More info on LIFECYCLE online:
lifecycle-project.eu

Report on review of interventions focused on lifestyle stressors, to improve life course health trajectories

Work package 9 - Task 9.2 - Subtask 9.2.4 - Deliverable 9.5

Authors:

Veit Grote, Anna Xu, Kathrin Gürlich

Organisation Name of Lead Contractor of this Deliverable:

Ludwig-Maximilians-Universität München (LMU)

Version 1.0

Delivery date: Month 48

Submission date 18.01.2021

Dissemination level:

Public

LIFECYCLE Project
Coordination and leadership:

Erasmus MC
Generation R (Na-2918)
PO box 2040
3000 CA Rotterdam
The Netherlands

Phone: +31 (0)10 704 3405
Email: lifecycle@erasmusmc.nl
Web: lifecycle-project.eu

This project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733206 (LifeCycle).

Table of Contents

1. Objective of Subtask 9.2.4

The objective of Task 9.2 was to review the available evidence of interventions focused on early-life stressors. Subtask 9.2.4 "Lifestyle of parents and young children" aimed to generate evidence on the impact of lifestyle interventions on long-term child health outcomes. Lifestyle stressors as defined in Task 9.1 and in Deliverable 9.1 include dietary behaviour, nutritional intake and status, physical activity, sleep and substance exposures in the prenatal and postnatal periods up to 2 years of age of the child. The outcomes comprise of a multitude of clinical health measures in cardio-metabolic, respiratory, and mental health fields occurring anytime from birth to early adulthood.
This systematic review focuses on evidence around the impact of nutrition intervention programs implemented during the first 1000 days of life on long-term child and adolescent health outcomes. We performed the literature searches based on the developed general review strategy from Task 9.1 (Deliverable 9.1). We examined characteristics of interventions commonly used to promote recommended nutrition and diet behaviour and to identify areas for evidence implementation and further research. The interventions of interest included programs conducted in high-income countries targeting diet behaviour, giving health information, increasing health knowledge, and providing support or education for healthy nutrition lifestyles.

This systematic review addresses four main objectives:

- What is the evidence on the long-term health impacts of early nutrition interventions?
- What type of interventions are used to promote recommended nutrition and diet behaviour?
- What is the quality and design of these trials?
- What should further research focus on and what recommendations can be made with the current evidence?

In April 2020, the review was registered on PROSPERO (International prospective register of systematic reviews) with the title "Nutrition interventions in the first 1000 days of life and long-term health outcomes in high-income countries: a systematic review of randomized controlled trials": https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=167893

2. Review question

What are the impacts of nutrition interventions implemented in the first 1000 days of life in high-income countries on long-term cardio-metabolic, respiratory, mental health, and dietary behaviour outcomes?

3. Eligibility criteria

Eligibility criteria for this review is summarized in the PICOT (population, intervention, comparator, outcome, time) table (Table 1).

Table 1: Summary of PICOT for research question

Study Design: Randomized controlled trials (RCTs), Cluster randomised trials	
Population	Healthy adults: preconception, prenatal Children up to 2 years of age Parents of children up to 2 years of age
Intervention	Nutrition programs targeted at diet lifestyle and improving nutritional knowledge and healthy dietary behaviours
Comparator	Standard Care, alternative non-nutrition program
Outcomes	Clinical outcomes in the child: • Cardio-metabolic • Respiratory • Mental health and development Behavioural outcomes in the child: • Diet practices • Nutritional intake • Health knowledge
Time	Minimum 12 months follow-up

3.1. Study Design

Randomized controlled trials (RCTS) and cluster randomised trials were included in this review. Observational studies such as cohort, cross-sectional, and case-control studies were excluded.

3.2. Participants/population

Targeted participants were parents of infants up to 2 years of age or infants up to 2 years of age. Studies with participants of a mixed age range were included if the mean age of child participants is under two years at the start of the intervention. Healthy adults in the preconception and prenatal periods were also included.

Studies should include a sample that is reflective of their communities. Studies focused on clinical samples (e.g. preterm infants, low-birth weight infants, pregnant women with high BMI) or specific demographic subsets (e.g. low-income families, certain ethic groups) were excluded as the results may not be generalizable. Studies that include participants from clinical subsets as a representative sample of the community were eligible. Studies conducted in neighbourhoods or communities with predominantly specialized populations (low-income, migrants) that do not restrict their inclusion criteria to these population subsets were included.

3.3. Interventions

Nutrition interventions were defined as programs focused on improving diet behaviour, nutritional intake, providing support, recommendations, or education to promote healthy dietary choices, lifestyles, and expand nutrition knowledge. The first 1000 days of life refer to the period from conception through pregnancy until the child's second birthday. Interventions had to be applied during this period on the child or parents.

Interventions can be a composite of different lifestyle factors with a nutrition component. Nutrition counselling targeted at specific diet choices (e.g. reduce sodium, increase intake of healthy fatty acids) were included. Programs that include breastfeeding support or diet manipulations as a component of a larger nutrition and health education intervention were eligible. Supplement studies that used a 3 arm-trial to include placebo with diet counselling with a control were included. Programs can be delivered in the community, at home, online, by a healthcare provider or a trained educator. No restrictions were applied to intensity or duration of intervention.

Supplements, or diet manipulations and breastfeeding interventions alone were excluded.

3.4. Comparator

The control groups should be receiving care in accordance with community standards. Studies that used a non-nutrition program (e.g. physical activity, composite lifestyle intervention not including nutrition) as a comparator were included.

Studies using an alternate nutrition program or supplementation as a control were excluded.

3.5. Primary outcomes

Primary outcomes are clinical endpoints or clinical measurements that have significant correlation with overall cardio-metabolic, respiratory, and mental health, as well as diet behaviour. Influence on behaviour and health knowledge are not clinical outcomes but are important targets of nutrition intervention programs.

Outcomes had to be measured in the offspring if the intervention targeted parents or were applied in the preconception or prenatal periods. If the intervention targeted children within two years of age directly, then the outcomes and follow-up had to be measured in these children.

Fetal outcomes, outcomes measured at birth, and within the first year of life were excluded. Outcomes related to overweight or obesity were also left out to exclude the subset of studies that focus solely on obesity, which has already been studied extensively (Hesketh et al 2010, Redsell et al 2016). The definition of obesity is continuously evolving, with the Canadian practice guidelines recently updating the definition of obesity as "a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications and reduces lifespan" (Wharton et al 2020). In line with this definition, BMI or anthropometric measures alone are not sufficient to diagnose obesity and additional risks for disease needs to be identified, which will be measurements included in cardio-metabolic outcomes. Outcomes of diet behaviour and nutrition intake measured with serum biomedical markers were excluded.

Cardio-metabolic outcomes:

- Cardiovascular disease (e.g. hypertension)
- Cardiovascular measures (e.g. blood pressure)
- Metabolic disease (e.g. diabetes mellitus)

Respiratory outcomes:

- Respiratory diseases (e.g. Wheezing, asthma, COPD)

Mental Health outcomes:

- Mental health diagnoses (e.g. ADHD (Attention Deficit Hyperactivity Disorder), ASD (Autism-Spectrum Disorder), Internalizing and Externalizing behavior)
- Self-assessment/reporting of mental health status

Child diet behaviour outcomes:

- Dietary intake (e.g. portions of fruits, vegetables, sodium intake)
- Diet quality (e.g. variation of intake)
- Nutrition knowledge

3.6. Secondary outcomes

Secondary outcomes include clinical measurements in cardio-metabolic, respiratory, and mental health that have associations but do not directly diagnose disease.

Cardio-metabolic outcomes:

- Serum Markers: Inflammatory measurements (e.g. CRP), Lipid measures (e.g. Fatty acids, Total cholesterol, Triglycerides), Blood Glucose (e.g. glucose, HbA1c, insulin)
- Other cardiovascular measures: E.g. carotid intima media thickness

Respiratory outcomes:

- Measure of Lung Function: E.g. FEV1, FVC, Bronchial hyperresponsiveness, Fractional exhaled nitric oxide

Mental health outcomes:

- Cognitive Measures: Psychomotor development (e.g. gross motor and fine motor), Executive Function (e.g. working memory), Intelligence (nonverbal) (e.g. IQ), Language

3.7. Context

The review focused on high-income countries with health contexts comparable to that of Western EU.

3.8. Time

Studies with follow-up greater or equal to 12 months were included. Interventions applied during the preconception and prenatal periods should followed-up until the infant is a minimum of 12 months of age for outcome measurement.

4. Search strategy and databases

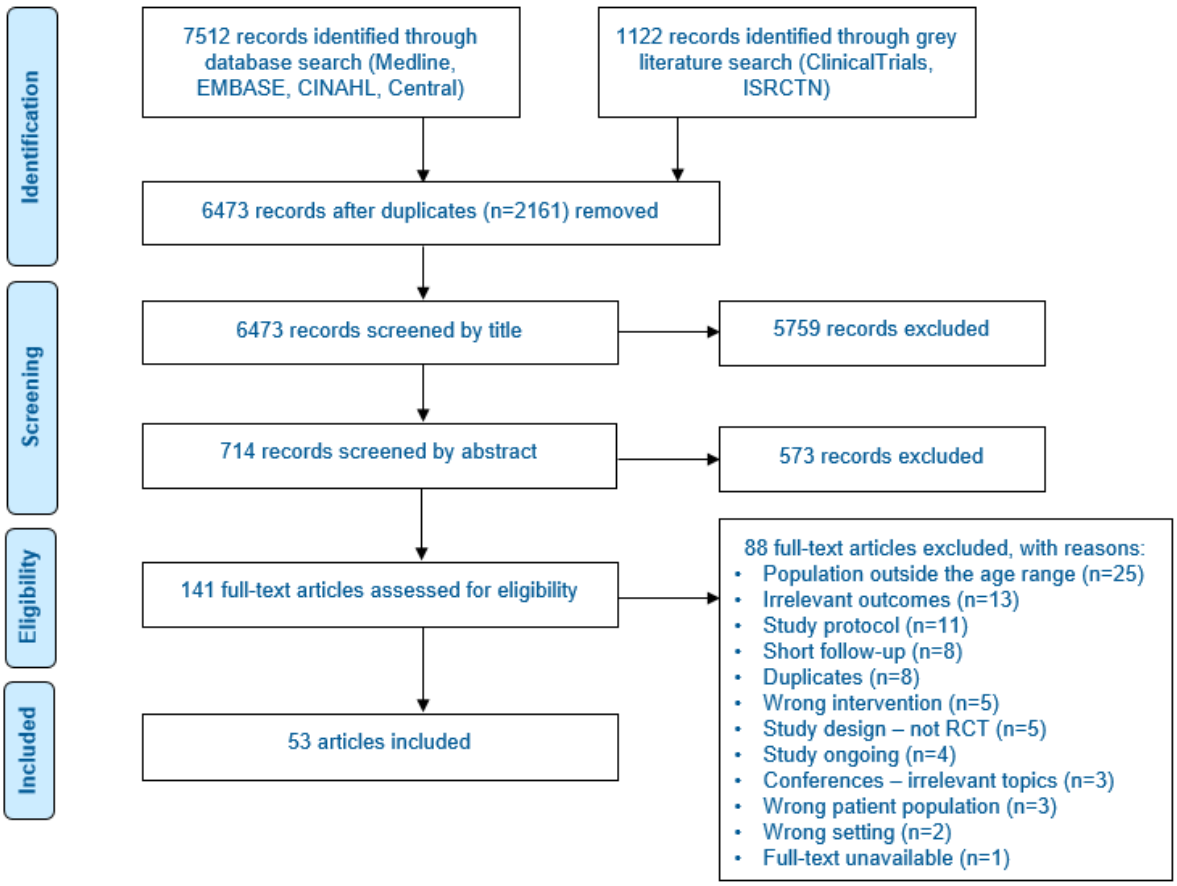
We applied no language or publication date restrictions in the search. The following databases were searched:

- MEDLINE/PubMed (see search strategy in Appendix I)
- EMBASE
- CINAHL
- Cochrane Register for Controlled Trials
- ISRCTN
- ClinicalTrials.gov

The search strategy was developed and tested for PubMed, then subsequently translated to the other databases. Search terms were developed using medical subject headings (MeSH) and free text. Searches were repeated with the addition of new terms and revisions until a high proportion of selected eligible studies were detected with a reasonable number of total hits in the final search strategy. To ensure literature saturation, reference lists of included studies were hand searched. Authors' personal files were also searched to capture relevant material.

5. Flow chart

Figure 1: PRISMA Flow Diagram for Study Screening and Selection



6. Data extraction

All identified records from the search process were imported into Endnote software and duplicates were removed. Two reviewers worked independently on the selection process. A. Xu (LMU) and M. Vafeiadi (UoC) did title screening. A. Xu (LMU) and K. Gürlich (LMU) did abstract and full-text screening. Data extraction was completed following the Cochrane data extraction template with Covidence (Covidence, 2020). A. Xu and K. Gürlich completed data extraction independently. Data items extracted included patient characteristics, intervention and comparator characteristics, trial design, trial size, duration of follow-up, outcome measures, results, and study conclusions. Differences in data extraction and interpretation were resolved through discussion.

7. Risk of bias assessment

Risk of bias assessment was conducted for all studies using the Cochrane risk of bias tool (Higgins et al, 2011). For each domain in the tool, information from the studies was presented, including verbatim quotes, and assigned a 'high' or 'low' risk rating. If there was insufficient data, then the risk of bias was 'unclear'. Risk of bias was assessed using the outcomes relevant to this review, rather than the original study, and at the latest follow-up reported.

The overall quality of included studies is presented in the risk of bias graph (Figure 2), produced by the Cochrane RobVis tool (McGuinness and Higgins 2020). As seen in Figure 2, no study was classified to be at low risk of bias overall. The blinding of participants and personnel (performance bias) was the domain with most concern, but expected for the nature of these interventions, as it is impossible to blind participants and personnel. An additional source of bias was incomplete outcome data (attrition bias), which is also expected for long-term trials. Finally, another domain of concern was other biases, including unclear bias regarding adherence to intervention and power of sample size. Thus, assessing the quality of studies excluding the blinding of participants and personnel aspect, most studies possess moderate concern for bias in terms of attrition bias and other biases. A breakdown of risk assigned for each study per domain is presented in Figure 3.

Figure 2: Risk of bias graph

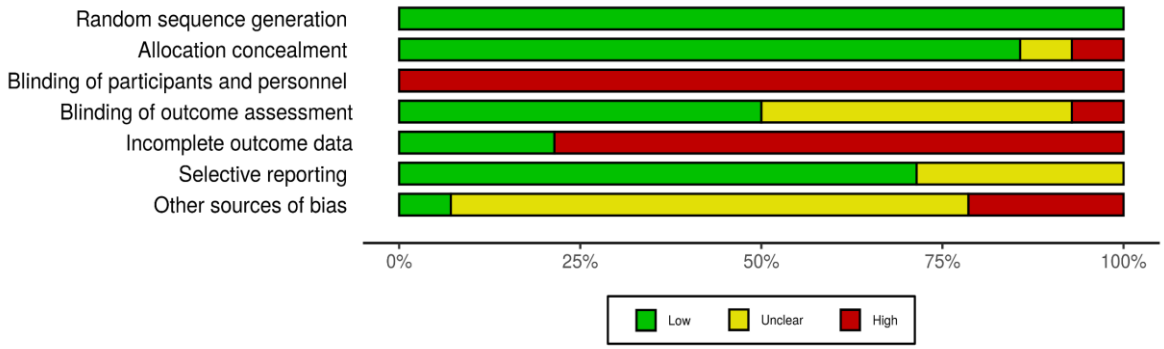
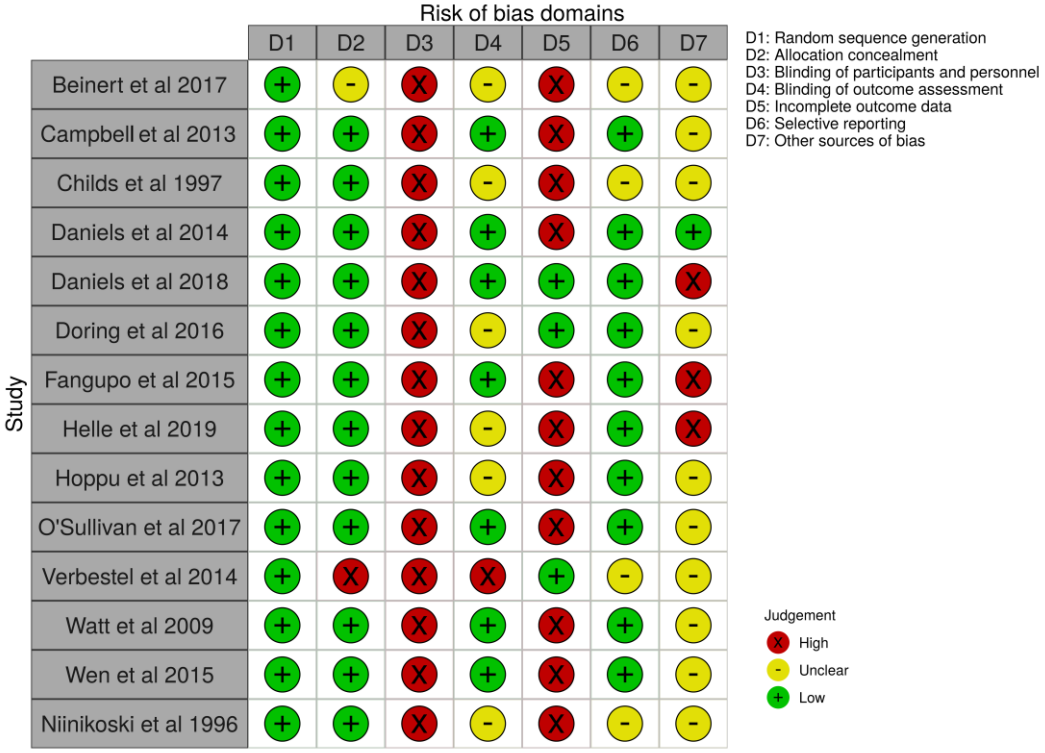


Figure 3: Risk of bias chart



8. Results

The final search yielded 6473 reports after duplicates were removed. The search strategy combined results from four databases and two trial registries. A remaining of 53 articles representing 14 different interventions were deemed eligible after title, abstract, and full-text screening (Figure 1). Reasons for exclusion are outlined in detail in the PRISMA flow diagram but were mainly due to population outside the age range (n = 25) and irrelevant outcomes (n = 13). 35 articles were from one RCT, the STRIP study from Finland.

8.1. Study characteristics

Eleven studies were randomized controlled trials, and three studies were cluster randomized controlled trials. The studies were from eight different countries: Australia, Norway, United Kingdom, New Zealand, Finland, Ireland, Sweden, and Belgium. The population included parents during pregnancy in two studies or parents with their infants in the remaining studies. The number of participants varied from 110 families to 1355 families. The follow-up was shorter term among the studies, with ten studies reporting outcomes at less than five years of age, three studies reported outcomes at five years of age, and one study reported outcomes at 20 years of age. A summary of study characteristics is presented in Table 2.

Table 2. Study characteristics of included studies

Randomized Controlled Trials

Study ID	Country	Setting	No. participants	Follow-up Age	Population Description
Beinert et al 2017	Norway	4 Healthcare Clinics with different socioeconomic areas in Kristiansand	110 families	24 months	Parents and their 4-6 months old infants; parents were highly educated, few were smokers, most were married or cohabitants
Childs et al 1997*	United Kingdom	2 inner city areas of high socioeconomic deprivation in Birmingham	1000 infants	18 months	Participants were largely Asian, around half were of low socioeconomic status and one-third of the mothers had no education or primary school only.
Daniels et al 2014 (NOURISH)	Australia	Child health clinics in Brisbane and Adelaide	698 mothers	5 years	First-time mothers were largely born in Australia, married, non-smokers, and over a half had a university degree.
Daniels et al 2018	New Zealand	Dunedin	206 mothers and infants	3 years	Included participants are mostly New Zealand Europeans, half had a university degree.
Fangupo et al 2015† (POI.nz)	New Zealand	Dunedin	802 mothers	3.5 years	Mothers were mostly New Zealand Europeans, 65% had a university degree or higher, 47% were primiparous, and 37% of households had low levels of deprivation
Helle et al 2019	Norway	Web-based, child health clinics in Norwegian municipalities	718 parents and children	2 years	Norwegian speaking mothers with 5 months old infants, mostly married or living with a partner, had high education, worked full time and were non-smokers.
Hoppu et al 2013‡	Finland	Maternal welfare clinics in the city of Turku and South-West Finland	256 mothers	4 years	Children of mothers participating from the first trimester of pregnancy. Most of the mothers had a high education level, 77.8% had a university or college degree and all were Caucasian, and 60% were first time mothers.
Niinikoski et al 1996 (STRIP study)	Finland	Well-baby clinics in the city of Turku	1054 families, 1062 children	20 years	Healthy children at the age of 7 months and their families, recruited from the general population in Turku, Finland.
O'Sullivan et al 2017	Ireland	Socio-economically disadvantaged communities in Dublin	233 pregnant women	4 years §	Pregnant women from a community in Dublin, which had above national average rates of unemployment, school dropout, lone-parent households, and public housing. About 50% were first-time mothers.

Watt et al 2009	United Kingdom	2 disadvantaged inner city London boroughs (Camden and Islington)	312 women and infants	18 months	Women were recruited from baby clinics in disadvantaged neighbourhoods, 50% were white ethnicity, 62% were first-time mothers¶. Infants were 10 weeks old.
Wen et al 2015	Australia	Socially and economically disadvantaged areas of Sydney	667 first-time mothers and infants	5 years	First-time mothers and their children in a socially and economically disadvantaged area of Sydney. Most were married, 63-65% were born in Australia, 60% were employed and 85% had a secondary or higher education.

* Childs 1997 reported as prospective cohort study, but participants had been randomized into intervention and control groups
†Fangupo 2015 is a 4-arm trial, including 3 interventions and 1 control group. Results reported compared intervention (grouping arms 1 and 2) against control (arms 3 and 4)
‡ Hoppu et al 2015 is a 3-arm trial, including 1) intervention and probiotic, 2) intervention and placebo, and 3) control and placebo group. Results were analysed comparing arm 1 and 3.
§Published paper follows up participants to 4 years of age (2-year follow-up) but authors have planned follow up until 9 years of age (11-year follow-up)
¶Watt et al 2009 originally included only first-time mothers but expanded eligibility criteria to increase sample size

Cluster Randomized Controlled Trials

Study ID	Country	Setting	Clusters	No. participants	Follow-up Age	Population Description
Campbell et al 2013 (InFANT Study)	Australia	Local Government Areas (LGAs) located within 60km radius of research centre in Melbourne	62 parent groups ≥6-8 parents per group	542 parents	5 years	Majorly Australian-born, English speaking, first-time parents, with at least secondary school education. Near 50/50 mixture of male and female infants at 4 months of age.
Doring et al 2016 (PRIMROSE Trial)	Sweden	Child Health Centres (CHC) in 8 counties	59 CHC units ≥ 1 CHC per unit (n = 7) People per cluster not reported	1355 families 1369 children	4 years	Restricted to Swedish-speaking families, >90% of mothers were born in Sweden, 61% had secondary or postsecondary education, and mostly non-smokers.
Verbestel et al 2014	Belgium	6 communities in Flanders, Belgium with range of socio-economic status scores	4-21 daycare centres per community (n=70) 16-80 children per community	203 children	1 year	Two communities with a low, two with a medium and two with a high SES. Consenting parents of all children aged 9–24 months within consenting day-care centres in selected communities were enrolled. Mean age of the children 15,51 months, 54% boys.

8.2. Summary of findings

The 14 studies included in this review reported outcomes in cardio-metabolic health (3 studies), mental health (4 studies), and dietary behaviour (14 studies). No studies reported respiratory health outcomes. The summary of findings can be found in Table 3.

The cardio-metabolic outcomes were grouped in five categories: blood pressure, metabolic syndrome, cardiovascular measures, biochemical profile and lipid profile. Results from one long-term trial suggests that nutrition interventions can be beneficial in reducing occurrence of adolescent metabolic syndrome, reduce blood pressure and can favour ideal cardiovascular scores (Niinikoski et al 1996). For other cardiovascular measures like brachial artery diameter basal, left ventricular mass and ideal glucose score no differences were found between intervention and control group (Niinikoski et al 1996). For biochemical profile and lipid profile mixed results were found.

All four studies (Fangupo et al 2015, O'Sullivan et al 2017, Wen et al 2015, and Niinikoski et al 1996) looking at mental health outcomes found no difference between intervention and control groups.

All 14 included studies reported dietary behaviour outcomes. The specific outcomes used to measure dietary behaviour among studies were grouped into 7 categories: food intake, nutrient intake, eating behaviour, food preferences, supplementation, diet scores/patterns and nutrition knowledge. There were mixed findings among studies for intervention effects across all measures. The most consistent finding was that in four studies interventions favoured a decrease in intake of unfavourable foods: sweet snacks, Campbell et al 2013 (SMD[1]: - 0.26 g/day, 95%CI: -0.47 to -0.05); sweet and savoury snacks, Verbestel et al 2017 (SMD: -0.26 g/day, p <0.001); desserts, Niinikoski et al 1996 (β-coeff: -4.10 g/day, 95%CI: -6.50 to -1.70, p<0.001); or sugary drinks, Döring et al 2014 (MD[2]: -0.49 times/week, 95%CI: -0.97 to -0.15, p=0.04).

[1] SMD: standardized mean difference

[2] MD: mean difference

Table 3. Summary of findings

Summary of findings

Outcomes	Study	Summary of Findings
Cardio-metabolic health		
Blood Pressure	Niinikoski et al 1996	Favoured intervention for decreasing incidence of blood pressure above 80th %tile, and systolic and diastolic blood pressure
Metabolic Syndrome	Niinikoski et al 1996	Favoured intervention for decreasing incidence of adolescent metabolic syndrome
Cardivascular measures	Niinikoski et al 1996	Favoured intervention for low ideal cardiovascular score, ideal cholesterol and blood pressure, but no difference found for brachial artery diameter basal, left ventricular mass and ideal glucose score
Biochemical profile	Daniels et al 2018 Niinikoski et al 1996	1 study found no difference across all measures 1 study favoured intervention for decreasing Insulin and Homa-IR, but found no difference in other measures
Lipid Profile	Beinert et al 2017 Niinikoski et al 1996	2 studies favoured intervention for decreasing HDL cholesterol, total cholesterol, fatty acids, but found no difference in other measures
Respiratory health		No studies reported outcomes for respiratory health
Mental Health and Development		
Self-Regulation Abilities	Fangupo et al 2015	4 studies found no difference across all measures
Cognitive Development	O'Sullivan et al 2017	
Quality of Life	Wen et al 2015	
Psychological well being	Niinikoski et al 1996	
School Performance	Niinikoski et al 1996	
Medication or supplement use	Niinikoski et al 1996	
Neurological Development	Niinikoski et al 1996	

Table continued

Summary of findings

Outcomes	Study	Summary of Findings
Dietary Behaviour		
Food Intake	Beinert et al 2017 Campbell et al 2013 Daniels et al 2014 Döring et al 2014 Fangupo et al 2015 Helle et al 2019 Niinikoski et al 1996 O'Sullivan et al 2017 Verbestel et al 2017 Watt et al 2009 Wen et al 2015	5 studies found no difference across all measures 4 studies favoured intervention in decreasing sweet snacks, savoury snack, dessert, or sugary drink intake 3 studies favoured intervention in increasing fruit or vegetable intake 1 study favoured intervention in increasing low-fat unsweetened dairy, vegetable-based oil fat, fish, and fibre-rich grain products intake 1 study favoured intervention in decreasing intake of french fries 1 study favoured control in decreased chips intake 1 study favoured control in decreased water intake
Nutrition Intake	Daniels et al 2018 Fangupo et al 2015 Hoppu et al 2013 Niinikoski et al 1996 Watt et al 2009	3 studies found no difference across all measures 2 studies favoured intervention in increasing Vitamin C intake 2 studies favoured intervention in increasing polyunsaturated
Supplementation	Beinert et al 2017 Niinikoski et al 1996	1 study favoured intervention in increasing cod liver oil supplementation for vitamin D, but not difference for cod liver oil supplementation 1 study reported results partially, no significance or effect was reported for supplement use or vitamin intake from supplement
Eating Behaviour	Daniesl et al 2014 Fangupo et al 2015 Helle et al 2019 Watt et al 2009	2 studies found no difference in eating behaviour 1 study favoured control for increasing food responsiveness and favoured intervention for increasing satiety responsiveness 1 study favoured intervention for increasing food responsiveness
Food Preferences	Beinert et al 2017 Daniels et al 2014 Helle et al 2019	2 studies found no difference in scepticism to new food or food neophobia 1 study favoured intervention for increasing percent of fruit liked
Dietary Pattern/Scores	Campbell et al 2013 Childs et al 1997 Daniels et al 2014 Fangupo et al 2015 Niinikoski et al 1996	2 studies found no difference in food scores 1 study favoured intervention for increasing obesity protective index score 1 study favoured intervention for increasing fruit and vegetable score 1 study favoured intervention for increasing ideal diet scores and reducing unfavourable diet score
Nutrition Knowledge	Niinikoski et al 1996	Favoured intervention on increasing food knowledge in the fat, health heart, and total scores

9. Conclusion and next steps

What is the evidence on the long-term health impacts of early nutrition interventions?

There is unclear evidence on the efficacy of early life nutrition intervention programs to improve long-term health outcomes in high-income countries, attributed to a lack studies in children in the first two years of life, appropriate long follow-up (>12 months) and lack of measurement of relevant clinical endpoints as outcomes in many studies. Areas of high heterogeneity between studies were identified in this review, especially for outcomes reported in mental health and dietary behaviours. Results from one long-term trial suggests that nutrition interventions can be beneficial in reducing occurrence of adolescent metabolic syndrome and reduce blood pressure (Niinikoski et al 1996). Nutrition interventions are also seen to be able to reduce some unfavourable dietary behaviour in decreasing consumption of sugary foods and increasing consumption of fruits and vegetables, however the clinical significance of these changes is yet to be determined. From the included studies, there are no mental health impacts demonstrated in early life nutrition interventions. Furthermore, no studies reported outcomes for respiratory health.

This review was unable to conclude a synthesized intervention effect of nutrition programs on long-term cardio-metabolic, respiratory or mental health outcomes because of high heterogeneity and mixed results across studies. Few studies report long-term clinical outcomes, and most studies report dietary behaviour outcomes in large variations.

What type of interventions are used to promote recommended nutrition and diet behaviour?

Most of the studies used multiple methods to deliver nutrition interventions or a composite lifestyle intervention, largely targeting the postpartum period and parents. More research is needed in prenatal and preconception nutrition interventions.

What is the quality and design of these trials?

All trials suffer from high attrition, high levels of missing data, and detection bias through the inability to blind participants.

What should further research focus on and what recommendations can be made with the current evidence?

Long-term follow-up of early nutrition intervention studies in humans are needed and should be emphasized. Further research requires innovative strategies to overcome limitations in lifestyle-related trials, such as high attrition. High attrition can complicate longer follow-up times. Harmonizing data collection across a network of study groups to investigate the impact of interventions targeting early life stressors can be a solution to these limitations. Future research should consider when intervention effects over time using respective statistical methods is more beneficial than analysis of one time point.

In Task 9.3 we will take the work of Task 9.2 forward and integrate the results of this review as far as possible into recommendations for feasible, effective and efficient intervention strategies before and during pregnancy or in infancy. Furthermore, we will identify knowledge gaps and priorities for improving and implementing future nutritional intervention studies.

10. References

Beinert, C., Hernes, S., Haugen, M. and Øverby, N., 2017. No long-term effect of a 2-days intervention on how to prepare homemade food, on toddlers' skepticism for new food and intake of fruits and vegetables and sweet beverages: a randomized, controlled trial. *BMC Research Notes*, 10(1).

Campbell, K., Lioret, S., McNaughton, S., Crawford, D., Salmon, J., Ball, K., McCallum, Z., Gerner, B., Spence, A., Cameron, A., Hnatiuk, J., Ukoumunne, O., Gold, L., Abbott, G. and Hesketh, K., 2013. A Parent-Focused Intervention to Reduce Infant Obesity Risk Behaviors: A Randomized Trial. *PEDIATRICS*, 131(4), pp.652-660.

Childs, F., Aukett, A., Darbyshire, P., Ilett, S. and Livera, L., 1997. Dietary education and iron deficiency anaemia in the inner city. *Archives of Disease in Childhood*, 76(2), pp.144-147.

Covidence. 2020. *Covidence - Better Systematic Review Management*. [online] Available at: <https://www.covidence.org/>.

Daniels, L., Mallan, K., Battistutta, D., Nicholson, J., Meedeniya, J., Bayer, J. and Magarey, A., 2014. Child eating behavior outcomes of an early feeding intervention to reduce risk indicators for child obesity: The NOURISH RCT. *Obesity*, 22(5), pp.E104-E111.

Daniels, L., Taylor, R., Williams, S., Gibson, R., Fleming, E., Wheeler, B., Taylor, B., Haszard, J. and Heath, A., 2018. Impact of a modified version of baby-led weaning on iron intake and status: a randomised controlled trial. *BMJ Open*, 8(6), p.e019036.

Fangupo, L., Heath, A., Williams, S., Somerville, M., Lawrence, J., Gray, A., Taylor, B., Mills, V., Watson, E., Galland, B., Sayers, R., Hanna, M. and Taylor, R., 2015. Impact Of An Early-Life Intervention On The Nutrition Behaviors Of 2-Y-Old Children: A Randomized Controlled Trial. *American Journal of Clinical Nutrition*, 102(3):704-712.

Heino, T., Kallio, K., Jokinen, E., Lagström, H., Seppänen, R., Välimäki, I., Viikari, J., Rönnemaa, T. and Simell, O., 2000. Sodium intake of 1 to 5-year-old children: the STRIP Project. *Acta Paediatrica*, 89(4), pp.406-410.

Helle, C., Hillesund, E., Wills, A. and Øverby, N., 2019. Examining the effects of an eHealth intervention from infant age 6 to 12 months on child eating behaviors and maternal feeding practices one year after cessation: The Norwegian randomized controlled trial Early Food for Future Health. *PLOS ONE*, 14(8), p.e0220437.

Hesketh, K., Campbell, K., 2010. Interventions to Prevent Obesity in 0–5 Year Olds: An Updated Systematic Review of the Literature. *Obesity* (Silver Spring), 18 Suppl 1:S27-35.

Hesketh, K., Campbell, K., Salmon, J., McNaughton, S., McCallum, Z., Cameron, A., Ball, K., Gold, L., Andrianopoulos, N. and Crawford, D., 2013. The Melbourne Infant Feeding, Activity and Nutrition Trial (InFANT) Program follow-up. *Contemporary Clinical Trials*, 34(1), pp.145-151.

Higgins, J., Altman, D., Gotzsche, P., Juni, P., Moher, D., Oxman, A., Savovic, J., Schulz, K., Weeks, L. and Sterne, J., 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, 343(oct18 2), pp.d5928-d5928.

Hoppu, U., Isolauri, E., Koskinen, P. and Laitinen, K., 2013. Diet and blood lipids in 1–4-year-old children. *Nutrition, Metabolism and Cardiovascular Diseases*, 23(10), pp.980-986.

Kaitosaari, T., Rönnemaa, T., Raitakari, O., Talvia, S., Kallio, K., Volanen, I., Leino, A., Jokinen, E., Välimäki, I., Viikari, J. and Simell, O., 2003. Effect of 7-Year Infancy-Onset Dietary Intervention on Serum Lipoproteins and Lipoprotein Subclasses in Healthy Children in the Prospective, Randomized Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) Study. *Circulation*, 108(6), pp.672-677.

Kaseva, K., Pulkki-Råback, L., Elovainio, M., Pahkala, K., Keltikangas-Järvinen, L., Hintsanen, M., Hakulinen, C., Lagström, H., Jula, A., Niinikoski, H., Rönnemaa, T., Viikari, J., Simell, O. and Raitakari, O., 2015. Psychological wellbeing in 20-year-old adults receiving repeated lifestyle counselling since infancy. *Acta Paediatrica*, 104(8), pp.815-822.

Lagström, H., 2021. *Nutrient Intakes By Young Children In A Prospective Randomized Trial Of A Low—Saturated Fat, Low-Cholesterol Diet*.

Lagström, H., Seppänen, R., Jokinen, E., Niinikoski, H., Rönnemaa, T., Viikari, J. and Simell, O., 1999. Influence of dietary fat on the nutrient intake and growth of children from 1 to 5 y of age: the Special Turku Coronary Risk Factor Intervention Project. *The American Journal of Clinical Nutrition*, 69(3), pp.516-523.

Laitinen, T., Nuotio, J., Juonala, M., Niinikoski, H., Rovio, S., Viikari, J., Rönnemaa, T., Magnussen, C., Jokinen, E., Lagström, H., Jula, A., Simell, O., Raitakari, O. and Pahkala, K., 2018. Success in Achieving the Targets of the 20-Year Infancy-Onset Dietary Intervention: Association With Insulin Sensitivity and Serum Lipids. *Diabetes Care*, 41(10), pp.2236-2244.

Lapinleimu, J., Raitakari, O., Lapinleimu, H., Pahkala, K., Rönnemaa, T., Simell, O. and Viikari, J., 2015. High Lipoprotein(a) Concentrations Are Associated with Impaired Endothelial Function in Children. *The Journal of Pediatrics*, 166(4), pp.947-952.e2.

Lehtovirta, M., Pahkala, K., Niinikoski, H., Kangas, A., Soininen, P., Lagström, H., Viikari, J., Rönnemaa, T., Jula, A., Ala-Korpela, M., Würtz, P. and Raitakari, O., 2018. Effect of Dietary Counseling on a Comprehensive Metabolic Profile from Childhood to Adulthood. *The Journal of Pediatrics*, 195, pp.190-198.e3.

Magarey, A., Mauch, C., Mallan, K., Perry, R., Elovaris, R., Meedeniya, J., Byrne, R. and Daniels, L., 2016. Child dietary and eating behavior outcomes up to 3.5 years after an early feeding intervention: The NOURISH RCT. *Obesity*, 24(7), pp.1537-1545.

Matthews, L., Rovio, S., Jaakkola, J., Niinikoski, H., Lagström, H., Jula, A., Viikari, J., Rönnemaa, T., Simell, O., Raitakari, O. and Pahkala, K., 2018. Longitudinal effect of 20-year infancy-onset dietary intervention on food consumption and nutrient intake: the randomized controlled STRIP study. *European Journal of Clinical Nutrition*, 73(6), pp.937-949.

McGuinness, L. and Higgins, J., 2020. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Research Synthesis Methods*.

Niinikoski, H., Jula, A., Viikari, J., Rönnemaa, T., Heino, P., Lagström, H., Jokinen, E. and Simell, O., 2009. Blood Pressure Is Lower in Children and Adolescents With a Low-Saturated-Fat Diet Since Infancy. *Hypertension*, 53(6), pp.918-924.

Niinikoski, H., Koskinen, P., Punnonen, K., Seppänen, R., Viikari, J., Ronnemaa, T., Irjala, K. and Simell, O., 1997. Intake and indicators of iron and zinc status in children consuming diets low in saturated fat and cholesterol: the STRIP baby study. Special Turku Coronary Risk Factor Intervention Project for Babies. *The American Journal of Clinical Nutrition*, 66(3), pp.569-574.

Niinikoski, H., Lagström, H., Jokinen, E., Siltala, M., Rönnemaa, T., Viikari, J., Raitakari, O., Jula, A., Marniemi, J., Näntö-Salonen, K. and Simell, O., 2007. Impact of Repeated Dietary Counseling Between Infancy and 14 Years of Age on Dietary Intakes and Serum Lipids and Lipoproteins. *Circulation*, 116(9), pp.1032-1040.

Niinikoski, H., Lapinleimu, H., Viikari, J., Ronnemaa, T., Jokinen, E., Seppanen, R., Terho, P., Tuominen, J., Valimaki, I. and Simell, O., 1997. Growth Until 3 Years of Age in a Prospective, Randomized Trial of a Diet With Reduced Saturated Fat and Cholesterol. *PEDIATRICS*, 99(5), pp.687-694.

Niinikoski, H., Pahkala, K., Ala-Korpela, M., Viikari, J., Ronnemaa, T., Lagstrom, H., Jokinen, E., Jula, A., Savolainen, M., Simell, O. and Raitakari, O., 2012. Effect of Repeated Dietary Counseling on Serum Lipoproteins From Infancy to Adulthood. *PEDIATRICS*, 129(3), pp.e704-e713.

Niinikoski, H., Pahkala, K., Viikari, J., Rönnemaa, T., Jula, A., Lagström, H., Simell, O. and Raitakari, O., 2021. *The STRIP Study: Long-Term Impact Of A Low Saturated Fat/Low Cholesterol Diet*.

Niinikoski, H., Viikari, J., Ro¨nnemaa, T., Lapinleimu, H., Jokinen, E., Salo, P., Seppa¨nen, R., Leino, A., Tuominen, J., Va¨lima¨ki, I. and Simell, O., 1996. Prospective Randomized Trial of Low-Saturated-Fat, Low-Cholesterol Diet During the First 3 Years of Life. *Circulation*, 94(6), pp.1386-1393.

Nupponen, M., Pahkala, K., Juonala, M., Magnussen, C., Niinikoski, H., Rönnemaa, T., Viikari, J., Saarinen, M., Lagström, H., Jula, A., Simell, O. and Raitakari, O., 2015. Metabolic Syndrome From Adolescence to Early Adulthood. *Circulation*, 131(7), pp.605-613.

Oranta, O., Pahkala, K., Ruottinen, S., Niinikoski, H., Lagstrom, H., Viikari, J., Jula, A., Loo, B., Simell, O., Ronnemaa, T. and Raitakari, O., 2013. Infancy-Onset Dietary Counseling of Low-Saturated-Fat Diet Improves Insulin Sensitivity in Healthy Adolescents 15-20 Years of Age: The Special Turku Coronary Risk Factor Intervention Project (STRIP) study. *Diabetes Care*, 36(10), pp.2952-2959.

O'Sullivan, A., Fitzpatrick, N. and Doyle, O., 2016. Effects of early intervention on dietary intake and its mediating role on cognitive functioning: a randomised controlled trial. *Public Health Nutrition*, 20(1), pp.154-164.

Øverby, N., Hernes, S. and Haugen, M., 2017. Effect of dietary interventions during weaning period on parental practice and lipoproteins and vitamin D status in two-year-old children. *Food & Nutrition Research*, 61(1), p.1350127.

Pahkala, K., Hietalampi, H., Laitinen, T., Viikari, J., Rönnemaa, T., Niinikoski, H., Lagström, H., Talvia, S., Jula, A., Heinonen, O., Juonala, M., Simell, O. and Raitakari, O., 2021. *Ideal Cardiovascular Health In Adolescence*.

Raitakari, O., Rönnemaa, T., Järvisalo, M., Kaitosaari, T., Volanen, I., Kallio, K., Lagström, H., Jokinen, E., Niinikoski, H., Viikari, J. and Simell, O., 2005. Endothelial Function in Healthy 11-Year-Old Children After Dietary Intervention With Onset in Infancy. *Circulation*, 112(24), pp.3786-3794.

Rask-Nissilä, L., Jokinen, E., Terho, P., Tammi, A., Lapinleimu, H., Rönnemaa, T., Viikari, J., Seppänen, R., Korhonen, T., Tuominen, J., Välimäki, I. and Simell, O., 2000. Neurological Development of 5-Year-Old Children Receiving a Low–Saturated Fat, Low-Cholesterol Diet Since Infancy. *JAMA*, 284(8), p.993.

Rask-Nissilä, L., Jokinen, E., Rönnemaa, T., Viikari, J., Tammi, A., Niinikoski, H., Seppänen, R., Tuominen, J. and Simell, O., 2000. Prospective, Randomized, Infancy-Onset Trial of the Effects of a Low-Saturated-Fat, Low-Cholesterol Diet on Serum Lipids and Lipoproteins Before School Age. *Circulation*, 102(13), pp.1477-1483.

Rask-Nissilä, L., Jokinen, E., Viikari, J., Tammi, A., Rönnemaa, T., Marniemi, J., Salo, P., Routi, T., Helenius, H., Välimäki, I. and Simell, O., 2002. Impact of Dietary Intervention, Sex, and Apolipoprotein E Phenotype on Tracking of Serum Lipids and Apolipoproteins in 1- to 5-Year-Old Children. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 22(3), pp.492-498.

Räsänen, M., Keskinen, S., Niinikoski, H., Heino, T., Simell, O., Rönnemaa, T., Helenius, H. and Viikari, J., 2003. Impact of nutrition counselling on nutrition knowledge and nutrient intake of 7- to 9-y-old children in an atherosclerosis prevention project. *European Journal of Clinical Nutrition*, 58(1), pp.162-172.

Räsänen, M., Lehtinen, J., Niinikoski, H., Keskinen, S., Ruottinen, S., Salminen, M., Rönnemaa, T., Viikari, J. And Simell, O., 2002. Dietary Patterns and Nutrient Intakes of 7-Year-Old Children Taking Part in an Atherosclerosis Prevention Project in Finland. *Journal of the American Dietetic Association*, 102(4), pp.518-524.

Räsänen, M., Niinikoski, H., Keskinen, S., Tuominen, J., Simell, O., Viikari, J. and Rönnemaa, T., 2001. Nutrition knowledge and food intake of seven-year-old children in an atherosclerosis prevention project with onset in infancy: the impact of child-targeted nutrition counselling given to the parents. *European Journal of Clinical Nutrition*, 55(4), pp.260-267.

Redsell, S.A., Edmonds, B., Swift J.A., Siriwardena A.N., Weng S., Nathan D., Glazebrook C., 2016. Systematic review of randomised controlled trials of interventions that aim to reduce the risk, either directly or indirectly, of overweight and obesity in infancy and early childhood. *Maternal & child nutrition* 12 (1):24-38.

Routi, T., Rönnemaa, T., Salo, P., Seppänen, R., Marniemi, J., Viikari, J., Ehnholm, C. and Simell, O., 1996. Effects of prospective, randomized cholesterol-lowering dietary intervention and apolipoprotein E phenotype on serum lipoprotein(a) concentrations of infants aged 7-24 mo. *The American Journal of Clinical Nutrition*, 63(3), pp.386-391.

Ruottinen, S., Lagström, H., Niinikoski, H., Rönnemaa, T., Saarinen, M., Pahkala, K., Hakanen, M., Viikari, J. and Simell, O., 2021. *Dietary Fiber Does Not Displace Energy But Is Associated With Decreased Serum Cholesterol Concentrations In Healthy Children*.

Salo, P., Viikari, J., Rask-Nissilä, L., Hämäläinen, M., Rönnemaa, T., Seppänen, R. and Simell, O., 1999. Effect of low-saturated fat, low-cholesterol dietary intervention on fatty acid compositions in serum lipid fractions in 5-year-old children. The STRIP project. *European Journal of Clinical Nutrition*, 53(12), pp.927-932.

Simell, O., Niinikoski, H., Rönnemaa, T., Lapinleimu, H., Routi, T., Lagström, H., Salo, P., Jokinen, E. and Viikari, J., 2000. Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP). *The American Journal of Clinical Nutrition*, 72(5), pp.1316s-1331s.

Simell, O., Niinikoski, H., Viikari, J., Rask-Nissilä, L., Tammi, A. and Rönnemaa, T., 1999. Cardiovascular disease risk factors in young children in the STRIP baby project. *Annals of Medicine*, 31(sup1), pp.55-61.

Simell O, Niinikoski H, Viikari J, Rask-Nissilä L, Tammi A, Rönnemaa T. Cardiovascular disease risk factors in young children in the STRIP baby project. Special Turku coronary Risk factor Intervention Project for children. *Ann Med*. 1999;31 Suppl 1:55-61.

Spence, A., McNaughton, S., Lioret, S., Hesketh, K., Crawford, D. and Campbell, K., 2013. A Health Promotion Intervention Can Affect Diet Quality in Early Childhood. *The Journal of Nutrition*, 143(10), pp.1672-1678.

Talvia, S., Lagström, H., Räsänen, M., Salminen, M., Räsänen, L., Salo, P., Viikari, J., Rönnemaa, T., Jokinen, E., Vahlberg, T. and Simell, O., 2004. A Randomized Intervention Since Infancy to Reduce Intake of Saturated Fat. *Archives of Pediatrics & Adolescent Medicine*, 158(1), p.41.

Talvia, S., Räsänen, L., Lagström, H., Pahkala, K., Viikari, J., Rönnemaa, T., Arffman, M. and Simell, O., 2005. Longitudinal trends in consumption of vegetables and fruit in Finnish children in an atherosclerosis prevention study (STRIP). *European Journal of Clinical Nutrition*, 60(2), pp.172-180.

Taylor, R., Gray, A., Heath, A., Galland, B., Lawrence, J., Sayers, R., Healey, D., Tannock, G., Meredith-Jones, K., Hanna, M., Hatch, B. and Taylor, B., 2021. *Sleep, Nutrition, And Physical Activity Interventions To Prevent Obesity In Infancy: Follow-Up Of The Prevention Of Overweight In Infancy (POI) Randomized Controlled Trial At Ages 3.5 And 5 Y*.

Verbestel, V., De Coen, V., Van Winckel, M., Huybrechts, I., Maes, L. and De Bourdeaudhuij, I., 2013. Prevention of overweight in children younger than 2 years old: a pilot cluster-randomized controlled trial. *Public Health Nutrition*, 17(6), pp.1384-1392.

Watt, R., Tull, K., Hardy, R., Wiggins, M., Kelly, Y., Molloy, B., Dowler, E., Apps, J. and McGlone, P., 2008. Effectiveness of a social support intervention on infant feeding practices: randomised controlled trial. *Journal of Epidemiology & Community Health*, 63(2), pp.156-162.

Wen, L., Baur, L., Simpson, J., Xu, H., Hayes, A., Hardy, L., Williams, M. and Rissel, C., 2015. Sustainability of Effects of an Early Childhood Obesity Prevention Trial Over Time. *JAMA Pediatrics*, 169(6), p.543.

Wharton, S., Lau, D., Vallis, M., Sharma, A., Biertho, L., Campbell-Scherer, D., Adamo, K., Alberga, A., Bell, R., Boulé, N., Boyling, E., Brown, J., Calam, B., Clarke, C., Crowshoe, L., Divalentino, D., Forhan, M., Freedhoff, Y., Gagner, M., Glazer, S., Grand, C., Green, M., Hahn, M., Hawa, R., Henderson, R., Hong, D., Hung, P., Janssen, I., Jacklin, K., Johnson-Stoklossa, C., Kemp, A., Kirk, S., Kuk, J., Langlois, M., Lear, S., McInnes, A., Macklin, D., Naji, L., Manjoo, P., Morin, M., Nerenberg, K., Patton, I., Pedersen, S., Pereira, L., Piccinini-Vallis, H., Poddar, M., Poirier, P., Prud'homme, D., Salas, X., Rueda-Clausen, C., Russell-Mayhew, S., Shiau, J., Sherifali, D., Sievenpiper, J., Sockalingam, S., Taylor, V., Toth, E., Twells, L., Tytus, R., Walji, S., Walker, L. and Wicklum, S., 2020. Obesity in adults: a clinical practice guideline. *Canadian Medical Association Journal*, 192(31), pp.E875-E891.

Appendix I.

Table 1. Search Strategy for PubMed

ID	PUBMED
1	"Prenatal Education"[Mesh] OR "Preconception Care"[Mesh] OR "Early Intervention, Educational"[Mesh] OR "Healthy People Programs"[Mesh] OR "Health Education"[Mesh] OR "Community Health Services"[Mesh] OR "health planning"[Mesh] OR "Social Support"[Mesh] OR "Health Knowledge, Attitudes, Practice"[Mesh] OR "Health Promotion"[Mesh:NoExp] OR "Program Evaluation"[Mesh:NoExp]
2	intervention*[ti] OR program*[ti] OR counsel*[ti] OR advice[ti] OR initiative*[ti] OR education*[ti] OR promotion*[ti] or early intervention or early education
3	**1 or 2**
4	"Nutritional Physiological Phenomena"[Mesh:NoExp] OR "Child Nutritional Physiological Phenomena"[Mesh:NoExp] OR "Infant Nutritional Physiological Phenomena"[Mesh:NoExp] OR "Maternal Nutritional Physiological Phenomena"[Mesh] OR "Diet"[Mesh:NoExp] OR "Feeding Behavior"[Mesh:NoExp] OR "Food Preferences"[Mesh] OR "Diet, Healthy"[Mesh] OR "Nutritional Requirements"[Mesh] OR "Nutritional Status"[Mesh]
5	("Diet, Food, and Nutrition"[Mesh]) NOT "Nutritional Physiological Phenomena"[Mesh]
6	diet[tiab] OR diets[tiab] OR dietary[tiab] OR nutrition*[tiab]
7	food*[tiab] OR feeding[tiab] OR meal*[tiab] OR breakfast*[tiab] OR lunch*[tiab] OR dinner*[tiab] OR snack*[tiab] OR vegetable*[tiab] OR fruit[tiab] OR eating habit* OR feeding habit* OR eating behavi* OR feeding behavi* OR food behavi* OR food preference*
8	**4-7/or**
9	3 AND 8
10	nutrition counsel* OR nutritional counsel* OR nutrition advice* OR nutritional advice* or nutrition education* OR nutritional education* OR nutrition promotion* OR nutritional promotion* OR nutrition intervention* OR nutritional intervention* OR nutrition program* OR nutritional program* OR nutrition initiative* OR nutritional initiative* OR nutrition information
11	diet counsel* OR dietary counsel* OR diet advice* OR dietary advice* or diet education OR dietary education* OR diet promotion* OR dietary promotion* OR diet intervention* OR dietary intervention* OR diet program* OR dietary program* OR diet initiative* OR dietary initiative*
12	10 or 11
13	9 or 12
14	infan*[tiab] OR preschool*[tiab] OR pre-school*[tiab] OR toddler*[tiab] OR nursery[tiab] OR nurseries[tiab] OR kindergarten*[tiab] OR early years[tiab] OR early years of life [tiab] OR early life[tiab] OR first year of life[tiab] OR first years of life[tiab]
15	preconception[tiab] or periconception[tiab] or pre-conception[tiab] or peri-conception[tiab] or prepregnancy[tiab] or pre-pregnancy[tiab]
16	prenatal[tiab] OR antenatal[tiab] OR antepartum[tiab] OR pregnancy[tiab] OR pregnant[tiab]
17	postnatal[tiab] OR postpartum[tiab]

18	parent[tiab] OR parents[tiab] OR parenting[tiab] Or mothers[tiab] OR fathers[tiab] OR newborn[tiab] OR child[tiab] OR children[tiab] OR childhood[tiab] OR baby[tiab] OR babies[tiab]
19	14-18/ or
20	13 AND 19
21	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR clinical trials as topic [mesh: noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] not humans[mh])
22	20 AND 21
23	LMIC filter (Cochrane LMIC filter 2012 - https://epoc.cochrane.org/lmic-filters)
24	22 NOT 23