Working method for drawing up dietary recommendations for pregnant women

No. 2021/26-A1e, The Hague, June 22, 2021

Background document to:
Dietary recommendations for pregnant women
No. 2021/26, The Hague, June 22, 2021

Health Council of the Netherlands

inhoud

01 introduction

In this introductory chapter, the committee describes the scope of the advisory report and explains its working method. Chapter 2 provides a more detailed description of the dietary topics that the committee has selected. The committee explains in Chapter 3 what outcome measures were evaluated to establish the dietary recommendations. The approach to literature reviews is described in Chapter 4.
In Chapter 5, the committee describes how it reaches conclusions in the background documents. Finally, it describes in Chapter 6 how the conclusions in the background documents are translated and integrated into recommendations.

1.1 The scope of the advisory report

In this advisory report, dietary recommendations for pregnant women are established. Healthy nutrition is part of a healthy lifestyle. Other lifestyle factors in addition to diet are also important for the health of both mother and baby, such as sufficient physical activity and not smoking. These other lifestyle factors are beyond the scope of this advisory report.

The dietary recommendations are aimed at pregnant women in the general population. The focus is on promoting favourable pregnancy outcomes and preventing unfavourable ones (see Chapter 3).
The recommendations describe the nutritional choices that can be made to improve health during pregnancy in the Netherlands.

1.2 Working method for assessing the state of scientific knowledge

The Committee on Dietary Recommendations for Pregnant Women has described the state of scientific knowledge and assessed it in four[a] background documents.

- Health effects of food consumption and dietary patterns during pregnancy[1]
- Health effects of nutrient intake from supplements during pregnancy[2]
- Health effects related to weight change during pregnancy[3]
- Harmful effects of substances and microorganisms in the diet during pregnancy[4]

One background document is about food safety: the risks of harmful effects from substances in the diet (e.g. nutrients, contaminants, aroma compounds) and the risks of microorganisms. The committee has primarily based that background document on existing risk assessments that have been carried out by other committees and organisations (paragraphs 3.3, 4.2 and 5.2).

For the three other background documents, the committee has evaluated the published studies itself based on systematic reviews and meta-analyses (paragraphs 3.1, 3.2, 4.1 and 5.1). When doing so,

[a] Paragraph 6.2 covers the addition of a fifth background document at a later moment in the advisory process to underpin the recommendation about fish species and fish fatty acids.

the committee adopted the working methods of the *Dutch dietary guidelines 2015* and the *Physical activity guidelines 2017* as the guiding principle.[5,6]

The committee has established the recommendations (Chapter 6) based on these four background documents. Additional information has been gathered and used where necessary (see paragraph 6.2). When writing the paragraph on fish in the advisory report, the committee concluded that these recommendations required an additional background document on the evaluation of fish species and the recommended dosage of fish-fatty-acid supplements. Dietary reference values sometimes play a part in the considerations by the committee in the advisory report. Dietary reference values describe the nutrient intake level which is sufficient to meet the nutrient requirement of virtually all individuals in the population group (in this case: pregnant women) and also describe the upper intake limit for the nutrient.

02 background documents: nutrition topics that have been evaluated

2.1 Origins of the topics

At the time this advisory process was started, the dietary recommendations for pregnant women were mostly based on the current recommendations by the Netherlands Nutrition Centre, although an inventory by the National Institute for Public Health and the Environment (RIVM) shows that there was some variation in dietary recommendations issued for pregnant women between various Dutch organisations and websites (Appendix A).

The recommendations by the Netherlands Nutrition Centre at the time of this project have been used in the evaluation as a guiding principle, alongside the dietary factors that were included in the *Dutch dietary guidelines 2015*. Additionally, not only the Netherlands Nutrition Centre but also professionals in the field and members of the committee have been able to propose additional topics, which the committee has also assessed.

2.2 Overview of all topics

Table 1 gives an overview of all the topics evaluated, both based on existing guidelines and as newly proposed topics.

Table 1 Dietary topics to be evaluated

Type of topic	Health effects of dietary patterns, foods and weight change during pregnancy	Health effects of nutrient supplements	Harmful effects of substances and microorganisms
Topics originating from the advice by the Netherlands Nutrition Centre	Dietary patterns Fish, including fish species Dairy Weight change during pregnancy	Folic acid around the time of conception Vitamin D Iron	Acrylamide Alcohol and alcoholic drinks Caffeine Herbal preparations, kitchen herbs and herbal teas Mercury and dioxins from predatory fish Lead from calabash chalk Vitamin A, liver and liver products Glycyrrhizin from liquorice (sweet or salty candy and tea with pieces of the liquorice plant root) *Listeria monocytogenes* *Toxoplasma gondii* and other microorganisms in the diet
New topics	Elimination diets Ramadan Gluten-free diets Vegetables Fruit Grain and cereal products Legumes Nuts and seeds Eggs Meat Potatoes Fats and oils Salt (sodium/potassium) Tea Coffee Water Sugar-containing beverages Artificially sweetened beverages	Continued use of folic acid in pregnancy Calcium Calcium and vitamin D Vitamin B12 Magnesium Fish fatty acids Iodine Multivitamin and/or multimineral supplements	Furans Soy isoflavones. Additives with E-numbers* Probiotics Superfoods

*The committee has not evaluated these because the European Food Safety Authority (EFSA) is updating the risk assessments for additives.[7]

03 background documents: outcome measures

3.1 Dietary patterns, foods and weight change during pregnancy

The committee has used systematic reviews to evaluate the effects of dietary patterns, foods and weight change during pregnancy on a fixed set of outcome measures.

The measures of outcome for this evaluation can be broken down into perinatal outcomes (offspring), pregnancy complications (mother) and long-term effects for the offspring – see Table 2. Some of these outcomes are 'hard' measures: illness, death, and complications. Both cohort studies and RCTs have been evaluated for these hard outcome measures.

Another subset are 'intermediate' outcome measures: outcome measures which are related to increased risks for mother or child (e.g. preterm birth or a low or high birth weight considering the gestational age).

The committee did not consider epigenetic effects (such as methylation of the DNA) as measures of outcome because it is not yet clear what these epigenetic effects mean for health.[8]

Table 2 Measures of outcome for the health effects of dietary patterns, foods and weight change during pregnancy

'Hard' outcome measures	'Intermediate' outcome measures
Perinatal outcome measures (offspring) • Congenital abnormalities • Miscarriages • Mortality	**Perinatal outcome measures (offspring)** • Foetal growth restriction/intrauterine growth retardation • *Large for gestational age*/macrosomia • *Small for gestational age* • Premature birth (duration of pregnancy)
Pregnancy complications (mother) • Complications during delivery • Gestational diabetes • Hypertensive disorders of pregnancy (e.g. preeclampsia)	
Long-term effects (offspring) • Asthma and allergies • Type 2 diabetes • Abnormal cognitive development (IQ) • Behavioural problems listed in DSM-5	**Long-term effects (offspring)** • Cardiovascular outcome measures: blood pressure, glucose, triglycerides • Body composition (BMI and fat percentage) • Outcomes of cognitive tests • Behavioural symptoms (e.g. emotional problems, aggression, but not listed in DSM-5)

3.2 Nutrient supplements

In evaluating the health effects of nutrient supplements, the committee did not pre-define the outcome measures in order to be able to evaluate any unintended effects of supplementation. In practice, most studies covered the hard and intermediate outcome measures presented in Table 2. Where available, the committee also described other hard outcome measures, such as postnatal depression.

3.3 Harmful effects of substances and microorganisms in the diet

With regard to harmful effects of substances and microorganisms in the diet, the committee did not pre-define the outcome measures in advance in order to be able to evaluate any unintended effects.

04 background documents: literature review on health effects

4.1 Dietary patterns, foods, nutrient supplements and weight change during pregnancy

For the three background documents on the health effects of dietary patterns, foods, nutrient supplements, and weight change during pregnancy, the committee evaluated the available studies themselves. The approach is described in this chapter.

4.1.1 Systematic reviews and meta-analyses of RCTs and cohort studies

Pooled analyses, meta-analyses, and systematic reviews of prospective studies are central to evaluating the health effects of dietary patterns, foods, nutrient supplements, and weight change during pregnancy.

The focus is on prospective research: RCTs and cohort studies

Prospective research is taken to mean: RCTs and cohort studies, with the latter being a catch-all for prospective cohort studies, nested patient control studies, and patient cohort studies. RCTs and cohort studies complement each other. Cohort studies are particularly valuable due to their long follow-up time, large number of participants, and the representativeness of both the participants and the range of intake levels for the general population or demographic in question. The strength of RCTs lies in their ability to provide compelling evidence for causality by eliminating confounding.

The committee does not consider case-control studies, mechanistic studies, and animal studies, because these studies do not provide sufficient evidence to formulate dietary recommendations for the general population. Case-control studies were not included because of their relatively high sensitivity to recall bias. The cases may report differently about their diet than the controls, which may affect the results of the study. To avoid this type of bias as much as possible, the committee has chosen to base its recommendations only on prospective research: cohort studies and RCTs.

With regard to most rare complications and outcomes, only case-control studies are available (not cohort studies or RCTs). This means that potential effects on these outcome measures have not received proper attention in the advisory report. The committee notes that case-control research, due to the lower evidence level, could at most be supportive to dietary recommendations based on stronger evidence. Therefore, the choice to disregard case-control studies does not affect dietary recommendations.

Starting from meta-analyses and systematic reviews

In evaluating the literature, meta-analyses, and systematic reviews of prospective studies were used wherever possible. In meta-analyses, findings from several original studies with similar questions and approaches are combined into a new risk estimate. This can be based either on the average effects in the studies (meta-analysis or meta-

regression analysis) or on individual participant data from these studies (pooled analysis). In a meta-analysis and meta-regression analysis, the correction for confounders may differ between studies, whereas said correction is uniform across all data in a pooled analysis. Intermediate forms also exist.

Combining findings from multiple studies leads to greater statistical power and more accurate estimates of the effect or association than provided by the original studies. By using pooled analyses, meta-analyses and systematic reviews, the committee has efficiently used the preliminary work done by others. The background documents explain which pooled analyses and meta-analyses were found. If applicable, they elucidate why certain publications have not been taken into account. These reasons may consist of methodological issues or insufficient information about the method used, characteristics, or outcomes. Earlier publications that included only part of the available research were disregarded if a more recent or comprehensive publication of high quality was available.

4.1.2 Methodological considerations with regard to RCTs and cohort studies

Considerations with regard to RCTs

The committee has evaluated RCTs that solely study the effect of diet (intervention and control treatments concern only the diet). The exception is the background document on gestational weight change, in which findings were described for RCTs with diet-only interventions, with physical-activity-only interventions and with combined interventions (diet and physical activity).

Blinding and dietary compliance are important aspects when interpreting the findings of RCTs. Blinding revolves around whether participants and/or researchers are aware of which intervention group the participants were assigned to. If participants are aware of the intervention, for instance, there is a chance that they will also alter other aspects of their behaviour, which may be a confounder. If researchers, on the other hand, know which group a particular participant has been assigned to, there is a chance that they may treat participants in the intervention group differently than those in the control group. Dietary compliance revolves around whether participants are able to adhere to the intervention, as the participants' degree of dietary compliance can also affect results.

The extent to which bias due to lack of blinding and lack of dietary compliance can be mitigated varies between different types of interventions, of which, broadly speaking, there are two: interventions consisting of nutritional advice or intervention consisting of the actual provision of a nutrient supplement, food, or complete diet. With nutritional advice, blinding is impossible (for the participants). When providing nutrient supplements, on the other hand, blinding is relatively easy, as the control group can be given a placebo that resembles the supplement in

terms of taste and appearance. With foods and diets, single-blind studies are the best possible option, with the person determining the outcome not knowing which food or diet was assigned to each participant.

With regard to dietary compliance, adherence to dietary advice can be more difficult than consuming a certain nutrient supplement, food or complete diet provided. Studies sometimes use an indicator of dietary compliance, such as the level of certain fatty acids in the blood.[9]

Participants in RCTs are usually not a representative sample of pregnant women overall, as these studies commonly use selection and exclusion criteria.

Considerations with regard to cohort studies

In cohort studies, the method of determining nutritional intake and the risk of confounding need consideration.

Many studies use a food frequency questionnaire, asking participants about their intake over a certain period of time, e.g. the past month. The quality of such questionnaires, i.e. their reproducibility and reliability, differs per questionnaire and per target food and depends in part on how often or how regularly participants eat a certain food. The questionnaires are usually completed by the participants themselves. Although these questionnaires allow researchers to determine who ate a particular food relatively little or relatively often, determining absolute quantities is more difficult, which complicates comparison with other cohort studies. Furthermore, comparing different cohort studies is also restricted by the fact that studies use different definitions for dietary patterns and product groups, do not all ask participants to record their intake of the same number of food items, and use different cut-off values to define low intake and high intake.

Finally, in cohort studies, certain potentially confounding variables, such as gender, age, or socioeconomic status can never be ruled out completely. Although the analyses correct for confounders, the possibility of residual confounding must be taken into account. Therefore, it is of great value if associations reported in cohort studies are confirmed in RCTs.[9]

4.1.3 General population, risk groups and patient groups

The focus is on studies of pregnant women in the general population. Because RCTs are often conducted among high-risk groups (e.g. pregnant women with high blood pressure or pre-diabetes), RCTs conducted only among high-risk groups were also included, due to the fact that this type of study is particularly significant in assessing causality.

4.1.4 Search engine and end date of literature review

The committee used PubMed and Psychinfo to search the literature for its review. The literature review covers publications published up to July 2019. The background documents outline the exact search strategies used.

The literature searches for the background document on foods and dietary patterns and the background document on weight change during pregnancy were carried out by Pallas, an independent research and consultancy firm specialising in health and healthcare, at the start of the advisory process. The updates up to and including July 2019 were carried out by the Secretariat of the Health Council of the Netherlands. The literature searches for the background document on nutrient supplements were carried out by the Secretariat of the Health Council of the Netherlands in their entirety i.e. the initial search and any updates.

Furthermore, the committee members were able to put forward studies and public consultations were observed for the background documents with the aim of discovering whether the committee had missed any important publications that fit within the methodology used (see paragraph 5.3).

4.2 Harmful effects of substances and microorganisms in the diet

Risk assessments of a toxicological nature (harmful effects of substances of foods other than nutrients) or a microbiological nature (microorganisms) have been described in various international reports. The committee has based its conclusions primarily on the risk assessments carried out by toxicology committees of the Health Council of the Netherlands and/or the European Food Safety Authority (EFSA). If these were not available, the committee used risk assessments published by other organisations (Table 3). The committee checked whether additional research had been published after the risk assessment in question. Such additional research was considered as well by the committee when reaching its final conclusions. A public consultation was observed with the aim of discovering whether the committee had missed any important publications that fit within the methodology used (see paragraph 5.3).

Table 3 List of organisations that published risk assessments used by the committee in the background document on harmful substances and microorganisms

Primary organisations
The Netherlands • Health Council of the Netherlands (HC)
Europe • European Food Safety Authority (EFSA)
Other organisations to consult in the absence of up-to-date reports by HC and EFSA
The Netherlands • Netherlands Food and Consumer Product Safety Authority (NVWA) • National Institute of Public Health and the Environment (RIVM)
Europe • Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), France • Food Standards Agency, United Kingdom • Bundesinstitut für Risikobewertung (BfR), Germany • European Commission and European Parliament
United States • Food and Drug Administration (FDA)

05 background documents: formulating conclusions

The previous chapters show that the approach taken in the background documents on the health effects of dietary patterns, foods, nutrient supplements and weight change during pregnancy differs from the approach taken in the background document on food safety (harmful substances and microorganisms). This distinction is reflected in the method used to formulate the conclusions, which is described in this chapter.

5.1 Dietary patterns, foods, nutrient supplements and weight change during pregnancy

In the background documents on the health effects of dietary patterns, foods, nutrient supplements and weight change during pregnancy, the committee evaluated the state of the science regarding effects (for RCTs) and associations (for cohort studies) for each individual topic. The method used to draw conclusions about effects and associations is outlined below.

5.1.1 Summary of findings in standardised tables

Each individual evaluation begins with a summary table with a standardised format (Table 4).

Table 4 Summary table per effect or association in the background documents on health effects.

Feature	Description
Selected studies	The committee specifies the number of meta-analyses and/or systematic reviews and the number of RCTs or cohort studies on which its conclusion is based.
Heterogeneity	No / yes; if 'yes', the committee provides an explanation if possible. Meta-analyses are tested for the statistical heterogeneity between the original studies. If this test shows little or no heterogeneity (I^2<25%), 'no' is entered in the table. The same applies for moderate heterogeneity (I^2 25-50%), although moderate heterogeneity will always be addressed in the accompanying text. Only in case of significant heterogeneity (I^2>50% and p<0.10) will the table say 'yes'. In the absence of a heterogeneity test, the committee will assess the overlap between the confidence intervals of the original studies or meta-analyses and the direction of the effect or risk estimates. The committee distinguishes between heterogeneity with regard to the *size* versus the *direction* of the effect/association. In case of heterogeneity with regard to the size of the effect/association, it is not possible to quantify the effect/association. In case of heterogeneity with regard to the direction, the findings on the effect / association are considered to be *contradictory.*
Strength of the effect/ association	If it proves possible to quantify the effect/association, the committee will specify the effect estimate or risk estimate with the 95% confidence interval. If possible the change of the associated dietary component is quantified as well. If a meta-analysis presents the effects based on both fixed effects and random effects models, the committee will always adopt the results of the random effects model.
Population studied	For cohort studies, the committee will specify in which continent the study took place (Europe, North America, Australia & New Zealand, Asia, Africa and South America). In the case of RCTs, the committee will specify which groups and/or risk groups were studied.

5.1.2 Five conclusion options per evaluation

Below the summary table, one will find the conclusion, with the committee choosing one of five fixed options (Table 5). These conclusions are formulated differently for intervention studies than for cohort studies, as intervention studies allow one to draw conclusions about effects (causality), while cohort studies only allow for conclusions about associations. If the

available publications suggest an effect or association, the committee will indicate whether it considers the evidence to be strong or limited.

Table 5 Conclusions on health effects in the background documents.

Option	Conclusion	Description
1	*High or low exposure increases or decreases the risk of disease (based on RCTs), or high or low exposure is associated with a higher or lower risk of disease (based on cohort studies).* *The evidence is strong or limited.*	For conclusions of this type, the committee will specify the strength of evidence based on the availability of studies, the presence or absence of heterogeneity with regard to the direction and size of the effect/association, the strength of the effect/association (confidence interval, statistical significance, and possibly the magnitude of the risk estimate) as well as any additional considerations specified in the text. If the conclusion relates to a specific population or level of exposure, this is specified. If the evidence is strong and there is little heterogeneity in terms of the direction and the size of the effect/association, the committee quantifies the effect/association. If the evidence is strong and there is considerable heterogeneity in terms of the size of the effect/association, or if the evidence is limited, a qualitative conclusion will be given (see the decision tree in the appendix).
2	*An effect/association is unlikely.*	This conclusion will be given if there are sufficient studies that do not indicate an effect/association. For studies with continuous outcome measures, the estimate will be close to zero (no effect/association) with a narrow confidence interval. For studies with a dichotomous outcome measure, the estimate (such as a relative risk or an odds ratio) will be close to one (no effect/association) with a narrow confidence interval.
3	*The effect/association is contradictory.*	This conclusion indicates that there is uncertainty about the direction of the effect/association. The conclusion is used if one of the following two situations applies: 1) A meta-analysis has found significant and unexplained heterogeneity in the direction of effect/association. 2) No measure of heterogeneity is available, but the findings of the original studies show significant differences in the direction of effects or associations, with (near) significant findings in both directions.
4	*Too little research has been done to make a statement about the effect/association.*	One or more of the following situations applies: 1) No more than two original studies are summarised in a systematic review or more than two studies are summarised, but the number of participants/ cases is insufficient (see paragraph 5.1.3 for the definition of ‘insufficient’). 2) Three or four studies are summarised, but the available studies are of insufficient quality to make a statement about the effect/association, for example due to publication bias or insufficient correction for confounding. 3) Three or four studies are summarised, but all available studies are from one research group and are therefore not independent.
5	*No conclusion can be drawn based on the available studies.*	Five or more original studies are summarised in a systematic review, but there is some degree of uncertainty as to whether a effect/association exists (the width of the confidence interval does not allow one to draw a conclusion and the original publications do not demonstrate convincing heterogeneity with regard to effect direction).

The conclusion is followed by a text in which the conclusion is explained and in which the committee presents the publications assessed in connection with the conclusion. In said text and in the corresponding table or tables, the committee presents the research data used for the summary table.

5.1.3 Decision tree

The committee used the accompanying decision tree to draw its conclusions (see Appendix B). In doing so, it used criteria for the number of studies and participants per type of conclusion. These criteria were based on experience with the *Physical Activity Guidelines 2017* by the Health Council. In order to conclude that there is strong evidence for an effect or association, or that an effect or association is unlikely, there must be at least five studies with a total of at least 150 participants (RCTs with continuous outcome measures) or 500 cases (cohort studies). In order to conclude that there is limited evidence, there must be three or four studies with at least 90 participants (RCTs with continuous outcome measures) or 300 cases (cohort studies). In the event of one or two studies, the conclusion will be that too little research has been done. Table 5 shows that the latter conclusion may also have some other causes that are related to study outcomes, study quality, and study groups.

Because of the large number of RCTs with dichotomous outcome measures that studied the health effects of nutrient supplements during pregnancy, the committee introduced an additional criterion for the number of cases required for these studies. In addition to the criteria mentioned above, the committee requires there to be at least 100 cases in the intervention or control group to conclude that there is strong evidence for an effect or association, or that an effect or association is unlikely, and that there be at least 60 cases in the intervention or control group to conclude that there is limited evidence. The number of participants needed in individual RCTs obviously depends on the difference between the outcome measure and the expected effect size. The committee's experience is that these cut-off values are useful in practice.

5.2 Harmful effects of substances and microorganisms in the diet

In formulating its conclusions about the harmful effects of substances and microorganisms in the diet, the committee primarily relies on the assessments of national and international organisations, and – if available – on additional research published after the risk assessment (see paragraph 4.2). The committee has not created its own decision model for weighing the strength of evidence of harmful effects, but will indicate whether its conclusions are based on human, animal and/or in vitro research. Where possible, the exposure and the effect or association will be quantified. For harmful substances that are known to exceed tolerable intake levels, the focus in the committee's advisory report will mainly be on foods that are to be avoided.

5.3 Public comment periods for background documents

Drafts of the four background documents in which the committee described the state of the science were temporarily published on the Health Council's website in 2019 to give stakeholders the opportunity to comment on their content:

- Health effects of food consumption and dietary patterns during pregnancy[1]
- Health effects of nutrient intake from supplements during pregnancy[2]
- Health effects related to weight change during pregnancy[3]
- Harmful effects of substances and microorganisms in the diet during pregnancy[4]

Organisations of professionals involved in pregnancy care were sent an e-mail to notify them of the public consultation, as well as a second e-mail at the start of this period.

The purpose of the public consultation was twofold:

1. Did the committee miss any important publications that fit within the working method used?
2. Are there any mistakes in the background documents?

After these public consultations, the background documents were finalised. All comments received on the content of the documents and the committee's responses to these comments can be found on the Health Council's website (these are only available in Dutch).

06
the advisory report: from conclusions to recommendations

The previous chapters described the working method used in drawing up the background documents accompanying this advisory report. This chapter outlines how the conclusions drawn in the background documents were combined with additional relevant literature to arrive at the recommendations published in the advisory report.

6.1 Selection of conclusions from background documents relevant to the advisory report

The dietary recommendations for pregnant women are based on the conclusions from the background documents.

The background document on food safety (harmful substances and microorganisms) ends with a paragraph for each topic in which the committee formulates its conclusion on the exposure in question. This final conclusion was then incorporated into the advisory report.

In the three other background documents, separate conclusions per outcome measure were formulated for each exposure, specifically for findings based on RCTs (effects) or cohort studies (associations). The dietary recommendations are primarily based on the conclusions with a strong evidence level. The recommendation on the use of vitamin D supplements is an exception: it is based on multiple findings with a limited evidence level.

In these three background documents, each exposure ends with a concluding paragraph in which the committee indicates which conclusions are relevant to mention in the advisory report (main findings) and how other conclusions relate to these main findings. Conclusions with a strong evidence level warrant inclusion in the advisory report. Other conclusions do not necessarily have to be included in the advisory report, as they do not affect the recommendations. In this concluding chapter of the background documents, the committee also discusses the following types of conclusions:

- Conclusions that an effect or association is unlikely. These cannot contradict the conclusions with a strong evidence level and therefore have no added value with regard to establishing recommendations. As such, they need not be included in the advisory report. However, as these conclusions require the same amount of research as conclusions supported by a strong evidence level, they are highlighted here.
- Conclusions based on limited evidence. There is no need to include these conclusions in the advisory report if they point in the same direction as conclusions with a strong evidence level: in that case, they will not affect the recommendations. If they point in the opposite direction to the conclusions with a strong evidence level, they do warrant inclusion in the advisory report.
- With regard to topics on which the committee concluded that too little research had been done to draw a conclusion, there are some for which the few studies available did demonstrate statistically significant

effects or associations. These findings are not relevant when it comes to drawing up recommendations, but the committee will state in this concluding paragraph of the background document whether the study outcome is consistent with the findings with a strong evidence level.

Conclusions that the results of the available studies are contradictory are not considered by the committee in preparing its advisory report.

In the advisory report, all findings for which the evidence level is not mentioned have strong evidence levels. Where possible, the effect or association is quantified for conclusions with a strong evidence level, but it must be noted that this was not possible for all conclusions with a strong evidence level (see the explanation in the background document in question). The relevance of the findings to the situation in the Netherlands depends on the circumstances of the study. Thus, where necessary, the committee checked whether the average intake levels of the study populations were comparable to those in the Netherlands.

The committee's findings cover a wide range of outcome measures. The committee pondered whether, based on the severity of the outcomes and their prevalence in the Netherlands, it was possible to rank the various recommendations. The committee concluded that such ranking was not feasible. Effects on infrequent but very serious outcome measures cannot be valued to be more or less important than effects on more frequent but less serious outcome measures in the Netherlands. The committee therefore considers most of its recommendations to be equally relevant.

6.2 Additional information and the involvement of experts not on the committee

In the context of this advisory process, RIVM investigated various topics at the behest of the committee.

- The dietary recommendations for pregnant women that were being promoted by various organisations and websites at the beginning of this advisory process.
- Available Dutch publications on food consumption and nutrient intake by pregnant women, and on the nutritional status of pregnant women (nutritional status generally refers to nutrient concentrations in the blood or in urine).
- The fat content of relevant fish species.

The committee prepared an additional new background document in a late stage of the advisory process, to establish the recommendation on fish species and on the dosage of fish-fatty-acid supplements.[10] The committee assesses the fish species based on the information available on the levels in fish of methylmercury, dioxins, and PFAS. The committee explains the

considerations leading to the recommended dosage of fish-fatty-acid supplements.

In the final phase, some specific issues concerning the findings on food safety (harmful substances and microorganisms) were presented to experts who were not members of the committee: Dr. L.A.P. Hoogenboom of the Wageningen Food Safety Research Institute; Dr P. Boon, G. van Donkersgoed, Dr S. Jeurissen and Dr R. de Jonge of the National Institute for Public Health and the Environment (RIVM); Dr J. Castenmiller and Dr A.E.I. de Jong of the Netherlands Food and Consumer Product Safety Authority (NVWA), and Dr Sophie van der Krieken and W. van der Vossen of the Netherlands Nutrition Centre.

6.3 Closed comment period for professional bodies and review by the standing committee

The draft of the advisory report and the accompanying background documents were submitted to organisations of professionals involved in pregnancy care: the professional bodies of midwives, gynaecologists, dieticians, general practitioners, paediatricians, and weight counsellors. The main purpose of this second comment period was to determine the feasibility of the advisory report. The council asked the professional bodies to highlight any parts of the advisory report that may be problematic upon implementation. The comments received and the committee's responses to them can be found on the Health Council's website.

The advisory report was then reviewed by the Standing Committee of the Health Council of the Netherlands, a body that discusses draft versions of advisory reports to be published by the council, checking their scientific quality and consistency with the Council's other advisory reports and identifying issues that may play an important role in the implementation of the recommendations.

references

1 Health Council of the Netherlands. *Health effects of food consumption and dietary patterns during pregnancy. Background document to Dietary recommendations for pregnant women*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/26-A2e.

2 Health Council of the Netherlands. *Health effects of nutrient intake from supplements during pregnancy. Background document to Dietary recommendations for pregnant women*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/26-A3e.

3 Health Council of the Netherlands. *Health effects related to weight change during pregnancy. Background document to Dietary recommendations for pregnant women*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/26-A4e.

4 Health Council of the Netherlands. *Harmful effects of substances and microorganisms in the diet during pregnancy. Background document to Dietary recommendations for pregnant women*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/26-A5e.

5 Health Council of the Netherlands. *Methodology for the evaluation of the evidence for the Dutch dietary guidelines 2015 - Background document Dutch dietary guidelines 2015.* The Hague: Health Council of the Netherlands, 2015; publication no. A15/03E.

6 Health Council of the Netherlands. *Methodology for the evaluation of evidence. Background document to Physical activity guidelines 2017.* The Hague: Health Council of the Netherlands, 2017; publication no. 2017/08Ae.

7 European Food Safety Authority (EFSA). *Food additive re-evaluations*. https://www.efsa.europa.eu/en/topics/topic/food-additive-re-evaluations. Consulted: 04-10-2018.

8 Green BB, Marsit CJ. *Select Prenatal Environmental Exposures and Subsequent Alterations of Gene-Specific and Repetitive Element DNA Methylation in Fetal Tissues*. Curr Environ Health Rep 2015; 2(2): 126-136.

9 Grobbee D, Hoes A. *Clinical epidemiology. Principles, methods, and applications for clinical research.* Jones and Bartlett Publishers, Inc.; 2007.

10 Health Council of the Netherlands. *Assessment of fish species and dosage of fish-fatty-acid supplements. Background document to Dietary recommendations for pregnant women*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/26-A6e.

annexes

A variation in dietary recommendations for pregnant women at the start of this advisory process [a,b]

Topic	Option 1 (source)	Option 2 (source)	Option 3 (source)	Sources that do not mention the topic	Conclusion on the situation in 2017
Use a folic acid supplement before and after conceiving	Dosage: 400 micrograms. Period: From the moment you start trying to conceive until the 10th week of pregnancy. Start at least 4 weeks before conceiving (1, 5, 8, 9).	Dosage: 400-500 micrograms. Period: From the moment you start trying to conceive up to and including the 8th week of pregnancy. Some of these sources add: start at least 4 weeks before you start trying. (2-4,6).	Dosage: 400-500 micrograms. Period: From the moment you start trying to conceive until at least the 8th week of pregnancy. You will no longer need to take the supplement after 10 weeks (7).	None	All sources recommended taking folic acid supplements. Differences between sources pertained to (1) dosage, (2) the recommendation of starting at least 4 weeks before conceiving, and (3) the week in which to stop taking supplements.
Use a supplement with 10 micrograms of vitamin D per day	Target group: All pregnant women (1,3,5,7-9).	Target group: Only pregnant women in risk groups (e.g. dark skin, low sun exposure) (4,6).	Target group: The supplement was recommended for one of the risk groups: pregnant women with dark skin. For other pregnant women, including all other risk groups, the source adds: “It is up to you to decide whether to take extra vitamin D, as is recommended by the Health Council of the Netherlands.” (2).	None	Differences between the sources pertained to the target audience.
Varied diet	Eat a varied diet (1-4). The Netherlands Nutrition Centre adds several considerations for people with a vegetarian or vegan diet.	Not all sources mentioned the same considerations for people with a vegetarian or vegan diet.		5-9	This topic was not discussed in all sources.
Iron-rich foods	Get plenty of iron (1, 2, 4, 8, 9). Eat products high in vitamin C, such as fruit and vegetables, with every meal to promote the absorption of iron (1, 4, 8, 9).			3, 5-7	This topic was not discussed in all sources.
Caffeine	Max. 1 cup of coffee or 1 glass of energy drink per day, with a moderate intake of tea and cola (1, 4).	Limit coffee, max. 1 energy drink per day (2).	Max. 4 cups of coffee per day. Or max. 8 glasses/cups of cola or tea per day if you do not drink coffee (7). Limited intake of caffeinated beverages (6). Max. 200-300 mg caffeine (9).	3, 5, 8	Differences between sources pertained to (1) whether the topic was discussed or not, (2) the quantities specified, and (3) the products specified.

Topic	Option 1 (source)	Option 2 (source)	Option 3 (source)	Sources that do not mention the topic	Conclusion on the situation in 2017
Product group fish:					
• Oily fish	Max. twice a week (1, 7, 9).	Once a week (6).	No maximum specified (8).	2-5	Differences between sources pertained to (1) whether the topic was discussed or not, (2) whether or not a maximum amount was specified.
• Predatory fish	Avoid predatory fish, with the exception of canned tuna (1, 8, 9).			2-7	This topic was not discussed in all sources.
• Eel	Avoid Dutch eel (and mitten crab) (1,7,9).			2-6, 8	This topic was not discussed in all sources.
• Raw fish	Avoid raw fish and sushi (1, 3, 5, 6, 9). Avoid raw seafood (1, 9).	Raw fish or sushi need not be avoided, with the exception of pre-packaged, store-bought options (8).		2, 4, 7	Differences between sources pertained to (1) whether the topic was discussed or not, (2) the seafood specified, (3) whether or not packaged/store-bought options were distinguished from fresh options.
• Smoked fish	Avoid (1, 6-9)			2-5	This topic was not discussed in all sources.
• Pre-packaged fish	Avoid (3, 7-9).			1, 2, 4-6	This topic was not discussed in all sources.
Product group meat:					
• Raw or semi-raw meat/meat products	Avoid (1, 3, 4, 6, 7, 9).	Avoid, or freeze if absolutely necessary (2, 8).		5	Differences between the sources pertained to (1) whether or not this topic was discussed, (2) whether or not the option of freezing food was addressed.
• Liver and liver products	Avoid liver (1-8). Avoid liver products or eat liver products in moderation (e.g. max. 1 sandwich per day) (1, 3, 4, 6, 8, 9).				This topic is mentioned in all sources. Differences between the sources pertained to how the liver products were specified.
• Use of vitamin A supplements	Avoid vitamin A medicines and remedies (1, 8).	Exercise caution when taking medicines containing vitamin A (3).		2, 4-7, 9	Differences between sources pertained to (1) whether the topic was discussed or not, (2) the definitions of “avoiding” or “exercising caution”, (3) the definition of “remedies” or “medicines”.
Product group milk and milk products:					
• Raw milk	Avoid (1, 2, 6, 7).			3, 4, 5, 8, 9	This topic was not discussed in all sources.
• Raw-milk cheese	Avoid (1-9).				This recommendation was given by all sources.
• Calcium-rich foods	Eat plenty of dairy (2-3 servings of dairy, 40g of cheese) (1,8,9).			2-7	This topic was not discussed in all sources.
• Calcium supplements	High doses not recommended (8)			1-7, 9	This topic was not discussed in all sources.

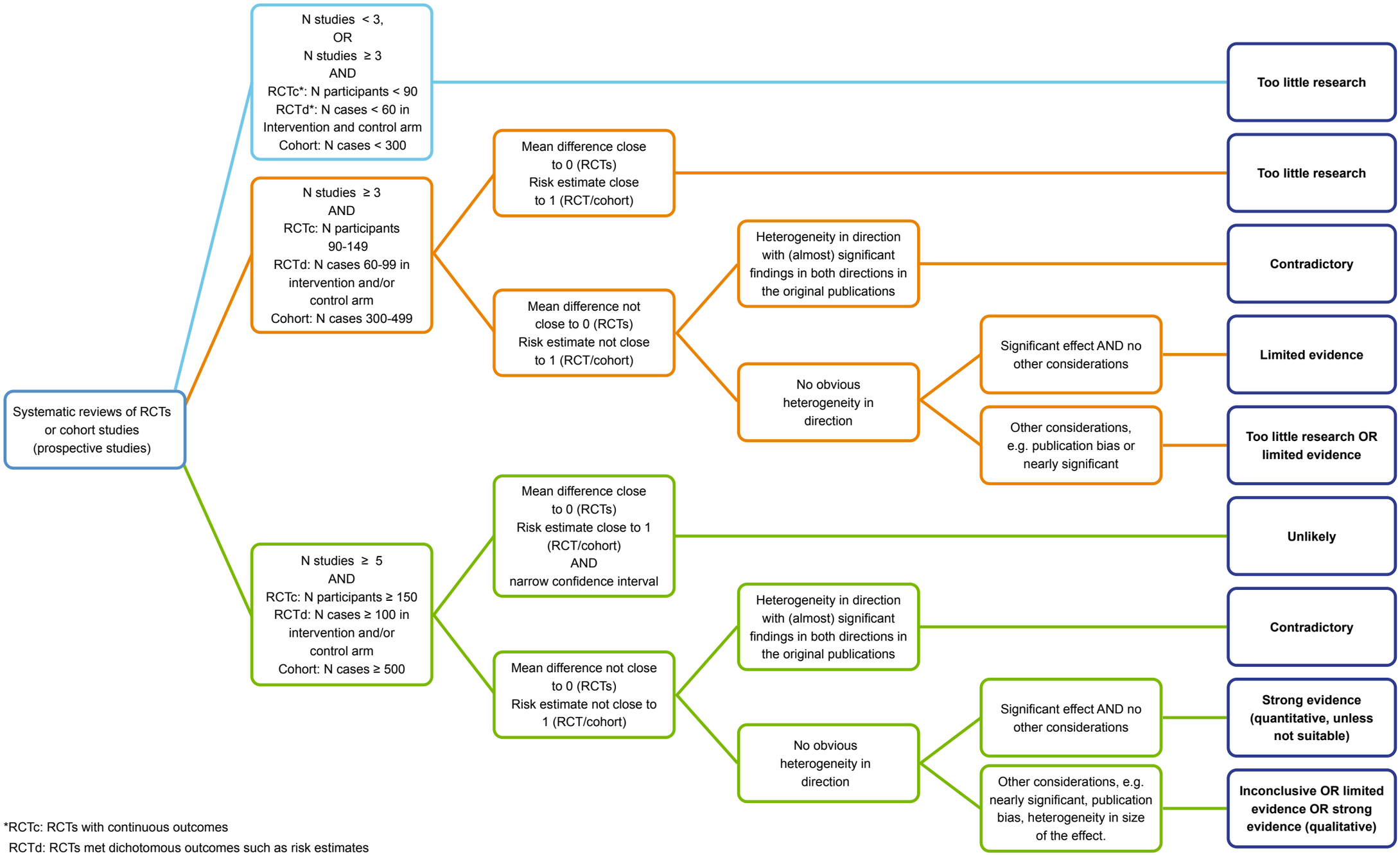
Topic	Option 1 (source)	Option 2 (source)	Option 3 (source)	Sources that do not mention the topic	Conclusion on the situation in 2017
Raw egg and products made with raw egg	Avoid (1-3, 5-8).			4, 9	This topic was not discussed in all sources.
Fruit and vegetables	Eat plenty of fruit and vegetables. Avoid raw sprouted vegetables (1). Hygiene measures (1, 4, 6, 8, 9).			2, 3, 5, 7	This topic was not discussed in all sources.
Fluids	Drink plenty of fluids (1.5-2 litres per day) (1, 4).			2, 3, 5-9	This topic was not discussed in all sources.
Alcohol	Avoid (1-9). Be careful with tiramisu, as it may contain alcohol (1, 8).				This recommendation was given by all sources.
Herbs and spices	Avoid/eat in moderation: • aniseed (1, 8). • basil (pesto), tarragon, cinnamon (1, 7, 8). • dong quai, mace, nutmeg, pepper, allspice, sassafras (1). • fenugreek, hawthorn, feverfew, nigella, senna (1, 9). • fennel seed (1, 7).	Avoid: • aniseed (7, 9). • Avoid as much as possible: • fenugreek, hawthorn, feverfew, nigella seed, senna (7, 8). • Avoid/eat in moderation: • sage (8, 9).	Avoid: • wormwood, aloe, buckwheat, dong quai, ephedra, coltsfoot, kava kava, borage, sassafras, comfrey, fennel (7-9).	2, 3, 4, 5, 6	Differences between sources pertained to (1) whether the topic was discussed or not, (2) the spices specified.
Herbal remedies	Avoid herbal remedies (pills) and herbal essential oils (1, 2).			3-6	This topic was not discussed in all sources.
Herbal tea	Fennel and aniseed tea: 1-2 glasses per day (1).	Avoid fennel and aniseed tea (9).		2-8	Differences between sources pertained to (1) whether the topic was discussed or not, (2) the recommendation.
Liquorice tea	Liquorice tea: 1-2 glasses per day (1, 9). Max. 2-3/ a few pieces of liquorice a day (1, 7, 9).			2-8	This topic was not discussed in all sources.
Salt	Salt is part of the so-called Wheel of Five (1).	Do not consume too many products that are high in salt (ready-made sauces, soups and flavourings) (7).		2-6, 8	This topic was not discussed in all sources.
Miscellaneous	Avoid dried superfoods (1).	Consume rhubarb in moderation (9).	Avoid soft-serve ice cream (6).	2-5, 7,8	This topic was not discussed in all sources.
Supplements / remedies	Avoid Calabash Chalk during pregnancy due to the possible presence of lead (1, 9).			2-8	This topic was not discussed in all sources.

[a] The table was based on an overview created by the National Institute for Public Health and the Environment (RIVM) for the committee at the start of the advisory process (in 2017).

[b] In the table, the sources (consulted in 2017) are numbered as follows:

1: The Netherlands Nutrition Centre
2: Leaflet on “Pregnancy”. This is a countrywide leaflet with information and advice from midwives, gynaecologists, general practitioners and other professional organisations involved in pregnancy care (National Institute for Public Health and the Environment RIVM).
3: Website strakszwangerworden.nl by the College Perinatale Zorg, a Dutch network organisation on perinatal care
4: The Dutch professional body of midwives (KNOV)
5: Website dieetditdieetdat.nl by the Dutch professional body of dieticians
6: Website thuisarts.nl by the Dutch professional body of general practitioners
7: Website www.babyvandaag.nl
8: Website www.wij.nl/zwanger-info
9: Website www.24baby.nl/zwanger

B decision tree



*RCTc: RCTs with continuous outcomes
RCTd: RCTs met dichotomous outcomes such as risk estimates

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