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European Food Safety Authority

Public Consultation on the draft scientific opinion on appropriate age for introduction of complementary feeding into an infant's diet

Fields marked with * are mandatory.

General Information

*First name

Helen

*Last name

Crawley

*E-mail

helen@firststepsnutrition.org

*Select your country

United Kingdom

*Category

NGO

*Name of employer *(insert N/A if not applicable)*

First Steps Nutrition Trust

Public consultation on a draft opinion on appropriate age for introduction of complementary feeding into an infant's diet

*Select the chapters you want to comment

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1. Introduction
- 1.1. Background and Terms of Reference as provided by the requestor - not for comment
- 1.2. Previous assessments
- 1.3. Definitions
- 1.4. Need for complementary foods for infants
- 1.5. Interpretation of the Terms of Reference
- 1.6. General considerations on the outcomes assessed

1.3. Definitions

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on lines 735-736 it is stated that:

The Panel considers that the appropriate age of introduction of CFs (which is the subject of this mandate) should not be regarded as synonymous with the optimal duration of exclusive breast feeding.

The age of appropriate introduction of foods other than breastmilk to an infant has to include the considerable body of evidence that shows that breastfeeding, and its exclusivity, is a key factor in reducing morbidity. To look at these separately in a review that uses the title 'appropriate age for introduction' is nonsensical. It is well known and acknowledged in the review (on lines 725-7) that as complementary foods are introduced that the amount of breastmilk consumed will reduce, therefore it is unrealistic to view the introduction of complementary foods separately to evidence about the optimal duration of breastfeeding. We beleive that this review answers the wrong question and has a misleadign title.

1.4. Need for complementary foods for infants

- 1.4.1. Nutritional adequacy of exclusive breast-feeding
- 1.4.2. Nutritional adequacy of exclusive breast-feeding: overall conclusions

1.4.2. Nutritional adequacy of exclusive breast-feeding: overall conclusions

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Lines 837-840 say that:

The Panel concludes that exclusive breast-feeding is nutritionally adequate up to 6 months for the majority of healthy infants born at term from healthy well-nourished mothers. However, some infants at risk of iron depletion may need CFs, especially foods that are a source of iron, before 6 months of age in addition to breast-feeding.

The first sentence acknowledges that most infants do not nutritionally require complementary foods until about 6 months of age, which begs the question why would you then introduce them earlier just because 'you can'? We do not believe adequate data is presented in this review to make the generalised statement relating to iron deficiency here, which is included without any reference. We review this in more detail in comments on section 15.

1.5. Interpretation of the Terms of Reference

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In the terms of reference, and throughout the document, the age of introduction of complementary foods and the duration of breastfeeding (or of formula feeding or, as is often the case, of mixed breast and formula feeding) are treated as two separate entities. They are not; the earlier complementary foods are introduced, the shorter the duration of exclusive breastfeeding and the total amount of breastmilk given to an infant. If, as shown by a large body of research worldwide, the benefits of breastmilk are proportional to its duration, then shortening it unnecessarily may cause harms. It is probably true that if an infant is given his or her first complementary foods when he or she is developmentally ready, there will be no harm (and this is true if developmental readiness occurs at 4 or 5 months, but also at 7 or 8 months). Labelling ultra-processed complementary foods from 4 months will promote the use of these foods before developmental readiness, both by the direct effect of marketing and by the indirect effect of health workers recommending products at an earlier age. The Panel did not appear to debate and consider this.

2. Data and Methodologies

- [x] 2.0. Data and Methodologies
- [ ] 2.1. Data
- [ ] 2.2. Methodologies
- [ ] 2.3. Protocol amendments

2.0. Data and Methodologies

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There are more than 20 complex pages on data and methodologies and it would have taken the 21 members of the panel and the support staff at EFSA a considerable amount of hard work to go through the thousands of available papers, to decide on the many exclusion criteria cited and the suitability of papers to review. It is impossible for reviewers of this EFSA opinion to repeat the search and analysis in the few weeks the consultation is open. It would have been easier to consider the studies reviewed, and conclusions, if the scope was restricted to the question which should have been at the heart of this review, which is the impact of adding commercial ultra-processed cereal-based and baby foods to the diets of infants and whether there is any rationale for ecouraging the intake of solid food before 6 monthts of age.

As it has not been possible to review all the sections of this report we have focused on a few sections to illustrate that, in our opinion, the evidence review does not appear in places to have been accurate. We think this may raise doubts about the results from other sections, and the overall conclusions of the review.

We would also like to comment on the lack of information provided about conflicts of interest in studies reported.

3. Assessment of the developmental readiness of the term infant to receive CFs

- [x] 3.0. Assessment of the developmental readiness of the term infant to receive CFs

- 3.1. Gastro-intestinal function
- 3.2. Renal function
- 3.3. Neuromuscular coordination and neurodevelopment
- 3.4. Developmental readiness of the term infant to receive CFs: conclusions

3.0. Assessment of the developmental readiness of the term infant to receive CFs

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In this and other sections of chapter 3, the lower end of the development range is continuously emphasized. The range for an infant sitting without support, for example, an essential developmental milestone for readiness to complementary foods, is reported between 3.8 to 9.2 months; but the members of the panel seem to privilege the lower side of the range, omitting the fact that at 6 months many infants would not be ready for complementary foods based on this parameter. This is probably a consequence of the decision to restrict the review to analysis of outcomes of complementary feeding before 6 months of age. Infants introduced to complementary foods at 7 or 8 months, because that's the age at which they can sit without support, could have better outcomes than those given foods earlier, but this evidence is ignored in this review.

In chapter 3, lines 1715 to 1719; it is suggested that greater neurological control of the tongue movements start at 2-4 months of age, but then say the Panel was unable to retrieve empirical data for this estimation. In lines 1729- 1731 it is suggested that an infant has to be able to ‘move the upper lip down to wipe food from a spoon when being spoon fed’, but does not challenge whether spoon feeding (and what is being fed) is the best estimate of readiness for solids. In the discussion on the evidence relating to the swallowing reflex it is suggested that this develops alongside jaw stability, which develops alongside head and trunk stability and control.

Very limited evidence is presented in lines 1748-1766 relating to head stability when lying or sitting aided, and this generally suggests that head control is not achieved well in infants under 5 months of age. The one study from Japan which reported that the majority of infants could maintain the head (based on ‘pulling on the arms’) at 3.25 months was based on reported data from the 4m health check, and it is not clear how the measurement was made, or its significance. As is reported, infants in this study were on average 6.66m before they could sit unaided, a measure of trunk and head stability. Other data reported in lines 1767- 1779 suggest lower ages at which infants are able to sit unaided. However, the majority of these studies reported that most infants were greater than 5m of age when they could sit unaided, and babies who were born small for gestational age were 6-7m of age. The data on lower birthweight infants from the study by Yokoyama et al, 2011 is not reported in the review, but was 6.65m. In our opinion this section therefore fails to provide evidence for the ability of most infants to sit up unaided before about 6m of age.

In lines 1780–1800 the ability of infants to reach out was examined, but limited evidence is provided. For example, no evidence is given on how reaching movements are structured, with evidence suggesting that straighter reaching movements are not achieved until about 6m of age (van Hofsten, 1991) and that reaching movements are linked to trunk stability and that control of both is needed, and this occurs at about 6m of age (Hopkins and Rönnquist, 2001).

In lines 1825-26 the panel "concludes from the available developmental data that most term infants are ready to be introduced to CFs between about 3-4 months of age and around 6 months of age", thus leaving out all the infants who reach developmental readiness after 6 months of age. The panel seems to contradict in its conclusions those of Naylor and Morrow in their 2001 review (Naylor and Morrow, 2001), despite citing it often in section 3. There is no explanation of the divergence, given the fact that many studies were used in both reviews.

Throughout this section the authors repeatedly acknowledge that there is biological variability when infants develop the necessary motor skills for the introduction of solids, ranging from 3-4 months to around 6 months of age, but this is not supported by the data presented. It appears as if it was agreed in advance that the 3-4 months to 6 months age range would be suggested throughout the document, regardless of evidence presented. We suggest this whole section needs further critical review.

Hopkins B and Rönnqvist L (2011) Facilitating postural control: effects on the reaching behaviour of 6m olds. Developmental Psychobiology, 40, 168-182.

Von Hofsten (1991) Structure of early reaching movements a longitudinal study. J Motor Behavior, 23, 282-290

5. Assessment of the data on BMI and related endpoints in term infants or mixed populations

- ☐ 5.1. BMI: final body of evidence
- ☐ 5.2. BMI: endpoint and study selection
- ☑ 5.3. BMI: summary of the evidence
- ☐ 5.4. BMI: conclusions and grading of the confidence in the evidence

5.3. BMI: summary of the evidence

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Lines 2189-2191:
For BMIZ or attained BMI, the evidence derived from the two RCTs (Jonsdottir et al., 2014; Perkin et al., 2016) did not show an effect of the timing of introduction of CFs at 3-4 months of age compared with the introduction at 6 months on these endpoints assessed up to 3 years of age.
The study by Jonsdottir et al (2014) looked only at exclusively breastfed infants and the impact of the introduction of complementary foods at 4 months or at 6 months, but this is not highlighted. It is a relatively small study, father's weight was not included as an explanatory variable and there was a significant difference between the groups in terms of mode of delivery with significantly more babies in the group exclusively breastfed for 6 months being born by caesarean delivery. Whilst this study did at least intend to report on weight as an outcome, the study by Perkin et al (2016) aimed to look at the impact of the introduction of specific allergenic foods on allergy development, and weight outcomes were not stated outcome measures. Again, all babies were exclusively breastfed and it appears that the reviewers may have trawled through the supplementary papers to this study to find data related to weight as none are reported in the paper. Supplementary papers are not referenced. It is unlikely the study was powered to consider secondary outcome measures. It is odd that if such a data fishing exercise was undertaken such a firm conclusion is reached, and that the conclusion does not mention that these studies are only relevant to breastfed infants.

6. Assessment of the data on obesity and overweight in term infants or mixed populations

- ☑ 6.1. Obesity and overweight: final body of evidence
- ☐ 6.2. Obesity and overweight: endpoint and study selection
- ☐ 6.3. Obesity: summary of the evidence
- ☐ 6.4. Overweight: summary of the evidence
- ☐ 6.5. Obesity and overweight: conclusions and grading of the confidence in the evidence

6.1. Obesity and overweight: final body of evidence

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In lines 2324-2327 it is concluded:
The main line of evidence consists of six prospective cohort studies and no RCT (Reilly et al., 2005; Brophy et al., 2009; Neutzling et al., 2009; Huh et al., 2011; Layte et al., 2014; Zheng et al., 2015). For these studies, which mainly investigated introduction of CFs at <3-4 months of age, the result of the meta-analysis did not show a statistically significant association between the age of introduction of CFs and the chance of developing obesity up to 11 years of age.

There are a number of studies that have looked at the age of introduction of complementary foods and overweight, and it is not clear how these six prospective studies were chosen. Data is included from China and Brazil as well as the USA and UK, so they were not chosen due to geographical relevance. However, a number of other studies (6) in this subject area that have been included in a meta-analysis of prospective studies (Wang et al, 2016) were not included. The meta-analysis by Wang et al (2016) concluded that introducing complementary foods before 4 months of age compared to at 4 to 6 months was associated with an increased risk of being overweight. This study had clear inclusion criteria and used a relatively consistent cut-off age to define an early (<4 months or ≤3 months) versus late (≥6 months) introduction to complementary foods.

In their conclusion the EFSA Panel give no age range for the timing of introduction of complementary foods in terms of risk of obesity development, and as highlighted earlier the summary at the end of the section (lines 2459 – 2463) the terms early and later introduction are extremely confused:

'The ages of introduction of CFs ranged between <1 month and <4 months for early introduction and >2 months and ≥6 months for later introduction'.

The suggestion here that early introduction of complementary foods is not associated with obesity even in very young infants is concerning.

Wang J, Yuangue W, Cuoping X, Chao T et al (2016) Introduction of complementary feeding before 4 months of age increases the risk of childhood overweight or obesity: a meta-analysis of prospective cohort studies. Nutrition Research, 36, 759-770.

12. Assessment of the data on infections in term infants or mixed populations

- [x] 12.1. Infections: final body of evidence
- [ ] 12.2. Infections: endpoint and study selection
- [x] 12.3. Gastro-intestinal infections: summary of the evidence
- [x] 12.4. Upper respiratory tract infections: summary of the evidence
- [x] 12.5. Lower respiratory tract infections: summary of the evidence
- [x] 12.6. Infections in general: summary of the evidence
- [ ] 12.7. Infections: conclusions and grading of the confidence in the evidence

12.1. Infections: final body of evidence

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The evidence presented in this section appears contradictory because introduction of complementary foods before 6 months of age displaces breastmilk and leads to a shorter duration of exclusive breastfeeding and

is therefore associated with an increased risk of a range of infections. For example, from one of the cited studies by Quigley et al (2007): 'each additional month of EBF reduced the risk of hospitalisation for diarrhoea and LRTI'. Milk feeding practices in the reviewed studies are not considered adequately, and the influence these may have on the findings and their generalisability is not discussed.

The selection of studies also appears to be questionable. The evidence reviewed includes 3 RCTs and 7 prospective studies. However, 2 of the RCTs were conducted in Honduras and we question the appropriateness of the poorly defined exclusion criteria used to justify their inclusion: 'human studies were not considered pertinent if they: investigated the outcome 'infections' in low and lower-middle income countries in settings with poor hygiene conditions.'

In the EFSA summary conclusion on infections in lines 246-250 it is stated that:

'For infections, there is no evidence that in countries with hygiene conditions that are similar to those in high-income countries the introduction of complementary foods <6 months of age compared with thereafter is associated with an increased risk of 1) gastro-intestinal infections (low level of confidence in the evidence) lower respiratory tract infections (moderate level of confidence in the evidence) or 3) infections in general (moderate level of confidence in the evidence). The evidence for upper respiratory tract infections is conflicting and insufficient to draw conclusions'.

Cohen et al (1994), authors of one of the 2 RCTs the panel included, state in their paper that
'Subjects came from poor neighbourhoods in which environmental sanitation was poor (only 60% of the households had indoor piped water)'.

12.3. Gastro-intestinal infections: summary of the evidence

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Only one of the four studies cited was explicitly designed to look at infection as an outcome of early introduction of solid foods (Forsyth et al 1993). Including studies in which morbidity data was not collected as a pre-specified outcome, as is the case for all three RCTs cited, is questionable. We particularly disagree with the appropriateness of including the 'Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants' by Perkin et al (2016), in which vomiting and diarrhoea subsequent to introduction to specific allergenic foods were reported as 'undesirable events' in a supplementary appendix (not the main paper). The justification to consider the diarrhoea ('no effect of the timing of CF') but not the vomiting ('earlier introduction of complementary foods related to a higher incidence of vomiting') is also not clear. It would also be appropriate to highlight that the data on morbidity that was collected in all 3 studies was retrospectively reported by parents, weakening its validity.

Line 4150, relating to the reviewed RCTs, is misleading
'all of which compared the introduction of CFs at 3-4 months with 6 months of age'
and we would like to highlight that Cohen et al (1994) and Dewey et al (1999) compared non-infection outcomes of infants exclusively breastfed to 6 months with those given complementary foods at 4 months, while the Perkins et al (2016) trial (the relevance of which we question above) compared non-infection outcomes of infants exclusively breastfed to 6 months with those given complementary foods at 3 months. Whilst the results of the prospective cohort by Noppornlertwong and Tantibhaedhyangkul (2016) do not inform the panel's conclusions, an incorrect summary of some results is presented: reporting GI infections between 5 and 15 months of age, not 4 and 18 months of age (line 4167).

Four further studies are cited as supportive evidence; three prospective cohorts and a cross sectional study. The design of two of the cohort studies (Morgan et al 2004 and Wright et al 2004) is inappropriate to support

a conclusion comparing ‘introduction of complementary foods at <6 months with thereafter’. The findings of the third prospective cohort (Lopez-Alacron et al 1997) and the cross-sectional analysis by Quigley et al (2009) are both mispresented, as outlined below. The findings of the prospective cohort by Morgan et al (2004) do not support the panel’s conclusions as they compare the morbidity of infants given complementary foods at <3 months with those given foods at >3 months.

The prospective cohort by Wright et al (2004) is also irrelevant to the conclusion as it compares prevalence of parent reported diarrhoea by age at introduction of complementary foods at <3 months with 3-4 months and >4 months. Nonetheless it is interesting to see the higher odds of diarrhoea among those introduced at <3 months compared to thereafter (prevalence by age group: 31% at <3 months, 19% at 3-4 months and 14% at >4 months) (nb. it should be noted that lines 4195-4198 incorrectly summarise these findings stating the comparison was between introduction at <4 months with thereafter, when it was with <3 months and thereafter). If this data were relevant, the appropriateness of dwelling on the lack of significant difference in the proportions of children with diarrhoea who were brought to a doctor could be questioned as the sample size was small and this result may have been due to a lack of power.

On lines 4191-4192 from the prospective cohort by Lopez-Alarcon et al (1997) it is reported that authors: ‘did not find an association between the timing of introduction of CFs and the odds of diarrhoea between birth and 6 months of age’. However, this is misleading, as the study actually reported:
‘Incidence, prevalence, and duration of individual episodes of diarrhea were lower in breast-fed infants. Incidence (r=-0.17, P <0.02) and prevalence (r =-0.19, P <0.008) were negatively associated with duration of full breast-feeding. Introduction of solid food was not associated with further episodes of diarrhea’, and the text clarifies that logistic regression was carried out to examine the coincidence of an episode of diarrhea occurring immediately after solid food was introduced.

In lines 4185-4188 it is stated that the cross-sectional analysis by Quigley et al (2009) reported the monthly risk of diarrhoea between birth and 8 months depending on whether complementary food had been introduced or not. This is incorrect as the outcome they reported on was hospitalisation for diarrhoea (or lower respiratory tract infection).

The presented evidence does not appear to be sufficient to support the conclusion presented, and it is inappropriate to say there is:
‘no evidence that the introduction of complementary foods <6 months of age increases gastro-intestinal infections’.

12.4. Upper respiratory tract infections: summary of the evidence

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Four studies are used as the ‘main line of evidence’; the 3 RCTs already cited (Perkin et al 2016; Dewey et al 1999; Cohen et al 1994) and the prospective cohort cited above (Forsyth et al 1993).

These studies do not all report on upper respiratory tract infections or define these in the same way and this should have been reflected in the conclusions. The inclusion of studies in which morbidity data was not collected as a pre-specified outcome is questionable, as is the case for all three RCTs cited. However, given that they are included, a number of issues can be highlighted: data on upper respiratory tract infections is not included in the paper by Perkin et al (2016) and any supplementary papers in which this may have been included are not referenced; and the paper by Dewey et al (1999) reports on ‘nasal discharge’, not upper respiratory tract infections.

The study by Forsyth et al (1993) was explicitly designed to look at infection as an outcome of early introduction of solid food, but it does not allow conclusions to be drawn in relation to the question of timing of introduction of complementary foods at < 6months compared to thereafter as it compares infants given complementary foods at <8 weeks, 8-12 weeks and >12 weeks. Nevertheless, this study is reported as showing significant differences in the prevalence (not incidence as reported, line 4215) of respiratory illness (defined as persistent cough, wheeze and coryza) among children 14-26 weeks of old, by age at introduction of complementary foods: highest in the <8 weeks, lowest in the >12 weeks. i.e. the one relevant study shows early introduction of complementary foods is associated with higher prevalence of respiratory infection in infants 14-26 weeks old.

To conclude, we believe that the summary on lines 4226-4231 is inappropriate (and inaccurate) and here and elsewhere in the report the available evidence for this outcome should simply be given as 'insufficient' to reach any conclusion. Again, it would be more appropriate to consider this question in light of the evidence that prolonged duration of exclusive breastfeeding is protective against respiratory infections. In their evidence review SACN in the UK reported that 'the early introduction of solids at three to four months is associated with greater risk of gastrointestinal, respiratory and ear infections than is continuing to breastfeed exclusively.' (SACN, 2018)

12.5. Lower respiratory tract infections: summary of the evidence

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The RCT by Perkin et al (2016) is used for the 'main line of evidence' and the 2 prospective cohorts cited above (Wright et al 2004 and Morgan et al 2004) and the cross-sectional study by Quigley et al (2009) as 'supportive evidence'.

These studies do not all report on lower respiratory tract infections or define these in the same way and this should have been reflected in the conclusions.

The appropriateness of including studies in which morbidity data was not collected as a pre-specified outcome should be questioned, as is the case for Perkin et al (2016), and this data is not reported in this paper but in unreferenced supplementary tables.

The findings of the prospective cohort study by Morgan et al (2004) do not support the conclusions as they compare the morbidity of infants given complementary foods at <3 months with those given at >3 months and the only mention of lower respiratory tract infections in the paper is as follows:
'There was no effect of the age of weaning on the proportions of term infants developing atopy, lower respiratory tract infections, or gastroenteritis'. There was no data presented.

The prospective cohort by Wright et al (2004) is also irrelevant to the conclusion as it compares prevalence of parent reported chest infections by age at introduction of complementary foods at <3 months with 3-4 months and >4 months.

In lines 4247-4250 it is stated that the cross-sectional analysis by Quigley et al (2009) reported the monthly risk of lower respiratory tract infections between birth and 8 months depending on whether complementary foods had been introduced or not. This is incorrect as the outcome they reported on was hospitalisation for lower respiratory tract infection (or diarrhoea).

It therefore appears to be misleading and inappropriate to report (lines 246-249) there is
'no evidence that the introduction of complementary foods <6 months of age compared with thereafter is associated with an increased risk of lower respiratory tract infections' and for EFSA to classify its level of

confidence in the evidence as ‘moderate’.

Again, the lack of review of the importance of exclusive breastfeeding on the reduction in infections means that evidence has not been included which would show a relationship between early introduction of complementary foods with lower respiratory tract infection. SACN (2018) concluded that: The introduction of solid foods or infant formula before 6 months of age is associated with greater risk of gastrointestinal, and lower and upper respiratory infections than continuing to breastfeed exclusively. Quigley et al (2007) reported that 27% of all lower respiratory tract infections could be prevented with each month of exclusive breastfeeding.

12.6. Infections in general: summary of the evidence

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Firstly, this endpoint is not clearly defined, and the two studies included measured more specific outcomes which could have been included in the other sections; e.g. Stordal et al (2017):
‘When we analyzed all infections regardless of hospitalization, introduction of complementary foods <4 months was associated with an increased risk for gastrointestinal intections, upper respiratory tract infections, and frequent infections but not for lower respiratory tract infection’.

It is not clear why this data was excluded from review of evidence relating to gastrointestinal and upper respiratory tract infections.

Stordal et al (2017) concluded that:
‘Breast-fed children who received complementary foods at 4 to 6 months of age had similar risk for infection as those receiving complementary foods after 6 months’.

The fact that their findings related to breastfed children, and this is only one of two studies included for this outcome, is not adequately reflected in the overall conclusion (lines 249-250).

It would also have been relevant to highlight that the authors stated that the introduction of complementary food before 4 months was found to be risky:
‘Age at introduction of complementary foods was a significant predictor for hospitalization for infections among infants who were breastfed for a minimum of 6 months … This association was driven by a higher risk for hospitalization in those with introduction of complementary foods at <4 months of age’.

The overall conclusion was ‘In this large birth cohort, we found a small but significant trend for lower risk for hospitalizations for infections for each month of delaying complementary foods in breastfed infants’.
The summary referring to Stordal et al (2017) on lines 4287-4290 appears incorrect and misleading.

The second study cited by Heinig et al (1993) is stated as being in exclusively breastfed infants (line 4261), whereas the authors reported:
‘We examined if the timing of introduction of solid foods was related to growth, intake, morbidity, activity or motor development among infants either breast fed or formula fed until >= l2 months of age’.
It appears both misleading and inappropriate that in including only two papers it is stated that (lines 246-249) there is ‘no evidence that the introduction of CFs <6 months of age compared with thereafter is associated with an increased risk of infections in general’ and for EFSA to classify its level of confidence in the evidence as ‘moderate’.

Again, it should be highlighted that it would be more appropriate to consider the question of infection risk in infancy in light of the evidence that prolonged duration of exclusive breastfeeding is protective against a range of infections. In their evidence review SACN in the UK reported that 'The introduction of solid foods or infant formula before 6 months of age is associated with greater risk of gastrointestinal, and lower and upper respiratory infections than continuing to breastfeed exclusively.' (SACN, 2018)
The EFSA review did not consider ear infections and it is not clear why.

Lastly, it would be relevant to share where papers have a conflict of interest. This is the case in the studies by Perkins et al (2016), Heinig et al (1993) and Cohen et al (1994).

15. Assessment of the data on indicators of nutrient status in term infants or mixed populations

- ☐ 15.1. Nutrient status: final body of evidence
- ☐ 15.2. Nutrient status: endpoint and study selection
- ☑ 15.3. Iron status: summary of the evidence
- ☑ 15.4. Iron status: conclusions and grading of the confidence in the evidence

15.3. Iron status: summary of the evidence

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We have divided our comments across sections 15.3 and 15.4 as not enough characters were available here.

Three RCTs are cited to provide the evidence to support the conclusion that
Lines 4558- 4568
'there is high confidence in the evidence that the introduction of complementary foods at 4 months of age compared with 6 months of age reduces the risk of iron depletion in exclusively breast-fed infants at 6 months of age'
This sentence is misleading as it appears to make a generalisation for all infants

'Exclusively breast-fed infants that may benefit from an early introduction of CFs that are a source of iron are infants born to mothers with a low iron status, infants with early umbilical cord clamping (<1 minute after birth), infants born pre-term, infants born small-for-gestational age, and infants with a high growth velocity'.

This sentence listing the groups that 'may benefit from early introduction of CF' lacks the requisite evidence base from the cited RCTs. Even if this were supportable with the presented evidence, it seems irrelevant to the consultation question which pertains to the labelling of commercial foods available to the general public among which such infants will be a small proportion.

We suggest that 3 RCTs cannot provide 'high confidence' for a broad recommendation, and this is especially the case given the questionable relevance of any of these trials to the current European setting. The two by Dewey et al were conducted in a low-income country and studied a majority of low birthweight infants. In the exclusion criteria for this opinion in line 976 it states that studies are excluded 'if they investigated growth or iron status in populations with high prevalence of undernutrition'. Honduras had a stunting rate of 23% in 2012 and this would have been higher when the studies were undertaken, therefore it is not clear why these studies were considered appropriate for this review. In addition, the trial by Jonsdottir et al (2012) was conducted before delayed cord clamping became common practice.

We also have concerns about how the data from these studies is presented. Selected results from these trials are given in a misleading manner by failing to highlight that differences between groups (exclusively breastfed for 6 months compared to introduction of complementary foods at 4 months alongside

breastfeeding) were not statistically significant: Dewey et al (1998), lines 4484-4486; Dewey et al (2004), lines 4479-4480, and Jonsdottir et al (2012), lines 4488-4489 and 4490-4492.

None of the 3 trials presented conclusions or recommendations in line with the panel's overall conclusion.

Dewey et al (1998) highlighted that although infants given complementary foods from 4 months consumed far more iron than the exclusively breastfed group, this did not fully eliminate the risk of developing anaemia by 6 months of age. They actually recommended that iron drops are given to low birth weight breastfed infants, exclusively breastfed infants over 3000g do not need any additional iron before 6 months and that more research is needed on whether iron drops or complementary foods are more effective at preventing iron deficiency before 6 months in breastfed infants born weighing 2500-3000g.

The study by Dewey et al (2004) examined iron drops and complementary foods, and the panel failed to point out that the results presented (lines 4479-4480) were from a sub-group analysis (as well as lacking statistical significance). In infants who did receive iron drops at 4–6 months, haemoglobin, haematocrit and transferrin saturation levels were actually higher in the exclusively breastfed group than in the group receiving complementary foods from 4 months. Over the entire 6 month study period, the cumulative probability of remaining non-anemic at 6 months without the use of iron drops was virtually identical in the two intervention groups. The authors recommended maintenance of exclusive breast-feeding to 6 months for low birth weight infants while providing supplemental iron drops.

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15.4. Iron status: conclusions and grading of the confidence in the evidence

5000 character(s) maximum

In the paper by Jonsdottir et al (2012), the authors conclude that 'No difference was seen between groups in iron deficiency anemia, iron deficiency, or iron depletion'.

In addition, none of the trials reported functional outcomes. Infants usually have serum ferritin values near the cut-off reflective of depletion, though a value near the cut-off does not necessarily imply functional iron deficiency .

Because of the criteria used for the review, data that might have contradicted the evidence presented was not considered. For example, a more recent study looking at iron deficiency among infants in Colombia exclusively breastfed for 4-5 months versus 6 months showed no difference in iron status at 6 months (Olaya et al, 2017).
Lastly, it would be relevant to share where papers have a conflict of interest. This is the case in the Jonsdottir et al (2012) trial which was funded by Mead Johnson.

We are concerned that the statements made in this review about iron status are potentially misleading and that the Panel's scrutiny of the relevance of the data presented may have been inadequate. If no relevant RCT were available to consider this outcome, then that should have been made clear.

20. Conclusions

5000 character(s) maximum

1. In the conclusion in lines 5259-60 it is stated that 'this opinion should not be interpreted as providing public health recommendations for the introduction of complementary foods.'
However, it will inevitably be used in this way. We believe that this opinion will contribute to maintaining low

rates of exclusive breastfeeding recorded in European countries (see Lancet series on breastfeeding, 2016) and the inappropriate provision of solid foods at even earlier ages than present. The constant recommendation of the 3-4m time period for introducing complementary foods has to be brought into question.

2. In line 5277 it states 'Most infants do not need complementary foods for nutritional reasons up to around 6 months of age. Allowing the labelling of ultra-processed commercial complementary foods 'from 4 months' or 'from 3-4 months' will inevitably shorten the duration of exclusive breastfeeding, and lead to well documented harmful impacts on the health of infants and mothers.

3. In lines 5320-24 it states that 'The available data do not allow the determination of a precise age at which complementary foods should be introduced to all infants living in Europe. The appropriate age depends on the individual's characteristics and development ... In most infants, this age is between about 3-4 months and around 6 months'.

How can the Panel state that the appropriate age is between 3-4 and 6 months, if 'the available data do not allow the determination of a precise age' and this 'depends on the individual's characteristics and development'?

Upload file(s) if necessary

*Do you need to upload file(s)?

- ○ YES
- ◉ NO

Background Documents

00_Draft Opinion_Age of introduction of Complementary Feeding_no appendix A

01_Appendix A - Age of introduction of Complementary Feeding

1_Annex A - Outcome of the data extraction from the included studies

2_Annex B - Result of the assessment of the risk of bias

3_Annex C - List of papers excluded at full text screening

4_Annex D - Funnel plots for the assessment of the publication bias

5_Annex E - Sensitivity analysis

6_Privacy statement EFSA Public Consultation

Contact

nda_admin@efsa.europa.eu