Quality of Evidence | So far as possible should be based on assessments reported in the included systematic reviews. | Appropriate |
| Analysis | Summary of review results; additional analyses may be undertaken for comparisons across reviews, typically indirect comparisons of multiple interventions. | Not Appropriate /insufficient (Narrative summary of results with no comparison between SRs. Error in reporting of results by Hooper et al.) |
| **Global evaluation** | **Low methodological quality, Excluded.** | |

**Table a1.5. SRs excluded with motivation.**

| **SRs excluded** | **Reason for exclusion** |
|---|---|
| Askie et al. 2020 [20] | Not appropriate (evaluates health education interventions on the mother) |
| Azaïs-Braesco et al. 2017 [21] | Not appropriate (survey reviews in 11 countries) |
| Bailey et al. 2018 [22] | Not appropriate. (Data on nutrients intake) |
| Blake-Lamb et al. 2016 [23] | Low methodological quality. Not appropriate. (Not evaluating single nutrient intake). |
| Borg et al. 2019 [24] | Not appropriate. (Data on nutrients intake) |

| | |
|---|---|
| Brown et al. 2019 [25] | Reporting aggregate data 1-5 years. |
| Das et al. 2019 [26] | Not appropriate. (in LIC, Low-Income Countries) |
| Eichler et al. 2019 [27] | Not appropriate. (children aged 5-15 years) |
| English et al. 2019 [28] | (Primary studies quantify food consumption, not the intake of specific nutrients. ) |
| Grote et al. 2014 [29] | Low methodological quality. (Narrative review) |
| Hooper et al. 2015 [30] | Not appropriate. (children aged > 24 mo) |
| Huang et al. 2019 [31] | Not appropriate. (studies on adult population) |
| Larqué et al. 2019 [32] | Low methodological quality. (Narrative review) |
| Laving et al. 2018 [33] | Low methodological quality. (Narrative review) |
| Lin et al. 20et al. 20 [34] | Not appropriate. (nutrients supplementation in preterm and SGA children) |
| Kikuchi et al. 2018 [35] | Not appropriate. (not including CF studies ) |
| Malik et al. 2013 [36] | Not appropriate. (not including CF studies ) |
| Mazarello Paes et al. 2015 [37] | Not appropriate. (not including CF studies) |
| Mela et al. 2018 [38] | Not appropriate. (Perspective on the topic: sugar, total, added, or free?) |
| Micha et al. 2018 [39] | Not appropriate. (assesses dietary habits, not including studies on CF). |
| Naude et al. 2018 [40] | Not appropriate. (age 2-18 years) |
| Obbagy et al. 2019 [41] | Not appropriate. (primary studies quantify meat intake, not protein) |
| Ojha et al. 2020 [42] | Not appropriate. (Evaluates the efficiency of health education to caregivers) |
| Park et al. 2019 [43] | Not appropriate. (LIC) |
| Pieścik-Lech et al. 2017 [44] | Not appropriate. (CF studies are not included) |
| Pimpin et al. 2019 [45] | Not appropriate. (premature children, low weight or malnourished) |
| Pitangueira et al. 2015 [46] | Low methodological quality. Not appropriate. (CF not evaluated) |
| Redsell et al. 2015 [47] | Not appropriate. (not evaluate the number of nutrients) |

| | |
|---|---|
| Reilly et al. 2017 [48] | Not appropriate. (SR critical review) |
| Roberts et al. 2017 [49] | Not appropriate. (children aged > 2 years ) |
| Roberts et al. 2017 [50] | Not appropriate. (children aged > 2 years, assesses fiscal measures ) |
| Shulkin et al. 2018 [51] | Data from CF studies combined with data from supplementation studies at birth. |
| Smithers et al. 2011 [52] | Not appropriate. (Assesses dietary indices. Not specifically on CF) |
| Stanhope et al. 2017 [53] | Low methodological quality. (Narrative review). Not appropriate. (CF studies are not included) |
| Stewart et al. 2020 [54] | Not appropriate. (LIC children) |
| Tang et al. 2019 [55] | Low methodological quality. (Narrative review). Not appropriate. (primary studies quantify meat intake, not protein intake) |
| Ter Borg et al. 2019 [56] | Not appropriate. (not PICO adherent) |
| Vargas-Garcia et al. 2017 [57] | Not appropriate. (not PICO adherent) |
| Wang et al. 2013 – AHRQ [58] | Not appropriate. (age population 2-18 years) |
| Zalewski et al. 2015 [59] | Low methodological quality. (SR of GL before 2015) |
| Zhou et al. 2014 [60] | Not appropriate. (CF not evaluated) |

**Tablea1.6. Appraisal of the Studies**

| | **Newcastle Quality Assessment Scale COHORT STUDIES** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Selection** | | | | **Comparability** | **Outcome** | | | |
| **Study** | **Representativeness of the exposed cohort** | **Selection of the non exposed cohort** | **Ascertainment of exposure** | **Demonstration that outcome of interest was not present at the start of the study** | **Comparability of cohorts based on the design or analysis** | **Assessment of outcome** | **Was follow-up long enough for outcomes to occur?** | **Adequacy of follow up of cohorts** | **Total** |
| Jen et al. 2019 [61] | 1a | 1a | 1b | 1a | 1a<br>1b | 1a | 1a | 1a | 9 |
| Nguyen et al. 2020 [62] | aa | 1a | 1b | 1a | 1a<br>1b | 1a | 1a | 1a | 9 |
| Voortman et al. 2016 [63] | 1a | 1a | 1b | 1a | 1a<br>1b | 1a | 1a | 1a | 9 |

**Table a1.7. Excluded studies with reasons for exclusion.**

| Excluded | Reason for exclusion |
|---|---|
| Au et al. 2018 [64] | Not appropriate (only descriptive) |
| Bailey et al. 2018 [65] | Not appropriate (usual intake estimated and primary food source for added sugars) |
| Beyerlein et al. 2017 [66] | Not appropriate (children at risk for DM1) |
| Breeze et al. 2018 [67] | Not appropriate (assesses trade policy intervention) |
| Campbell et al. 2016 [68] | Not appropriate (Evaluates different interventions. Single nutrients not evaluated) |
| Enö Persson et al. 2018 [69] | Not appropriate (No CF) |
| Gross et al. 2016 [70] | Not appropriate (No CF) |
| Gui et al. 2017 [71] | Not appropriate (No CF. conducted in China) |
| Ha et al. 2017 [72] | Not appropriate (for the outcomes considered) |
| Han et al. 2013 [73] | Not appropriate (for the outcomes considered. No CF) |
| Herran et al. 2018 [74] | Not appropriate (Inequalities. No CF.) |
| Hesketh et al. 2020 [75] | Not appropriate (Evaluates the effectiveness of a multilevel health education intervention to caregivers.) |
| Kostecka et al. 2020 [76] | Not appropriate (assesses factors inhibiting and facilitating the implementation of GL). |
| Lim et al. 2018 [77] | Not appropriate (only descriptive) |
| Morgen et al. 2018 [78] | Low methodological quality (high loss at follow-up, differences in baseline characteristics between study participants and those lost to follow-up.) |
| Mustila et al. 2018 [79] | Not appropriate (multilevel counseling intervention) |
| Nguyen et al. 2020 [80] | Not appropriate (dietetical intervention, nutrients not differentiated) |
| Nier et al. 2018 [81] | Not appropriate (only on obese children fructose consumption) |
| Niinikoski et al. 2012 [82] | Not quantify for carbohydrate intake in the CF period, but the whole duration of follow-up up to 9 years. |
| Okubo et al. 2015 [83] | Not appropriate (Does not assess individual nutrients but the overall Diet Quality Index (DQI)) |
| Pan et al. 2014 [84] | Low quality (Nutrients not quantified, high loss at follow-up). |
| Papanikolaou et al. 2018 [85] | Not appropriate (assesses nutrient patterns associated with both consumption/nonconsumption of eggs) |
| Pettigrew et al. 2015 [86] | Not appropriate (No CF) |
| Pigeot et al. 2016 [87] | Not appropriate (No CF. In German) |
| Pimpin et al. 2016 [88] | Low quality (High lost at follow up >50% and partial data) |
| Reifsnider et al. 2018 [89] | Not appropriate (No CF) |
| Rigo et al. 2018 [90] | Not appropriate (No CF) |
| Scully et al. 2017 [91] | Not appropriate (No CF, mothers' perception of commonly consumed pre-school drinks) |
| Sonneville et al. 2015 [92] | Low quality (Nutrients not quantified, high loss at follow-up) |
| Tang et al. 2014 [93] | Very short follow-up (from 5 to 9 mo of age) |
| Vard et al. 2019 [94] | Not appropriate (No CF) |
| Wasser et al. 2017 [95] | Not appropriate (multi-level complex intervention.) |
| Zuccotti et al. 2014 [96] | Not appropriate (only descriptive) |

## A1.a. RECOMMENDATIONS OF THE GLs, RESULTS OF THE SRs AND STUDIES

| | |
|---|---|
| - *Does an energy intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?*<br><br>- *Does a carbohydrate intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?*<br><br>- *Does a protein intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?*<br><br>- *Does a lipid intake above age-recommended levels from 6 to 24 months of age result in different short- and long-term nutritional and metabolic outcomes compared to an intake that meets recommended levels?* | **a.**<br>**P In the healthy infant, in the period 6-24 months,**<br>**I an energy intake above the recommended levels for age**<br>**C compared with an intake corresponding to recommended levels**<br>**O results in different short- and long-term nutritional and metabolic outcomes?**<br><br>**b.**<br>**P In the healthy infant, in the period 6-24 months,**<br>**I a carbohydrate intake above the recommended levels for age**<br>**C compared with an intake corresponding to recommended levels**<br>**O results in different short- and long-term nutritional and metabolic outcomes?**<br><br>**c.**<br>**P In the healthy infant, in the period 6-24 months,**<br>**I a protein intake above the recommended levels for age**<br>**C compared with an intake corresponding to recommended levels**<br>**O results in different short- and long-term nutritional and metabolic outcomes?**<br><br>**d**<br>**P In the healthy infant, in the period 6-24 months,**<br>**I a lipid intake above the recommended levels for age**<br>**C compared with an intake corresponding to recommended levels**<br>**O results in different short- and long-term nutritional and metabolic outcomes?** |

**Table a1.8. Clinical Guidelines and Guidance Documents Appraisal.**

| Guidelines and Clinical Guidance Documents | Recommendations | Grading |
|---|---|---|
| SIEDP-SIP 2018 [1] | Protein intake is suggested to be below 15% of daily energy in the first 2 years of life.<br><br>Reducing lipid intake in the first 2 years of life to percentages appropriate to those of adulthood is not recommended.<br><br>The use of sweet drinks in the first 2 years of life should be avoided. | Evidence level I, strength of recommendation B.<br>Ref. #349, 357-360<br><br>Evidence level II, strength of recommendation D.<br>Ref #361<br><br>Evidence level III, strength of recommendation A.<br>#362 |

**Table a1.9. Characteristics, Results, and Conclusions of the included SRs.**

| Systematic Reviews | Population and Purpose of SRs. | Results | Conclusions |
|---|---|---|---|
| Hörnell et al. 2013 [16] Bibliography closed February 2012 | The aim is to evaluate the effects of different levels of protein intake in infancy on health, in healthy full-term children living in northern European countries. | 37 studies included: 8 non-randomized controlled trials, 19 prospective cohort studies, 10 cross-sectional studies.<br><br>Study quality assessment based on AHRQ (Agency for Healthcare Research and Quality) criteria.<br><br>**A** Studies have an acceptably low level of bias and the results are considered valid.<br>**B** Studies may have some bias, but not enough to invalidate the results.<br>**C** Studies have a significant bias that may invalidate the results.<br><br>Studies adhering to PICOs<br><br>**Growth, BMI:**<br><br>*Cohort studies*<br><br>Gunnarsdottir et al. (3), graded B<br>Children in the highest quartile of protein intake (E%) at age 9-12 mo had a significantly higher BMI at 6 years compared to the lowest and second-lowest quartiles (17.8±2.4 vs 15.6±1.0 and 15.3±0.8 - P = 0.039 and P = 0.01, respectively).<br>Energy intake was not different between the groups.<br>Günther et al. (33), graded B,<br>Higher habitual protein intake between 12 and 24 mo was associated with a higher BMI-SDS at the time of AR in girls, but not in boys.<br>Günther et al. (34), graded A,<br>The relationship between different protein intakes at 6-24 mo and BMI and body fat percentage (% BF) at 7 years was evaluated using data from the DONALD study in Germany.<br>A sustained high protein intake at 12-18 and 24 mo was independently related to a higher mean BMI SDS and % BF at 7 years and a higher risk of having a BMI or % BF above the 75th percentile.<br>There was no association with protein intake at 6 mo.<br>Günther et al. (35), graded A<br>The age groups of 12 mo and 5-6 years were identified as critical periods in which higher intakes of total and animal, but not vegetable, protein were positively related to body fat at 7 years. E% animal protein at 12 mo was positively associated with BMI SDS at 7 years.<br><br>Hoppe et al. (36), graded B,<br>Danish 10-year-old children (n = 142 at 9 mo, n = 105 at 10 years) in relation to protein intake at 9 mo. | **Growth, BMI:** Convincing evidence (grade 1) that higher protein intake in infancy and early childhood is associated with greater growth and/or higher body mass index during childhood. |

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| | | Overall, 7.8% of boys and 7.5% of girls were overweight, none were obese. Protein intake (E%, g/day but not g/kg/day) at 9 mo was predictive of weight and height at 10 years.<br>Öhlund et al. (4), graded B<br>Protein intake in particular, but also total energy and carbohydrate intake at 17/18 mo and 4 years, were positively associated with BMI at 4 years.<br>Scaglioni et al. (38), graded B<br>The prevalence of overweight at age 5 was strongly associated with parental overweight (P=0.0001), and overweight children had a higher protein intake at age 1 than non-overweight children (22E% vs 20E%, P = 0.024).<br>*Cross-sectional*<br>No relevant studies.<br>**Adiposity rebound**<br>*Cohort studies*<br>Dorosty et al. (32), graded B<br>no evidence of an association between protein intake at 18 mo, or any other dietary variable, and the timing of AR.<br>Günther et al. (33), graded B,<br>no coherent relationship between habitual protein intake in early childhood and the timing of AR, but higher usual protein intake between 12 and 24 mo was associated with higher BMI-SDS in girls, but not in boys.<br>**Glucose/insulin**: no relevant studies.<br>**Hypertension:** no relevant studies. | |
| Pearce et al. 2013 [17]<br>Bibliography closed End June 2012 | Evaluate the evidence on the impact of different foods administered during the complementary feeding period on BMI or body composition in children aged 4-12 years.<br>Only include observational studies, evaluated with NOS, on healthy children.<br>Exposure: Nutrient intake in the CF period up to and including 12 mo.<br>Outcomes: BMI, BMI z-score, and body composition at 4-12 years, not self-reported.<br>Study data: 1959-2009. | 10 articles met the selection criteria, with numbers ranging from 90 to 881 participants.<br>4/10 examined the impact of macronutrient or energy intake in childhood and its effect on childhood BMI or % BF (body fat).<br>**BMI**<br>Gunnarsdottir et al.<br>Günther et al.<br>Günther et al.<br>Hoppe et al. | There is some evidence that high energy intake in early infancy may lead to higher BMI and BF% during infancy, but this is data from a single study on formula composition (Ong et al. 23): not conclusive.<br>There is limited evidence on protein intake at 4-12 mo. High protein intake (% energy) at 12 mo of age and high animal and LV protein intake (% energy) at 12 mo may result in higher BMI and % BF during infancy. |
| Ferrè et al. 2021 [18]<br>Bibliography closed | To evaluate the effects of protein intake during the second year of life on weight and | Included 14 references from 9 studies | There is moderate evidence for an association between protein intake during the second year |

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| 30 May 2020 | fat mass gain and the subsequent risk of developing obesity later in childhood.<br><br>Including all studies with this aim, research closure 30.05.2020.<br><br>Population: healthy children, without growth problems, born at term, living in developed countries.<br><br>Exposure: protein intake during the second year of life.<br><br>Outcomes:<br><br>% body fat (% BF), body fat mass (FM) (kilograms) or body fat mass index (BMI) (kilograms/meter2),<br><br>body mass index (BMI) (kilograms/meter2 or z score) and<br><br>Risk of excess weight (risks of overweight and obesity) (RR, OR, or frequency<br><br>Secondary outcomes: growth rate, adiposity rebound. | **<u>Growth</u>**<br><br>Outcome not considered<br><br>**<u>Risk of obesity/overweight</u>**<br><br>Günther et al. (32).<br><br>The DONALD cohort supported the hypothesis of an increased risk of being overweight by having a persistently higher protein intake during the first two years of life (compared to only the first year of life). The results of the Gemini cohort did not support this hypothesis. The contradictory results could be due to several factors: the Gemini cohort was performed on twins and included preterm infants, thus possibly low birth weight infants with different growth patterns than the target population.<br><br>Furthermore, in the Gemini cohort, protein intake was assessed at a mean age of 21 mo, within a range of 17-34 mo.<br><br>Therefore, some of the intake data were obtained during the third year of life instead of the second. In addition, these results were obtained at a single point in time, which could not be representative of what happened during the second year, which could hinder the extrapolation of conclusions.<br><br>**<u>Adiposity rebound</u>**<br><br>Several studies have investigated possible mechanisms supporting the association between the extent of protein intake in the 2nd year of life and early adiposity rebound.<br>Rolland-Cachera et al. (31)<br>Protein intake (% energy vs. protein) at 2 years of age was the start of AR ($r = 0.2$, $p = 0.02$).<br>Children with early AR (before 4 years of age) had a higher protein intake at 2 years of age than those children showing late AR (after 8 years of age) (16.6 2.1% vs. 14.9 2.1%, $p < 0.01$).<br><br>Dorosty et al (44)<br>Günther et al (45)<br><br>The available evidence consistently supports the hypothesis that protein intake during the second year of life may lead to an earlier onset of AR.<br>The DONALD and Gemini cohorts provided contradictory results. This could be due to several reasons: on the one hand, children in the Gemini cohort had a higher proportion of preterm infants and low birth weight infants who might have a different growth pattern and/or maturation rate.<br>The predicted AR as a consequence of increased protein intake during the second year of life was not confirmed by Dorosty et al. [44] in the ALSPAC cohort.<br>Another possible confounding factor could be the speed of sexual development.<br><br>**<u>BMI</u>** | of life and increased body fat at 2 years. The evidence supporting an increased risk of overweight or obesity at later ages was inconclusive.<br><br>Overall, the quality of evidence on effects on overweight and obesity is limited and based on observational cohort studies.<br><br>Definitive conclusions can be derived from randomized controlled intervention studies. In the Cochrane database of registered clinical trials, there is one ongoing RCT with more than 1600 children already recruited as infants (TOMI study, <u>formula, sponsored</u> by Nestlé, Clinical trials.gov, NTC02907502). |

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| | | Rolland-Cachera et al. (31)<br>Newborns in the highest quintile of protein intake at 2 years of age showed earlier AR and a greater increase in BMI after 4 years, showing a higher BMI at 8 years of age.<br><br>Günther et al. (32)<br>Günther et al. (33)<br><br>Karaolis-Danckert et al. (34)<br>Higher sustained protein intake during the first 2 years of life modulated the BMI z-score at 2 years (= 0.36 ±0.13, p = 0.005 for the HH group compared to the HL) but did not affect the longitudinal change in BMI z-score between 2 and 5 years.<br><br>Children with rapid growth (0-2 years) showed a higher BMI z-score (-0.016± 0.99 versus 0.41 ±0.90, p < 0.001) at 5 years. However, the distribution of fast-growing children was similar between the groups of high and low protein intakes during the first 2 years (H-H vs. H-L).<br>(high loss at follow-up).<br><br>Cowin et al. (35)<br>Protein intake at 18 mo of age was not associated with changes in BMI z score at 31 mo but was associated with height (r = 0.176)<br>(high loss at follow-up)<br>Garden et al. 2011 (36)<br>Protein intake (g/day) at 18 mo of age was associated with a higher BMI z-score at 8 years of age (10 g/day protein intake was associated with an increased BMI z-score in BMI 0.47 SD. Meat intake was also associated with BMI z-score and waist circumference at 8 years.<br>(high loss at follow-up)<br>Garden et al. 2012 (37)<br>Different sex-specific BMI growth trajectories (normal, persistent early increase, and late increase) up to the age of 11.5 years were not associated with different protein intakes at 18 mo of age.<br>(high loss at follow-up)<br><br>Öhlund et al. (38)<br><br>Pimpin et al. (39)<br>Protein intake at 21 ±1.2 mo above 16.3% of total energy intake was associated with greater weight gain up to 5 years of age (= 0.330 kg, CI 95% 0.182-0.478 for highest vs. lowest quintile).<br>(The cohort included 43.5% preterm infants).<br><br>Morgen et al. (41) | |

| | | | |
|---|---|---|---|
| | | Protein intake from dairy products at 18 mo (for 5 g/day) increased the BMI z-score at 7 years (: 0.012, 95% CI: 0.003,0.021; p = 0.007)<br>Protein intake from meat and fish at 18 mo (by 2 g/day) increased BMI = 0.010 SD (95% CI: 0.004, 0.017; p = 0.003) or 0.013 (95% CI: 0.005, 0.020; p = 0.002) at 7 and 11 years, respectively.<br>(High drop-out rate (72%). Very little information on dietary registration.<br>Anthropometric data at 7 and 11 years reported by parents.)<br><br>The available evidence from the study cohorts suggests a possible association between protein intake during the second year of life and an increase in BMI z score thereafter. There was little evidence of this association due to the heterogeneity and considerable bias observed in the cohort studies, especially for ref.31,32,36,38,39,41. | |

**Table a1.10. Characteristics and Results of Included Studies.**

| Study | Study Design | Population | Test | Primary Outcome | Secondary Outcomes | Follow-up | Results |
|---|---|---|---|---|---|---|---|
| Nguyen et al. 2020 [62] | Cohort prospective | 3629 children from *Generation R Study*, a population-based cohort study from fetal life onwards in Rotterdam, The Netherlands. | Dietary intake in early childhood was assessed using a validated semi-quantitative food frequency questionnaire (FFQ) at the age of 12.9 (12.7-19.9) mo of the child.<br>Nutrient intake was calculated using the Dutch food composition table.<br>Validation of the FFQ about three calls, 24 hours apart, in a representative sample of 32 Dutch children, showed a moderate to good ranking for nutrient intake.<br>The children's dietary intake was then assessed at the age of 8 years and the dietary quality score, a measure of adherence to age-specific dietary guidelines, was calculated. | To evaluate the association of carbohydrate intake at 12 mo with metabolic parameters such as BMI, *fat mass index* (FMI) (fat mass(kg)/height(m)2, and *fat-free mass index* (FFMI) (fat-free mass(kg)/height(m)2 at 10 years.<br>(FFMI) fat-free mass(kg)/height(m)2 at 10 years. | To evaluate the association between carbohydrate intake at 12 mo, examining the role of different macronutrient substitutions, on triglyceride, total cholesterol, HDL-cholesterol, and insulin concentrations. | 10 years | The total carbohydrate intake at the age of 12.9 mo was 191.7 ± 58.9 g/day, which corresponds to 58.3 ± 6.1 E%.<br>A (cm) (n = 2984 =82%) 118.2 ± 5.2<br>P (kg) (n = 2984) 21.8 (20.2 - 24.0)<br>Body mass index (kg/m2) (n = 2984) 15.7 (15.10-16.7)<br>The results do not support that carbohydrate intake or its subtypes in early childhood is associated with different BMI/FFMI, but suggest that higher carbohydrate intake in childhood, particularly monosaccharides and disaccharides, may be associated with higher triglyceride levels and lower HDL. |
| Voortman et al. 2016 [63] | Cohort prospective | 2911/3629 (80%) children from *Generation R Study*, a population-based cohort study from fetal life onwards in Rotterdam, The Netherlands. | See **Nguyen 2020**<br><br>To assess the effect of proteins independently of their energy content, the dietary intake of proteins and other macronutrients was adjusted for total energy intake using the nutrient residue method. | To study the associations between protein intake at age 1 and BMI, fat mass index (FMI), and lean mass index (FFMI) at age 6. | Assess these associations in a subgroup of children for protein intake at age 2 years; examine whether the associations differed by gender, ethnicity, children's genetic | 6 years | At the age of 1 year, children's mean (± s.d.) daily protein intake was 41.2 g (± 12.9), which corresponds to 12.9% of their total energy intake.<br>Although this amount is higher than recommended for this age group, it is similar to the protein intake observed in other Western pediatric populations. |

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| | | | | | risk score for BMI, birth weight or catch-up growth, or by protein source. | | The mean animal protein intake was 8.1 E% (± 2.4) and the mean vegetable protein intake was 4.7 E% (± 1.4). Boys had a higher absolute protein and energy intake than girls, but the relative protein intake was the same for boys and girls (12.9 E%).<br><br><u>Macronutrient composition of the diet</u><br>Total protein intake, mean(E%) 12.9 (2.4)<br>Total fat intake (E%) 28.6 (5.6)<br>Total carbohydrate intake (E%) 58.4 (6.0)<br><br><u>Child characteristics at the 6-year visit - mean (SD)</u><br><br>A (cm) = 118.2 (5.2)<br>P (kg) = 22.4 (3.4)<br>Body mass index (kgm-2) = 16.0 (1.6)<br>Fat mass index (kgm-2) = 3.8 (1.2)<br>Fat-free mass index (kgm-2) = 11.9 (0.9) |
| Jen et al. 2019 [61] | Cohort prospective | 573/3629 (98%) children from *Generation R Study*, a population-based cohort study from fetal life onwards in Rotterdam, The Netherlands. | See **Voortman 2016**<br>Children's dietary intake was updated to their average age of 8.0 years | Evaluate longitudinal associations of total protein intake and protein from different sources in childhood with growth and detailed measures of body composition up to the age of 10 years. | To examine whether these associations were independent of protein intake and general dietary quality in late childhood. | 10 years | The mean ± SD total protein intake at the age of 1 year was 42.1 ± 13.4 g/day, corresponding to approximately 4.1 g/kg/bodyweight based on the study population averages. The mean animal protein intake was 26.5 ± 10.6 g/day and the mean vegetable protein intake was 15.1 ± 5.9 g/day. The proportion of total energy intake derived from protein intake increased from 12.9 ± 2.4% at 1 year to 16.5 ± 2.2% at 8 years.<br><br><u>Child characteristics at the 10-year growth assessment</u><br>Age (years) = 9.7 ± 0.3<br>Height (cm) = 141.6 ± 6.5<br>Weight (kg) = 34.7 ± 6.7<br>BMI (kg / m2) = 17.2 ± 2.5<br><br>In this large prospective population-based cohort study, higher protein intake, mainly from animal food sources, in childhood was persistently associated with adiposity until the age of 10 years. |

| | | | | | | | |
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| | | | | | | | These associations were independent of protein intake or diet quality in late childhood, suggesting that an excessively high protein diet in childhood may have a lasting impact on adiposity risk. A more appropriate protein intake during this critical period of development may help in the early prevention of adiposity in childhood. |

## A1.a. EVIDENCE PROFILE GRADE

**Table a1.11. Amount of carbohydrates. Risk of overweight/obesity.**

**[carbohydrate intake above age-recommended levels, 6-24 months] compared to [intake that meets recommended levels] in order to [different short- and long-term nutritional and metabolic outcomes]**

**Patient or population:** [healthy infant, 6-24 months of age]

**Setting:** outpatient

**Intervention:** [carbohydrate intake above the recommended levels for the age group]

**Comparator:** [adequate intake]

| Certainty assessment | | | | | | | Impact | Certainty of evidence | Importance |
|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study Design | Distortion risk | Lack of reproducibility of results | Lack of generalisability | Inaccuracy | Further considerations | | | |
| **Risk of overweight/obesity at 6 patient-years (assessed by: BMI)** | | | | | | | | | |
| 2 [1,2] | Observational studies | Serious [a] | Not relevant | Not relevant | Not relevant | All plausible residual confounders could reduce the demonstrated effect | Inconsistency of results, conflicting data [a] | ⨁⨁◯◯ LOW | Important. |

**CI:** Confidence interval

**Explanations**

a. Inconsistency of results: Pan et al. document a higher risk of obesity at 6 years of age (17.0% vs 8.6%), in Nguyen et al. results do not support that intake of carbohydrates or its subtypes in early childhood is associated with different BMI.

**References**

1. Pan et al. 2014 [84]

2. Nguyen et al. 2020 [62]

**Table a1.12. Amount of protein. Risk of overweight/obesity.**

**[protein intake above age-recommended levels, 6-24 months] compared to [intake that meets recommended levels] in order to [different short- and long-term nutritional and metabolic outcomes]**

**Patient or population:** [healthy infant, 6-24 months of age]

**Setting:** outpatient

**Intervention:** [protein intake above the recommended levels for the age group]

**Comparator:** [adequate intake]

| Certainty assessment | | | | | | | Impact | Certainty of evidence | Importance |
|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study Design | Distortion risk | Lack of reproducibility of results | Lack of generalisability | Inaccuracy | Further considerations | | | |
| **Risk of overweight/obesity (follow-up: average 6-10 patient-years; assessed by: BMI)** | | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 16 [1,2,3,4,5,a] | Observational studies | Serious [b,c] | Not relevant | Not relevant | Not relevant | all residual plausible confounders would suggest a spurious effect, whereas no effect was observed | There is evidence of an association between protein intake during the second year of life and increased BMI at 6-10 years. However, the evidence supporting an increased risk of overweight or obesity at later ages is inconclusive, both because of its limited quality and because the results are conflicting.[b,c] | ⊕⊕◯◯ LOW | Important. |

**Early adiposity rebound (follow up: interval 4 to 8 patient-years; evaluated with: % of children with adiposity rebound before the age of 4 years)**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 3 [6] | Observational studies | Serious [b] | Not relevant | Not relevant | Not relevant | all residual plausible confounders would suggest a spurious effect, whereas no effect was observed | Conflicting results: in 2 studies (Dorosty et al. and Günther et al.) there was no association between protein intake at 18 mo or any other dietary variable, and the timing of RA. in 1 study (Rolland-Cachera et al.) children with early RA (before 4 years of age) had a higher protein intake at 2 years of age than those children showing late RA (after 8 years of age) (16.6 ± 2.1% vs 14.9 ± 2.1%, $p<0.01$). | ⊕⊕◯◯ LOW | Important |

**CI:** Confidence interval

**Explanation**

a. Further References

- Pearce et al. 2013 [17]
- Patro-Golab et al. 2016 [19]
- Weng 2012 et al. [58]

b. Inconsistency: conflicting results.

c. Low methodological quality due to: 1. high loss to follow-up, often >50%, 2. uncertain quantification of the exposure factor (amount of nutrient intake per period of supplementary feeding), 3. uncertain detection of outcomes (self-reported P and A), 4. failure to assess important confounding factors, particularly total energy intake after 2 years of age, percentage of a nutrient considered concerning total energy intake, physical activity.

**References**

1. Foterek K, et al. 2016. [97]

2. Voortman et al. 2016 [63]

3. Jen et al. 2019 [61]

4. Gunnarsdottir,et,al.,(3),Günther,et,al.,2006, (33),Günther,et,al.,2007,(34),Hoppe,et,al.,(36),Öhlund,et,al.,(4),Scaglioni,et,al.,(38)

In Hörnell et al. 2013 [16]

5. Garden,,et,al.,2011,(36),,Garden,,et,al.,2012,(37),,Cowin,,et,al.,(35),,Rolland-Cachera,et,al. (31), Karaolis-Danckert,,et,al.,(34), Pimpin,,et,al.(39), Morgen,et,al. (41).

In Ferrè et al. 2021 [18]

6. Dorosty,et,al,(44),Günther,et,al,(45),Rolland-Cachera,et,al.. (31)

In Ferrè et al. 2021 [18]

**Table a1.13. Amount of lipid. Risk of overweight/obesity.**

**[lipid intake above age-recommended levels, 6-24 months] compared to [intake that meets recommended levels] in order to [different short- and long-term nutritional and metabolic outcomes]**

**Patient or population:** [healthy infant, 6-24 months of age]

**Setting:** outpatient

**Intervention:** [lipid intake above the recommended levels for the age group]

**Comparator:** [adequate intake]

| Certainty assessment | | | | | | | Impact | Certainty of evidence | Importance |
|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study Design | Distortion risk | Lack of reproducibility of results | Lack of generalisability | Inaccuracy | Further considerations | | | |
| **Long-term risk of overweight/obesity (follow-up: average 14 years; assessed by: BMI)** | | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 [1] | Randomized Studies | Very serious [a] | Not relevant | Not relevant | Not relevant | all residual plausible confounders would suggest a spurious effect, whereas no effect was observed | the STRIP study, on 1062 infants from 7 mo of age, at high cardiovascular risk, who were fed a low lipid diet (30-35% of calories/day, with a good saturated/unsaturated fat ratio). At 14 years there were no differences in BMI between the diet group and the control group without lipid restriction. [b] | ⊕⊕⊕◯ Moderate | Important |

**CI:** Confidence interval

**Explanations**

a. Exposure is not relevant to PICO on CF: it does not quantify intake during the period of CF, but throughout follow-up up to 9 years.

b. the STRIP study, on 1062 infants from 7 mo of age, at high cardiovascular risk, on a low lipid diet (30-35% of calories/day, with a good saturated/unsaturated fat ratio). At 14 years there were no differences in BMI between the diet group and the control group without lipid restriction.

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# Recommendation 8

**A1.b. Salt and hypertension**

***- Can excessive salt intake during the CF period lead to hypertension later in life?***

**P.** In a healthy infant aged 6-24 months
**I** lower or higher intakes of salt with the complementary diet
**C.** compared to the recommended intake
**O.** leads to a different risk of hypertension at later ages

**Systematic reviews research**

**PubMed**

("Sodium Chloride"[Mesh] OR "salt"[All Fields]) OR "Sodium, Dietary"[Mesh] OR "Sodium Chloride, Dietary"[Mesh]) AND "Hypertension"[Mesh] AND ((Meta-Analysis[ptyp] OR systematic[sb]) AND ("*2009/10/16"[PDat] : "2021/06/25*"[PDat]) AND "humans"[MeSH Terms] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms])

**EMBASE**

('sodium chloride'/exp OR 'salt intake'/exp) AND 'hypertension'/exp AND [2017-2021]/py AND ('meta analysis'/de OR 'systematic review'/de) AND ([child]/lim OR [infant]/lim OR [young adult]/lim)

**COCHRANE**

*hypertension* AND *sodium chloride* in Title Abstract Keyword - with Cochrane Library publication date Between Jun 2009 and Mar 2021, in Cochrane Reviews (Word variations have been searched)

**Studies Research**

**PubMed**

#1

(("Sodium Chloride"[Mesh] OR "salt"[All Fields]) OR "Sodium, Dietary"[Mesh] OR "Sodium Chloride, Dietary"[Mesh]) AND "Hypertension"[Mesh] AND ((Clinical Trial[ptyp] OR Observational Study[ptyp] OR Pragmatic Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp]) AND ("2017/03/01"[PDAT] : "2019/03/15"[PDAT]) AND "humans"[MeSH Terms] AND ("infant"[MeSH Terms] OR "child"[MeSH Terms] OR "adolescent"[MeSH Terms]))

#2

(("Sodium Chloride"[Mesh] OR "Sodium, Dietary"[Mesh] OR "Sodium Chloride, Dietary"[Mesh]) OR "salt"[All Fields]) AND "Hypertension"[Mesh] AND ("Infant Nutritional Physiological Phenomena"[Mesh] OR "Weaning"[Mesh]))

**EMBASE**

('sodium chloride'/exp OR 'salt intake'/exp) AND 'hypertension'/exp AND [2009-2021]/py AND ('case control study'/de OR 'cohort analysis'/de OR 'controlled study'/de OR 'cross sectional study'/de OR 'intervention study'/de OR 'major clinical study'/de OR 'observational study'/de OR 'prospective study'/de OR 'randomized controlled trial'/de) AND ([child]/lim OR [infant]/lim OR [young adult]/lim)

**COCHRANE**

*hypertension AND sodium chloride* in Title Abstract Keyword - in Cochrane Reviews, Trials with 'Child Health' in Cochrane Groups (Word variations have been searched) Cochrane Library publication date from Mar 2017 to Mar 2021in Trials with Child Health in Cochrane Groups (Word variations have been searched)

**Figure a1.4. Guidelines search flow diagram (from General hypertension)**

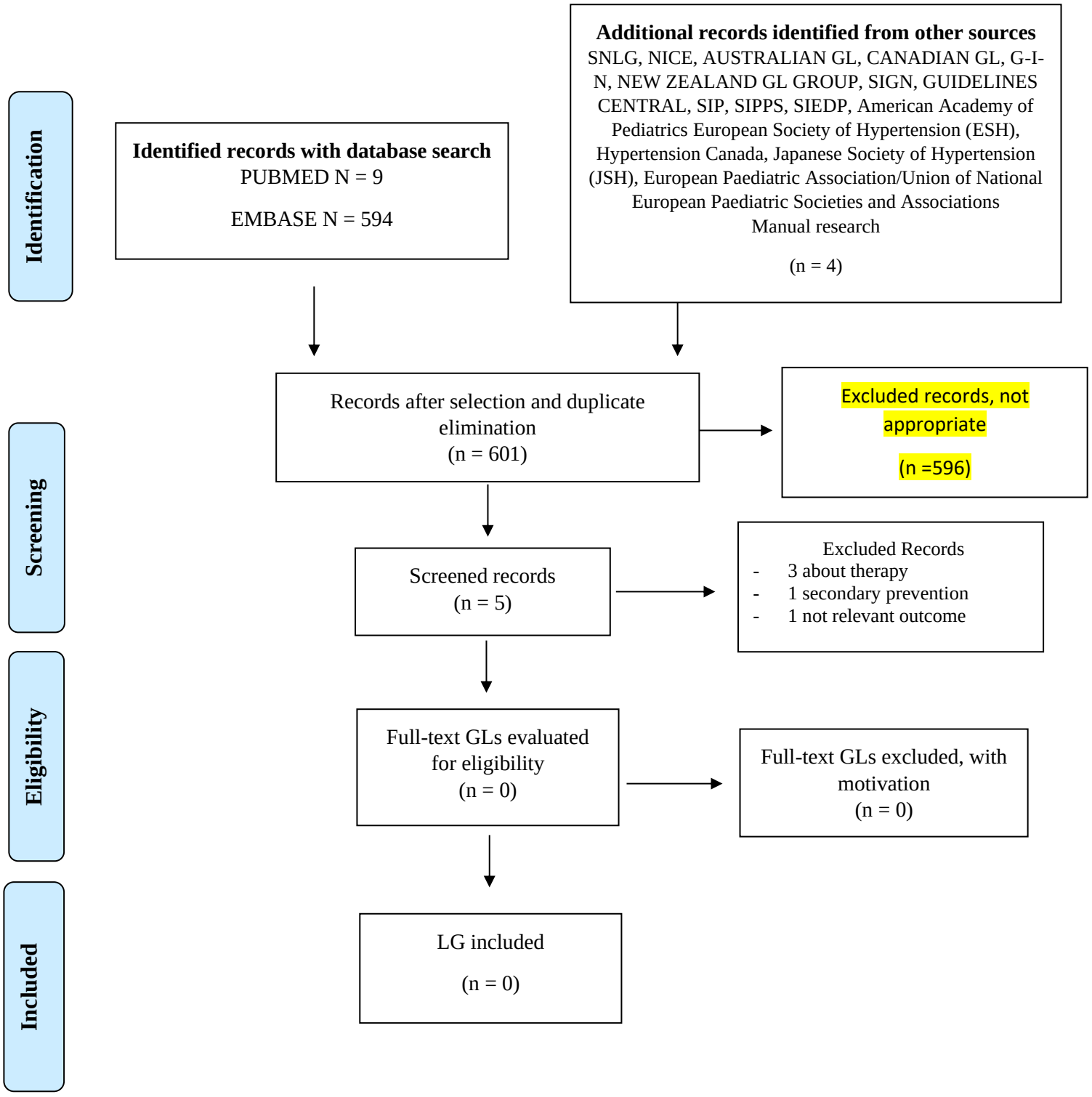


**Figure a1.5. SRs search flow diagram**

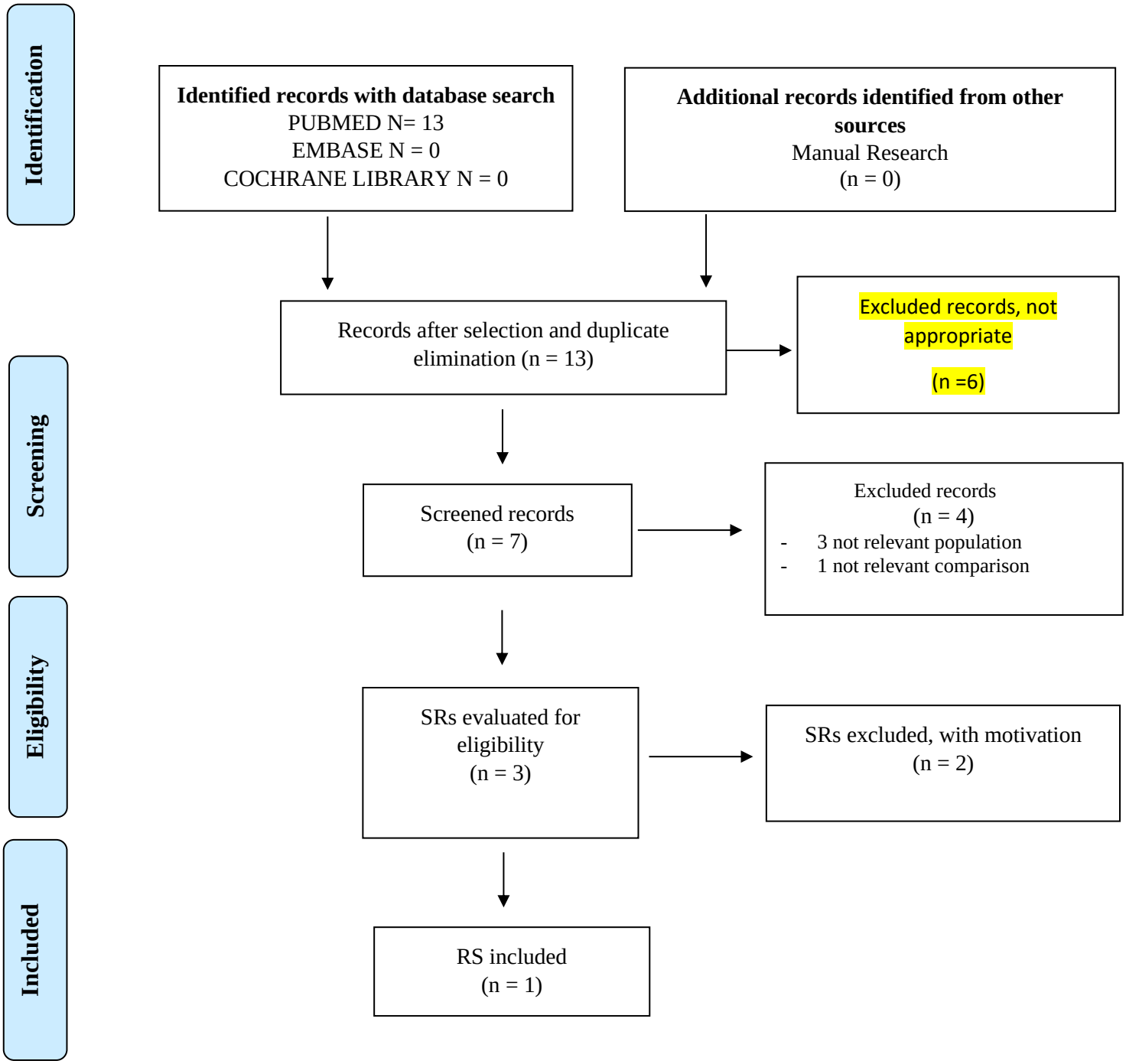
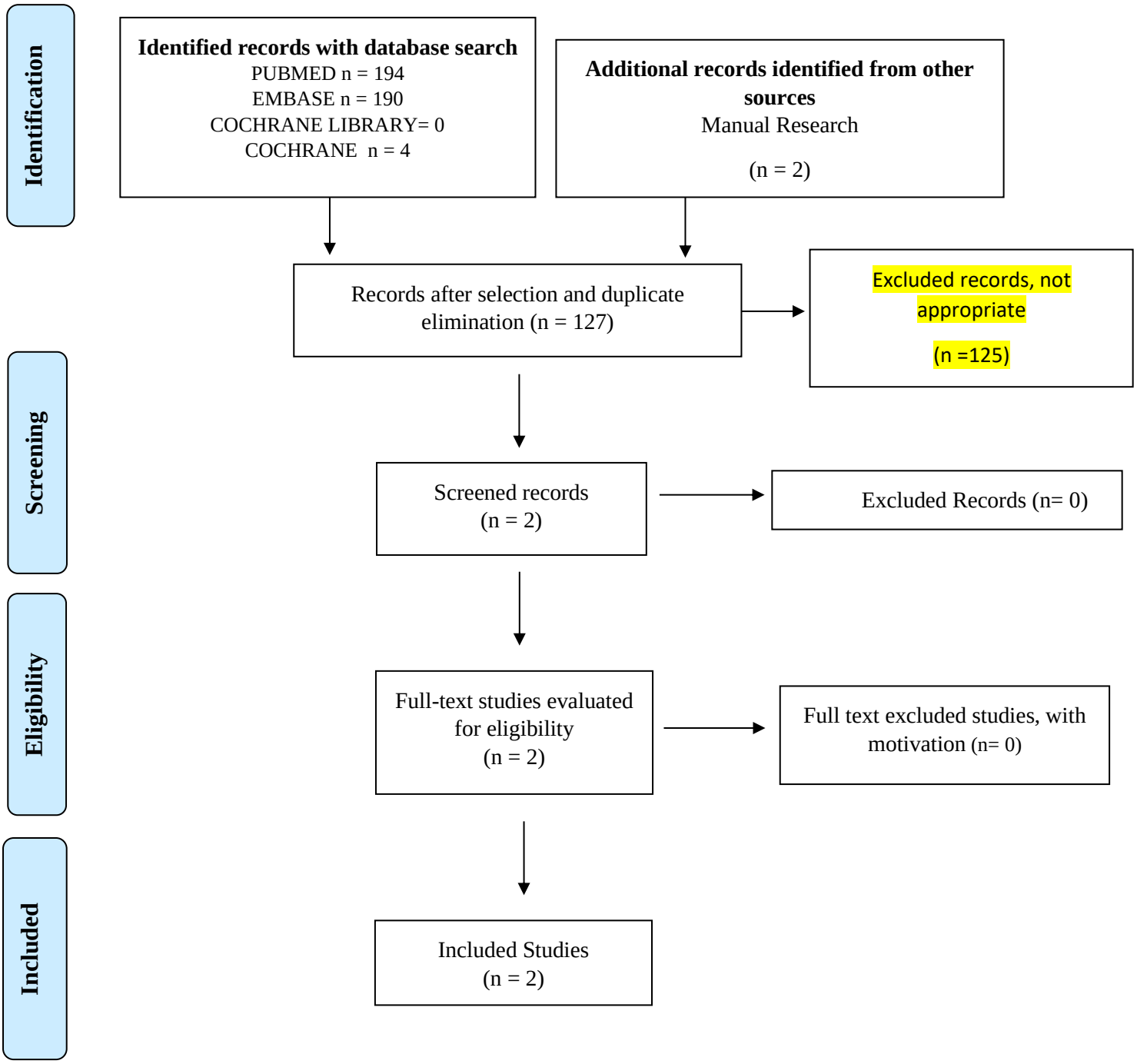


**Figure a1.6. Studies search flow diagram**.



## A1.b. METHODOLOGICAL EVALUATION

**Appraisal of the Clinical Guidelines and Documents**

None included

**Table a1.14. Appraisal of the Systematic Reviews.**

| **AMSTAR 2** | Leyvraz et al. 2018 [1] |
|---|---|
| **1. Did the research questions and inclusion criteria for the review include the components of PICO?**<br>**(Yes/No)** | No |
| **2. Did the report of the review contain an explicit statement that the review methods were established before the conduct of the review and did the report justify any significant deviations from the protocol?**<br>**(Yes/Partial Yes/No)** | Yes |
| **3. Did the review authors explain their selection of the study designs for inclusion in the review?**<br>**(Yes/No)** | Yes |
| **4. Did the review authors use a comprehensive literature search strategy?**<br>**(Yes/Partial Yes/No)** | Yes |
| **5. Did the review authors perform study selection in duplicate?**<br>**(Yes/No)** | Yes |
| **6. Did the review authors perform data extraction in duplicate?**<br>**(Yes/No)** | Yes |
| **7. Did the review authors provide a list of excluded studies and justify the exclusions?**<br>**(Yes/Partial Yes/No)** | No |
| **8. Did the review authors describe the included studies in adequate detail?**<br>**(Yes/Partial Yes/No)** | Partial Yes |
| **9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?**<br>**(Yes/Partial Yes/No/Includes only NRSI-RCT)** | Yes |

| | |
|---|---|
| | Yes |
| **10. Did the review authors report on the sources of funding for the studies included in the review?**<br>**(Yes/No)** | No |
| **11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?**<br>**(Yes / No / No meta-analysis conducted)** | Yes |
| **12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?**<br>**(Yes / No / No meta-analysis conducted)** | Yes |
| **13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?**<br>**(Yes/No)** | Yes |
| **14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?**<br>**(Yes/No)** | Yes |
| **15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?**<br>**(Yes / No / No meta-analysis conducted)** | Yes |
| **16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?**<br>**(Yes/No)** | Yes |
| **OVERALL EVALUATION** | **Good Quality** |

**Table a1.15. SRs excluded with motivation.**

| SRs excluded | Reason for exclusion |
|---|---|

| | |
|---|---|
| Strazzullo et al. 2012 [2] | Includes only 2 pediatric studies, but on infants and with follow-up less than the first 6 months of life (Hofman 1983 and Pomeranz 2002; also contained in the included RS of Leyvraz 2018). |
| Zalewski et al. 2017 [3] | Review of recommendations from the previous RS. |

**Table a1.16. Appraisal of the Studies.**

| | **Newcastle Quality Assessment Scale CROSS-SECTIONAL STUDIES** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Selection** | | | | **Comparability** | **Outcome** | | |
| **Study** | **Representativeness of the sample** | **Sample size:** | **Non-respondents** | **Ascertainment of the exposure (max 2)** | **Comparability between groups, confounders are controlled (Maximum 2 stars)** | **Outcome evaluation (max 2)** | **Statistical test** | **Total** |
| Lakatos et al. 2015 [4] | 0 c | 0b | 1a | 1a | 1a<br>1b | 2a | 1a | **7** |

**Figure 1.7 Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies** [5]

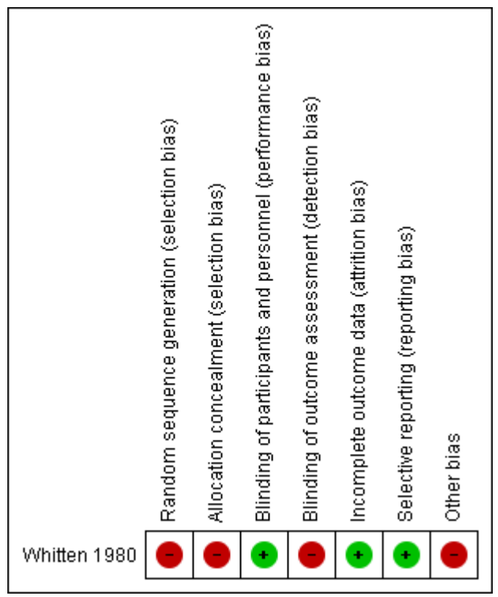



**Table a1.17. Excluded studies with motivation.**

| **Excluded studies.** | **Reason for exclusion** |
|---|---|
| Schachter et al. 1979 (cohort perspective) [6] | A cohort followed only up to 6 months |
| Pomeranz et al. 2002 (RCT) [7] | Infants in the first 6 months of life<br>Comparison of low-sodium and high-sodium formula |
| Hofman et al. 1983 (RCT) [8] | Infants in the first 6 months of life<br>Comparison of low-sodium formula and normal-sodium formula |
| Dominguez Cancino et al. 2017 (cross-sectional) [9] | Prevalence study >15 years of age |
| Chmielewski et al. 2018 (cross-sectional; Survey) [10] | Study on subjects >12 years of age |

## A1.b. RECOMMENDATIONS OF THE GLs, RESULTS OF THE SRs AND STUDIES

| | |
|---|---|
| ***Can excessive salt intake during the Complementary Feeding period lead to hypertension later in life?*** | **P.** In a healthy infant aged 6-24 months<br>**I** lower or higher intakes of salt with the complementary diet<br>**C.** compared to the recommended intake<br>**O.** leads to a different risk of hypertension at later ages |

**Table a1.18. Characteristics, Results, and Conclusions of SRs**

| Systematic Review | Population and purpose of the SR | Results | Conclusions |
|---|---|---|---|
| Leyvraz et al. 2018 [1]<br>Bibliography closed March 2017<br><br>RS of RCTs and observational studies (only 6 studies with subjects < 2 years old) | Children or adolescents (0-18 years) without selection for sex, initial weight, and baseline blood pressure level. Studies involving children and adults were included only if data for children could be extracted separately.<br><br>Primary objective: to demonstrate whether there is an association between sodium intake and blood pressure in children and adolescents.<br><br>Secondary objective: to assess whether this association differs according to age and body weight. | A meta-analysis of intervention studies (11 papers, after elimination of outliers) showed an increase in systolic blood pressure at the end of follow-up of 0.6 mmHg (IC95% 0.5-08) and diastolic blood pressure of 1.2 mmHg (IC95% 0.4-1.9).<br><br>Differences, as assessed by subgroup meta-analysis of regression coefficients, were greatest in overweight children, in those with lower potassium intakes, and, for systolic blood pressure, in children under one year of age (but with excessively large IC95%) and preadolescents and adolescents. | Experimental and observational studies with sodium intake and high-quality blood pressure measurement methods consistently showed that sodium intake was associated with increased systolic and diastolic blood pressure. The association between sodium intake and blood pressure tended to be stronger among overweight children and children with a low potassium intake. Exploratory dose-response gradient analysis showed an almost linear increase in systolic and diastolic blood pressure within the usual range of daily sodium intake. |

**Table a1.19. Characteristics and Results of Included Studies.**

| Study | Study Design | Population | Test | Primary Outcome | Secondary Outcomes | Follow-up | Results |
|---|---|---|---|---|---|---|---|
| Whitten et al. 1980 [5] | In parallel groups, controlled | 27 healthy infants enrolled at 3 months of age.<br>One group with controlled Na+ intake of 2 mEq/100 Kcal, one group 9 mEq/100 Kcal | One group with controlled Na+ intake of 2 mEq/100 Kcal, one group 9 mEq/100 Kcal | Blood pressure at 4 and 8 months | Blood pressure at 8 years of age | 5 months (last measured at 8 months of age) | Non-significant differences in systolic and diastolic pressures at all ages. |
| Lakatos et al. 2015 [4] | Cross-sectional | N = 200<br><br>Age 1-18 years (7 under 3 years) | Na+ and K+ intakes (from urinary excretion determination/24 hours) | Measurement of Sodium and Potassium intakes<br>Relationships between Sodium and Potassium Intake and Hypertension, with adjustments for age, sex, and BMI | / | / | The correlation between dietary salt intake and systolic blood pressure was not significant after logistic regression analysis. |

## A1.b. EVIDENCE PROFILE GRADE

**Table a1.20. Quantity of salt. Risk of Hypertension.**

**[higher salt intake with CF, in a healthy infant aged 6-24 months] than [recommended intake] for [leads to a different risk of hypertension at later ages].**

**Patient or population**: In a healthy infant aged 6-24 months

**Setting**: Outpatient

**Intervention**: [increased salt intake with Supplementary Feeding ].

**Comparator**: [recommended intake]

| Certainty assessment | | | | | | | Impact | Certainty of evidence | Importance |
|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study Design | Distortion risk | Lack of reproducibility of results | Lack of generalisability | Inaccuracy | Further considerations | | | |

**Blood pressure (exposure time: interval 5 months to 8 years; assessed with: mm Hg).**

| Certainty assessment | | | | | | | | Impact | Certainty of evidence | Importance |
|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study Design | Distortion risk | Lack of reproducibility of results | Lack of generalisability | Inaccuracy | Further considerations | | | | |
| 2 [1,2] | Observational studies [a] | Serious [a] | Not relevant | Not relevant | Not relevant | All plausible residual confounders could reduce the demonstrated effect | In both studies: non-significant differences in systolic and diastolic pressures, at all ages | | ⨁⨁◯◯ LOW | Important |

**CI:** Confidence interval

**Explanations**

a. Whitten 1980 non-randomized controlled clinical trial

**References**

1. Whitten et al. 1980 [5]
2. Lakatos et al. 2015 [4]

**Appendix 1b. References**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