Optimal Timing of Introduction of Complementary Feeding: A Systematic Review and Meta-Analysis

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Abstract

Background: The timing of introducing complementary feeding (CF) accompanies a critical window of vulnerability as failure to consume adequate energy, protein, vitamins, and minerals is a significant concern and can lead to poor growth outcomes, increased susceptibility to infections, allergies, and lower developmental potential. It is therefore of utmost importance to determine the most optimal time to start CF for infants. The objective of this systematic review is to evaluate the impact of timing of CF introduction on health, nutrition, and developmental outcomes among infants.

Methods: The protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42020218517). The search was conducted in electronic databases till March 01, 2021. Data were meta-analysed separately for normal term infants and for preterm/ low birth weight (LBW) /small for gestational age (SGA) infants; and data from randomised controlled trials (RCTs)experimental studies and observational studies were also separately synthesised for the following two comparisons:

- Early introduction of CF (i.e., introduction of CF at any time before six months of age)
- Late introduction of CF (i.e., introduction of CF at any time after six months of age)

Included studies were further classified according to common time points reported for early and late introduction of CF by the study authors. We summarised the findings of this review for primary outcomes as per the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria.

Results: This review synthesises data from 240 documents; including nine RCTs (from 26 papers) and 214 observational studies. Out of the total included studies, eighty-seven studies (RCTs: 7; observational: 80) including a total of 384,716participants were meta-analysed.

Among normal term infants; the evidence for RCTs did not show a difference of early introduction on any of the primary and secondary outcomes. While, low certainty evidence from observational studies suggest that early introduction of CF (< 6 months compared to ≥ 6 months) might increase BMI, BMI z-score, and overweight+obesity; while early introduction of CF at < 3 months compared to ≥ 3 months might increase BMI and odds of LRTI, and early introduction of CF at < 4 months compared to ≥ 4 months might increase height, LRTI, and systolic and diastolic blood pressure. The limited subgroup analysis by country suggested

mixed evidence on diarrhea from a very small study and increase in anemia and the limited evidence by subgroup analysis by feeding practices suggested greater effect of formula fed infants for BMI and overweight and obesity. Among normal term infants, the evidence for RCTs did not show an effect of late introduction on any of the primary and secondary outcomes. Low certainty evidence from observational studies suggests that among normal term infants, late introduction of CF (at > 6 months) may decrease height, BMI, and systolic and diastolic blood pressure, and it might increase odds of intestinal helminth infection.

Among preterm / LBW / SGA infants; the evidence from RCTs suggests no difference of early introduction of CF (at 3 months compared to at 4 months; at 4 months compared to at 6 months) on any primary or secondary outcomes. While, low certainty evidence from observational studies suggests increased WAZ among infants initiated on CF at < four months compared to ≥ four months; while there was no difference in all the outcomes assessed for early or late introduction on CF. Thus, the evidence is insufficient to make any meaningful conclusions on any other outcomes of this review.

Conclusion: Findings from this review should be interpreted with caution due to design limitations of the included studies. Limited evidence with low certainty from observational studies in normal term infants suggests that early introduction of CF might be associated with overweight, obesity and increased BP, while there is no conclusive effect on morbidity like diarrhea and LRTI, but this warrants further exploration. The evidence is limited and inconclusive for preterm/LBW/SGA. The evidence till now calls for remaining with the existing recommendations. Future robust studies, especially from LMIC settings, evaluating different feeding practices and underlying determinants are required with standardised outcomes measures and long-term follow-ups to assess the actual impact on growth, morbidity, non-communicable diseases, development, and mortality among term infants as well as other subgroups of infants (including preterm, SGA and LBW infants).

Background

The condition

Complementary feeding (CF) is the process of initiating any solid or liquid food other than breast milk or infant formula when breast milk alone does not remain sufficient to meet the nutritional requirements of infants (1, 2). According to the World Health Organization (WHO), adequate infant and young child feeding (IYCF) includes the practice of breastfeeding and the timely introduction of appropriate CF (2). The World Health Organisation (WHO)/ United Nations International Children's Emergency Fund (UNICEF) guidelines recommend early initiation of breastfeeding within an hour of birth; exclusive breastfeeding (EBF) for the first six months of life; and introduction of nutritionally adequate and safe complementary foods at six months of age together with continued breastfeeding up to two years of age or beyond (2, 3). While EBF for six months is adequate for normal growth in healthy infants, the continuation of breastfeeding is more important with introduction of CF at six months for long term optimal growth (4).

The initial two years of life are very crucial for the infant's growth including both physical and cognitive growth; this is the time when the development of the child is vulnerable due to poor dietary intake and diseases; and therefore, this is considered a 'critical window' for the children(5, 6). Nutritional inadequacy in infancy can lead to malnutrition which is comprised of both undernutrition (stunting and wasting) and overnutrition (overweight and obesity) (7). Approximately 45% of all deaths under the age of five years are associated with malnutrition; and as of 2020, 47 million children under the age of five years are wasted, 14.3 million are severely wasted, and 144 million are stunted (8). Evidence from variable sources has established the association of poor dietary intake during infancy years with increased risk of morbidities, mortality, impaired neurodevelopment, and delayed development outcomes in the short-term (7, 9); and impaired intellectual performance, work capacity, poor reproductive, increased cardiovascular and autoimmune disorders, and overall health outcomes in the long run (10, 11).

The intervention

CF practices vary widely between countries and time. The percentage of infants introduced to CF before six months was reported to be 58% in India (2017) (12), 47.8% in Pakistan (2018-2019)(12), 40.7% in Turkey (2018) (12), 24% in Vietnam (2014) (12),37% in northwest Italy (2007/08) (13), 25.8% in the United States of America (USA) (2017-18)(12), and 30% in the United Kingdom (UK) (in a birth cohort of 2010) (14, 15). In the

Asia Pacific region, China initially recommended the introduction of CF at four months, which has now been updated to 6 months; however, Japan still introduces CF at a child's 100th day following birth, which consists of a traditional ceremony where a child is introduced with fruit juice and soup (16). The prevalence of introduction of CF by six months is 93.8% in Sri Lanka (2016), 41.2% Somalia (2018), 95.3% Oman (2017), 46.5% in Bangladesh (2006), and 86%% in Nepal (2019) (12). Studies suggest a range of maternal and infant related factors that are associated with the early introduction of complementary food, which includes culture, maternal age, her education, body mass index (BMI), postnatal weight gain, psychosocial factors, infant size at birth, early initiation and exclusive breastfeeding (17).

Exclusive breastfeeding fulfils the energy requirement by the infant during the first six months or even longer, however, the iron, zinc, vitamin D, and other micronutrients requirement cannot be met by milk alone (18). Systematic reviews have shown that the iron status of healthy full-term infants could be positively altered by an earlier introduction of iron-fortified or adequate complementary foods (19, 20). Similarly, zinc requirements are partially met from prenatal stores which tends to decrease with the course of lactation (21, 22).

How the intervention might work

The CF period accompanies a critical window of vulnerability. During this time, failure to consume adequate energy, protein, vitamins, and minerals is a significant concern and can lead to poor growth outcomes, increased susceptibility to infections, allergies, and diseases, and lower developmental potential. The early introduction of CF has been associated with increased morbidity due to gastrointestinal diseases (such as diarrheal diseases), particularly in areas where food and water hygiene is a concern (18). Early and inappropriate CF is also associated with poor growth and malnourishment (23), while long-term health impacts are unclear but may relate to risk of atopy and allergic reactions, type 1 and 2 diabetes, obesity, and neuromuscular development (11, 24, 25). In contrast, late introduction of CF leads to micronutrient deficiencies including low iron and zinc levels, which affects cognitive and neurological development and may also lead to feeding difficulties (16). The type of feeding adopted in the first years of life is also associated with adverse outcomes later in childhood and adulthood (26-31). It is therefore imperative to evaluate the

consequences of both early and late introduction of CF since optimal timing of introduction may have potential short- and long-term health effects (11).

Why it is important to do this review

There are a few discrepancies between existing recommendations for the introduction of CF and little evidence is available on the timing of the introduction of CF. The timing of introduction of CF during infancy influences the lifelong health. Building on the prior recommendations, Those recommendations vary between four and six months by the societies such as the American Academy of Pediatrics (AAP) encouraged delaying the introduction of solid foods at about 6 months (32, 33), the WHO recommends that infants should be introduced to complementary foods at six months of age (7), and the similar guidelines such as the European Society for Peadiatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee, NASPGHAN and the European Academy of Allergy and Clinical Immunology (EAACI), which recommend that complementary foods be introduced between 17 and 26 weeks (1, 3, 34). Despite the inconsistencies, none of the guidelines recommend initiating CF before four months (23, 35-37). It is therefore of utmost importance to determine the most optimal time to start CF for different populations of infants. Thus, our review aims to study the impact of early and late introduction of CF on infant health, nutrition, and developmental outcomes.

Objectives

The objective of this systematic review is to evaluate the impact of timing of CF introduction on health, nutrition, and developmental outcomes in infants (including term, preterm, small for gestational age (SGA), and low birth weight (LBW) infants) for the following two comparisons:

- Early introduction of CF (i.e., introduction of CF at any time before six months of age)
- Late introduction of CF (i.e., introduction of CF at any time after six months of age)

Methods

Criteria for considering studies for this review

Types of studies

Eligible study designs included randomized controlled trials (RCTs); (cluster or individually randomized), non-randomized controlled trials, and observational studies with a concurrent comparison group (cohort

(prospective and retrospective), controlled before-after studies, cross-sectional, and nested case-control studies). Case reports, case series, opinions, editorials, commentaries, conference abstracts, qualitative studies, and reviews or systematic reviews were excluded from this review.

Types of participants

Participants included both male and female infants, including term, preterm, SGA, and LBW infants, living in any low-, middle-, or high-income countries. Studies were excluded if these were explicitly done on infants with any pre-existing health condition including HIV, congenital abnormalities, metabolic disorders, cancer, diabetes, etc.

Types of interventions

Studies were eligible for inclusion if they compared the effect of the timings of introducing CF. We aimed to define the timing of the introduction of CF as follows:

- Early introduction of CF (i.e., introduction of CF at any time before six months of age)
- Late introduction of CF (i.e., introduction of CF at any time after six months of age)

Included studies were further classified according to common time points of early and late introduction of CF as reported by the study authors, keeping the plausibility of results in mind. Moreover, we included studies that had appropriately defined the timing and constitution of CF (i.e., foods and beverages other than human milk or infant formula including liquids, semisolids, and solid food).

Types of outcomes

We aimed to assess the effect of early and late introduction of CF on the health, nutrition, and developmental outcomes at any time point in life, regardless of the type of milk-feeding (breastfed, formula-fed, or mixed-fed) provided to the infant.

Primary Outcomes

- Anthropometric measures (height/length; height/length gain; weight/weight gain; head circumference; stunting (height-for-age z-score (HAZ) <-2 SD); wasting (weight-for-height z-score (WHZ) <-2 SD); underweight (weight-for-age z-score (WAZ) <-2 SD); overweight; obesity; body mass index (BMI); HAZ; WAZ; WHZ)
- Morbidity (including fever, upper respiratory infections, lower respiratory infections, diarrhea, malaria, other infections, atopic dermatitis, etc.)

- Anemia
- Child developmental measures (cognitive, socio-behavioral, motor, etc.)
- Food preferences
- Dietary patterns/dietary diversity
- Food allergies
- Non-communicable diseases (NCD) including glucose intolerance, diabetes, hypertension, cardiac, inflammatory, or auto-immune diseases, cancers
- Infant and child mortality

Secondary Outcomes

- Hemoglobin level
- Micronutrient status (including serum micronutrient levels for iron, serum ferritin, transferrin receptor, vitamin A, zinc, folic acid, B12, and fatty acids)
- Waist circumference
- Skinfold thickness
- Gut health and the microbiome
- Bone mineral density/bone mineral content
- Maternal outcomes: Lactational amenorrhea, maternal birth spacing

Type of settings

All settings within any low-, middle-, or high-income country were considered for this review.

Search methods for identification of studies

Reporting and protocol

The protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42020218517).

Electronic searches

The search strategy was formulated using the PICO methodology based on medical subject headings (MeSH) and keywords detailed in **Appendix** (**Table 1**). Electronic searches were conducted in the following databases: MEDLINE, Embase, Web of Science Index Medicus, CINAHL, LILACS, the Cochrane Central Register of Controlled Trials CENTRAL, eLENA (WHO), Index Medicus for the WHO Eastern Mediterranean Region

(IMEMR), Western Pacific Region Index Medicus (WPRIM), Index Medicus for South-East Asia Region (IMSEAR), and African Index Medicus. Searches were conducted for ongoing trials from clinicaltrials.gov. There were no restrictions on publication date, however, only studies published in English were included. The date of the final search was March 01, 2021.

Searching other sources

We also searched the reference list of all the included studies and relevant systematic reviews to look for studies missing from the electronic search.

Data collection and analysis

Selection of studies

Title, abstract and full-text screening were managed using Covidence, a web-based software platform for systematic reviews (38). At both title/abstract and full-text screening stages, two review authors independently scanned and screened all records retrieved by the searches for relevance based on selection criteria (**Table 1**). Any disagreements were resolved through discussion or by a third review author when necessary.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria
● Low-, middle-, or high-income country
● Normal term, preterm, LBW, SGA infants or children who have received CF
● Types of interventions ○ Timing of introduction of CF was clearly defined ▪ Early introduction of CF (i.e., introduction of CF at any time before six months of age) ▪ Late introduction of CF (i.e., introduction of CF at any time after six months of age)
● Relevant study designs: ○ Randomized controlled trials (RCTs) (individually or cluster) ○ Quasi-randomized controlled trials (q-RCTs) ○ Non-randomized controlled trials (NRTs) ○ Controlled before-after studies (CBA) ○ Cohort studies (prospective and retrospective) ○ Cross-sectional studies ○ Nested case control studies
Exclusion Criteria
● Recruitment of infants explicitly with an existing illness such as cancer, diabetes, metabolic disorder, HIV, congenital abnormalities, etc.
● Recruitment of infants explicitly with a family history of atopy, etc.
● Irrelevant study designs: case reports, case-control studies, case series, opinions, editorials, commentaries, letters, conference abstracts, and reviews or systematic reviews.

- Studies which have not explicitly defined the timing of introduction of complementary feeding and the foods introduced

Data extraction and management

Two review authors independently extracted data from each included study onto a standardized data extraction form in Excel that had been piloted. All studies were matched between the two review authors, and any disagreements or discrepancies were resolved through discussion, or by a third independent reviewer. Attempts were made to contact the authors of included studies to obtain clarifications or additional data.

We extracted the following information from each included study: source (e.g., contact details); study characteristics (e.g., study design, location of study, years of data collection, etc.); population characteristics (e.g. number, mean age, age range, gender, inclusion criteria, exclusion criteria, infant feeding prior to and after the introduction of CF, birth weight, gestational age, potential key confounders (e.g. education, socioeconomic status, sex of caregiver, maternal/paternal age, race and/or ethnicity, milk feeding practices (breast milk, infant formula, or both)); intervention/comparison characteristics (e.g., exposure, description, duration of intervention/exposure, and comparison group description); outcomes (e.g., primary and secondary outcomes specified and collected, time points reported, and extraction methods used, etc.); data analysis methods; control of confounding; funding obtained, and any conflict of interests.

Assessment of risk of bias in included studies

Two independent authors assessed the quality of all eligible studies and disagreements were resolved by consensus or contacting a third author. The Cochrane Risk of Bias tool was used to assess the methodological quality of RCTs and the overall risk of bias judgment was given to each study (low, high, some concerns) (39). The tool assessed trials in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases.

The risk of bias from non-randomized studies of intervention and prospective cohorts was assessed using ROBINS-I (40). The ROBINS-I tool assessed non-randomized trials in the following domains: bias due to confounding, bias in the selection of study participants, bias in classification of interventions/exposure, bias due to deviations from intended interventions/exposure, bias due to missing data, bias in the measurement

of outcomes, and bias in the selection of the reported results. Each study was given an overall risk of bias judgment (low, moderate, serious, critical).

For retrospective cohort studies, we have used the National Institute of Health NHLBI tool (41), and studies were rated as good, fair, or poor, based on fourteen criteria covering the research question, participant population, analyses, timeframe, independent and dependent variables, attrition, and control of confounding variables.

Data synthesis

Separate analysis was conducted for 'normal term infants' and 'preterm / LBW / SGA infants'; and data from RCTs were also separately synthesized from observational studies. Normal term infants were defined where studies did not explicitly included infants who were LBW, preterm or SGA. Based on the data reported from the included studies, analysis was conducted for the following comparisons:

- Early introduction of CF (i.e., introduction of CF at any time before six months of age)
    - Randomised control trials:
        - Early introduction of CF at ≤ four months of age compared to six months of age
        - Early introduction of CF at four months of age compared to six months of age
        - Early introduction of CF at three months compared to at four months of age
    - Observational studies:
        - Early introduction of CF < six months of age compared to ≥ six months of age
        - Early introduction of CF < three months of age compared to ≥ three months of age
        - Early introduction of CF < four months of age compared to ≥ four months of age
- Late introduction of CF (i.e., introduction of CF at any time after six months of age)
    - Observational studies:
        - Late introduction of CF (> six months) compared to ≤ six months of age
        - Late introduction of CF (> eight months) compared to ≤ eight months of age

We didn't meta analyse studies which reported introduction of CF at or less than 2 months or at 12 months of age or even studies in the 'early initiation' and 'late initiation' comparison where the 'exposure group' included infants who were started CF at 6 months. For dichotomous outcomes, we used risk ratio (RR) while

for the continuous outcomes, mean difference (MD) or standardized mean difference (SMD) along with a 95% confidence interval (CI) were used. Data reported as medians and interquartile ranges were converted to means and standard deviations using standard formulas. We undertook meta-analyses only where it was meaningful, i.e., if the exposures, participants, and the underlying clinical question were sufficiently similar for pooling. We performed a random-effects analysis for all comparisons, using inverse-variance and Mantel-Haenszel methods to calculate the weights for continuous and categorical outcomes. This is a more conservative approach, as we expected the data to be heterogeneous. For experimental studies, we planned to include both individually randomized as well as cluster-randomized trials in the analyses, however we did not find any cluster randomized trials. We meta-analysed effect sizes and standard errors using RevMan software.

Statistical heterogeneity was assessed using τ^2, I^2, and significance of the χ^2 test; we also assessed heterogeneity by visually inspecting forest plots. Based on prior clinical knowledge, we expected clinical and methodological heterogeneity in included studies and therefore, we attempted to explain any observed statistical heterogeneity using subgroup analysis (where data permitted). We planned to create and examine a funnel plot to explore possible small-study and publication biases, however, we could not explore publication bias since none of the plots included more than 10 studies.

Quality assessment

We constructed Summary of Finding (SoF) tables for primary outcomes for all the comparisons summarizing the quality of evidence according to the outcomes as per the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria (42-44). It covers consideration of the within-study risk of bias, directness of evidence, heterogeneity, the precision of effect estimates, and the risk of publication bias. We rated the certainty of the evidence for each key outcome as “high” (indicating that an outcome will/will not have an effect), “moderate” (indicating that the outcome ‘probably’ have/not have an effect), “low” (indicating that the outcome ‘might’ have/not have an effect), or “very low” (indicating that the outcome effect is ‘uncertain’). For non-randomized studies, the evidence quality was upgraded based on the large magnitude of effect, dose-response relationship, and effect of all plausible confounding factors in reducing the effect (where an effect is observed) or suggesting a spurious effect (when no effect is observed).

Sub-group analysis

We performed sub-group analysis based on the following groups:

- By type of feeding before the introduction of CF - breastfed, formula-fed
- By income regions - Low- and middle-income countries, high-income countries

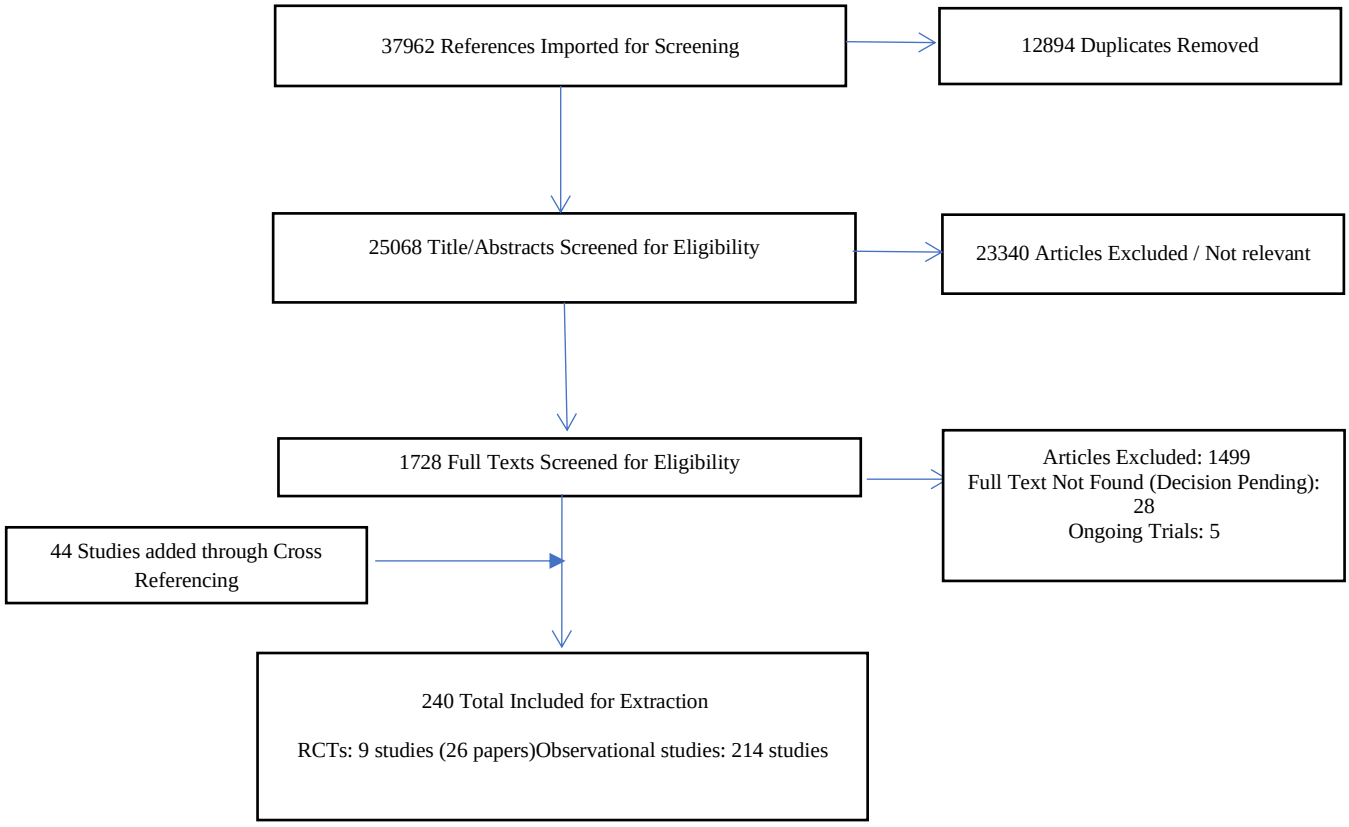
Sensitivity Analysis

We planned to perform sensitivity analysis to examine only studies that had controlled for potential confounders, however the limited number of studies included under each outcome did not permit this analysis.

Results

Our search identified a total of 37,962 records for screening; out of which 25,068 records were screened for eligibility based on titles/abstracts after removing the duplicates. A total of 1728 full texts were reviewed: with an addition of 44 studies from cross-referencing. We included a total of 240 documents in our review: including nine RCTs (from 26 papers) and 214 observational studies. A total of 1,499 studies were excluded from this review. **Figure 1** depicts the search flow diagram.

Figure 1: PRISMA Flow Diagram



Characteristics of the included studies

A total of 240 studies including 846,592 participants were included in this review. Among the included RCTs, the included infants were breast fed (n= 4), formula fed (n= 2), or both breast fed, and formula fed (n=1) infants; while in two studies feeding practices were not clearly mentioned. Studies were conducted in high- middle- and low- income countries including the United States of America (n=28), the United Kingdom (n=25), the Netherlands (n=16), India (n=11), Australia (n=8), Ethiopia (n=10), Germany (n=6), Brazil (n=5), Bangladesh (n=5), Canada (n=5), China (n=5), Norway (n=5), Indonesia (n=4), Denmark (n=4), France (n=4), Korea (n=4), Finland (n=3), Ireland (n=3), Mexico (n=3), Palestine (n=3), Iceland (n=3), Honduras (n=2), New Zealand (n=2), Egypt (n=2), Ghana (n=2), Iran (n=2), Italy (n=2), Malawi (n=2), Nigeria (n=2), Senegal (n=2), South Africa (n=2), Taiwan (n=2), Turkey (n=2), Belgium (n=1), Cameroon (n=1), Croatia (n=1), Greece (n=1), Israel (n=1), Japan (n=1), Jordan (n=1), Malaysia (n=1), Myanmar (n=1), Pakistan (n=1), Pacific Island (n=1), Peru (n=1), Philippines (n=1),Sri Lanka (n=1), Singapore (n=1), Sweden (n=1), Tanzania (n=1), Togo (n=1), Thailand (n=1), and Vietnam (n=1). Ten studies were multi-country studies and nine studies failed to report.

Data from 87 studies were available for meta-analysis comprising of seven RCTs and 80 observational studies. Fifty-nine studies (RCTs: 7; observational: 52) focused on the early introduction of CF (i.e., introduction of CF at any time before six months of age); 13observational studies focused on the late introduction of CF (i.e., introduction of CF at any time after six months of age); while 15 observational studies focused on both early and late introduction of CF. Within each comparison, included studies were further categorised into sub-comparisons based on the time of introduction of CF reported by the included studies. For early introduction of CF, the following sub-comparisons were made based on the timings reported in the included studies:

- Early introduction of CF (≤ four months of age) compared to six months of age
- Early introduction of CF at four months of age compared to six months of age
- Early introduction of CF at three months compared to at four months
- Early introduction of CF (< six months of age) compared to ≥ six months of age
- Early introduction of CF (< three months of age) compared to ≥ three months of age
- Early introduction of CF (< four months of age) compared to ≥ four months of age

For late introduction of CF, included studies were further categorised into the following sub-comparisons:

- Late introduction of CF (> six months) compared to ≤ six months of age
- Late introduction of CF (> eight months) compared to ≤ eight months of age

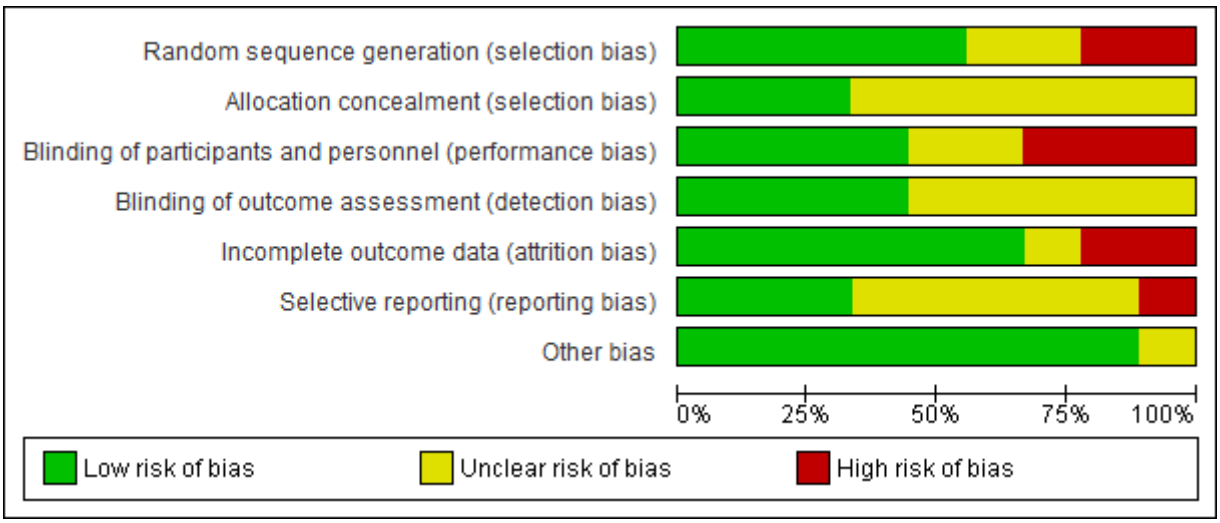
The sample size in the included studies ranged from 36 to 90,596 infants. Two hundred and seven studies focused on normal term infants; ten studies focused on preterm/LBW/SGA infants, and six studies included both term and preterm infants. Outcomes were separately analysed for normal term infants and preterm/SGA/LBW infants. Among primary outcomes, included studies reported height, weight, head circumference, wasting, stunting, underweight, HAZ, WAZ, WHZ, overweight, obesity, anemia, infant mortality, food acceptance, dietary diversity, meal frequency, food allergies, morbidity, NCDs, and child developmental measures. Among secondary outcomes, included studies reported hemoglobin level, micronutrient status, waist circumference, skinfold thickness, bone mineral content (BMC), and lactational amenorrhea. Characteristics of the included studies are summarised in **Appendices** (**Tables 2 and 3**).

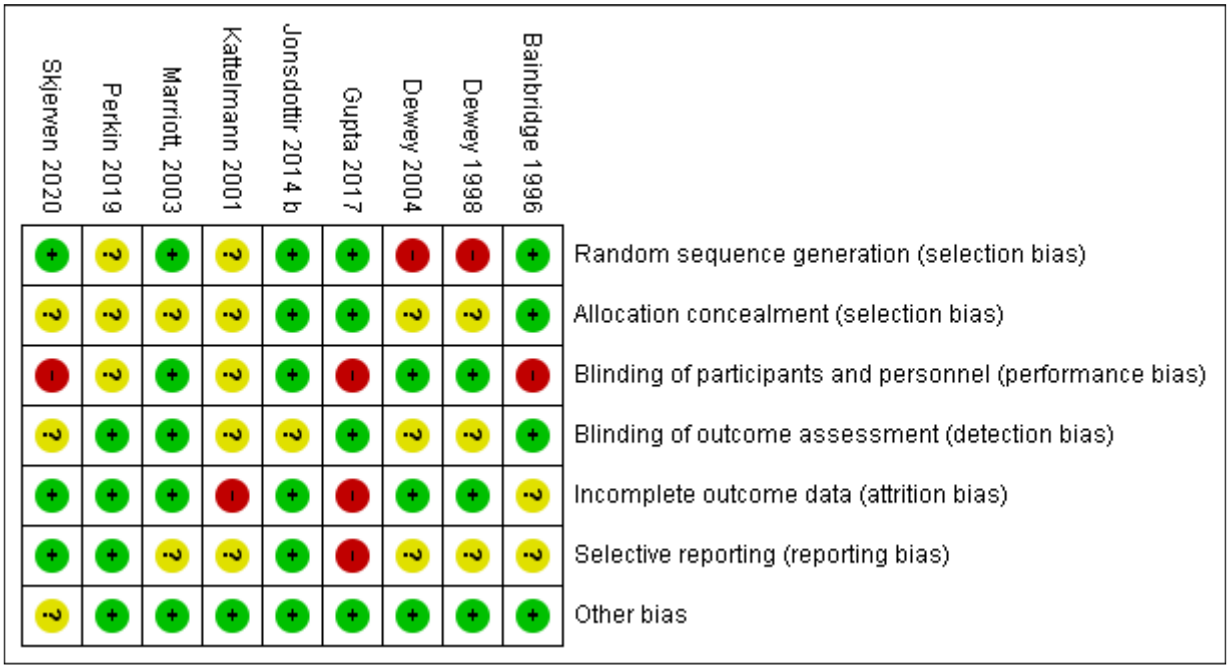
Quality of the included studies

RCTs

The Cochrane Risk of Bias tool was used to assess the methodological quality of RCTs. For sequence generation, five studies were judged to be at low risk of bias; two studies were judged to be at high risk of bias; while two studies did not provide sufficient information to permit judgement. For allocation concealment, three studies were judged to be at low risk of bias; while all other studies failed to provide sufficient information to make a judgement on allocation concealment. For blinding of participants and personnel, four studies were judged to be at low risk of bias; three studies were judged to be at high risk; while the information provided in two studies was insufficient to permit any judgement. For blinding of the outcome assessment, four studies were judged to be at low risk of bias; while all the other studies lacked sufficient information to permit judgement. For attrition bias, six studies were judged to be at low risk of bias; two studies were judged to be at high risk of bias; while one study did not provide sufficient data to permit judgement. For selective reporting, three studies were judged to be at low risk of bias; one study was judged to be at high risk of bias; while five studies did not provide enough data to permit any judgement on selective reporting bias. All the included studies, except one study was judged to have unclear risk of bias for other biases. **Table 4** in **Appendices** and **Figure 2** summarises the risk of bias from RCTs.

Figure 2: Risk of Bias in RCTs

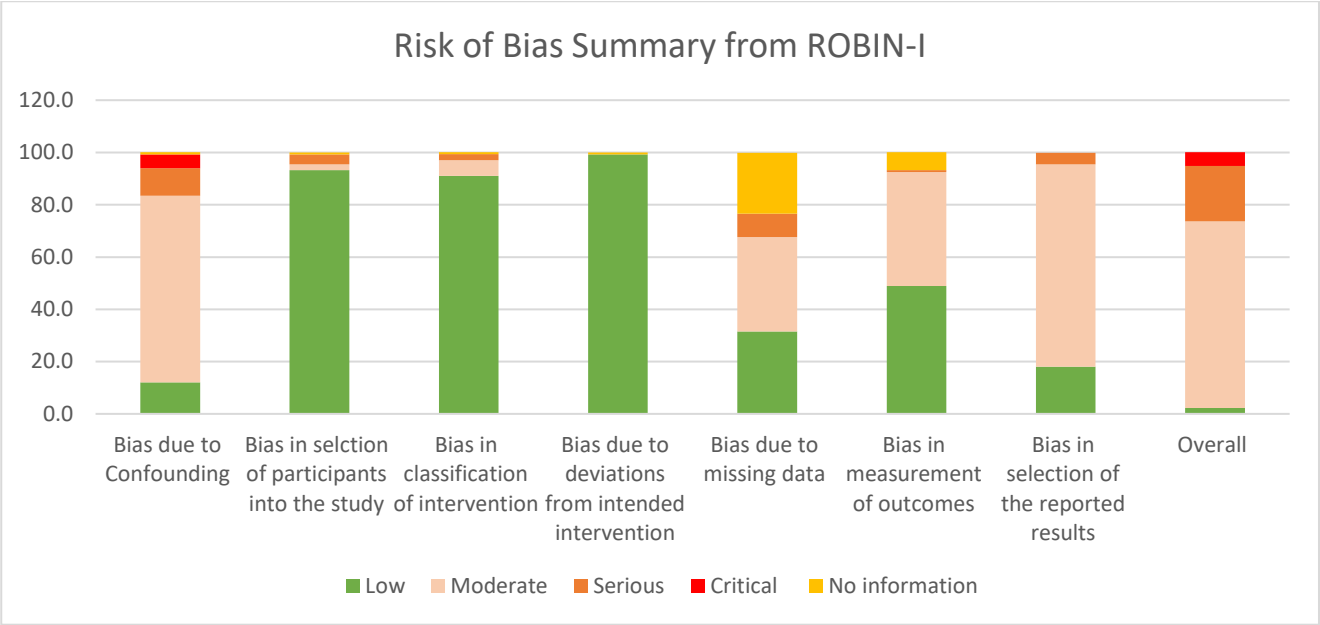


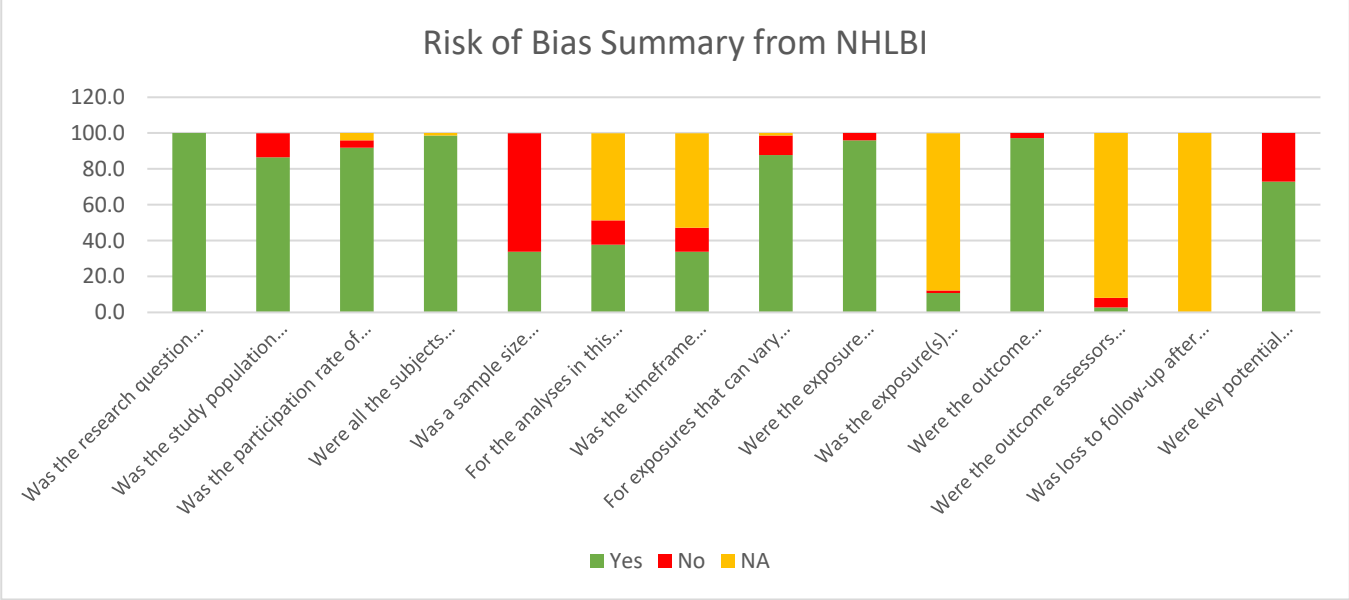


Observational Studies

The risk of bias from non-randomized studies of intervention and prospective cohorts was assessed using ROBINS-I. Based on the ROBIN-I assessment, the majority of the studies were judged to be at either moderate, serious, or critical risk of bias for confounding; missing data; and selection of reported results. The majority of the included studies were judged to be at low risk for bias in the selection of participants; classification of intervention; and deviation from intended intervention. For retrospective cohort and cross-sectional studies, we have used the NHLBI tool. Based on the NHLBI assessment, the majority of the studies were judged to be at high risk of bias for statistical power to capture the association between timing of introduction of CF and health outcomes. The majority of the studies were judged to be at low risk for clear research objective; defined study population; participation rate; examining different levels of exposures; clear definitions of exposure measurement; and defined outcome measurement. **Figure 3** summarises the risk of bias from the non-randomized studies of intervention, prospective cohorts, retrospective cohort, and cross-sectional studies.

Figure 3: Risk of Bias in non-RCTs





Effect of intervention

Based on the availability of data, a total of 87 studies (RCTs: 7; observational: 80) including a total of 384,716 participants were meta-analysed. For early introduction of CF; 59 studies (RCTs: 7; observational: 52) with 284,842 participants were meta-analysed; for the late introduction of CF, 13 studies (RCTs: 0; observational: 13) with 75,352 participants were meta-analysed, and for both late and early introduction of CF 15 studies (RCTs: 0; observational: 15) with 24,522 participants were meta-analysed. **Table 2** summarises the number of studies meta-analysed within all the comparisons.

Forest plots for all the outcomes are attached as **Figures** in the appendix; while the developmental outcomes could not be pooled and are presented descriptively and also some morbidity outcomes and NCD outcomes

that could not be pooled are presented in **Appendix Table 5 and 6**. Subgroup analysis was attempted for the outcomes where data permitted; however, there were a low number of studies under each comparison. The forest plots for the subgroup analysis are attached as **Figures** in the appendix.

Table 2: Summary of the comparisons and number of studies included in the meta-analysis for each comparison

Comparison		Number of Studies	
		RCTs	Observational
Term Infants			
Early Introduction	Early introduction of CF (≤ four months of age) compared to six months of age	4	-
	Early introduction of CF (< six months of age) compared to ≥ six months of age	-	45
	Early introduction of CF (< three months of age) compared to ≥ three months of age	-	5
	Early introduction of CF (< four months of age) compared to ≥ four months of age	-	30
Late Introduction	Late introduction of CF (> six months) compared to ≤ six months of age	-	22
	Late introduction of CF (> eight months) compared to ≤ eight months of age	-	5
Preterm/LBW/SGA Infants			
Early Introduction	Early introduction of CF at four months of age compared to six months of age	3	-
	Early introduction of CF at three months compared to at four months	1	-
	Early introduction of CF (< six months of age) compared to ≥ six months of age	-	1
	Early introduction of CF (< four months of age) compared to ≥ four months of age	-	1
Late Introduction	Late introduction of CF (> six months) compared to ≤ six months of age	-	1

Normal Term Infants

Early introduction of CF - Evidence from RCTs

- Early introduction of CF (≤ four months of age) compared to six months of age

A total of four RCTs with 415 participants were included in the meta-analysis under this comparison. We were unable to meta-analyze developmental outcomes, which are descriptively given in **Appendix Table 6. Table 3** summarises the findings for the outcomes under this comparison.

Primary outcomes:

Findings from RCTs suggest that among normal term infants, early introduction of CF at less than or equal to four months of age when compared to six months of age might not have any effect on height/length (SMD: 0.05; 95% CI: -0.16 to 0.27; n=429; 4 studies; **Figure 4**), weight (SMD: -0.06; 95% CI: -0.26 to 0.13; n=429; 4

studies; **Figure 5**), head circumference (SMD: 0.03; 95% CI: -0.20 to 0.26; n=288; 3 studies), BMI (MD: 0.02; 95% CI: -0.41 to 0.45; n=100; 1 study), BMI z-score (MD: -0.15: 95% CI: -0.48 to 0.18; n=100; 1 study), and overweight (RR: 3.70; 95% CI: 0.43 to 31.61; n=77; 1 study). We are uncertain of the effect of early introduction of CF at less than or equal to four months on anemia, severe anemia, and food acceptance among normal term infants.

None of the included studies under this comparison reported stunting, underweight, wasting, HAZ, WAZ, WHZ, dietary pattern/diversity, food allergies, NCD, and infant /child mortality.

Subgroup analysis by country and feeding practices, based on very limited evidence, suggested that there might be no effect by HIC and LMIC for length, weight, head circumference, and anemia.

Secondary Outcomes:

Findings from RCTs suggest a non-significant effect of early introduction of CF at less than or equal to four months of age compared to six months of age on haemoglobin levels, serum ferritin, low ferritin levels, serum zinc levels, tricep thickness, subscapular thickness, suprail thickness, BMC, amenorrhea and duration of lactational amenorrhea among term infants.

None of the included studies under this comparison reported waist circumference, and gut health/microbiome.

Subgroup analysis by country, based on very limited evidence from a single study, suggests increase in Hb (MD: 5.00; 95% CI: 1.54 to 8.46; 1 study), and serum ferritin (MD: 18.9; 95% CI: 0.74 to 37.06; 1 study) levels among normal term infants from LMIC. Moreover, the study also provided iron-fortified complementary food to the intervention group.

Subgroup analysis by feeding practices, based on very limited evidence from a single study, suggested increase in serum ferritin levels (MD: 18.9; 95% CI: 0.74 to 37.06; 1 study) among breastfed infants.

Figure 4: Forest plot of early introduction of CF (≤ four months of age) compared to six months of age among normal term infants (RCTs)- Outcome: Length/Height

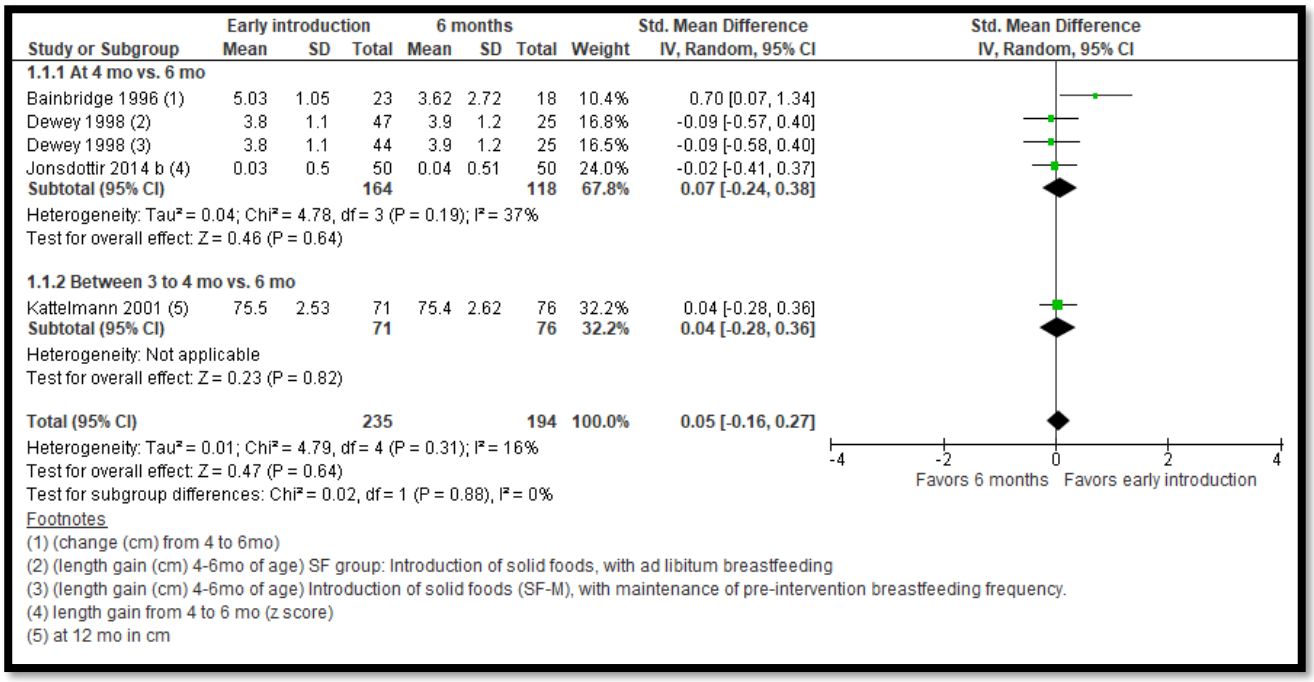


Figure 5: Forest plot of early introduction of CF (≤ four months of age) compared to six months of age among normal term infants (RCTs)- Outcome: Weight

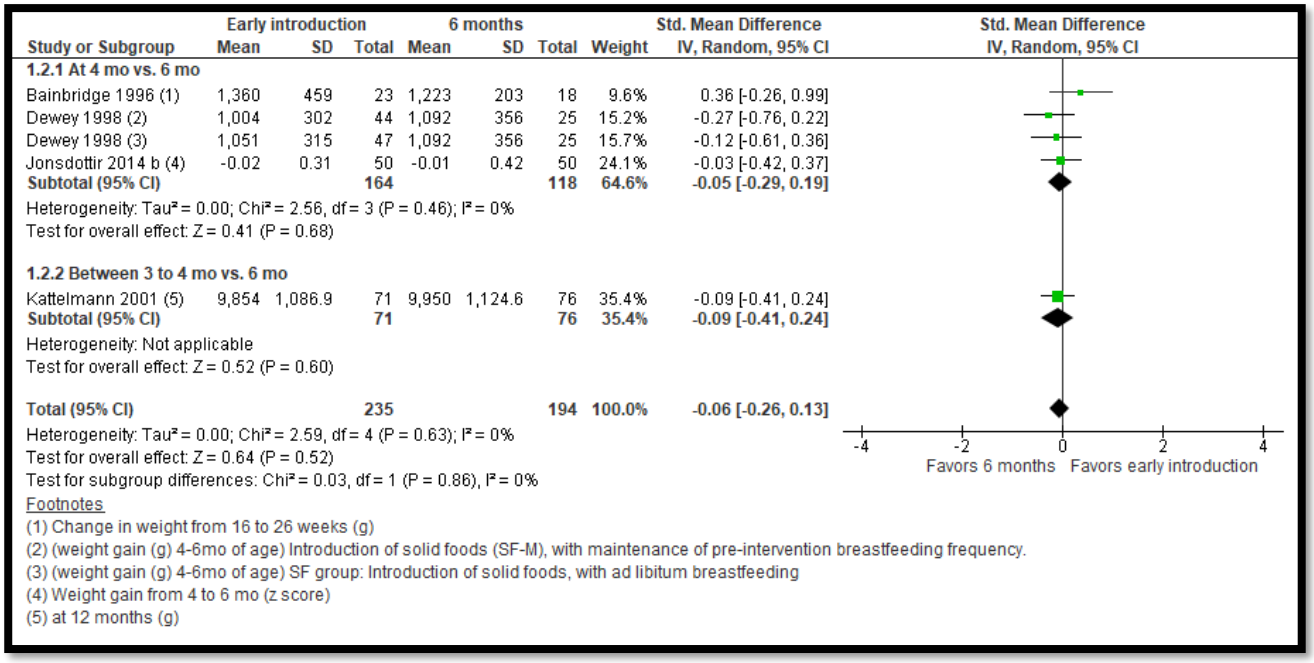


Table 3: Early introduction of CF (≤ four months of age) compared to six months of age among normal term infants (RCTs)

Comparison: Early initiation (<=4mo) vs 6 months among normal term infants (RCTs)			
Outcome	**At 4 months Vs. 6 months**	**Between 3 to 4 months Vs. 6 months**	**Overall**
Height/Length	SMD 0.07 [-0.24, 0.38] (n= 282; 3 studies)	SMD 0.04 [-0.28, 0.36] (n= 147; 1 study)	SMD 0.05 [-0.16, 0.27] (n=429; 4 studies)
Weight	SMD -0.05 [-0.29, 0.19] (n= 282; 3 studies)	SMD -0.09 [-0.41, 0.24] (n= 147; 1 study)	SMD -0.06 [-0.26, 0.13] (n=429; 4 studies)
BMI (kg/m^2)	MD 0.02 [-0.41, 0.45] (n=100; 1 study)		MD 0.02 [-0.41, 0.45] (n=100; 1 study)
BMI for age	MD -0.15 [-0.48, 0.18] (n=100; 1 study)		MD -0.15 [-0.48, 0.18] (n=100; 1 study)
Overweight	RR 3.70 [0.43, 31.61] (n=77; 1 study)		RR 3.70 [0.43, 31.61] (n=77; 1 study)
Anemia	RR 0.83 [0.63, 1.10] (n=139; 1 study)	RR 0.42 [0.04, 4.40] (n=77; 1 study)	RR 0.83 [0.63, 1.08] (n=216; 2 studies)
Severe Anemia	RR 0.77 [0.45, 1.33] (n=139; 1 study)		RR 0.77 [0.45, 1.33] (n=139; 1 study)
Skin fold thickness (triceps)	MD -0.72 [-1.88, 0.44] (n=41; 1 study)		MD -0.72 [-1.88, 0.44] (n=41; 1 study)
Skin fold thickness (subscap)	MD 0.32 [-0.26, 0.90] (n=41; 1 study)		MD 0.32 [-0.26, 0.90] (n=41; 1 study)
Skin fold thickness (suprail)	**MD 0.72 [0.06, 1.38] (n=41; 1 study)**		**MD 0.72 [0.06, 1.38] (n=41; 1 study)**
Head circumference/occipital frontal circumference (OFC)	SMD 0.06 [-0.27, 0.39] (n=141; 2 studies)	SMD 0.0 [-0.32, 0.32] (n=147; 1 study)	SMD 0.03 [-0.20, 0.26] (n=288; 3 studies)
Food acceptance score	MD 0.00 [-0.18, 0.18] (n=125; 1 study)		MD 0.00 [-0.18, 0.18] (n=125; 1 study)
Hemoglobin levels (g/l)	MD 2.47 [-2.23, 7.16] (n=237; 2 studies)	MD 2.00 [-2.17, 6.17] (n=77; 1 study)	MD 2.26 [-0.71, 5.24] (n=314; 3 studies)
Serum Ferritin (ug/L)	MD 18.90 [0.74, 37.06] (n=139; 1 study)	MD 1.0 [-13.20, 15.20] (n=12; 1 study)	MD 9.02 [-8.43, 26.47] (n=151; 2 studies)
Ferritin (ug/L) <12 ug/L	RR 0.43 [0.16, 1.16] (n=135; 1 study)	RR 3.00 [0.15, 61.74] (n=12; 1 study)	RR 0.66 [0.13, 3.27] (n=147; 2 studies)
Ferritin (ug/L) <15 ug/L	RR 0.34 [0.13, 0.88] (n=135; 1 study)		RR 0.34 [0.13, 0.88] (n=135; 1 study)
Serum zinc levels		MD -0.20 [-1.70, 1.30] (n=79; 1 study)	MD -0.20 [-1.70, 1.30] (n=79; 1 study)
Serum zinc <9.2 umol/L		RR 0.38 [0.04, 4.00] (n=79; 1 study)	RR 0.38 [0.04, 4.00] (n=79; 1 study)
Amenorrhea	RR 0.84 [0.50, 1.41] (n=108; 1 study)		RR 0.84 [0.50, 1.41] (n=108; 1 study)
Duration of lactational amenorrhea	MD -3.73 [-41.57, 34.10] (n=108; 1 study)		MD -3.73 [-41.57, 34.10] (n=108; 1 study)
BMC (g)		MD -2.00 [-11.80, 7.80] (n=147; 1 study)	MD -2.00 [-11.80, 7.80] (n=147; 1 study)
RR: Risk ratio; MD: Mean difference; SMD: Standard Mean Difference; BMI: body mass index; BMC: Bone mineral content			

Early introduction of CF - Evidence from Observational Studies

- ### Early introduction of CF (< six months of age) compared to ≥ six months of age –normal term infants

A total of 45 studies with 214,844 participants were included in the meta-analysis under this comparison. **Table 4** summarises the outcomes reported under this comparison. We were unable to meta-analyze developmental outcomes, which are descriptively given in **Appendix Table 6.** Seven studies reported on the introduction of complementary feeding and the exposure group of 'early initiation' included infants who were started at six months, hence were excluded from the meta-analyzed (45-51).

Primary outcomes:

Findings from observational studies suggest among normal term infants, early introduction of CF at less than six months of age compared to greater than or equal to six months of age might increase BMI (MD: 0.13; 95% CI: 0.05 to 0.21; n= 3532; 3 studies; **Figure 6**), BMI z-score (MD: 0.19; 95% CI: 0.09 to 0.29; n= 2447; 1 study; **Figure 7**), and overweight+obesity (OR: 1.34; 95% CI: 1.09 to 1.65; n= 9078; 4 studies; **Figure 8**). Early introduction of CF at less than six months of age might not have any effect on HAZ (MD: 0.03; 95% CI: -0.13 to 0.19; n= 1349; 2 studies), WAZ (MD: 0.08; 95% CI: -0.12 to 0.27; n= 713; 1 study), WHZ (MD: -0.00; 95% CI: -0.01 to 0.00; n= 1995; 1 study), overweight (OR: 1.17; 95% CI: 0.89 to 1.54; n= 8423; 4 studies), obesity (OR: 1.06; 95% CI: 0.95 to 1.19; n=13818; 4 studies), atopic dermatitis (OR: 1.04; 95% CI: 0.71 to 1.52; n= 1425; 1 study), lower respiratory tract infection (LRTI) (OR: 1.11; 95% CI: 0.90 to 1.38; n= 110035; 3 studies), and food allergy (OR: 0.90; 95% CI: 0.60 to 1.35; n= 2396; 2 studies). The evidence is uncertain for stunting, underweight, wasting, thinness, height/length, weight, head circumference, diarrhea, asthma, wheeze, eczema, rickets, respiratory illness, gastro-intestinal illness, anemia, and iron deficiency anemia.

None of the included studies under this comparison reported food preferences, NCDs, and infant/child mortality.

Subgroup analysis by country, based on very limited evidence, suggests decrease in odds of diarrhea (OR: 0.39; 95% CI: 0.27 to 0.55, 1 study), and increase in odds of anemia (OR: 2.45; 95% CI: 1.69 to 3.54; 1 study) among infants in LMIC; and increase in BMI (MD: 0.13; 95% CI: 0.05 to 0.22; 2 studies), and overweight (OR: 1.55; 95% CI: 1.08 to 2.22; 2 studies) among infants in HIC. There was no difference by HIC and LMIC for stunting, wasting, underweight, HAZ, length, weight, obesity, LRTI, and asthma.

Subgroup analysis by feeding practices, based on very limited evidence, suggests increase odds of overweight and obesity (OR: 2.26; 95% CI: 1.10 to 4.63; 1 study) among infants on formula feeding and there was no effect by breast fed and formula fed infants for HAZ, WAZ, length, weight, BMI, overweight, and obesity.

Figure 6: Forest plot of early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies)- Outcome: BMI

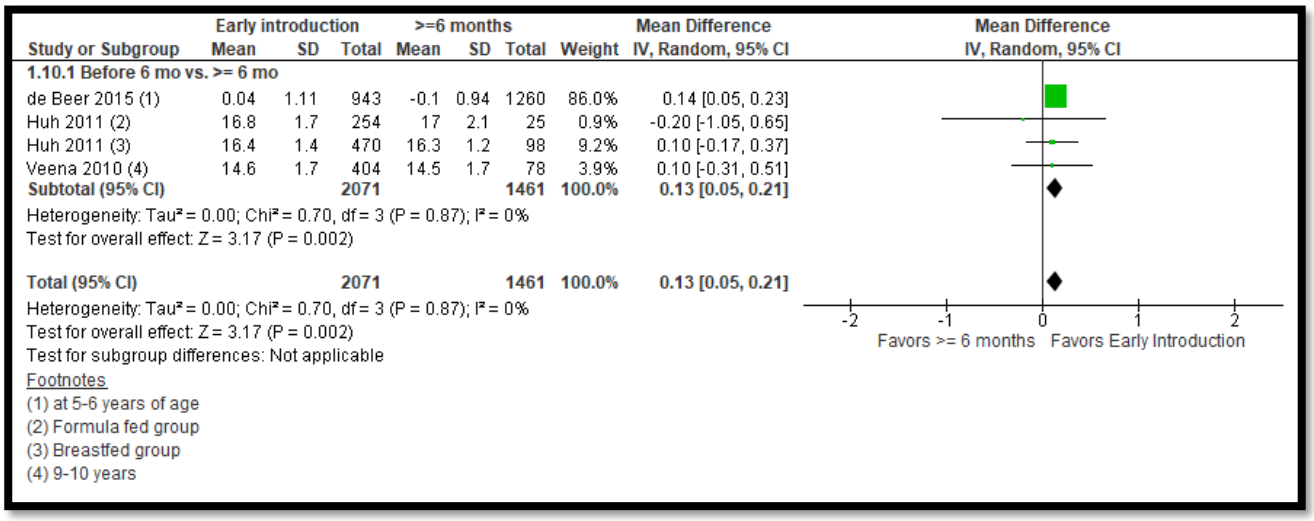


Figure 7: Forest plot of early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies) - Outcome: BMI z-score

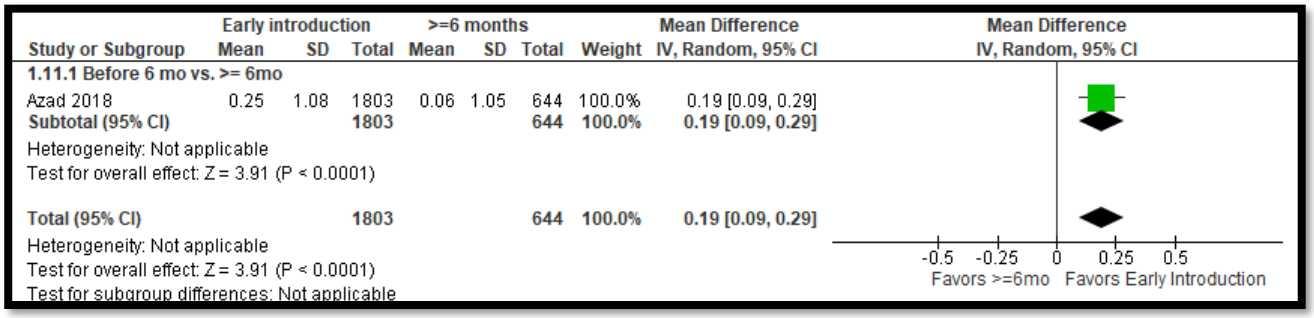
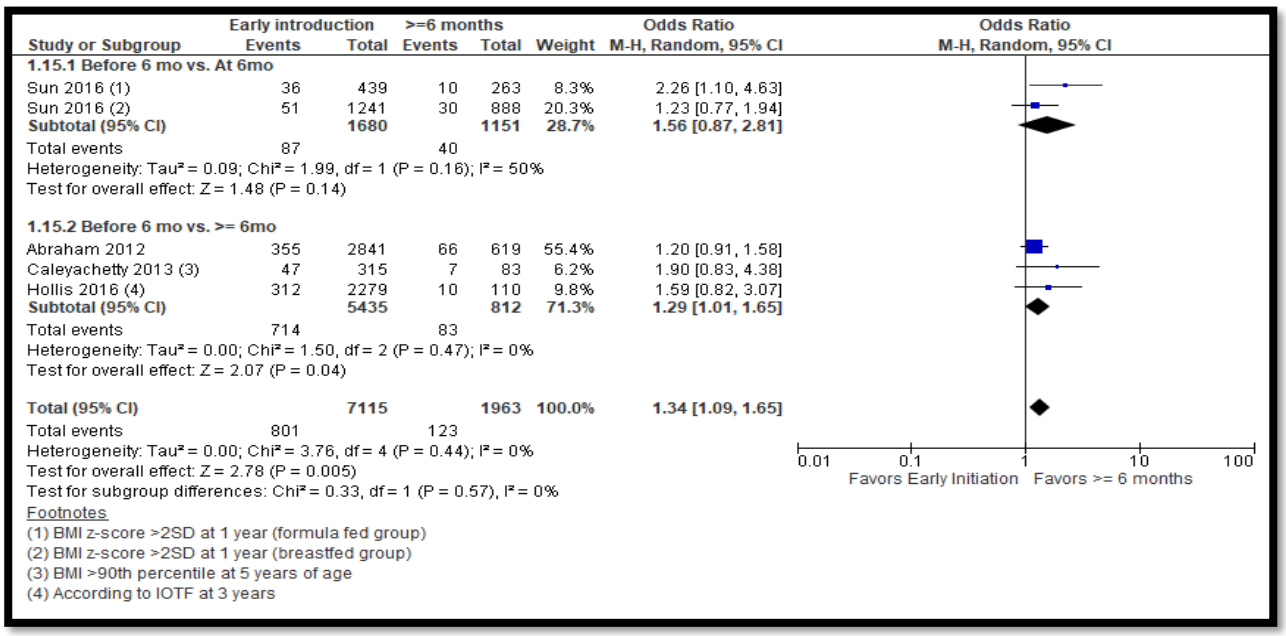


Figure 8: Forest plot of early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies)- Outcome: Overweight+Obesity



Secondary Outcomes:

Findings from the observational studies suggest a non-significant effect of early introduction of CF at less than six months of age compared to greater than or equal to six months of age on haemoglobin level, serum ferritin, iron deficiency, and skinfold thickness.

None of the included studies under this comparison reported BMC, waist circumference, gut health/microbiome, and maternal outcomes.

Subgroup analysis by setting, based on very limited evidence, suggests no effect by HIC and LMIC for skin fold thickness.

Table 4: Early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies)

Comparison: Early initiation (< 6mo) vs. at or after 6 months among normal term infants (Observational studies)			
Outcome	<6mo Vs at 6 months	<6mo Vs at and after 6 months	Overall
Stunting	OR 1.02 [0.77, 1.35] (n= 1026; 3 studies)	OR 1.19 [0.66, 2.12] (n= 11790; 7 studies)	OR 1.16 [0.77, 1.75] (n= 12816; 10 studies)
Underweight	OR 0.90 [0.60, 1.36] (n= 549; 2 studies)	**OR 1.39 [1.15, 1.68] (n= 5390; 4 studies)**	**OR 1.29 [1.08, 1.53] (n= 5939; 6 studies)**
Wasting	OR 0.94 [0.62, 1.44] (n= 549; 2 studies)	OR 2.03 [1.02, 4.03] (n= 1291; 4 studies)	OR 1.55 [0.91, 2.62] (n= 1840; 6 studies)
Thinness		OR 2.70 [0.62, 11.79] (n= 139; 1 study)	OR 2.70 [0.62, 11.79] (n= 139; 1 study)
Height for Age Z-score		MD 0.03 [-0.13, 0.19] (n= 1349; 2 studies)	MD 0.03 [-0.13, 0.19] (n= 1349; 2 studies)
Weight for Age Z-score		MD 0.08 [-0.12, 0.27] (n= 713; 1 study)	MD 0.08 [-0.12, 0.27] (n= 713; 1 study)
Weight for Height Z-score		MD -0.00 [-0.01, 0.00] (n= 1995; 1 study)	MD -0.00 [-0.01, 0.00] (n= 1995; 1 study)
Height/Length	SMD -0.14 [-0.75, 0.48] (n= 41; 1 study)	SMD -0.12 [-0.57, 0.34] (n= 2581; 6 studies)	SMD -0.12 [-0.54, 0.30] (n= 2559; 7 studies)
Weight	SMD 0.17 [-0.44, 0.78] (n= 41; 1 study)	SMD 0.13 [-0.04, 0.30](n= 2036; 5 studies)	SMD 0.13 [-0.02, 0.29] (n= 2077; 6 studies)
BMI		**MD 0.13 [0.05, 0.21] (n= 3532; 3 studies)**	**MD 0.13 [0.05, 0.21] (n= 3532; 3 studies)**
BMI Z-score		**MD 0.19 [0.09, 0.29] (n= 2447; 1 study)**	**MD 0.19 [0.09, 0.29] (n= 2447; 1 study)**
Head circumference	MD 0.20 [-0.34, 0.74] (n= 41; 1 study)		MD 0.20 [-0.34, 0.74] (n= 41; 1 study)
Overweight		OR 1.17 [0.89, 1.54] (n= 8423; 4 studies)	OR 1.17 [0.89, 1.54] (n= 8423; 4 studies)
Obesity		OR 1.06 [0.95, 1.19] (n= 13818; 4 studies)	OR 1.06 [0.95, 1.19] (n= 13818; 4 studies)
Overweight and obesity	OR 1.56 [0.87, 2.81] (n= 2831; 1 study)	**OR 1.29 [1.01, 1.65] (n= 6247; 3 studies)**	**OR 1.34 [1.09, 1.65] (n= 9078; 4 studies)**
Skinfold thickness (triceps)		MD 0.30 [-0.47, 1.07] (n= 529; 1 study)	MD 0.30 [-0.47, 1.07] (n= 529; 1 study)
Skinfold thickness (subscapular)		MD 0.05 [-0.51, 0.61] (n= 529; 1 study)	MD 0.05 [-0.51, 0.61] (n= 529; 1 study)
Skinfold thickness (triceps + subscapular)		MD 0.11 [-0.56, 0.78] (n= 1376; 2 studies)	MD 0.11 [-0.56, 0.78] (n= 1376; 2 studies)
Anemia	**OR 2.45 [1.69, 3.54] (n= 477; 1 study)**	**OR 1.27 [1.13, 1.42] (n= 18446; 1 study)**	OR 1.72 [0.90, 3.27] (n= 18923; 2 studies)
Iron deficiency anemia		**OR 0.34 [0.18, 0.63] (n= 870; 1 study)**	**OR 0.34 [0.18, 0.63] (n= 870; 1 study)**
Hemoglobin		SMD -0.01 [-0.31, 0.28] (n= 18519; 2 studies)	SMD -0.01 [-0.31, 0.28] (n= 18519; 2 studies)
Serum ferritin		MD 3.70 [-2.93, 10.33] (n= 73; 1 study)	MD 3.70 [-2.93, 10.33] (n= 73; 1 study)
Iron deficiency		**OR 0.57 [0.43, 0.75] (n= 1489; 2 studies)**	**OR 0.57 [0.43, 0.75] (n= 1489; 2 studies)**
Atopic dermatitis		OR 1.04 [0.71, 1.52] (n= 1425; 1 study)	OR 1.04 [0.71, 1.52] (n= 1425; 1 study)
Diarrhea		OR 0.64 [0.21, 1.97] (n= 107407; 2 studies)	OR 0.64 [0.21, 1.97] (n= 107407; 2 studies)
Gastrointestinal illness		OR 1.05 [0.48, 2.28] (n= 233; 1 study)	OR 1.05 [0.48, 2.28] (n= 233; 1 study)
Asthma		OR 0.99 [0.71, 1.38] (n=4938; 3 studies)	OR 0.99 [0.71, 1.38] (n=4938; 3 studies)
Respiratory illness		OR 1.51 [0.68, 3.35] (n= 233; 1 study)	OR 1.51 [0.68, 3.35] (n= 233; 1 study)
LRTI		OR 1.11 [0.90, 1.38] (n=110035; 3 studies)	OR 1.11 [0.90, 1.38] (n=110035; 3 studies)
Wheeze		OR 0.93 [0.69, 1.25] (n= 2320; 1 study)	OR 0.93 [0.69, 1.25] (n= 2320; 1 study)
Eczema		OR 1.12 [0.89, 1.42] (n= 2290; 1 study)	OR 1.12 [0.89, 1.42] (n= 2290; 1 study)
Food Allergy		OR 0.90 [0.60, 1.35] (n= 2396; 2 studies)	OR 0.90 [0.60, 1.35] (n= 2396; 2 studies)
Rickets		OR 3.17 [0.40, 25.03]	OR 3.17 [0.40, 25.03]

		(n= 233; 1 study)	(n= 233; 1 study)
OR: Odds ratio; MD: Mean difference; SMD: Standard Mean Difference; BMI: Body mass index; LRTI: Lower respiratory tract infection			

- Early introduction of CF (< three months of age) compared to ≥ three months of age

A total of five studies with 17,892 participants were included in the meta-analysis under this comparison. **Table 5** summarises the findings from the outcomes under this comparison. Nine studies reported on introduction of CF and the exposure group of 'early initiation' included infants who were started at less than or equal to three months, hence were excluded from the meta-analysis (51-59).

Primary outcomes:

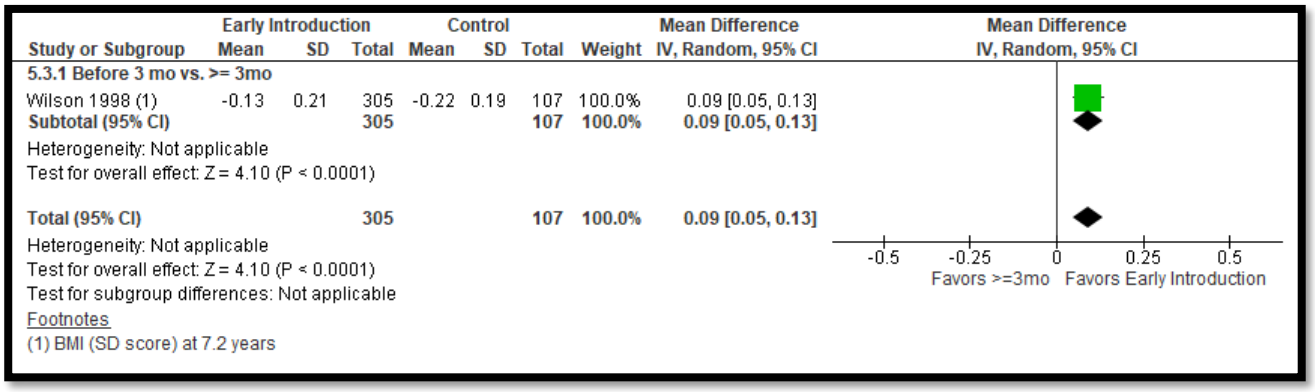
Findings from the observational studies among normal term infants suggest that early introduction of CF at less than three months compared to greater than or equal to three months of age might increase BMI (MD: 0.09; 95% CI: 0.05 to 0.13; n= 412; 1 study; **Figure 9**), and odds of LRTI (OR: 1.51; 95% CI: 1.12 to 2.03; n= 106132; 1 study). Early introduction of CF at less than three months of age might not have any effect on WAZ (MD: -0.20; 95% CI: -0.52 to 0.12; n= 317; 1 study), weight (MD: 0.04; 95% CI: -0.07 to 0.14; n= 412; 1 study), and diarrhea (OR: 1.19; 95% CI: 0.95 to 1.49; n= 212258; 2 studies).

The evidence is uncertain for chest infection, eczema, ear infection, respiratory illness, gastro-intestinal illness, rickets, systolic blood pressure, and diastolic blood pressure.

None of the included studies under this comparison reported stunting, underweight, wasting, HAZ, WHZ, height/length, head circumference, overweight, obesity, overweight+obesity, anemia, developmental outcomes, food preferences, dietary diversity, food allergies, and infant/child mortality.

Subgroup analysis by country, based on very limited data, suggests no difference by HIC and LMIC. Subgroup analysis by feeding practices, based on very limited evidence, suggests increase in weight (MD: 0.18; 95% CI: 0.11 to 0.25; 1 study), BMI (MD: 0.12; 95% CI: 0.05 to 0.19; 1 study), and diastolic blood pressure (MD: 0.90; 95% CI: 0.16 to 1.64; 1 study) among infants on formula feeding; while early introduction might increase BMI (MD: 0.09; 95% CI: 0.04 to 0.14; 1 study), and diastolic blood pressure (MD: 0.71; 95% CI: 0.05 to 1.37; 1 study) among infants on breast feeding. There was no effect by breast fed and formula fed infants for systolic blood pressure.

Figure 9: Forest plot of early introduction of CF (< three months of age) compared to ≥ three months of age among normal term infants (Observational studies)- Outcome: BMI



Secondary Outcomes:

None of the included studies under this comparison reported on skinfold thickness, haemoglobin, micronutrient status, BMC, waist circumference, gut health/microbiome, and maternal outcomes.

Table 5: Early introduction of CF (< three months of age) compared to ≥ three months of age among normal term infants (Observational studies)

Comparison: Early initiation (< 3mo) vs at or after 3 months among normal term infants (Observational studies)	
	Overall **Comparison: <3mo Vs at and after 3 months**
Weight for Age Z-Score	MD -0.20 [-0.52, 0.12] (n= 317; 1 study)
Weight	MD 0.04 [-0.07, 0.14] (n= 412; 1 study)
BMI	**MD 0.09 [0.05, 0.13]** **(n= 412; 1 study)**
Diarrhea	OR 1.19 [0.95, 1.49] (n= 212258; 2 studies)
Gastrointestinal illness	OR 1.05 [0.48, 2.28] (n= 233; 1 study)
LRTI	**OR 1.51 [1.12, 2.03]** **(n= 106132; 1 study)**
Respiratory illness	OR 1.51 [0.68, 3.35] (n= 233; 1 study)
Chest infection	OR 1.13 [0.32, 3.94] (n= 97; 1 study)
Eczema	OR 1.22 [0.57, 2.61] (n= 178; 1 study)
Ear infection	OR 1.18 [0.04, 31.99] (n= 34; 1 study)
Systolic BP	MD -0.21 [-10.40, 9.98] (n= 40; 1 study)
Diastolic BP	MD 0.86 [-0.53, 2.25] (n= 40; 1 study)
Rickets	OR 3.17 [0.40, 25.03] (n= 233; 1 study)
OR: Odds ratio; MD: Mean difference; BMI: Body mass index; LRTI: Lower respiratory tract infection; BP: Blood pressure	

- Early introduction of CF (< four months of age) compared to ≥ four months of age

A total of 30 studies with 136,330 participants were included in the meta-analysis under this comparison.

Table 6 summarises the findings from the outcomes reported under this comparison. Seven studies reported

on introduction of CF and the exposure group of 'early initiation' included infants who were started at four months, hence were excluded from the meta-analysis (45, 50, 53, 56, 60-62).

Primary outcomes:

Findings from observational studies suggest that among normal term infants, early introduction of CF at less than four months compared to greater than or equal to four months of age might increase stunting (OR: 1.46; 95% CI: 1.01 to 2.11; n= 807; 1 study), height (SMD: 0.18; 95% CI: 0.06 to 0.30; n= 3764; 4 studies; **Figure 10**), LRTI (OR: 1.43; 95% CI: 1.19 to 1.73; n= 106132; 1 study), systolic blood pressure at 5 years of age (OR: 1.50; 95% CI: 0.11 to 2.89; n= 2203; 1 study), and diastolic blood pressure at 5 years of age (OR: 1.30; 95% CI: 0.27 to 2.33; n= 2203; 1 study), and might not have any effect on wasting (OR: 0.92; 95% CI: 0.54 to 1.59; n= 796; 1 study); head circumference (OR: 0.86; 95% CI: 0.49 to 1.49; n= 796; 1 study), overweight (OR: 0.97; 95% CI: 0.83 to 1.13; n= 9865; 5 studies), and diarrhea (OR: 1.36; 95% CI: 0.97 to 1.91; n= 106677; 2 studies).

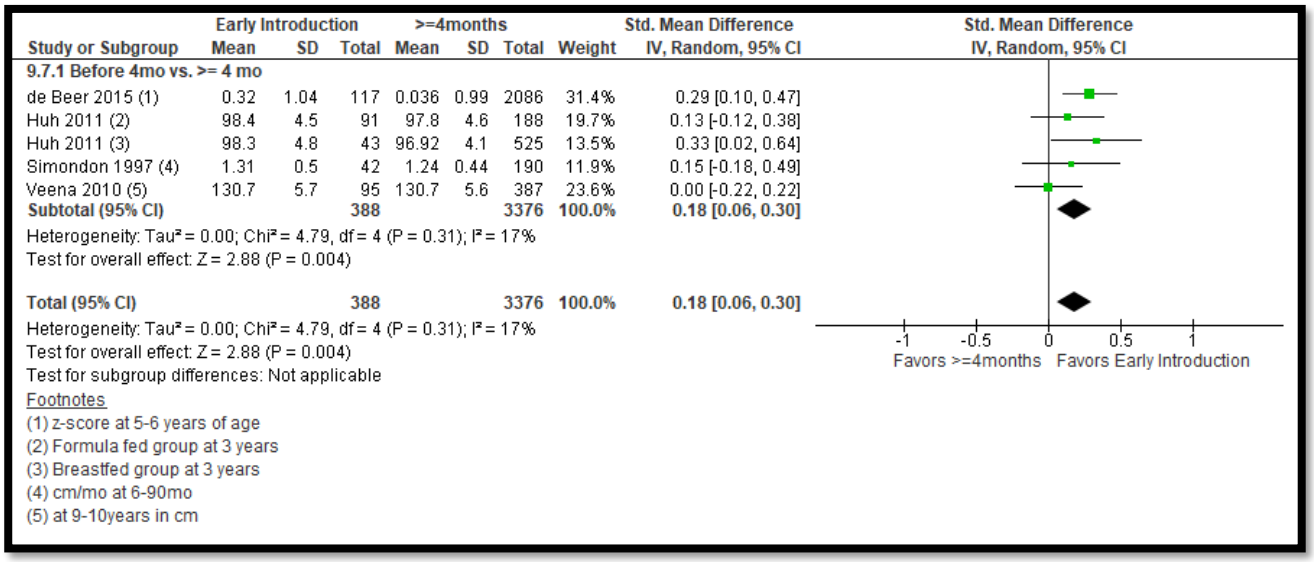
The evidence is uncertain for underweight, HAZ, WAZ, WHZ, weight, BMI, BMI z-score, obesity, overweight and obesity, atopic dermatitis, asthma, wheeze, eczema, and food allergy.

None of the included studies under this comparison reported anemia, developmental outcomes, food preferences, dietary diversity, NCDs, and infant/child mortality.

Subgroup analysis by country, based on very limited evidence, suggest increase in odds of underweight (OR: 1.67; 95% CI: 1.16 to 2.40; 1 study), BMI (MD: 13.4; 95% CI: 12.91 to 13.89; 1 study), and diarrhea (OR: 1.71; 95% CI: 1.06 to 2.77; 1 study) in LMIC, and increase in height/length (MD: 0.25; 95% CI: 0.11 to 0.38; 2 studies) in HIC. There was no effect by HIC and LMIC for underweight, HAZ, length, weight, overweight, obesity, overweight+obesity, atopic dermatitis, and asthma.

Subgroup analysis by feeding practices, based on very limited evidence, suggests decrease in the odds of underweight (OR: 0.44; 95% CI: 0.26 to 0.75; 1 study), and increase in WAZ (MD: 0.35; 95% CI: 0.09 to 0.61; 1 study), weight (MD: 0.32; 95% CI: 0.07 to 0.57; 1 study), BMI (MD: 0.60; 95% CI: 0.15 to 1.05; 1 study), BMI z-score (MD: 0.40; 95% CI: 0.12 to 0.68; 1 study), and obesity (OR: 4.96; 95% CI: 2.34 to 10.52; 1 study) among infants on formula feeding. There was no effect by breast fed and formula fed infants for HAZ, height, overweight, and overweight and obesity.

Figure 10: Forest plot of early introduction of CF (< four months of age) compared to ≥ four months of age among normal term infants (Observational studies) - Outcome: Height/length



Secondary Outcomes:

Findings from observational studies suggest a non-significant effect of early introduction of CF at less than four months compared to greater than or equal to four months on waist circumference and skinfold thickness.

None of the included studies under this comparison reported haemoglobin, micronutrient status, BMC, waist circumference, gut health/microbiome, and maternal outcomes.

Table 6: Early introduction of CF (< four months of age) compared to ≥ four months of age among normal term infants (Observational studies)

Comparison: Early initiation (<4mo) vs at or after 4 months among normal term infants (Observational studies)		
	<4mo Vs at and after 4 months	**Overall**
Stunting	**OR 1.46 [1.01, 2.11] (n= 807; 1 study)**	**OR 1.46 [1.01, 2.11] (n= 807; 1 study)**
Underweight	OR 0.98 [0.60, 1.61] (n= 6643; 3 studies)	OR 0.98 [0.60, 1.61] (n= 6643; 3 studies)
Wasting	OR 0.92 [0.54, 1.59] (n= 796; 1 study)	OR 0.92 [0.54, 1.59] (n= 796; 1 study)
Height for Age Z-score	MD 0.15 [-0.03, 0.32] (n= 892; 2 studies)	MD 0.15 [-0.03, 0.32] (n= 892; 2 studies)
Weight for Age Z-score	MD 0.16 [-0.23, 0.55] (n= 892; 2 studies)	MD 0.16 [-0.23, 0.55] (n= 892; 2 studies)
Weight for Height Z-score	**MD -7.40 [-12.65, -2.15] (n= 45; 1 study)**	**MD -7.40 [-12.65, -2.15] (n= 45; 1 study)**
Height/Length	**SMD 0.18 [0.06, 0.30] (n= 3764; 4 studies)**	**SMD 0.18 [0.06, 0.30] (n= 3764; 4 studies)**
Weight	SMD 0.04 [-0.26, 0.35] (n= 1127; 3 studies)	SMD 0.04 [-0.26, 0.35] (n= 1127; 3 studies)
BMI	MD 2.53 [-0.16, 5.23] (n= 26221; 5 studies)	MD 2.53 [-0.16, 5.23] (n= 26221; 5 studies)
BMI Z-score	MD 0.14 [-0.12, 0.39] (n= 3294; 2 studies)	MD 0.14 [-0.12, 0.39] (n= 3294; 2 studies)
Head circumference <-2 Z-score	OR 0.86 [0.49, 1.49] (n= 796; 1 study)	OR 0.86 [0.49, 1.49] (n= 796; 1 study)
Overweight	OR 0.97 [0.83, 1.13] (n= 9865; 5 studies)	OR 0.97 [0.83, 1.13] (n= 9865; 5 studies)
Obesity	OR 0.86 [0.30, 2.45] (n= 9389; 6 studies)	OR 0.86 [0.30, 2.45] (n= 9389; 6 studies)
Overweight and Obesity	OR 1.22 [0.55, 2.71] (n= 29178; 5 studies)	OR 1.22 [0.55, 2.71] (n= 29178; 5 studies)
Waist circumference	**MD 2.10 [0.67, 3.53] (n= 106; 1 study)**	**MD 2.10 [0.67, 3.53] (n= 106; 1 study)**
Skinfold thickness (triceps + subscapular)	MD 0.02 [-1.25, 1.30] (n= 847; 1 study)	MD 0.02 [-1.25, 1.30] (n= 847; 1 study)
Atopic dermatitis	OR 1.38 [0.53, 3.54] (n= 22332; 5 studies)	OR 1.38 [0.53, 3.54] (n= 22332; 5 studies)
Asthma	OR 1.22 [0.72, 2.09] (n= 2595; 2 studies)	OR 1.22 [0.72, 2.09] (n= 2595; 2 studies)
Wheeze	OR 0.77 [0.46, 1.31] (n= 1894; 1 study)	OR 0.77 [0.46, 1.31] (n= 1894; 1 study)
Diarrhea	OR 1.36 [0.97, 1.91] (n= 106677; 2 studies)	OR 1.36 [0.97, 1.91] (n= 106677; 2 studies)
LRTI	**OR 1.43 [1.19, 1.73] (n= 106132; 1 study)**	**OR 1.43 [1.19, 1.73] (n= 106132; 1 study)**
Eczema	OR 0.98 [0.69, 1.39] (n= 16959; 2 studies)	OR 0.98 [0.69, 1.39] (n= 16959; 2 studies)
Food allergy	OR 1.16 [0.74, 1.82] (n= 1239; 1 study)	OR 1.16 [0.74, 1.82] (n= 1239; 1 study)
Systolic BP	**MD 1.50 [0.11, 2.89] (n= 2203; 1 study)**	**MD 1.50 [0.11, 2.89] (n= 2203; 1 study)**
Diastolic BP	**MD 1.30 [0.27, 2.33] (n= 2203; 1 study)**	**MD 1.30 [0.27, 2.33] (n= 2203; 1 study)**
OR: Odds ratio; MD: Mean difference; SMD: Standard Mean Difference; BMI: Body mass index; LRTI: Lower respiratory tract infection; BP: Blood pressure		

Late introduction of CF - Evidence from RCTs

None of the included RCTs reported outcomes under this comparison.

Late introduction of CF - Evidence from Observational Studies

- Late introduction of CF (> six months) compared to ≤ six months of age

A total of 22 studies with 95,779 participants were included in the analysis under this comparison. **Table 7** summarises the findings from the outcomes reported under this comparison. Thirteen studies reported on introduction of CF and the exposure group of 'late initiation' included infants who were started at equal to six months, hence were excluded from the meta-analysis (52-54, 56, 57, 63-70).

Primary outcomes:

Findings from observational studies suggest that among normal term infants, late introduction of CF at greater than six months of age compared to less than or equal six months may decrease height (MD: -0.12; 95% CI: -0.21 to -0.04; n= 2357; 2 studies; **Figure 11**), BMI (MD: -0.14; 95% CI: -0.23 to -0.05; n= 2203; 1 study; **Figure 12**), systolic blood pressure (MD: -1.20; 95% CI: -1.80 to -0.60; n= 2203; 1 study), diastolic blood pressure (MD: -0.72; 95% CI: -1.22 to -0.22; n= 2203; 1 study), and might increase odds of intestinal helminth infection (OR: 173.00; 95% CI: 39.17 to 764.05; n= 404; 1 study). Late introduction of CF at greater than six months of age might not have any effect on overweight (OR: 0.94; 95% CI: 0.69 to 1.29; n= 41152; 3 studies), obesity (OR: 0.85; 95% CI: 0.59 to 1.21; n= 40510; 1 study), and LRTI (OR: 1.09; 95% CI: 0.86 to 1.37; n= 3903; 2 studies). The evidence is uncertain for stunting, underweight, wasting, thinness, overweight+obesity, weight, asthma, wheeze, eczema, diarrhea, atopic dermatitis, food hypersensitivity, and anemia.

None of the included studies under this comparison reported HAZ, WHZ, WAZ, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Subgroup analysis by country, based on very limited evidence, suggested that late introduction of CF at greater than six months of age compared to less than or equal six months might decrease in weight (MD: -0.04; 95% CI: -0.68 to -0.12; 1 study) in HICs.

Subgroup analysis based on feeding practices, based on very limited evidence, suggested that there might be an increase in odds of overweight and obesity (OR: 2.76; 95% CI: 1.10 to 6.95; 1 study) among normal term infants on formula feeding and there might be decrease in height (MD: -0.12; 95% CI: -0.20 to -0.04; 1 study) among normal term infants on breastfeeding.

Figure 11: Forest plot of late introduction of CF (> six months) compared to ≤ six months of age among normal term infants (Observational studies) - Outcome: Height/Length

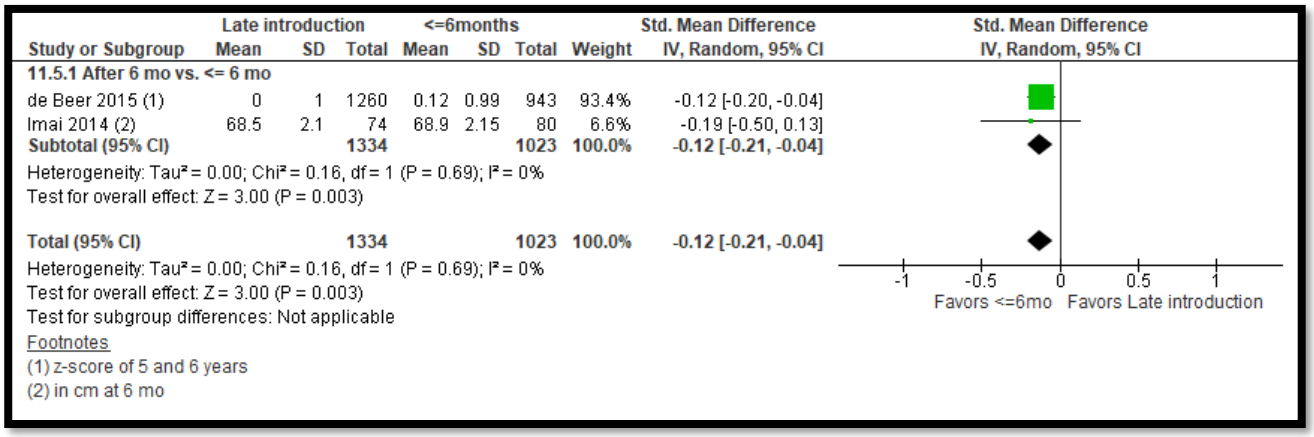
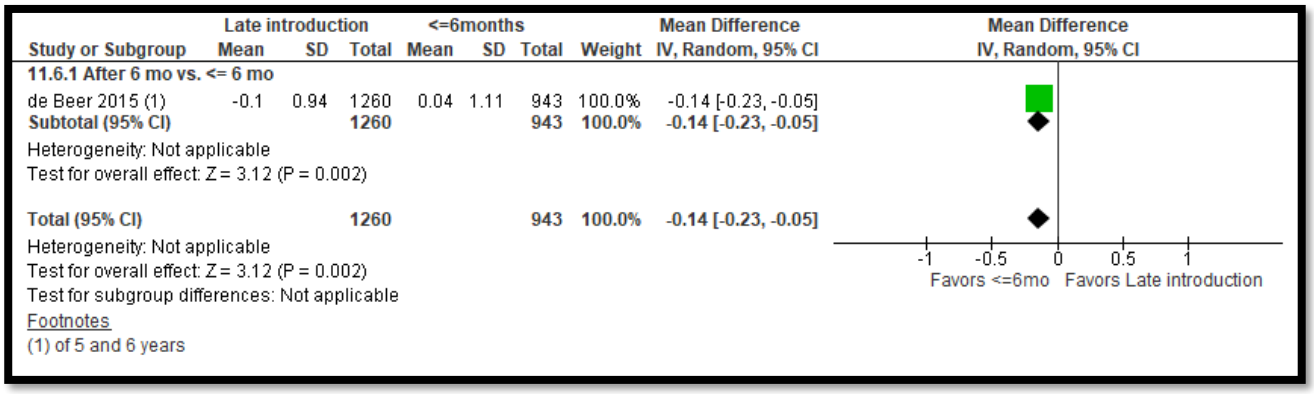


Figure 12: Forest plot of late introduction of CF (> six months) compared to ≤ six months of among normal term infants (Observational studies) - Outcome: BMI



Secondary Outcomes:

None of the included studies under this comparison reported haemoglobin, micronutrient status, BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 7: Late introduction of CF (> six months) compared to ≤ six months of age among normal term infants (Observational studies)

Comparison: Late initiation (>6mo) vs at or before 6 months among normal term infants (Observational studies)	
	Overall **Comparison: >6mo Vs at and before 6 months**
Stunting	OR 1.19 [0.71, 2.00] (n= 11872; 7 studies)
Underweight	OR 1.35 [0.65, 2.78] (n= 1107; 4 studies)
Wasting	OR 0.42 [0.07, 2.56] (n= 540; 3 studies)
Thinness	OR 0.37 [0.08, 1.62] (n= 139; 1 study)
Height/Length	**MD -0.12 [-0.21, -0.04](n= 2357; 2 studies)**
Weight	MD -0.11 [-0.69, 0.48] (n= 7588; 2 studies)
BMI	**MD -0.14 [-0.23, -0.05]** **(n= 2203; 1 study)**
Overweight	OR 0.94 [0.69, 1.29] (n= 41152; 3 studies)
Obesity	OR 0.85 [0.59, 1.21] (n= 40510; 1 study)
Overweight and Obesity	OR 0.76 [0.10, 5.92] (n= 5239; 2 studies)
Anemia	OR 2.49 [0.02, 359.68] (n= 704; 2 studies)
Atopic dermatitis	OR 0.98 [0.79, 1.20] (n= 18773; 1 study)
Asthma	OR 0.95 [0.61, 1.46] (n= 2343; 1 study)
Wheeze	OR 0.93 [0.69, 1.25] (n= 2320; 1 study)
Eczema	OR 1.04 [0.79, 1.36] (n= 2301; 1 study)
LRTI	OR 1.09 [0.86, 1.37] (n= 3903; 2 studies)
Diarrhea	OR 1.58 [1.10, 2.28] (n= 597; 1 study)
Food hypersensitivity	0.56 [0.10, 3.08] (n= 56; 1 study)
Intestinal helminth infection	**OR 173.00 [39.17, 764.05]** **(n= 404; 1 study)**
Systolic BP	**MD -1.20 [-1.80, -0.60]** **(n= 2203; 1 study)**
Diastolic BP	**MD -0.72 [-1.22, -0.22]** **(n= 2203; 1 study)**
OR: Odds ratio; MD: Mean difference; BMI: Body mass index; LRTI: Lower respiratory tract infection; BP: Blood pressure	

- Late introduction of CF (> eight months) compared to ≤ eight months of age

A total of five studies with 3,997 participants were included in the analysis under this comparison. **Table 10** summarises the findings from the outcomes reported under this comparison. Two studies reported on introduction of CF and the exposure group of 'late initiation' included infants who were started at equal to eight months, hence were excluded from the meta-analysis (61, 71).

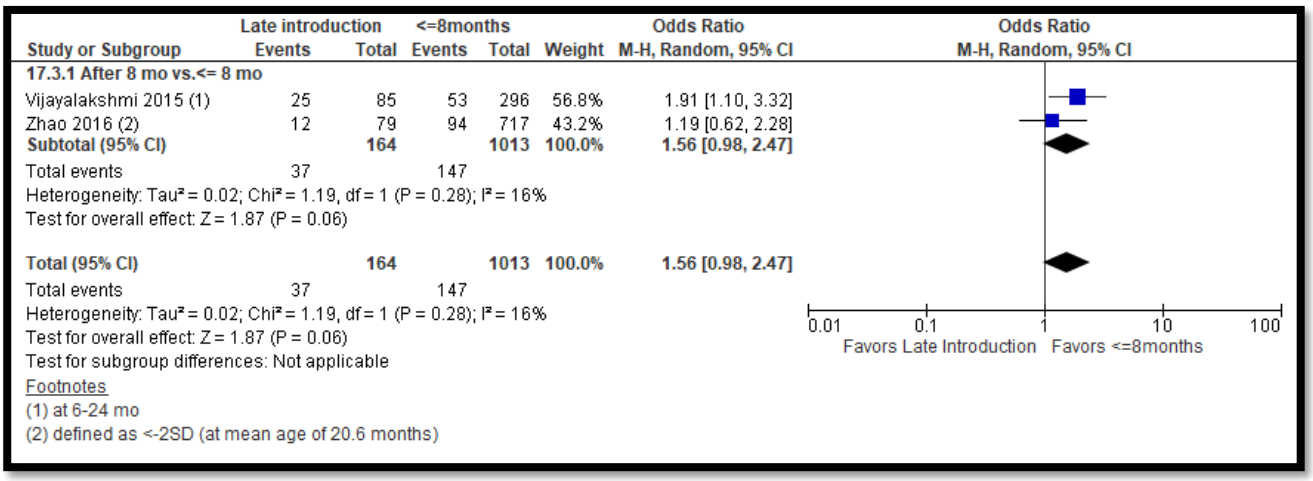
Primary outcomes:

Findings from observational studies suggest that among normal term infants, late introduction of CF at greater than eight months of age compared to less than or equal to eight months of age might increase HAZ (MD: 0.50; 95% CI: 0.09 to 0.91; n= 636; 1 study), and it might not have any effect on wasting (OR: 1.56; 95%

CI: 0.98 to 2.47; n= 1177; 2 studies; **Figure 13**), head circumference (OR: 0.95; 95% CI: 0.47 to 1.91; n= 796; 1 study), and diarrhea (OR: 1.44; 95% CI: 0.78 to 2.67; n=545; 1 study). The evidence is uncertain for stunting, underweight, gastro-intestinal illness, and anaemia.

None of the included studies under this comparison reported WAZ, WHZ, BMI, BMI z-score, overweight, obesity, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Figure 13: Forest plot of late introduction of CF (> eight months) compared to ≤ eight months of age among normal term infants (Observational studies) - Outcome: Wasting



Secondary Outcomes:

Findings from an observational study suggests a non-significant effect of late introduction of CF at greater than eight months of age compared to less than or equal to eight months of age on head circumference.

None of the included studies under this comparison reported haemoglobin, micronutrient status, BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 10: Late introduction of CF (> eight months) compared to ≤ eight months of age among normal term infants (Observational studies)

Comparison: Late initiation (>8mo) vs at or before 8 months among normal term Infants (Observational studies)	
	Overall **Comparison: >8mo Vs at and before 8 months**
Stunting	OR 1.66 [0.88, 3.14] (n= 1824; 3 studies)
Underweight	OR 1.95 [0.56, 6.83] (n= 1187; 2 studies)
Wasting	OR 1.56 [0.98, 2.47] (n= 1177; 2 studies)
Height for Age Z-score	**MD 0.50 [0.09, 0.91]** **(n= 636; 1 study)**
Head circumference <-2 Z-score	OR 0.95 [0.47, 1.91] (n= 796; 1 study)
Anemia	**OR 0.34 [0.12, 0.93]** **(n= 150; 1 study)**
Diarrhea	OR 1.44 [0.78, 2.67] (n= 545; 1 study)
Gastrointestinal illness	OR 0.78 [0.28, 2.12] (n= 213; 1 study)
OR: Odds ratio; MD: Mean difference	

Preterm /SGA / LBW Infants

Early introduction of CF-Evidence from RCTs

- Early introduction of CF (at four months of age) compared to six months of age

A total of three RCTs (72-74) with 428 participants were included in the meta-analysis under this comparison. Of these studies, two studies included LBW, term infants (SGA) (72, 73), and one study included preterm infants (74). We were unable to meta-analyze developmental outcomes, which are descriptively given in **Appendix Table 6. Table 9** summarises the findings from the outcomes reported under this comparison.

Primary outcomes:

Findings from RCTs among LBW/SGA infants, suggest that early introduction of CF at four months compared to six months of age has an uncertain evidence for length, weight, and severe anemia. Findings from an RCT among preterm infants, suggest that early introduction of CF at four months compared to six months of age has an uncertain effect on WAZ, acceptable minimum dietary diversity, minimum acceptable diet, diarrhea, LRTI, sepsis, systolic blood pressure, diastolic blood pressure, and infant mortality.

None of the included studies under this comparison reported stunting, underweight, wasting, HAZ, WHZ, food preferences, food allergies, or any other NCDs.

Secondary Outcomes:

Findings from RCTs suggest that there is an effect of early introduction on LBW/SGA infants on serum ferritin (SMD: 0.72; 95%CI: 0.10 to 1.33; n= 45; 1 study) and a non-significant effect on haemoglobin levels,

ferritin deficiency, serum vitamin A, percentage transferrin saturation, serum folate, serum vitamin B12, and serum zinc. Findings from an RCT suggest that there is a non-significant effect on serum ferritin, BMC on preterms. None of the included studies under this comparison reported waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 9: Early introduction of CF (at four months of age) compared to six months of age among Preterm/ LBW/ SGA infants (RCTs)

Comparison: Early initiation at 4mo vs 6 months among Preterm/LBW/SGA Infants (RCTs)	
Outcome	**Overall Comparison: At 4 months Vs. 6 months**
LBW/ SGA term infants	
Height/Length	MD -0.23 [-0.57, 0.12](n=147; 2 studies)
Weight	MD -7.91 [-121.91, 106.09] (n=147; 2 studies)
Severe anemia (% Hb <100g/L)	RR 0.32 [0.11, 0.94] (n=116; 1 study)
Hemoglobin level	MD 3.08 [1.68, 4.48] (n=116; 1 study)
Serum Ferritin (ug/L)	SMD 0.72 [0.10, 1.33] (n=45; 1 study)
Ferritin (% <12 ug/L)	RR 0.61 [0.13, 2.83] (n=48; 1 study)
Ferritin (% <20 ug/L)	RR 0.35 [0.12, 1.07] (n=48; 1 study)
Percentage Transferrin Saturation	MD -2.39 [-7.03, 2.25] (n=44; 1 study)
Percentage Transferrin Saturation (<12%)	RR 3.82 [0.16, 89.24] (n=48; 1 study)
Plasma Vitamin A	MD 0.02 [-0.13, 0.17] (n=47; 1 study)
Plasma Vitamin A (% <0.7 umol/L)	RR 3.22 [0.31, 33.03] (n=47; 1 study)
Plasma folate nmol/L	MD -1.00 [-9.77, 7.77] (n=47; 1 study)
Plasma Vit B12 pmol/L	MD -19.00 [-71.95, 33.95] (n=47; 1 study)
Plasma Vitamin B12 (%<96 pmol/L)	RR 0.40 [0.05, 3.33] (n=47; 1 study)
Plasma Vitamin B12 (%<136 pmol/L)	RR 0.69 [0.20, 2.33] (n=47; 1 study)
Plasma zinc umol/L	MD -0.20 [-1.31, 0.91] (n=45; 1 study)
Plasma zinc (% <9.2 umol/L)	RR 3.00 [0.29, 30.69] (n=45; 1 study)
Preterm Infants	
Weight for Age z-score	MD 0.0 [-0.25, 0.25] (n=373; 1 study)
Serum Ferritin (ug/L)	SMD -0.01 [-0.23, 0.20] (n=333; 1 study)
Ferritin (% <12 ug/L)	RR 1.02 [0.90, 1.16] (n=333; 1 study)
Acceptable minimum dietary diversity	RR 1.09 [0.92, 1.30] (n=372; 1 study)
Minimum acceptable diet	RR 1.08 [0.90, 1.29] (n=373; 1 study)
Systolic BP (mm of Hg)	MD 0.00 [-2.12, 2.12] (n=141; 1 study)
Diastolic BP (mm of Hg)	MD -0.30 [-2.13, 1.53] (n=143; 1 study)
BMC (g)	MD -5.80 [-13.99, 2.39] (n=270; 1 study)
Infant Mortality	RR 1.94 [0.36, 10.48] (n=400; 1 study)
Diarrhea	RR 1.88 [0.71, 4.99] (n=373; 1 study)
LRTI	RR 1.49 [0.71, 3.13] (n=373; 1 study)
Sepsis	RR 3.08 [0.32, 29.36] (n=373; 1 study)
RR: Risk ratio; MD: Mean difference; BMC: Bone mineral content; LRTI: Lower respiratory tract infection; BP: Blood pressure	

- Early introduction of CF at three months compared to at four months

A total of one RCT (75) with 68 preterm/LBW/SGA participants were included in the analysis under this comparison. **Table 10** summarises the outcomes reported under this comparison.

Primary outcomes:

Findings from the RCT suggests that among preterm/LBW/SGA infants, early introduction of CF at three months compared to introduction of CF at four months might not have any effect on length (MD: 0.20; 95% CI: -0.04 to 0.44; n=64; 1 study), weight (MD: 1.40; 95% CI: -8.21 to 11.01; n=64; 1 study), and head circumference (MD: 0.00; 95% CI: -0.13 to 0.13; n=64; 1 study).

None of the included studies under this comparison reported stunting, underweight, wasting, HAZ, WHZ, WAZ, BMI, BMI z-score, overweight, obesity, anemia, morbidity, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Secondary Outcomes:

Findings from RCT suggests a non-significant effect of early introduction of CF at three months compared to at four months on haemoglobin, serum ferritin, and serum iron among preterm/SGA infants.

None of the included studies under this comparison reported BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 10: Early introduction of CF at three months compared to at four months among Preterm/SGA/LBW infants (RCTs)

Comparison: Early initiation at 3 months vs. at 4 months among Preterm/SGA/LBW Infants (RCTs)	
	Overall **Comparison: At 3 months Vs. At 4 months**
Height/Length	MD 0.20 [-0.04, 0.44] (n=64; 1 study)
Weight	MD 1.40 [-8.21, 11.01] (n=64; 1 study)
Head circumference	MD 0.00 [-0.13, 0.13] (n=64; 1 study)
Hemoglobin (g/l)	MD 6.00 [-19.56, 31.56] (n=61; 1 study)
Serum Ferritin (ng/ml)	MD 1.50 [-6.34, 9.34] (n=61; 1 study)
Serum Iron (ng/ml)	**MD 2.80 [0.31, 5.29]** **(n=61; 1 study)**
RR: Risk ratio; MD: Mean difference	

Early introduction of CF-Evidence from Observational Studies

- Early introduction of CF (< six months of age) compared to ≥ six months of age

A total of one study with 2,280 participants among preterms were included in the analysis under this comparison. **Table 12** summarises the findings of the outcomes reported under this comparison. One study

reported on early introduction of CF at less than or equal to six months of age among preterms, which was not meta-analysed (76).

Primary outcomes:

Findings from observational study suggest that among preterm infants suggest that early introduction of CF at less than six months of age compared to greater than or equal to six months of age might not have any effect on underweight (OR: 0.94; 95% CI: 0.76 to 1.16; n= 2280; 1 study).

The included study under this comparison did not report on weight, height/length, head circumference, stunting, wasting, WHZ, HAZ, WAZ, BMI, BMI Z-score, anemia, overweight, obesity, morbidity, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Secondary Outcomes:

The included study did not report on haemoglobin, micronutrient status, BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 12: Early introduction of CF (< six months of age) compared to ≥ six months of age among Preterm infants (Observational studies)

Comparison: Early initiation (<6mo) vs at or after 6 months among Preterm infants (Observational studies)	
	Overall **Comparison: <6mo Vs at and after 6 months**
Underweight	OR 0.94 [0.76, 1.16] (n= 2280; 1 study)
OR: Odds Ratio	

- Early introduction of CF (< four months of age) compared to ≥ four months of age

A total of one study with 691 preterm participants were included in the analysis under this comparison. **Table 14** summarises the findings from the outcomes reported under this comparison.

Primary outcomes:

Findings from an observational study among preterm infants suggest that early introduction of CF at less than four months of age compared to greater than or equal to four months of age might increase WAZ (MD: 0.32; 95% CI: 0.14 to 0.50; n= 691; 1 study).

The included study did not report on stunting, wasting, underweight, HAZ, WHZ, BMI, BMI z-score, anemia, overweight, obesity, morbidity, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Secondary Outcomes:

The included study did not report on haemoglobin, micronutrient status, BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 14: Early introduction of CF (< four months of age) compared to ≥ four months of age among Preterm infants (Observational studies)

Comparison: Early initiation (<4mo) vs at or after 4 months among Preterm Infants (Observational studies)	
	Overall **Comparison: <4mo Vs at and after 4 months**
Weight for Age Z-score	**MD 0.32 [0.14, 0.50]** **(n= 691; 1 study)**
MD: Mean difference	

Late introduction of CF - Evidence from RCTs

None of the included RCTs on preterm/LBW/SGA infants reported outcomes under this comparison

Late introduction of CF - Evidence from Observational Studies

- Late introduction of CF (> six months) compared to ≤ six months of age – Preterm infants

A total of one study with 98 preterm participants was included in the analysis under this comparison. **Table 15** summarises the findings reported for the outcomes under this comparison. One study reported on the late introduction of CF at greater than or equal to six months of age, which was not meta-analysed (77).

Primary outcomes:

The findings of an observational study among preterm infants, suggest uncertain effect of late introduction of CF at greater than six months of age compared to less than or equal to six months of age on WHZ, weight, height, BMI z-score and head circumference.

The included study did not report on underweight, stunting, wasting, HAZ, WAZ, BMI, anemia, overweight, obesity, morbidity, developmental outcomes, food preferences, food allergies, NCDs, and infant/child mortality.

Secondary Outcomes:

The included study did not report on haemoglobin, micronutrient status, BMC, waist circumference, skinfold thickness, gut health/microbiome, and maternal outcomes.

Table 15: Late introduction of CF (> six months) compared to ≤ six months of age among Preterm infants (Observational studies)

Comparison: Late initiation (>6mo) vs at or before 6 months among Preterm Infants (Observational studies)	
	Overall **Comparison: >6mo Vs at and before 6 months**
Weigh for height Z-score	**MD -0.49 [-0.92, -0.06]** **(n= 98; 1 study)**
Height/Length	MD -0.04 [-0.50, 0.42] (n= 98; 1 study)
Weight	MD -0.37 [-0.82, 0.08] (n= 98; 1 study)
BMI Z-score	**MD -0.46 [-0.90, -0.02]** **(n= 98; 1 study)**
Head circumference (Z-score)	MD 0.03 [-0.46, 0.52] (n= 98; 1 study)
MD: Mean difference	

Discussion

Summary of the Evidence

The findings from this review summarise data from 240 documents: including nine RCTs (from 26 papers) and 214 observational studies. Data were available for meta-analysis from 87 studies (RCTs: 7; observational: 80) including a total of 384,716 participants. **Table 16** summarises the evidence GRADE for all the primary outcomes reported under each comparison.

Among normal term infants, the evidence did not show an effect of early introduction on any of the primary and secondary outcomes. While, low certainty evidence from observational studies suggest that early introduction of CF (< 6 months compared to ≥ 6 months) might increase BMI, BMI z-score, and overweight+obesity; while early introduction of CF at < 3 months compared to ≥ 3 months might increase BMI and odds of LRTI, and early introduction of CF at < 4 months compared to ≥ 4 months might increase stunting, height, LRTI, and systolic and diastolic blood pressure. The limited subgroup analysis by country suggested mixed evidence on diarrhea from a very small study and increase in anemia and the limited evidence by subgroup analysis by feeding practices suggested greater effect of formula fed infants for BMI and overweight and obesity.

Among normal term infants, the evidence for RCTs did not show an effect of late introduction on any of the primary and secondary outcomes. Low certainty evidence from observational studies suggests that among normal term infants, late introduction of CF (at > 6 months) may decrease height, BMI, and systolic and diastolic blood pressure, and it might increase odds of intestinal helminth infection.

Among preterm / LBW / SGA infants; the evidence from RCTs suggests no difference of early introduction of CF (at 3 months compared to at 4 months; at 4 months compared to at 6 months) on any primary or secondary outcomes. While, low certainty evidence from observational studies suggests increased WAZ among infants initiated on CF at < four months compared to ≥ four months; while there was no difference in all the other outcomes assessed for early or late introduction on CF. Thus, the evidence is insufficient to make any meaningful conclusions on any other outcomes of this review.

Table 16: GRADE Summary of Evidence for Normal Term and Preterm /SGA/ LBW infants

COMPARISON	GRADE	OUTCOMES	SUMMARY OF FINDING
NORMAL TERM INFANTS			
Early introduction of CF (≤ four months of age) compared to six months of age (RCTs)	**Low**	Height/length	SMD 0.05 [-0.16, 0.27]; (n=429; 4 studies)
		Weight	SMD -0.06 [-0.26, 0.13]; (n=429; 4 studies)
		Head circumference	SMD 0.03 [-0.20, 0.26]; (n=288; 3 studies)
		Overweight	RR 3.70 [0.43, 31.61]; (n=77; 1 study)
		BMI	MD 0.02 [-0.41, 0.45]; (n=100; 1 study)
		BMI for age	MD -0.15 [-0.48, 0.18]; (n=100; 1 study)
	Very Low	Anemia	RR 0.83 [0.63, 1.08]; (n=216; 2 studies)
		Severe anemia	RR 0.77 [0.45, 1.33]; (n=139; 1 study)
		Food acceptance score	MD 0.00 [-0.18, 0.18]; (n=125; 1 study)
Early introduction of CF (< six months of age) compared to ≥ six months of age (Observational Studies)	**Low**	Height for age Z-score	MD 0.03 [-0.13, 0.19]; (n= 1349; 2 studies)
		Weight for age Z-score	MD 0.08 [-0.12, 0.27]; (n= 713; 1 study)
		Weight for height Z-score	MD -0.00 [-0.01, 0.00]; (n= 1995; 1 study)
		BMI	MD 0.13 [0.05, 0.21]; (n= 3532; 3 studies)
		BMI Z-score	MD 0.19 [0.09, 0.29]; (n= 2447; 1 study)
		Overweight	OR 1.17 [0.89, 1.54]; (n= 8423; 4 studies)
		Obesity	OR 1.06 [0.95, 1.19]; (n= 13818; 4 studies)
		Overweight and Obesity	OR 1.34 [1.09, 1.65]; (n= 9078; 4 studies)
		Atopic dermatitis	OR 1.04 [0.71, 1.52]; (n= 1425; 1 study)
		LRTI	OR 1.11 [0.90, 1.38]; (n=110035; 3 studies)
		Food allergy	OR 0.90 [0.60, 1.35]; (n= 2396; 2 studies)
	Very Low	Stunting	OR 1.16 [0.77, 1.75]; (n= 12816; 10 studies)
		Underweight	OR 1.29 [1.08, 1.53] ; (n= 5939; 6 studies)
		Wasting	OR 1.55 [0.91, 2.62]; (n= 1840; 6 studies)
		Thinness	OR 2.70 [0.62, 11.79]; (n= 139; 1 study)
		Weight	SMD 0.13 [-0.02, 0.29]; (n= 2077; 6 studies)
		Height/Length	SMD -0.12 [-0.54, 0.30]; (n= 2559; 6 studies)
		Head circumference	MD 0.20 [-0.34, 0.74]; (n= 41; 1 study)
		Anemia	OR 1.72 [0.90, 3.27]; (n= 18923; 2 studies)
		Iron deficiency anemia	OR 0.34 [0.18, 0.63]; (n= 870; 1 study)
		Asthma	OR 0.99 [0.71, 1.38]; (n=4938; 3 studies)
		Diarrhea	OR 0.64 [0.21, 1.97]; (n= 107407; 2 studies)
		Wheeze	OR 0.93 [0.69, 1.25]; (n= 2320; 1 study)
		Eczema	OR 1.12 [0.89, 1.42]; (n= 2290; 1 study)
		Gastrointestinal illness	OR 1.05 [0.48, 2.28]; (n= 233; 1 study)
		Respiratory illness	OR 1.51 [0.68, 3.35]; (n= 233; 1 study)
		Rickets	OR 3.17 [0.40, 25.03]; (n= 233; 1 study)
Early introduction of CF (< three months of age) compared to ≥ three months of age (Observational Studies)	**Low**	Weight for age Z-score	MD -0.20 [-0.52, 0.12]; (n= 317; 1 study)
		Weight	MD 0.04 [-0.07, 0.14]; (n= 412; 1 study)
		BMI	MD 0.09 [0.05, 0.13]; (n= 412; 1 study)
		LRTI	OR 1.51 [1.12, 2.03]; (n= 106132; 1 study)
		Diarrhea	OR 1.91 [0.95, 1.49]; (n= 212258; 2 studies)
	Very Low	Chest Infection	OR 1.13 [0.32, 3.94]; (n= 97; 1 study)

		Eczema	OR 1.22 [0.57, 2.61]; (n= 178; 1 study)
		Ear Infection	OR 1.18 [0.04, 31.99]; (n= 34; 1 study)
		Systolic BP	MD -0.21 [-10.40, 9.98]; (n= 40; 1 study)
		Diastolic BP	MD 0.86 [-0.53, 2.25]; (n= 40; 1 study)
		Gastrointestinal illness	OR 1.05 [0.48, 2.28]; (n= 233; 1 study)
		Respiratory illness	OR 1.51 [0.68, 3.35]; (n= 233; 1 study)
		Rickets	OR 3.17 [0.40, 25.03]; (n= 233; 1 study)
Early introduction of CF (< four months of age) compared to ≥ four months of age (Observational Studies)	**Low**	Stunting	OR 1.46 [1.01, 2.11]; (n= 807; 1 study)
		Wasting	OR 0.92 [0.54, 1.59]; (n= 796; 1 study)
		Height	SMD 0.18 [0.06, 0.30]; (n= 3764; 4 studies)
		Head circumference <-2 Z-score	OR 0.86 [0.49, 1.49]; (n= 796; 1 study)
		Overweight	OR 0.97 [0.83, 1.13]; (n= 9865; 5 studies)
		Diarrhea	OR 1.36 [0.97, 1.91]; (n= 106677; 2 studies)
		LRTI	OR 1.43 [1.19, 1.73]; (n= 106132; 1 study)
		Systolic BP	MD 1.50 [0.11, 2.89]; (n= 2203; 1 study)
		Diastolic BP	MD 1.30 [0.27, 2.33]; (n= 2203; 1 study)
	Very Low	Underweight	OR 0.98 [0.60, 1.61]; (n= 6643; 3 studies)
		Height for age Z-score	MD 0.15 [-0.03, 0.32]; (n= 892; 2 studies)
		Weight for age Z-score	MD 0.16 [-0.23, 0.55]; (n= 892; 2 studies)
		Weight for height Z-score	MD -7.40 [-12.65, -2.15]; (n= 45; 1 study)
		Weight	SMD 0.04 [-0.26, 0.35]; (n= 1127; 3 studies)
		BMI	MD 2.53 [-0.16, 5.23]; (n= 26221; 5 studies)
		BMI Z-score	MD 0.14 [-0.12, 0.39]; (n= 3294; 2 studies)
		Obesity	OR 0.86 [0.30, 2.45]; (n= 9389; 6 studies)
		Overweight and Obesity	OR 1.22 [0.55, 2.71]; (n= 29178; 5 studies)
		Atopic dermatitis	OR 1.38 [0.53, 3.54]; (n= 22332; 5 studies)
		Asthma	OR 1.22 [0.72, 2.09]; (n= 2595; 2 studies)
		Wheeze	OR 0.77 [0.46, 1.31]; (n= 1894; 1 study)
		Eczema	OR 0.98 [0.69, 1.39]; (n= 16959; 2 studies)
		Food Allergy	OR 1.16 [0.74, 1.82]; (n= 1239; 1 study)
Late introduction of CF (> six months) compared to ≤ six months of age (Observational Studies)	**Low**	Height	MD -0.12 [-0.21, -0.04]; (n= 2357; 2 studies)
		BMI	MD -0.14 [-0.23, -0.05]; (n= 2203; 1 study)
		Overweight	OR 0.94 [0.69, 1.29]; (n= 41152; 3 studies)
		Obesity	OR 0.85 [0.59, 1.21]; (n= 40510; 1 study)
		Atopic dermatitis	OR 0.98 [0.79, 1.20]; (n= 18773; 1 study)
		LRTI	OR 1.09 [0.86, 1.37]; (n= 3903; 2 studies)
		Intestinal helminth infection	OR 173.00 [39.17, 764.05]; (n= 404; 1 study)
		Systolic BP	MD -1.20 [-1.80, -0.60]; (n= 2203; 1 study)
		Diastolic BP	MD -0.72 [-1.22, -0.22]; (n= 2203; 1 study)
	Very Low	Stunting	OR 1.19 [0.71, 2.00]; (n= 11872; 6 studies)
		Underweight	OR 1.35 [0.65, 2.78]; (n= 1107; 4 studies)
		Wasting	OR 0.42 [0.07, 2.56]; (n= 540; 3 studies)
		Weight	MD -0.11 [-0.69, 0.48]; [n= 7588; 2 studies]
		Thinness	OR 0.37 [0.08, 1.62]; (n= 139; 1 study)
		Overweight and Obesity	OR 0.76 [0.10, 5.92]; (n= 5239; 2 studies)
		Anemia	OR 2.49 [0.02, 359.68]; (n= 704; 2 studies)

		Asthma	OR 0.95 [0.61, 1.46]; (n= 2343; 1 study)
		Wheeze	OR 0.93 [0.69, 1.25]; (n= 2320; 1 study)
		Eczema	OR 1.04 [0.79, 1.36]; (n= 2301; 1 study)
		Diarrhea	OR 1.58 [1.10, 2.28]; [n= 597; 1 study]
		Food sensitivity	OR 0.56 [0.10, 3.08]; [n=56; 1 study]
Late introduction of CF (> eight months) compared to ≤ eight months of age (Observational Studies)	**Low**	Wasting	OR 1.56 [0.98, 2.47]; (n= 1177; 2 studies)
		Height for age Z-score	MD 0.50 [0.09, 0.91]; (n= 636; 1 study)
		Head circumference <-2 Z-score	OR 0.95 [0.47, 1.91]; (n= 796; 1 study)
		Diarrhea	OR 1.44 [0.78, 2.67]; (n= 545; 1 study)
	Very Low	Stunting	OR 1.66 [0.88, 3.14]; (n= 1824; 3 studies)
		Underweight	OR 1.95 [0.56, 6.83]; (n= 1187; 2 studies)
		Anemia	OR 0.34 [0.12, 0.93]; (n= 150; 1 study)
		Gastrointestinal illness	OR 0.78 [0.28, 2.12]; (n= 213; 1 study)
Preterm/LBW/SGA Infants			
Early introduction of CF at four months of age compared to six months of age (RCTs)	**Very Low**	Weight for age Z-score	MD 0.0 [-0.25, 0.25]; (n=373; 1 study)
		Height/length	MD -0.23 [-0.57, 0.12]; (n=147; 2 studies)
		Weight	MD -7.91 [-121.91, 106.09]; (n=147; 2 studies)
		Infant mortality	RR 1.94 [0.36, 10.48]; (n=400; 1 study)
		Severe anemia	RR 0.32 [0.11, 0.94]; (n=116; 1 study)
		Acceptable minimum dietary diversity	RR 1.09 [0.92, 1.30]; (n=372; 1 study)
		Minimum acceptable diet	RR 1.08 [0.90, 1.29]; (n=373; 1 study)
		Diarrhea	RR 1.88 [0.71, 4.99]; (n=373; 1 study)
		LRTI	RR 1.49 [0.71, 3.13]; (n=373; 1 study)
		Sepsis	RR 3.08 [0.32, 29.36]; (n=373; 1 study)
		Systolic BP	MD 0.00 [-2.12, 2.12]; (n=141; 1 study)
		Diastolic BP	MD -0.30 [-2.13, 1.53]; (n=143; 1 study)
Early introduction of CF at three months compared to at four months (RCTs)	**Low**	Length/Height	MD 0.20 [-0.04, 0.44]; (n=64; 1 study)
		Weight	MD 1.40 [-8.21, 11.01]; (n=64; 1 study)
		Head circumference	MD 0.00 [-0.13, 0.13]; (n=64; 1 study)
Early introduction of CF (< six months of age) compared to ≥ six months of age (Observational Study)	**Low**	Underweight	OR 0.94 [0.76, 1.16]; (n= 2280; 1 study)
Early introduction of CF (<four months of age) compared to ≥ four months of age (Observational Study)	**Low**	Weight for age Z-score	MD 0.32 [0.14, 0.50]; (n= 691; 1 study)
Late introduction of CF (> six months) compared to ≤ six months of age	**Very Low**	Weigh for height Z-score	MD -0.49 [-0.92, -0.06]; (n= 98; 1 study)
		Weight	MD -0.37 [-0.82, 0.08]; (n= 98; 1 study)
		Height	MD -0.04 [-0.50, 0.42]; (n= 98; 1 study)
		BMI Z-score	MD -0.46 [-0.90, -0.02]; (n= 98; 1 study)
		Head circumference (Z-score)	MD 0.03 [-0.46, 0.52]; (n= 98; 1 study)
RR: Risk ratio; MD: Mean difference; BMI: Body mass index; BMC: Bone mineral content; LRTI: Lower respiratory tract infection; BP: Blood pressure			

Diarrhea being an important aspect of complementary feeding was not extensively studied in the included papers. Of the few included studies on diarrhea, we were unable to conduct meta-analysis of seven studies which reported on diarrhea. Among these seven studies one study (78) indicated increased risk of diarrheal incidence among younger infants who were introduced CF before 6mo. Another study reported significantly lower rate of diarrhea among infants who started CF after 6mo than in infants who initiated CF between 4-6 mo (11% versus 27%) (79). Dhami et al. 2020 (80), showed that infants who were introduced to solid, semi-solid or soft foods between 6-8 months were more likely to experience diarrhea compared to those whose mothers delayed or introduced complementary foods earlier than 6-8 months in the Central India region. Popkin et al. 1990 (81) reported an increase in diarrhea morbidity when nutritive foods were added to breastfeed children at 2 and 4 months compared to children who were introduced food at or after six months. Eaton-Evans et al. 1987 (82) reported that infants who were introduced solids before 3 months had less chances of having diarrhea or vomiting (5%) than those children who were introduced solids after 3 months. (16%). Kalanda et al. 2006 (83) reported an insignificant decrease in diarrheal incidence among infants who were introduced complementary foods before 3mo, however a significant decrease in diarrheal incidence was observed in infants who were provided CF after 3 months of age. Mondal et al. 1996 (84) also reported that children weaned at 3 months or earlier had 3.02 times (95% CI 1.043-8.802) more risk of diarrhea compared to children who were introduced CF at 4 months or later (**Table 17**).

Table 17: Studies on Diarrhea

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
Kalanda 2006 (83)	Diarrhoea	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				0.87 (0.73, 1.01)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.73 (0.62, 0.84)	262
Khadivzadeh 2004 (79)	Diarrhea		EBF (6mo)			11/98			
			CF (4-6mo)			27/95			
Dhami 2020 (80)	Diarrhea		CF < 6mo		National Estimate			1 (reference)	
			6-8mo		National Estimate			1.06 (0.92, 1.21)	
Mondal 1996 (84)	Diarrheal Episodes		</= 3mo	1 year	No episode	98/127			
			</= 3mo		1 episode	12/127			
			</= 3mo		2 episodes	13/127			
			</= 3mo		3+ episodes	4/127			
			>/= 4mo		No episode	18/21			

			>/= 4mo		1 episode	3/21			
			>/= 4mo		2 episodes	0/21			
			>/= 4mo		3+ episodes	0/21			
		Incidence rate ratio						3.02 (95% CI 1.043-8.802)	
Eaton-Evans 1987 (82)	Diarrhea/Vomiting		0-3 mo (no description given on timing)	0-3 mo		Breast milk: 0/23 Mixed: 0/14 Bottle: 3/20 Subtotal: 3/57			
			3-6 mo	3-6 mo		Breast milk: 5/44 Mixed: 1/32 Bottle: 12/34 Subtotal: 18/110			
			6-9 mo	6-9 mo		Breast milk: 2/10 Mixed: 6/43 Bottle: 8/55 Subtotal: 16/108			
			9-12 mo	9-12 mo		Mixed: 8/24 Bottle: 19/71 Subtotal: 27/95			
Brown 1989 (78)	Diarrhea	Incidence of Diarrhea	0-2 mo			3.04 (1777 observations)		RR 1.61	
			3-5 mo			2.63 (9280 observations)		RR 1.79	
			6-8 mo			2.59 (10154 observations)		RR 1.00	
			9-11 mo			2.88 (9450 observations)		RR 1.00	
		Prevalence of Diarrhea	0-2 mo			19.5 (347 days)		RR 2.57	
			3-5 mo			17.1 (1585 days)		RR 3.35	
			6-8mo			14.4 (1467 days)		RR 1.00	
			9-11 mo			14.9 (1411 days)		RR 1.00	
Popkin 1990 (81)	Diarrhea	Diarrheal Morbidity	Breast Milk + Nutritive Foods/Solids at 6 mo	At 6 mo	Urban			RR 10.61 (4.63, 16.60)	
			Breast Milk + Non-nutritive Liquid	At 6 mo	Urban			RR 3.18 (2.53 3.84)	
			Breast Milk + Nutritive Foods/Solids at 6 mo	At 6 mo	Rural			RR 4.73 (3.95, 5.52)	
			Breast Milk + Non-nutritive Liquid	At 6 mo	Rural			RR 2.21 (2.07 2.35)	

Completeness and Applicability of the Evidence

Findings from this review are based majorly on data from observational studies since only nine RCTs were included in this review. All the included RCTs assessed the effect of early introduction of CF, while the findings

for the effect of late introduction of CF are based on observational studies only. The majority of the included RCTs were of reasonable quality; however, some studies were judged to be at high risk of bias or provided insufficient information on allocation concealment, blinding, and selective reporting. Among the non-RCTs, the majority of the studies were judged to be at either moderate, serious, or critical risk of bias for confounding, missing data, and selection of reported results. Among observational studies, the majority of the studies were not statistically powered to capture the association between the timing of introduction of CF and outcomes reported and were not adequately adjusted for the confounding variables. The included observational studies were also prone to misclassification bias due to ascertainment of exposure (timing of introduction of CF) based on recalls. Thus, the availability of the existing evidence is restricted to permit any strong causal association between the timing of the introduction of CF and any of the health, nutrition, and developmental outcomes assessed. However, the strength of observational studies is that they represent real world feeding practices.

Within each comparison, included studies varied widely for the cut-offs used to differentiate between the early and late introduction of CF, making it difficult to combine participants under each comparison. Therefore, studies were further categorised within each comparison into sub-comparisons to achieve sufficient consistency in the exposures and participants for meaningful pooling of the outcomes. This led to fewer studies and participants pooled under each outcome. Furthermore, there were inconsistencies in the definitions of the reported outcomes in the included studies, especially for reporting morbidity, NCDs, food allergies, and developmental outcomes. Hence, these outcomes could not be pooled due to a variety of measures used to report these outcomes in the included studies. There was very limited data reported on infant and child mortality for any meaningful conclusions.

Fifty-nine studies assessed the early introduction of CF, 13 studies assessed the late introduction of CF, while 15 studies assessed early and late introduction of CF. Although there were fewer studies in the later comparison, the direction of effect for a few outcomes is consistent with the former comparison. For example, low certainty evidence suggested increased height, BMI, BMI z-score, overweight and obesity, LRTI, systolic and diastolic blood pressure might be associated with early introduction of CF; while there is low certainty evidence suggesting that late introduction of CF might be associated with decreased BMI, height,

systolic and diastolic blood pressure. Studies included in this review were conducted in high-, middle-, and low-income countries. However, only three RCTs out of nine included RCTs which were conducted in LMICs, showing lack of evidence from these settings. Findings based on very limited evidence from subgroup analysis by country suggested differences in the effects of early introduction of CF among term infants in HIC and LMIC settings on outcomes like WAZ, WHZ, BMI, wasting, overweight, and Hb; and subgroup analysis by feeding practices suggested differences in the effects of early introduction of CF among breast fed and formula fed term infants for some outcomes like WAZ, weight, BMI, BMI z-score, obesity, overweight and obesity, and serum ferritin. These findings warrant future studies from different settings and population groups, along with feeding practices in order to explore any actual differences in the effect. We planned to conduct sensitivity analyses based on the risk of bias, major confounding variables including breast-feeding status, age at outcome assessment, and study settings. However, we could not draw any meaningful conclusions due to the limited number of studies under each comparison.

Agreement and Disagreement

The review by English et al. (85) summarising findings from 81 articles and concluded that early introduction of CF among term infants is probably not associated with weight status, body composition, body circumferences, weight, or length among term infants. The review by English et al. (85) also pointed out there is limited evidence suggesting that early introduction of CF before 4 months of age might be associated with higher odds of overweight and obesity. Data from our review also highlights that early introduction of CF might increase BMI, BMI z-score, overweight+obesity, systolic and diastolic blood pressure. This finding is reciprocated by the low certainty evidence of decreased height, BMI, and systolic and diastolic blood pressure associated with the late introduction of complementary feeding (> six months and > eight months) from our review. However, this should be highlighted that the evidence certainty for these associations remains low and these findings are mainly based on data from observational studies. Moreover, the review by English et al. (85) also concluded on the need for additional research to address gaps in the existing evidence on the timing of introduction of CF and growth, size, and body composition; simultaneously highlighting lack of RCTs that examine multiple outcomes accounting for potential confounders such as feeding practices and baseline growth status and considers issues of reverse causality.

Another recent review evaluating the appropriate age range for the introduction of CF into an infant's diet (44) suggested no convincing data suggesting any adverse health effects or benefits associated with the introduction of CF at any age investigated in the included studies (< 1 to < 6 months) and this further suggested that infants at risk of iron depletion including infant subgroups that are exclusively breastfed or born to mothers with low iron status, or with early umbilical cord clamping (< 1 min after birth), or born preterm, or born SGA or with high growth velocity might benefit from the earlier introduction of CFs (< 6 months of age) that are a source of iron. However, in our review we found uncertain evidence on the effect of timing of introduction of CF on anaemia or iron deficiency and also increased odds of anemia in LMICs for early introduction.

Implications and Conclusion

Findings from this review highlight lack of rigorous evidence on the appropriate timing of CF and its impact on health, nutrition, and developmental outcomes. Existing evidence, from both RCTs and observational studies, suggest no difference in effect of early introduction of CF on some anthropometric measures and morbidity but highlight concerns around increased BMI, obesity and BP measures. Future robust studies with long term follow-ups are required; especially from LMICs, since infants in disadvantaged settings are more vulnerable to the adverse effects, including mortality. Any future studies assessing the relationship between the timing of introducing CF and infant health outcomes should be designed with the following considerations:

- Future studies should focus not only on term infants but also on other subgroup of infants including preterm, LBW, SGA infants, who might be more vulnerable to the effects of the timing of introduction of CF.
- Studies need to ethically optimize both breastfeeding and CF practices, which might not reflect the real-life situation when exclusive breastfeeding is stopped at less than six months under trial conditions. On the contrary, observational studies represent real world practices but however would require more robust analysis adjusting for the various confounding variables.
- There is a need to account for the factors that might impact the association between timing of CF and health outcomes including breastfeeding practices, types of CF used, and baseline growth status.

- The outcomes measures in future studies need to be standardised especially for outcomes like adverse events, food allergies, and developmental outcomes so that the data can be synthesised for practical and policy implications.
- Future studies should focus on long-term follow-ups to assess any impact on future development of NCDs and mortality.

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Appendices

Table 1: Search Strategy

Medline

MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to March 15, 2021

Search Strategy:

#	Searches	Results
1	bottle feeding/ or exp breast feeding/	40116
2	infant food/ or infant formula/	14375
3	(breastfeed* or breast feed* or breastfed or breast fed or bottle feed* or bottle fed or breast milk or infant food or infant formula or baby formula).tw,kf.	58946
4	(wean* adj5 (milk or formula or infant? or baby or babies)).tw,kf.	2190
5	or/1-4	78834
6	Infant Nutritional Physiological Phenomena/	15360
7	(complementary feeding? or complementary food? or infant nutrition* physiology or infant nutritional physiological phenomen* or supplementary feeding? or supplementary food?).tw,kf.	3966
8	(introduc* adj5 (solid? or semisolid? or food? or fruit? or vegetable? or seed? or nut? or dairy or cheese? or meat? or egg? or grain? or legume? or bean? or peas or bread? or honey or juice?)).tw,kf.	6868
9	or/6-8	23687
10	5 and 9	9732
11	child nutrition disorders/ or exp infant nutrition disorders/	8573
12	body mass index/	131513
13	Pediatric Obesity/	9585
14	adolescent health/ or child health/	4293
15	(malnutrition or malnourish* or nutrition disorder? or overnutrition or over-nutrition or overnourish* or over-nourish* or undernutrition or under-nutrition or undernourish* or under-nourish*).tw,kf.	59861
16	(malnutrition or malnourish* or nutrition disorder? or overnutrition or over-nutrition or overnourish* or over-nourish* or undernutrition or under-nutrition or undernourish* or under-nourish* or obesity or obese or body mass index or BMI).tw,kf.	541101
17	(health* adj3 (infant* or child* or adolescen* or adult*)).tw,kf.	197783
18	(longterm outcome? or health outcome? or health status).tw,kf.	116889

19	or/11-18	847034
20	5 and 9 and 19	2728

Embase Classic+Embase 1947 to 2021 Week 10
Search Strategy:

#	Searches	Results
1	infant feeding/ or bottle feeding/ or exp breast feeding/	65221
2	artificial milk/	14881
3	(breastfeed* or breast feed* or breastfed or breast fed or bottle feed* or bottle fed or breast milk or infant food or infant formula or baby formula).tw,kw.	74704
4	(wean* adj5 (milk or formula or infant? or baby or babies)).tw,kw.	2786
5	or/1-4	102232
6	complementary feeding/	1183
7	(complementary feeding? or complementary food? or infant nutrition* physiology or infant nutritional physiological phenomen* or supplementary feeding? or supplementary food?).tw,kw.	5127
8	(introduc* adj5 (solid? or semisolid? or food? or fruit? or vegetable? or seed? or nut? or dairy or cheese? or meat? or egg? or grain? or legume? or bean? or peas or bread? or honey or juice?)).tw,kw.	10475
9	or/6-8	14608
10	nutritional disorder/ or malnutrition/ or overnutrition/	88853
11	body mass/	476305
12	childhood obesity/	16128
13	adolescent obesity/	2857
14	adolescent health/	9053
15	child health/	29538
16	(malnutrition or malnourish* or nutrition disorder? or overnutrition or over-nutrition or overnourish* or over-nourish* or undernutrition or under-nutrition or undernourish* or under-nourish* or obesity or obese or body mass index or BMI).tw,kw.	875917
17	(health* adj3 (infant* or child* or adolescen* or adult*)).tw,kw.	262610
18	(longterm outcome? or health outcome? or health status).tw,kw.	155325
19	or/10-18	1387895
20	5 and 9 and 19	1836

CINAHL

(MM "Infant+") OR "infant" OR (MM "Infant, Newborn+") OR (MM "Child+") OR "neonate" OR (MM "Child, Preschool")

AND

(MM "Infant Feeding, Supplemental") OR (MM "Infant Feeding+") OR (MM "Infant Feeding Schedules") OR "complementary feeding" OR (MM "Infant Nutritional Physiology+") OR (MM "Weaning") OR (MM "Breast Feeding+") OR "breastfeeding" OR "exclusive breastfeeding" OR "Infant, Young and Child Feeding"

AND

"timing" OR (MM "Time+") OR "time" OR "initiation" OR "introduction" OR "introduce" OR ''initiate''

Results: 2928 (humans filter)

LILAC
Search Hits: 319
Date: 19_02_2020 (Exported)

CENTRAL

Search Name: CENTRAL
Date Run: 18/02/2021 14:41:09

ID Search Hits
#1 MeSH descriptor: [Infant] explode all trees 32243
#2 MeSH descriptor: [Infant, Newborn] explode all trees 16060
#3 MeSH descriptor: [Child, Preschool] explode all trees 29651
#4 infant* 64436
#5 MeSH descriptor: [Child] explode all trees 56346
#6 child* 181148
#7 toddler* 2119
#8 baby or babies 9721
#9 neonate* 9390
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 207850
#11 MeSH descriptor: [Weaning] explode all trees 138
#12 MeSH descriptor: [Infant Nutritional Physiological Phenomena] explode all trees 2829
#13 'complementary feeding' 826
#14 #11 or #12 or #13 3450
#15 timing 15103
#16 time 407730
#17 introduction 70077
#18 initiation 25762
#19 #15 or #16 or #17 or #18 471854
#20 #10 and #14 and #19 1314

WHO Index Databases

(tw:(Infant OR Newborn OR Child OR neonate OR Preschool OR neonate)) AND (tw:(complementary feeding OR infant feeding OR complementary feed OR weaning)) AND (tw:(timing OR time OR initiation OR introduction OR introduce OR initiate OR early OR late))

Data 25_02_2021
Results:

African Index Medicus Database 5

Index Medicus for the Eastern Mediterranean Region (IMEMR): 41

WPRIM (for Western Pacific): 85

Table 2: Characteristics of the Included RCTs

Study Name	Study Design	Country	Study Participant	Intervention group	Comparison Group	Feeding Practices	Outcomes reported
1. Bainbridge 1996 (1)	RCT	Ohio, USA	Healthy, full-term infants (n=41)	Cereal group	Formula group	Formula fed	Weight; length; MUAC; triceps, suprail, and subscap skinfold thickness; occipital frontal, Chest, abdominal, and mid-thigh, circumference; ionized calcium, total calcium, phosphorus, vit D, parathyroid hormone, osteocalein, magnesium, and alkaline phosphate levels, Bone mineral radius, sleep, milk, and cereal volume
2. Dewey 1998 (2-8)	RCT	Honduras	141 women completed the intervention, healthy full-term infants	SF group and SF-M group	FBF group	Breast fed	Amenorrhea, duration of lactational amenorrhea, energy intake, weight gain, length gain, weight for age Z score, length for age z-score, weight for length z score, morbidity, food acceptance, food groups consumed
3. Dewey 2004 (5, 9-12)	RCT	Honduras	128 mothers and LBW infants, healthy, full-term infants	SF group	EBF group	Breast fed	Hemoglobin levels, ferritin, % transferrin saturation, plasma vitamin A, folate, plasma vitamin B-12 and plasma zinc levels, weight gain, length gain, morbidity
4. Gupta 2017 (13)	RCT	India	Infants less than 34 weeks of gestation and included SGA babies (n=403)	CF at 4 months	CF at 6 months	Unclear	Weight for age z-score, diagnosis/ morbidity, neurodevelopmental outcomes, fat and lean mass, BMC, fat percentage, cholesterol levels, ferritin, blood pressure, meal frequency, number of food groups offered, HOMA-IR, minimum acceptable diet, consumption of iron rich food
5. Jonsdottir 2014 (14-18)	RCT	Iceland	100 mother-infant pair, singleton, full-term healthy infants	CF group	EBF group	Breast fed	Developmental outcomes; weight, length, head circumference gain and z-score; hemoglobin levels; MCV; ferritin; total iron-binding capacity; red blood cell distribution width, BMI for age, overweight, obesity, lean and fat mass, breast milk intake
6. Kattelmann 2001 (19, 20)	RCT	Ohio, USA	Healthy, full-term, normal birth weight infants. (n=133)	Commercial Early Group (at 3-4 mo) Choice Early Group	- Commercial Late Group (at 6mo) - Choice Late Group	Formula fed	Dietary iron, zinc intake; weight; length; Occipito-frontal circumference; fat and lean mass; BMC, protein, fat, and carbohydrate levels; energy intake, calorie consumption
7. Marriott 2003 (21)	RCT	United Kingdom (England)	Preterm infants (n=68)	CF after 3 months	CF after 4 months	Unclear	Growth velocities, length, weight, energy intake, hemoglobin levels, serum ferritin ,iron levels, head circumference, daily vitamin C intake
8. Perkin 2018 (22, 23)	RCT	United Kingdom (England)	Full-term infants. (n=1303)	The early introduction group (EIG); CF at 3 months	The standard introduction group (SIG); CF at 6 months	Breast fed	Sleep, Allergy

9. Skjerven 2020 (24-26)	RCT	Norway and Sweden	Healthy Infants: 2397	Skin group Food group (CF at 3-4 months) Skin and food group	No intervention	Breast fed and Formula fed	Atopic dermatitis, number of hospitalization events

Table 3: Characteristics of the Included Observational Studies

Study Name	Study Design	Country	Study Participant	CF feeding comparison	Feeding Practices	Outcomes reported
1.Sloan 2007 (27)	Ambi-directional cohort study	Northern Ireland	Full term Infants (n=92), aged between 10-14 months	Before 4 months and after 4 months	Breast fed (68% mother initiated it) and some were given prelacteal feed	8 week, Weight Z-score (weight gain)
2.Sreedhara 2014 (28)	Retrospective cohort study	India	Full term Infants (n=100), aged between 9 months to 1 year	Less than 6 months, 7-9 months, more than 10 months	Breast fed (100% by one year) and 2% bottle fed	Weight, height, stunting, wasting
3.Sun 2016 (29)	Retrospective cohort study	Australia	Healthy, full term Infants (n=3153), aged between 9-15 months	Less than 4 months, at 4, 5, 6 months and more than 7 months	Breast fed and Formula fed	Weight, height, BMI z score, wasting
4.Shim 2011(30)	Retrospective cohort study	United States	Preschool children (n=129), aged between 2-3 years, mean age 2.97+/- 0.5 years	Before 4 months and before 6 months	Breast fed	Preference for specific food preparation, food phobia, food rejection
5.Zhao 2016 (31)	Retrospective cohort study	Myanmar	Healthy Children, (n= 642), aged between 6-36 months, mean age 20.6+/- 9.7 months	Less than 4 months, 4-8 months, more than 8 months	Breast fed	Weight, height, underweight, stunting, mean upper arm circumference, head circumference, hemoglobin level, morbidity (diarrhea, fever)
6.Miliku 2015 (32)	Prospective cohort	Netherlands	Singleton live births, (n= 6616)	Less than 4 months, 4-4.9 months, more than equal to 5 months	Some were breast fed	Kidney function, (eGFR, creatinine, kidney volume, microalbuminuria)
7.WHO working group 2002 (33)	Prospective cohort	China; India, Africa, Chile; Sweden; and Australia	Healthy Neonates (n=1252), average age 5 days	1-8, 9-16, 25-32 weeks	Breast fed	Attained height, height velocity, attained weight, weight velocity
8.Hua 2017 (34)	Prospective cohort study	Taiwan	Full term infants, (n=206)	Less than equal to 4 months, 5-6 months, more than equal to 7 months	Breast fed	Fecal eosinophilic cationic protein, Serum IgE levels.
9.Hollis 2016 (35)	Prospective cohort study	United Kingdom	Full term infants, (n=2389)	<4 months, ≥4 and <6 months, ≥6 months	Breast fed for ⩾4 months: (No: 32%; Yes:42%)	Height, Weight, BMI (overweight and obesity), food preference
10. Heinig 1993 (36)	Prospective cohort study	United States	Full term infants, (n=105)	Less than 26 weeks, more than 26 weeks	Breastfed and Formula fed infants	length gain, weight gain, developmental milestones.

11. Vijayalakshmi 2015 (37)	Retrospective cohort study	N/A	Full term infants, (n=500), 6-24 months of age	Less than 4, 4-5, 6-7,8-9, 10-12, 13-24 months	N/A	Weight, length, stunting, wasting, underweight and Knowledge and attitude regarding complementary feeding
12. Huh 2011 (38)	Prospective cohort	United States	847 healthy children	Less than 4, 4-5 and more than equal to 6 months.	Breastfed and Formula fed infants	Height, height z score, weight, weight z score, BMI, BMI z score, skinfold thickness
13. Ahmad 2018 (39)	Retrospective cohort study	Indonesia	Healthy children, aged between 6-23 months, (population included 13.5% LBW children) (n=392)	Before 6 months, start at 6 months	Breast fed	Weight for age (underweight) weight for height (wasting/ obesity) weight for length (stunting)
14. Eaton-Evans 1987 (40)	Prospective cohort	Australia	123 full term infants	Solid food given or not given	Three groups: breast fed only, bottle fed only and mixed feeding	Diarrhea, Vomiting
15. Barrera 2016 (41)	Retrospective cohort study	NA	1181 infants, healthy, term infants.	<4, 4–<6, and ≥6 months	N/A	Height, weight, and percent obese.
16. Bielemann 2018 (42)	Retrospective cohort study	Brazil	3427, live newborn infants	<3 mo 3–3.9 mo 4–5.9 mo, ≥6 mo	Breastfed	Consumption of ultra-processed foods.
17. Bell 2018 (43)	Prospective cohort	Australia	Children (n=953) with mean age of 29.8 (+/- 3.5 SD) months	Less than 17wks, 17-25 wks, more than equal to 26 wks	Breastfed	Weight, height, BMI z score
18. Carneiro 2015 (44)	Retrospective cohort	Brazil	51 infants, aged between 4-8 months.	At 4, 5 and 6 months	Breast fed (64.7%) and formula fed (31.2%)	Weight for age growth curve, Height for age growth curve.
19. Abraham 2012 (45)	Ambi-directional cohort study (Secondary analysis)	United Kingdom	Children (n=4493), aged between 9-12 months	0-3 months, 4-5 months, 6-10 months	Breast-feeding (n=3825) Ever breast-fed (n=2293) Never breast-fed (n=1532)	BMI z score (overweight, obesity) and dietary patterns
20. Asfaw 2015 (46)	Retrospective cohort study	South Ethiopia	Children, (n=779), aged between 6-59 months	</= 6 months or after 6 month	Exclusive breast fed plus with infants given prelacteal feed	Weight, height, MUAC, wasting
21. Baker 2004 (47)	Retrospective cohort study	Denmark	Healthy, full term infants (n=5530)	< 16wks, >/=16wks	Breast fed and formula fed (Never fed formula: n=1111; Ever fed formula: n=2657)	Weight at 1 year and length at 1 year
22. Caleyachetty 2013 (48)	Retrospective cohort study	India	Infants (n=585)	</=3, 4, 5, >/=6 months	Breast fed	Height, weight, BMI, skin fold thickness
23. Davies-Adetugbo 1997 (49)	Prospective cohort study	Nigeria	Healthy term infants (n=82)	Before 8 weeks, after 8 weeks	Breast fed	weight (underweight and severe underweight)

24. Grote 2011 (50)	Prospective cohort study	Belgium, Germany, Italy, Poland, and Spain	Healthy, singleton, term infants (n=687)	</= 13 week 14–17 week 18–21 week >/= 22 week	Formula fed	Weight, length, BMI, weight for length
25. Joseph 2011 (51)	Prospective cohort study	United States	594 infants, recruited at birth.	< 4 months, >/= 4 moths	Breast fed	Food sensitization measured via serum IgE
26. Johnson 2014 (52)	Retrospective cohort study	England and Wales	Healthy, term infants (n=4680)	Birth to 4 mo, 5, and 6+ months	Breast fed	Weight gain
27. Debarse 2017 (53)	Prospective cohort study (Gen R embedded study)	Netherlands	Full term infants, (n=4779)	< 4 months 4 – 4.9 months 5 – 5.9 months) *≥ 6 months*	Breast fed (90.7%)	Food fussiness.
28. Durmus 2012 (54)	Prospective cohort study (Gen R embedded study)	Netherlands	Children (n=779)	<4 mo, 4-5 mo, > 5 months	Breast fed (87.9% have ever breastfed)	Peripheral fat, central fat, total fat, via measurement of skinfold thickness
29. Kalanda 2006 (55)	Prospective cohort study	Malawi	Infants (n=494)	Before 3 months, after 3 months	Breast fed	Height, weight, morbidity (infection, malaria, diarrhea), MUAC
30. Leary 2015 (56)	Prospective cohort study	United Kingdom	Singleton, live born child, (n= 13 678)	At 3 months, or >/= 4 mo	Breast fed (Exclusive: 36.4%; Partial: 49.5% None: 14.1%)	Height, weight, BMI, fat mass, and lean mass
31. Rossiter 2013 (57)	Prospective cohort study	Canada	N= 483, healthy children	Before 4 months, after 4 months	Breast fed and Formula fed	Weight, height, BMI
32. Koplin 2010 (58)	Prospective cohort study	Australia	11-15 months old infants (n=2589)	<4, 4, 5, 6, or >6 months	Breast fed	Egg allergy
33. Makela 2014 (59)	Prospective cohort study	Finland	Healthy infants (n= 848)	<4, 4-6, >6 months	Breast fed	Weight, length, BMI, weight gain, BMI z score, weight z score
34. Lee 2020 (60)	Retrospective cohort study	Korea	1525 healthy children, aged between 1-3 years	<4, 4-5, >/=6 months	Breast fed and Formula fed	Atopic Dermatitis, Asthma
35. Luccioli 2014 (61)	Retrospective cohort study	United States	1363 healthy children	1-3, 4-5, 6-12 months	Exclusively Breastfed	Food allergies
36. Lin 2013 (62)	Prospective cohort study	China	7809 full term births	<3 Months 3–4 Months 5–6 Months 7–8 Months, > 8 Months	Breast fed (n= Never breastfed: 1773 Partially breastfed: 1336 Exclusively breastfed for >/=3 months 228)	Height, weight, BMI z score
37. Mannan 2018 (63)	Prospective cohort study	Australia	Healthy, singleton full term births (n=346)	</= 4 months vs >4 months	Breast fed	Height, weight, BMI (overweight and obesity)
38. Murcia 2019 (64)	Prospective cohort study	France	1028 children	<4, 4- <6, >/= 6 months	Breast fed and Formula fed	Sleep quality and quantity (sleep onset difficulty, night-time waking, sleep trajectory)

39. Messayke 2021 (65)	Prospective cohort study	France	Singleton or twin full-term births, (n=8696 infants)	<4, 4- 6, > 6 months	N/A	Sleep quality and quantity (sleep duration, night-time waking)
40. Metwally 2016 (66)	Retrospective cohort study	Egypt	655 healthy infants, aged between 6-24	Before 6 months, after 6 months	322 Breast fed, 240 bottle fed and 93 mixed fed infants	Hemoglobin levels, haematological parameters, micronutrient status, (Fe, Zn and Cu, Vit b12)
41. Nagahori 2016 (67)	Retrospective cohort study	Cameroon	212 Healthy children, aged between 5-24 months and 2-5 years of age.	≤4 months, ≥8 months and 5-7 months	Breast fed (6 7.9%) were breastfed during the first 6 months of life.)	height/length for age z score, weight for age z score weight for height /length z score
42. Onayade 2004 (68)	Prospective cohort study	Nigeria	Normal birthweight babies, (n=345), less than 14 days old	Before 4 months, between 4- 6 months	Breast fed (36%)	Mean monthly weights, morbidity (fever, diarrhea, acute respiratory infection)
43. Orlandi 2017 (69)	Prospective cohort study	Brazil	Healthy adolescents aged 18-19 years (n=4106).	</ = 1.00 1.01–2.00 2.01–3.00 3.01–4.00 4.01–5.00 > 5.00 months	Breast fed	Fat mass index and free fat mass index
44. Owais 2016 (70)	Prospective cohort study (Program evaluation)	Bangladesh	2189, 2074, 1969 and 1885 mother-child dyads at 3, 9, 16 and 24 months of infant age	</= 4 months, 5-6 months, >/= 7 months	Exclusive Breast fed (45%)	length-for-age (LAZ), weight-for-length (WLZ) z-scores and stunting
45. Padmadas 2002 (71)	Retrospective cohort study	India	89 777 ever-married women, 6226 infants	<6 months, 6 months, >6 months	Breast fed	Height for age, stunting
46. Papoutsou 2017 (72)	Retrospective cohort study	Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain, and Sweden	Healthy children (n=10,808)	1-3 months, 4-6 months, 7-12 months	EBF and/or in combination with milk formula	Height, weight, BMI
47. Davies 1977 (73)	Prospective cohort study	United Kingdom	821 full-term infants were chosen for the study	6 weeks to 3 months, < 6 weeks	Bottle fed	Weight gain, linear growth
48. Rodríguez-Cano 2020 (74)	Prospective cohort study	Mexico	Healthy full-term infants. (n=263)	< 4 months >/= 4 months	Breast fed	Length, weight, BMI, BMI z score, waist circumference, overweight, obesity, wasted
49. Crume 2014 (75)	Retrospective cohort study	United States	1077 participants, aged < 20 years	<3 Mos 3–6 Mos 7–11 Mos ⩾12 Mos	Breast fed (27% never breast fed)	Type 1 diabetes

50. Nopporlertwong 2016 (76)	Prospective cohort study	Thailand	Healthy, full term infants, aged between 16-20 weeks, (n=41)	4-6 months and at 6 months	Formula fed	Weight, length, head circumference, morbidity (Respiratory infections, GI infections, other infections) food preferences.
51. Meshram 2015 (77)	Retrospective cohort study	India	5457 children	<6, 6-8, 9-11 months	Breast fed	Height, weight, stunting, wasting, underweight
52. O'Donovan 2016 (78)	Prospective cohort study	Ireland	Healthy Maternal-infant dyads (n= 709)	< 17 weeks, > 26 weeks	Breast fed (By 6 mo some infants 22% were receiving infant formula with breastfeed)	Height, weight, waist circumference, atopic dermatitis, fat mass index
53. Morgen 2018 (79)	Prospective cohort study	Denmark	77,251 liveborn full term singleton births with no siblings in the cohort	< 4 month, >/= 4 months	Breast fed and Formula fed	Weight, height, BMI z score
54. Quigley 2008 (80)	Retrospective cohort study	United Kingdom	Healthy, full term infants (n=15 980)	</=1, 2 , 3 , 4, 5, >/= 6 months	Formula only: n=91842 Breast+formula: n= 12516 Breast milk only : n=23440	Diarrhea, LRTI
55. Moss 2014 (81)	Prospective cohort study	United States	Healthy, normal birth weight children (n=14,200)	<4 , 4–5, >/= 6 months	Breastfed	Overweight, obese
56. Vehapoglu 2014 (82)	Retrospective cohort study	Turkey	Healthy children, aged 2-14 years (n=4990)	< 4, 4–5, and >/= 6 months	Breast fed	Height, weight, BMI (overweight, obese)
57. Veena 2010 (83)	Prospective cohort study	India	Healthy, normal birthweight babies, (n=514), Preterm babies included	<4, 4, 5, >/= 6 months	Breast fed	cognitive function
58. vandenHooven 2016 (84)	Retrospective cohort study	Netherlands	Singleton, live born, healthy children (n=4919)	<4 months 4–4·9 months 5–5·9 months ≥6 months	Breast fed (92% ever breastfed)	(BMD)bone mineral density; (BMC) bone mineral content; (aBMC), area-adjusted BMC; (BA), bone area
59. Vafa 2012 (85)	Retrospective cohort study	Iran	healthy students (n=511). Sample includes LBW.	≤4 mos >4-6 mos >6 mos	Breast fed (75.7%), Formula fed (3.9%), Both (20.4%)	Height, weight, BMI (underweight, overweight)
60. Pluymen 2018 (86)	Prospective cohort study	Netherlands	Full -term infants (n=2611) LBW infants included	<4 or >/= 4 mos	Breast fed and Formula fed	Length, weight, BMI
61. Wang 2017 (87)	Retrospective cohort study (followup study)	China	Live singleton births, (n= 18,44)	3-6 months, >/= 6 months	Breast fed (n= Never: 1367; Primarily: 5184. Exclusively: 11,895)	Anemia (hemoglobin levels)

62. Wright 2004 (88)	Prospective cohort study	England (UK)	Full term healthy infants (N= 604)	<3 months 3–4 months > 4 months	Breast fed (Never: n= 322)	Weight gain, morbidity (diarrhea, rash, infections)
63. Rossem 2013 (89)	Prospective cohort study	Netherlands	Healthy full-term Children (n= 3184). Low BW babies included	0–3 months 3–6 months >/=6 months	Breast fed	Weight for height z-score
64. Mondal 1996 (90)	Prospective cohort study	India	Healthy full-term 148 infants	<3 months, > 4 months	Breast fed (2.7% not breastfed)	Diarrhea
65. Wen 2014 (91)	Prospective cohort study (secondary analysis of health beginnings trial	Australia	242 mothers in the analysis	</=2 3-5 61 (28) >/=6	Breast fed	Height, weight, BMI
66. Libuda 2016 (92)	Retrospective cohort study (secondary analysis of PINGU trial)	Germany	Healthy full term, newborns (n=83)	Before 6 months, after 6 months	Breast fed	Height, weight, Hemoglobin levels, haematological details
67. Gooze 2011 (93)	Retrospective cohort	United States	6750 children	>/= 6 months 4-5 months </=3 months	Formula fed	Weight for length percentile
68. Isherwood 1988 (94)	Retrospective cohort study	Bangladesh	Actual number of U5 children not given (200 families)	0-6 months > 7 months	Breast fed	Height, weight, (weight for height), MUAC
69. Zutavern 2006 (95)	Prospective cohort study	Germany	Healthy full-term infants (n=3097)	0-4 months 5-6 months >6 months	Exclusively breastfed: 57% Mixed: 37% Exclusively bottle-fed: 6%	Serum IgE levels, Atopic Dermatitis, Food allergies
70. Zutaverm 2008 (96)	Prospective cohort study	Germany	Healthy term infants (n= 3097)	0-4 months 5-6 months >6 months	Exclusively breastfed: 1224/2071 Mixed: 740/2071 Exclusively bottle-fed: 107/2071	Allergic rhinitis, Atopic dermatitis, food allergies, Serum IgE
71. Khadivzadeh 2004 (97)	Prospective cohort study	Iran	200 healthy, full-term infants	CF after 4 months vs. exclusive breastfeeding until the end of 6 months.	Breast fed	Height, weight, morbidity (diarrhea, Respiratory tract infection
72. Barton 2002(98)	Prospective cohort study	United States	Healthy full-term infants (n=52)	Before 4-6 months, after 4-6 months	Breastfed and Formula fed	Height, weight, head circumference
73. Grunwaldt 1960 (99)	Retrospective cohort study	United States	135 infants	At 3 months, >/= 6 months	N/A	Sleep quality and quantity

74. Quandt 1984 (100)	Prospective cohort study	United States	45 normal American infants consuming maternal-selected diets	Before 4 mons, after 4 months	Breast fed	Weight for age, length for age, weight for length
75. Wolman 1984 (101)	Prospective cohort study	NA	Healthy children (n=262)	1-12 weeks, >/= 13 weeks	Breast fed (not all were breast fed)	Height, weight, BMI
76. Winkelstein 1984 (102)	Retrospective cohort	NA	58 mothers and normal birthweight infants	Before 3 months, after 3 months.	Formula fed	Knowledge and attitude regarding complementary feed
77. Kalies 2005 (103)	Prospective cohort study	Germany	Healthy full-term neonates (n= 2624)	1- 3 months, 4-6 months and > 6 months	Breast fed	Weight gain
78. Tufa 2018 (104)	Retrospective cohort study	Ethiopia	Healthy children, (n= 342) aged 6-23 months	< 6 months, > 6 months	Breast fed	Length, weight, wasting, underweight
79. Vehapoglu 2017 (105)	Prospective cohort study	Turkey	Healthy children, (n= 4990)	<4 mons, 4-5 mons, >/= 6 mons	Breast fed	Weight, height, BMI (underweight, overweight, obesity)
80. Forsyth 1993 (106)	Prospective cohort study	Scotland	Full-term, normal birthweight infants (n=671)	< 8 weeks, 8-12 weeks, > 12 weeks	Breast fed only: n= 97 Partially breast fed: n= 130 Bottle fed: n= 264	Morbidity (diarrhea, vomiting, RTI, nappy dermatitis), asthma, atopic dermatitis, wheeze, weight
81. Yang 2012 (107)	Retrospective cohort study	China	Healthy, full-term Singleton infants aged 0–18 months. (n= 336)	<4 months, >6 months 4-6 months	Breast fed (n=336)	Weight, height, wasting, stunting, hemoglobin levels, micronutrient status
82. DeBeer 2016 (108)	Retrospective cohort study	Netherlands	Liveborn singleton infants (n=2227)	<4 months, >6 months 4-6 months	Unclear	Height, weight, BMI, systolic and diastolic BP
83. Gishti 2016 (109)	Prospective cohort study	Netherlands	Singleton children (n=3220)	< 3.9 mons, 4-4.9 mons, > 5 mons	Breast fed	BMI, systolic diastolic BP, retinal microvasculature assessment
84. Gishti 2014 (110)	Population-based prospective cohort study	Netherlands	School age children (n=3417)	< 3.9 mons, 4-4.9 mons, > 5 mons	Never breastfed N= 238 (92.6%) Ever breastfed N= 2982 (23.7%)	Height, weight, BMI, systolic and diastolic BP, (cardiometabolic risk factors, total cholesterol HDL cholesterol(mmol/l) LDL cholesterol (mmol/l) Triglycerides (mmol/l) Insulin (U/l) C-peptide (ng/ml)
85. Goodwin 1999 (111)	Prospective cohort study	Denmark	Children (n=200)	</= 2 weeks, >/= 3 weeks	Breast fed	Alcohol dependence

86. Salmanpera 1985 (112)	Retrospective cohort study	Finland	Healthy singleton, full-term infants (n=198)	3-6 months, 6-9 months 9-12 moths,	Breast fed	Length velocity, weight velocity, skin fold thickness, head circumference, BMI, micronutrient status
87. Stordal 2017 (113)	Prospective cohort	Norway	Singleton infants (n=70,511)	0-1 month, 1-3 months, 4-5 months, >/= 6 months	Breast fed	Morbidity (LRTI, URTI, gastroenteritis, otitis media, pneumonia, frequent infections)
88. Sit 2001 (114)	Retrospective cohort study	Canada	Healthy, full-term infants (n=130)	By 4 months	Breast fed and Formula fed	weight for age, height for age, weight for height
89. Yuan 2016 (115)	Prospective cohort	France	Infants (n=268)	<6 months, >/= 6 months	Breast fed and Formula fed	Dietary patterns
90. Gebreweld 2019 (116)	Retrospective cohort study	Ethiopia	Children aged 6 to 59 months. (n=404)	< 6 months, > months	N/A	Height, weight, underweight, stunted, wasted, Hb level
91. Elalfy 2012 (117)	Retrospective cohort study	Egypt	Healthy, full-term infants aged between 6 to 24 months (n=300)	</= 6 months, > 6 months	47 infants(15.7%) were predominantly breast-fed during the first 6months, 34 (11.3%) consumed only formula, 17 (5.7%) consumed only cow's milk, and 202 consumed a combination: 121 (40.3%) BF + formula and 81 (27%) BF + cow's. milk	Height, weight, underweight, stunting, Hb level
92. Ekelund 2021 (118)	Prospective cohort study	Norway	Children (n=3708)	≥ 6 months < 6 months	Breast fed and Formula fed	Atopic dermatitis, allergic rhinitis, asthma
93. Differding 2020 (a) (119)	Prospective cohort study	Canada	Healthy, singleton children. (n=392)	</= 4 months, > 4 months	Breast fed	weight, height, BMI z score, Gut microbiota diversity
94. Differding 2020 (b) (120)	Prospective cohort study	United States	Healthy singleton mother-infant pairs (n=67).	</= 3 months, > 3 months	Breast fed	Gut microbiota diversity, Gut microbiota composition, SCFA concentrations
95. Dhami 2019 (121)	Retrospective cohort study	India	Infant 6–8 months (n=13548)	Early introduction of solid foods, delayed introduction	Unclear	Stunting
96. Durmuş 2014 (122)	Prospective cohort study	Netherlands	Infants comprising of preterm, LBW and SGA (n=6616)	< 4 mons 4–4.9 mons >/= 5 mons	Breast fed (87.9% ever breastfed)	Height, weight, BMI, Android:gynoid fat, preperitoneal fat
97. Tessema 2013 (123)	Retrospective cohort study	Ethiopia	575 mother-infant pairs, aged between 0-23 months	< 6 months, at 6 months, > 6 months	Pre-lacteal fed(n=575) and Formula fed	Height, weight, BMI, stunting, head circumference

98. Malako 2018 (124)	Retrospective cohort study	Ethiopia	Children aged between 6-23 months. (n=485)	Before or after 6 months, at 6 months	Breast fed	Hemoglobin levels
99. Kleynhans 2006 (125)	Retrospective cohort study	South Africa	Mother and children pair, aged between 12-24 months. (n= 536)	0-1 month, >1 month	Breast fed	Height, weight, BMI, stunted, obese, overweight
100. Kamudoni 2015 (126)	Retrospective cohort study	Malawi	349 mother–infant pairs with the infants aged 0–12 months.	Before 6 mons, after 6 mons	Breast fed	Length for age z score, Weight for age z score,
101. Jeana 2017 (127)	Retrospective cohort study	Korea	Infants aged between 8-15 months (n=619)	< 6 months, >/= 6 months	Breast fed, Mixed feeding, Formula feeding	Height, Hb levels, haematological parameters, micronutrient status
102. Gingras 2019 (128)	Prospective cohort study	United States	1013 participants	< 6 months, >/= 6 months	69% were breastfed (at least partly) at 4 months, and 31% were never breastfed or no longer breastfed at 4 months (formula fed)	Adiposity outcomes (height, weight, BMI z score, Waist circumference, body fat percentage, DXA truncal fat mass, skinfold thickness, Skinfold ratio)
103. Fauzia 2020 (129)	Prospective cohort study	Indonesia	Children aged 36–71 months (n=165)	< 6 mons, >/= 6 mons	Breast Milk: 3.6%. Complementary Food: 13.3%. Formula Milk: 2.4 %. Other Sweet Drinks: 0.6%. Complementary Food and Formula Milk: 16.3%. Breast Milk and Combination: 63.6%	Dental carries
104. Chuang 2011 (130)	Prospective cohort study	Taiwan	Children (n=18773)	<4 months, 4–6 months, >6 months	Breast fed (16.7% not breastfed)	Atopic dermatitis
105. Kanoa 2011 (131)	Retrospective cohort study	Palestine	Preschool children aged 5 to 6 years. (n=571)	<4 months, 4–6 months, >6 months	Exclusively Breast fed	Height, weight, BMI, stunting, overweight, obesity
106. Hay 2008 (132)	Prospective cohort study	Norway	Healthy, full-term, singleton infant-mother dyads (n=364)	6 months, 12 months	Breast fed	Hb levels, haematological parameters, micronutrients (folate, cobalamin, HoloTC, HoloHC, MMA, tHcy)
107. Sirkka 2021 (133)	Prospective cohort study	Netherlands	3524 infants	< 4 mons, >/= 4 mons	Breast fed	Height, weight, BMI

108. Deisher 1954 (134)	Prospective cohort study	United States	Infants aged between 1-4 weeks (n=85)	Early (1-4 weeks) vs. Late (9-12 weeks)	Breast fed or Formula fed	Hemoglobin, RBC count
109. Shamim 2006 (135)	Retrospective cohort study	Pakistan	Healthy children under 3 years. (n=359)	<4 months, 4-6 months, > 6 months	N/A	Height, weight, weight for height
110. Zutavern 2004 (136)	Prospective cohort study	United Kingdom	Preschool children (n=551)	</= 3 months, > 3 months	Breast fed (62.3% ever breastfed)	Morbidity (atopy), atopic dermatitis, asthma, wheeze
111. Salah 2018 (137)	Retrospective cohort	Palestine	654 infants mother pairs. (n=654)	Before 6 mons, at 6 mons, after 6 mons	Breastfeeding: 38.2%. Partial breastfeeding and formula: 22.0%. Formula: 17.6%	Height, weight, stunting, wasting, Hb levels, haematological parameter
112. Hodgson 1978 (138)	Prospective cohort study	United Kingdom	Healthy babies under the age of one (n=301)	< 6 weeks, 6 weeks - 3 months, > 3 months	Breast fed	Weight
113. Zheng 2015 (139)	Prospective cohort study	China	Healthy children, (n=40 510)	</=3 mons, 4-6 mons, > 6 mons	Breast fed Never: 2682. Ever: 37,828	Height, weight, BMI z score
114. Grimshaw 2013 (140)	Nested, case-control within a cohort study	United Kingdom	123 infants	≥17 weeks vs <17 weeks	Breast fed or Formula fed	Food allergy
115. Wilson 1998 (141)	Retrospective cohort study	United Kingdom	545 infants	< 15 weeks, >/= 15 weeks	Exclusive Breast fed, Partial Breast fed, and Formula fed	Height, weight, BMI, morbidity (RTI, cough), Asthma, Skin fold thickness, Systolic Diastolic BP, total fat mass and lean mass
116. Baird 2008 (142)	Prospective cohort study	United Kingdom	Singleton, full term infants (n=1740)	<3 months 3 months 4 months 5 months >/=6 months	Breast fed or Formula fed	Height, weight, skinfold thickness
117. Sina 2019 (143)	Retrospective cohort study	Cyprus, Estonia, Germany, Hungary, Italy, Spain Sweden	5526 participants	</= 6 months, > 6 months	Exclusive Breastfeeding (EBF) 3.3/2.7 Combined Breastfeeding (BF&FMF) 7.2/6.3 Exclusive Formula Milk Feeding (EFMF) 4.1/8.1	Food preferences
118. Ejlerskov 2015 (144)	Prospective cohort study	Denmark	Singleton full-term infants (n=233)	3-4 months, 5 months, 6 months	Fully BF at 4 months: n= 233 Partial BF at 9 months: n=233 Formula at 9 months (g/d): n= 233	Weight for age, height for age, weight for heigh BMI z score, skin fold thickness, body composition
119. Lande 2005 (145)	Retrospective cohort study	Norway	Full term infants (n= 1441)	</= 4 mons, 4-5 mons, >5 mons	Breast fed or Formula fed	Height, weight, BMI

120. Layte 2014 (146)	Prospective cohort study	Ireland	9057 participants	<4 mons, < 5 mons, < 6 mons, 6+ mons	Breast fed	Height, weight, BMI
121. DeBeer 2015 (147)	Prospective cohort study	Netherlands	Full term children (n= 2227)	<4 months, 4-6 months, > 6 months	Breast fed	Height, weight, BMI, body composition (fat mass, free fat mass)
122. Zhou 2011 (148)	Nested case control study	China	Healthy children (n=162)	< 4 mons, </= 4 mons, > 6 mons	Breast fed, Formula fed or Mixed Feeding	Height, weight, BMI (Obesity)
123. Zheng 2019 (149)	Prospective cohort study	Australia	483 participants	< 6 mons, >/= 6 mons	Breastfeeding: Never: 2682 Ever: 37828	Height, weight, BMI
124. Simondon 1997 (150)	Prospective cohort study	Senegal	420 participants	2-3 months, 4-5 months, 6-7 months, > 6-7 month	Breast fed	Weight, Length, MUAC
125. Nirmolia 2018 (151)	Retrospective cohort study	India	Healthy children (n=624)	< 6 months, at 6 months, > 6 months	Breastfeed plus prelacteal feed	Morbidity (pneumonia)
126. Modjadji 2020 (152)	Retrospective cohort study	South Africa	Children aged less than 5 years (n= 404)	< 6 months, 6-12 months	Breastfed: Yes 384 (95.1) No 20 (4.9) Mixed feeding: Yes 268 (66.3) No 136 (33.7)	Height, weight, BMI, stunting, underweight hip circumference
127. Malako 2019 (153)	Retrospective cohort study	Ethiopia	Healthy children (n=477)	Earlier than 6 months, at 6 months	Breast fed	Height, weight, stunting, Hb levels
128. Griffiths 2009 (154)	Prospective cohort study	United Kingdom	Singleton, full-term infants (n=10 533)	Before 4 mons, after 4 mons	Breast fed (Never: 29%)	Weight gain.
129. Ferrara 2014 (155)	Retrospective cohort	Italy	Healthy full-term Children, aged between 8-36 months. (n=1250)	< 6 months, > 6 months	Cow milk	Height, weight, BMI, Hb level, haematological parameter
130. Eunice 2014 (156)	Retrospective cohort study	Malaysia	Healthy children and mother pairs (n=177)	< 6 months, >/+ 6 months	Breast fed (7.3% not breastfeeding)	Height for age, weight for age, weight for height (wasting), morbidity (GI or respiratory illness)
131. Demilew 2017 (157)	Retrospective cohort study	Ethiopia	Children (n=471)	< 6 months, at 6 months, > 6 months	N/A	Height, weight, stunting, wasting
132. Bournez 2019 (158)	Prospective cohort study	France	Infants born after 33 weeks of gestation (n=10,159)	<4 months, 4-6 months, >6 months	Breast fed	Frequency of use (SU) of added sugar, salt, and fat
133. Bindon 1985 (159)	Retrospective cohort study	United States	6,587 children	11-13 months, 22-26 months, 33-39 months	Breast fed, Formula fed or Mixed Feeding	Length/Height
134. Ahmed 1993 (160)	Nested case control study	Bangladesh	1085 children	</= 3 months, > 3 months	N/A	Height, diarrhea (shigellosis)

135. Abeway 2018 (161)	Retrospective cohort study	Ethiopia	Healthy children (n=410)	At 6 months, before or after 6 months	Breast fed (ever: 97.8); Given prelacteal feed (29.5%)	length
136. Hawkins 2009 (162)	Prospective cohort study	United Kingdom	Singleton children (n= 13188)	<17.4 weeks, >/= 17.4 weeks	Breast fed (Never: 30%)	Height, weight, BMI
137. Kim 2008 (163)	Retrospective cohort study	United States of America	Full-term Infants aged between 8-14 months, (n=8150)	< 4 months or after	Breast fed	Weight
138. Haschke 2000 (164)	Retrospective cohort study	Not mentioned	Healthy full-term children (n=2145)	< 4 mo or after	Breast fed	Height, weight, BMI
139. Sausenthaler 2011 (165)	Retrospective cohort study	Germany	3097 newborns	<5, 5-6, > 6 months	Mothers were advised to breastfeed exclusively during the strict intervention period of 4 mo, and formulas were provided only if breastfeeding was not feasible or wanted	Atopic dermatitis, asthma, wheeze, serum IgE levels, allergic rhinitis
140. Dhami 2020 (166)	Retrospective cohort study	India	Mother-children pairs with Children aged between 0-23 months, (N= 90596)	CF at 6-8 months of age	Breast fed, Predominant feeding, Formula fed	Diarrhea
141. Spiegler 2015 (167)	Prospective cohort study	Germany	981 premature infants with a birth weight of <1500 g	CF <4 months	Breast fed	Height and weight
142. Supadmi 2020 (168)	Retrospective cohort study	Indonesia	640 premature infants	<6 months vs. ≥ 6 months	Breast fed	Undernutrition and sever nutrition, normal and overweight children
143. Rodriguez 2018 (169)	Retrospective cohort study	United States	36 preterm toddlers, 18-to-24 month	<4 months vs. ≥ 4 months	Exclusive human milk: 11.1%; Human milk feedings with supplemental formula: 11.1%; Half human milk and half formula: 2.8%. Formula with supplementation with human milk: 8.3%. Exclusive formula: 66.7%	None

144. Morgan 2004 (170)	Retrospective cohort study	England	1600 infants (premature plus term infants)	<12 vs. ≥ 12 weeks	N/A	Weight and length gain, head circumference, skinfold thickness, sleep
145. Baldassarre 2020 (171)	Prospective cohort study	Italy	100 preterm infants	<4 months, 4-6 months, >6 months	Exclusive breast milk: 15 (15%); Exclusive formula: 35 (35%); Mixed: 50 (50%)	Timing of adiposity rebound
146. Brion 2020 (172)	Secondary analysis of a cohort	United States	204 premature infants	Homemade CF vs commercial CF (<17 weeks, 17–26 weeks, and >26 weeks)	Breast fed	Weight, length, BMI z score, fronto-occipital Circumference, weight for length z-score
147. D'Souza 1985 (173)	Prospective cohort study	NA	50 singleton preterm infants	Early: 2 weeks to 4 months vs late at between 4-6 months	Formula fed	Serum concentrations of sodium, potassium, urea, protein, and osmolality
148. Van't Hof 2000 (174)	Prospective cohort study	European group	Healthy infants (n=2145)	>4-5 months vs. <4-5 months and a control group	Breast fed	Length, weight, BMI
149. Gaffney 2012 (175)	Prospective cohort study	NA	691 infants born after 35 weeks of gestation	<4 months, between 4-6 months, ≥6 months	Breast fed and Formula fed	WAZ
150. Neutzling 2009 (176)	Prospective cohort study	Brazil	Live born children, recruited at birth. Adolescents (n=1204)	Before or after 4 months	Breast fed. With regard to the use of non-human milk, alone or in combination with breast milk, 21.2% received cow's milk, 33.5% formula and 18.1% both.	Height, weight, BMI, gut microbiome
151. Oliveira 2016 (177)	Secondary analysis/ Retrospective study	Brazil	singleton, full-term babies, healthy babies (n=150)	More than 240 days (8 months) vs < 8 months	Exclusively Breastfed	Height, stunting, hemoglobin level, micronutrient status
152. Moschonis 2017 (178)	Retrospective cohort study	Greece, Portugal, and the UK (European cohorts)	Healthy children from six cohorts: Greek-EuroPrevall at age 4 years (n = 309) Generation XXI at age 4 years (n = 3387) EDEN at age 5 years (n = 1070)	<4 months ≥4 to <5 months ≥5 to <6 months ≥6 months	Breast fed	Height z-score BMI z-score Fat mass

			ALSPAC at age 4 years (n = 6522) ALSPAC at age 9 years (n = 7540) ALSPAC at age 13 years (n = 6124)			
153. Taylor-Robinson 2016 (179)	Retrospective cohort study	United Kingdom	Children, (n=11 537) LBW infants included	Less than 4 months	Breast fed (Never: 30.2%) or Cow milk (54.2%)	Atopic dermatitis
154. Yeung 1981 (180)	Prospective cohort study	Canada	Healthy, full-term newborns (n=316)	At 2 months	Breast fed (38.9%) and Formula fed (61.1%)	Weight, length, head circumference, arm circumference, weight for length
155. Fairley 2015 (181)	Prospective cohort study	United Kingdom	Singleton, healthy babies (n=987)	6 and 12 weeks	Breast fed (Never: 27%)	Height, weight, BMI z-score
156. Griffiths 2010 (182)	Prospective cohort study	United Kingdom	11 653 singleton children	Less than 4 months	Breast fed (Never: 29%)	Height, weight
157. Anin 2020 (183)	Retrospective cohort study	Northern Ghana	581 children	CF at 6 months	Breast fed (96.4%)	Weight for age, length for age, weight for length (Wasting, underweight, stunting)
158. Wood 2020 (184)	(Prospective Cohort) Secondary analysis of Greenlight Intervention Study	NA	Healthy, full-term infants aged between 6- 16 weeks,(n= 469)	Before 4 months	Breast fed (96.4%) or Formula Milk (16%)	Rapid Gain WAZ, Rapid Gain WLZ
159. Saaka 2015 (185)	Retrospective cohort study	Northern Ghana	The assessment was made on a total of 1984 was the final sample, children 6–23 months	At 6 months	Breast fed (95.5%)	Length-for-age z-score, Weight-for-age z-score, Weight-for-height z-score, Stunting, wasting, underweight
160. Anjana 2015 (186)	Retrospective cohort study	India	110 healthy mother-child pairs, aged between 7 months to 3 years.	At 6 months	Breastfed/ Prelacteal feed	Weight
161. Birbilis 2013 (187)	Retrospective cohort study	Greece	2294 schoolchildren aged 9–13 years	≤4 months, 5-6 months, >6 months	Breast fed	Overweight, obesity
162. Ferris 1980 (188)	Prospective cohort study	United States	255 infants (92 were mother -female infant dyad	Solid before two months of age	Breast fed; Formula fed	Weight, length
163. Azad 2018 (189)	Prospective cohort study	Canada	2553 mother-infant dyads	<4, 4 to <5, 5 to <6, ≥6 months	Breast fed (96.6%)	BMI z score, weight gain velocity
164. Massion 2016 (190)	Retrospective cohort study	United Kingdom	11,764 children	CF > 4, <4 months	Breast fed (Never: 33.7%)	Overweight and obesity
165. Fergusson 1981 (191)	Prospective cohort study	New Zealand	1262 infants	CF > 4 months	Breast fed	Eczema

166. Venter 2009 (192)	Prospective cohort study	NA	969 families	Weaning before and after 16 weeks	Breast fed, Formula fed, Mixed feeding	Skin prick test positive, food hypersensitivity
167. Vogelezang 2018 (193)	Prospective cohort study	Netherlands	4444 children	<4 months, 4-4.9 months, ≥5months	Never breastfed (n = 333) Ever breastfed (n = 4111)	BMI, fat mass, visceral fat index, pericardial fat index, liver fat fraction
168. Iguacel 2018 (194)	Prospective cohort study	Australia	2186 children	CF > 4, <4 months	Breast fed	BMI Z-score
169. Aris 2018 (195)	Prospective cohort study	Singapore	858 infants	CF > 4, <4 months	Breast fed	BMI, BMI Z score, WHO BMI Z score, fat mass index, overweight
170. Sirkka 2018 (196)	Prospective cohort study	Amsterdam	3524 infants	Early (< 6 months) or late (≥6 months	Breast fed	Overweight
171. Lossius 2018 (197)	Prospective cohort study	Norway	41,020 children at 18 months	<4months, 4-5months, ≥6months	Breast fed (78%) and Formula fed (36% at 6 mo.)	Asthma
172. de Jonge 2013 (198)	Prospective cohort study	Netherlands	Singleton live births (n = 9506)	<4months, 4-5months, >5months	Breast fed (92.4%)	Blood pressure, pulse wave velocity, aortic root diameter, fractional shortening, left atrial diameter; left ventricular.
173. Larsson 2008 (199)	Prospective cohort study	Sweden	4779 children	Early introduction of solid food (<3 months)	N/A	Eczema
174. Sariachvili 2010 (200)	Nested case control study	Belgium	1128 children	Solid introduction in first 4 months	Breast fed and Formula fed	Eczema
175. Savilahti 2009 (201)	Prospective cohort study	Finland	6,209 healthy full-term newborns	Introduction of vegetables before and after 3.9 months	Breast fed, Formula fed and received Cow Milk	Type 1 diabetes
176. Martin 2004 (202)	Prospective cohort study	United Kingdom	7276 singleton, term infants	<3 months, at 3months, ≥4months	Breast fed (83%)	Blood Pressure
177. Simondon 2003 (203)	Prospective cohort study	Senegal	Mothers of singletons and of first-born twins were included (n = 855)	By 2–3 months, By 4–5 months, By 6–7 months, After 6–7 months	Breast fed	Resumption of ovarian activity
178. Ogbo 2018 (204)	Retrospective cohort study	Tanzania	Women children pair were interviewed, aged between 0-23 months (n = 10,139)	6-8 months	Breast fed and Formula fed	Diarrhea
179. Reilly 2005 (205)	Prospective cohort study	United Kingdom	Children aged between 4 months to 5 years (n=7758)	<1, 1-2, 2-3, 3-4, 4-6 months	Breast fed	Height, weight, BMI, and early adiposity rebound
180. Bammann 2014 (206)	Nested case control study	Belgium, Cyprus, Estonia,	Children aged 4-8 years of age. (n=1024)	Early introduction (before 4 months)	Breast fed	Height, weight, BMI, body composition

		Germany, Hungary, Italy, Spain, and Sweden.				
181. Briaux 2019(207)	Retrospective cohort study	Rural Togo	2,034 children aged 6–23 months	Early (<6 months) vs. Timely (6–8 months) v. Late (>8 months	Breast fed	Stunting, LAZ
182. Huffman 1987 (208)	Retrospective cohort study	Bangladesh	2455 married women	At 1-3 mo, 4-6 mo and 6+ months	Breast fed	Amennorhea (not given by complementary feeding, risk of resuming menses
183. Duncan 1993 (209)	Prospective cohort study	United States	1220 infants	Breastfeeding plus supplementary food at <4mo vs. 4-6 mo	Breast fed	Episodes of acute otitis media
184. Fergusson 1983 (210)	Prospective cohort study	New Zealand	1265 infants	Solid introduction between 0-4 months	Breast fed only and Breast fed with complement	Rate of eczema
185. Dunlop 2006 (211)	Prospective cohort study	United States	Birth cohort of 1990 infants	Solid introduction <4mo versus EBF ≥ 4mo	Breast fed; Formula fed	Atopic dermatitis
186. Haileamlak 2005 (212)	Nested case control study	Ethiopia	Children aged 1 to 5 years (n=7915)	Weaning at < 4mo, 4-6 mo, > 6mo	Unclear	Atopic Eczema
187. Lee 2017 (213)	Retrospective cohort study	Korea	Children 1-3 years old (n=2015)	≤ 4mo vs. > 4 mo	(29.1%) participants were exclusively breast-fed, 202 (11.3%) were exclusively formula-fed, and 1,134 (59.7%) had mixed feeding patterns	Atopic dermatitis
188. Kim 2011 (214)	Prospective cohort study	Korea	Birth cohort (n=1177)	<6mo vs. ≥ 6mo	Breast fed	Food allergy
189. Snijders 2008 (215)	Prospective cohort study	The Netherlands	Mother infant pairs (n=2558)	Introduction of food at 3mo, 4-6 mo and at > 7 mo	Breast fed (Never: 18%)	Atopic dermatitis and Eczema
190. Al-Suhiemat 2020 (216)	Retrospective cohort study	Jordan	100 anemic preschool children aged 36–59 months	Introduction of food at <2 mo, at 2 mo, at 4 mo, at 6 mo	Anaemic: Breastfed (18%); Formula fed (29%) Normal: Breastfed (29%); Formula fed (24%)	Anaemia
191. Asfaha 2018 (217)	Retrospective cohort study	Ethiopia	597 under-five children	Introduction of food after 6 mo vs. at 6mo	Breastfed	Diarrhea
192. Brown 1989 (218)	Prospective cohort study	Peru	153 singleton newborns	Introduction of food at 0-2 mo of age, 3-	Formula milk and Breast fed infants	Risk of Diarrhea

				5mo of age, 6-8 mo of age		
193. Estrada-Reyes 2007 (219)	Retrospective cohort study	Mexico	32 children of ≤ 3 years of age	Introduction of food after 6 mo vs. ≤ 6mo	NA	Atopic dermatitis and Food hypersensitivity
194. Fall 2011 (220)	Prospective cohort study	Brazil, Guatemala, India, Philippines, and South Africa (LMICs)	10,912 subjects in the age range of 15–41 years	Introduction of food: 0–3.00 mo, 3.01–6.00 mo, 6.01–9.00 mo, 9.01–12.00 mo, 12.01–18.00 mo	More than 90% of babies in all cohorts were initially breastfed	Adult blood pressure (BP), plasma glucose concentration and adiposity (skinfolds, waist circumference, percentage body fat and overweight/obesity)
195. Fallani 2011 (221)	Prospective cohort study	Five European countries (Sweden, Scotland, Germany, Italy, and Spain)	605 infants	Infants who started before weaning (at 6 weeks of age) and 4 weeks after the introduction of first solid foods	Fully breast-fed at 6 weeks 312 (54.2 %); Formula-fed at 6 weeks 163 (28.3 %); Mixed-fed at 6 weeks 101 (17.5 %)	Changes in microbiota
196. Fawzi 1997 (222)	Prospective cohort study	Israel	351 Israeli mother-infant pairs (North African descent)	Introduction of food at 1 mo, 2mo and at 3 mo of age	The rates of exclusive breast-feeding during infancy declined from 34% at I mo to 18% at 2 mo, to 6% at 3 mo	Infant weight
197. Ferris 1979 (223)	Prospective cohort study	United States	92 female infants and their mothers	Introduction of food at 1	Formula fed and breastfed infants	Triceps skinfold measurements
198. Franks 1985 (224)	Prospective cohort study	Pacific atolls	61 children	Introduction of food < 4mo vs. >4mo	Breastfed infants	Morbidity
199. Okubo 2016 (225)	Prospective cohort study	Japan	763 mother–child pairs	Introduction of food at <5 months; 5-5.9 months; and ≥6 months	Breastfed infants	Height and weight
200. Hop 2000 (226)	Prospective cohort study	Vietnam	300 newborns	Weaned from birth to 1 mo, 1 mo to 3 mo, and 6 to 12 mo	Breastfed infants	Length and weight gain
201. Imai 2014 (227)	Prospective cohort study	Iceland	250 Icelandic infants born	<6mo vs. >6mo	Breastfed and Formula Fed	Weight and length
202. Jimenez-Cruz 2010 (228)	Prospective cohort study	Mexico	810 mothers and their babies ranging from ages 5 to 24 months	Weaning ≤6 vs. ≥6 months	Thirty-five percent of infants were breastfed ≥6 month	Overweight and obesity

203. Kanoa 2011 (229)	Retrospective cohort study	Palestine	269 mothers of infants aged less than two years old	Age of CF introduction was <4 mo, 4-6 mo, >6mo	NA	Morbidity
204. Mehta 2012 (230)	Prospective cohort study	United States	550 pregnant women	Age of CF introduction was <4 mo, 4-6 mo, >6mo	92.6% initiated breastfeeding	Underweight, overweight and obesity
205. Popkin 1990 (231)	Prospective cohort study	Philippines	3000 mother-infant pairs	Introduced solid at 2mo, 4mo and 6 mo	Breastfed	Diarrhea
206. Rathnayake 2013 (232)	Retrospective cohort study	Sri Lanka	1087 preschool children	Initiation of Complementary feeding after 6 months	Formula fed and Breastfed infants	Overweight and obesity
207. Rippey 2020 (233)	Prospective cohort study	United States	2,794 infants	≤6 vs. ≥6 months	Formula fed and Breastfed infants	Morbidity
208. Robinson 2009 (234)	Prospective cohort study	United Kingdom	536 children	Age at introduction of solid foods Up to 3 months, Up to 4 months, Up to 5 months, and >5 months	Breastfed and non-breastfed children	Children with DXA measurements
209. Salahuddin 2017 (235)	Prospective cohort study	United States	4497 infants	Complementary food introduction prior to 4 months	Breastfed	BMI z-score
210. Škledar 2015 (236)	Prospective cohort study	Croatia	302 healthy Caucasian children	Complementary food < 6 months	Breastfed	Overweight and obesity
211. Thorisdottir 2019 (237)	Prospective cohort study	Iceland	250 Icelandic infants	Introduction of solid foods prior to 4 months	Breastfeeding initiation rate was high (99%) and 88% of infants were still breastfed when introduced to solid food	IgE sensitization
212. Vadiveloo 2019 (238)	Prospective cohort study	United States	449 women	CF < 4 months vs. ≥4 months	Not exclusively breast or formula feeding infants	Weight-for-length z-scores, healthy food scores
213. Werdani 2019 (239)	Retrospective cohort study	Indonesia	162 mothers with toddlers (6-59 months)	<6mo vs. ≥6mo	NA	Malnutrition
214. Khatun 2013 (240)	Retrospective cohort study	Bangladesh	180 child aged between 6-23 months	<6mo, just after 6mo, >6.1 mo	EBF: 54.3% in NNP area and 44% in non NNP area	Stunting, wasting, underweight
Note: Not all the studies have explicitly mentioned the type of feeding practice						

Table 4: Morbidity and NCD outcomes from studies not meta-analysed

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
RCTs									
Gupta 2017 (13)	Both diarrhoea and LRTI		4 mo	12 mo.		1/184			
			6 mo.			1/189			
Perkin 2019 (22, 23)	Prevalence of Allergy (%)		Early introduction (3 mo)			567 (5.6%)			
			Standard (EBF-6 mo)			595 (7.1%)			
	Prevalence of Egg Allergy (%)		Early introduction (3 mo)			569 (3.7%)			
			Standard (EBF-6 mo)			596 (5.4%)			
	Prevalence of Peanut Allergy (%)		Early introduction (3 mo)			571 (1.2%)			
			Standard (EBF-6 mo)			597 (2.5)			
Skjerven 2020 (24-26)	Atopic dermatitis		Skin Intervention	12 mo		64/575 (11%)			
			Food Intervention (CF between 12 and 16 weeks)			58/642 (9%)			
			Combined Intervention			31/583 (5%)			
	Possible AD	Possible atopic dermatitis was defined as observed eczema (excluding differential diagnoses to atopic dermatitis) and a history or signs of itch at the 3-, 6-, and 12-month investigations, or reported itchy rash of at least 4 weeks'	Skin Intervention			94/575 (16%)			
			Food Intervention (CF between 12 and 16 weeks)			101/642 (16%)			
			Combined Intervention			69/583 (12%)			
Dewey 2004 (LBW) (5, 9-12)	Diarrhea	% Of days	4 mo	16 to 26 weeks		2.8 ± 5.4			60
			6 mo			5.4 ± 8.5			59
	Cough		4 mo			29.2 ± 22.1			60
			6 mo			26.1 ± 20.3			59
	Fever		4 mo			7.3 ± 7.8			60
			6 mo			8.0 ± 7.2			59
Observational Studies									

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
Miliku 2015 (32)	Microalbuminuria		<4 mo	At 6 years				1.09 (0.64 to 1.85)	
			4-4.9 mo					1.01 (0.75 to 1.35)	
			>/=5.9 mo					1 (reference)	
Kalanda 2006 (55)	Eye	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				1.49 (1.30, 1.68)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				1.05 (0.13, 1.97)	262
	Malaria	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				1.31 (1.13, 1.49)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				1.04 (0.91, 1.17)	262
	Skin	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				0.31 (0.22, 0.40)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.27 (0.20, 0.34)	262
	Ear	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				0.07 (0.03, 0.11)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.09 (0.05, 0.13)	262
	Mouth	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				0.06 (0.02, 0.10)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.07 (0.04, 0.10)	262
Fauzia 2019 (129)	Posterior Decayed, extracted, filled tooth surface [defs] score		>/= 6 mo	59 months			Median (Min.-Max.) defs: 2.50 (0–40)		116
			<6mo				Median (Min.-Max.) defs: 5.00 (0–40)		49
Infections									
Noppornler twong 2016 (76)	Number of infections from enrollment to age 15 mo		4-to-6-months (starting complementary feeding between 4 and 6 months old)		enrollment to age 15 months		3.0 (1.0-4.0)		
			At-6-months				2.5 (0.5-4.5)		21
	Other Infections		4-to-6-months (starting complementary feeding between 4 and 6 months old)		enrollment to age 15 months		0 (0-1.0)		20
			At-6-months				0 (0-1.0)		21
Forsyth 1993 (106)	Nappy dermatitis		<8	53-104 weeks		4 (10.6%)			
			8 to 12			39 (17.5%)			
			>12			39 (20.2%)			
Duncan 1993 (209)	Episodes of Otitis Media		4-6 mo	0-12 mo		1.18 ± 1.55			185
			< 4mo			1.77 ± 1.91			189
			4-6 mo			1.52 ± 1.83			185

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
Fallani 2011 (221)	Proportions of bifidobacteria		< 6 weeks (before weaning (at 6 weeks of age))			40.9%			531 infants
			>6weeks (weeks after the introduction of first solid foods)			37.9%			
	Proportions of enterobacteria		< 6 weeks (before weaning (at 6 weeks of age))			7.3%			
			>6weeks (weeks after the introduction of first solid foods)			3.1%			
	Proportions of C. difficile+ C. perfringens species		< 6 weeks (before weaning (at 6 weeks of age))			3.2%			
			>6weeks (weeks after the introduction of first solid foods)			0.8%			
	Proportions of C. coccoides		< 6 weeks (before weaning (at 6 weeks of age))			5.4%			
			>6weeks (weeks after the introduction of first solid foods)			14%			
	Proportions of C. leptum		< 6 weeks (before weaning (at 6 weeks of age))			0.4%			
			>6weeks (weeks after the introduction of first solid foods)			1.6%			
GI Illness									
Noppornler twong 2016 (76)	Gastrointestinal infections	Number of infections from enrolment to age of 15 mo	4-to-6-months (starting complementary feeding between 4 and 6 months old)	enrollment to age 15 months		0.3 ± 0.8	0 (0-1.0)		20
			At-6-months			0.3 ± 0.8	0 (0-1.0)		21
Allergies and Sensitization									
Ekelund 2021 (118)	ARC- Allergic rhinoconjunctivitis		≥ 6 months	2 years (ever)		36/757			
			< 6 months			133/2127			
	ARC- Allergic rhinoconjunctivitis		≥ 6 months	6 years (current)		76/603			
			< 6 months			203/1591			
Koplin 2010 (58)	Egg allergy		<4	at 1 year		69 (4.4%)			
			4			354 (9%)			
			5			636 (8.8%)			
			6			996 (9.4%)			
			>6			106 (5.7%)			
Zutavern 2006 (95)	Early Skin or Allergic Symptoms		0-4 mo			315 (32%)			
			5-6 m0			476 (49%)			
			> 6 mo			187 (19%)			

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
	Early Skin or Allergic Symptoms Doctor-Diagnosed AD		5-6 m0	Months 6–24				1.08 (0.72–1.60)	
			> 6 mo					1.48 (0.91–2.40)	
	Early or Allergic Symptoms-Symptomatic		5-6 m0	Months 6–24				1.08 (0.73–1.59)	
			> 6 mo					1.51 (0.94–2.45)	
Zutavern 2004 (136)	Atopy		</= 3 mo	5.5 years		326 (14.4%)			
			> 3 mo			267 (18.8%)			
Venter 2009 (192)	Food hypersensitivity		before 16 weeks	At 1 year		10 (N not given)			
			after 16 weeks			28 (N not given)			
			before 16 weeks	At 3 years		17 (N not given)			
			after 16 weeks			38 (N not given)			
Luccioli 2014 (61)	New pFAb		1-3mo			461 (5.6%)		1 (reference)	
			4-5mo			542 (5.4%)		0.98 (0.53–1.80)	
			6-12 mo			236 (4.6%)		0.87 (0.37–1.89)	
	High-Risk pFAc		1-3mo			288 (11.1%)		1 (reference)	
			4-5mo			322 (8.7%)		0.91 (0.46–1.77)	
			6-12 mo			141(10.6%)		0.96 (0.40–2.20)	
Snijders 2008 (215)	Any Sensitization		3	at age 2		5/50			
			4 to 6			208/709			
			>7			7/23			
	Sensitization against cow milk		3			4/50			
			4 to 6			143/709			
			>7			3/23			
	Sensitization against hen's egg		3			1/50			
			4 to 6			44/709			
			>7			2/23			
	Sensitization against peanuts		3			1/50			
			4 to 6			39/711			
			>7			2/23			
	Sensitization against at Least 1 Inhalant Allergen		3			1/50			
			4 to 6			77/683			
			>7			6/23			
Thorisdottir 2019 (237)	Sensitization		<4mo					OR = 4.9 (95% CI = 1.4–16.6)	
Eczema									
Forsyth 1993 (106)	Eczema		<8	53-104 weeks		2 (5.4%)			

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
			8 to 12			36 (17%)			
			>12			18 (8.3%)			
Zutavern 2004 (136)	Eczema		</= 3 mo	5.5 years		326 (34.4%)			
			> 3 mo			267 (35%)			
Fergusson 1981 (191)	Eczema		CF at first 4mo of life (</=4mo)	2 years	Got Breast milk	54 (16.8%)			
			CF < 4 mo			82 (12%)			
			CF at first 4mo of life		No Breast milk	489 (13.7%)			
			CF < 4 mo			126 (7.9%)			
Larsson 2008 (199)	Incidence of Eczema	Crude values	> 6mo					1 (reference)	
			3-6 mo					0.95 (0.75-1.19)	2790
			< 3mo					2.43 (1.24-4.74)	47
Haileamlak 2005 (212)	Atopic Eczema		<4 mo	Children aged 1-5 years		19%			Overall N of cases is 306
			4-6 mo			67%			
			>6 mo			14%			
Fergusson 1983 (210)	Rate of Eczema	Rates of asthma per 100 children aged 0-4 years	Solid given by 0-4 mo (</=4 mo)	0-4 years	Total	58/802			
					BF-or complement fed	50/725			
					BF only	8/77			
			Solid given by not 0-4 mo		Total	19/308			
					BF-or complement fed	10/186			
					BF only	9/122			
Atopic Dermatitis									
O'Donovan 2016 (78)	Atopic dermatitis		<17 weeks (< 4mo)	12 mo		9 (8.2%)			
			>26 weeks (> 6mo)			4 (11.8%)			
Lee 2017 (213)	Atopic Dermatitis	Prevalence	</= 4mo	1 to 3 years of age		Mean ± SE: 12.7±4.2			180
			> 4mo			Mean ±SE: 87.3±4.2			1695
Asthma									
Larsson 2008 (199)	Asthma and/or Wheezing (Doctor diagnosed)	Crude values	> 6mo					1 (reference)	806
			3-6 mo					1.03 (0.81-1.31)	2620
			< 3mo					1.36 (0.59-3.14)	45
Wheeze									
Forsyth 1993 (106)	Wheeze		<8	53-104 weeks		3 (6.5%)			
			8 to 12			132 (4.5%)			
			>12			18 (9.4%)			
Zutavern 2004 (136)	Preschool Wheezing		</= 3 mo	5.5 years		326 (16.7%)			
			> 3 mo			267 (19.2%)			
	Transient wheezing		</= 3 mo			326 (31.6%)			
			> 3 mo			267 (28.6%)			
Respiratory									

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
Kalanda 2006 (55)	Respiratory	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				1.31 (1.13, 1.49)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.9 (0.78, 1.02)	262
Noppornler twong 2016 (76)	Respiratory tract infections	Number of infections from enrolment to age of 15 mo	4-to-6-months (starting complementary feeding between 4 and 6 months old) < 6mo	enrollment to age 15 months		2 ± 1.6	2.0 (1.0-3.0)		20
			At-6-months			1.8 ± 1.98	2.0 (0.5-3.0)		21
Khadivzadeh 2004 (97)	Respiratory Infection		EBF (6mo)			23/98			
			CF (after 4 mo)			35/95			
Forsyth 1993 (106)	Respiratory illness		<8	53-104 weeks		33 (82%)			
			8 to 12			194 (86%)			
			>12			149 (78.9%)			
Larsson 2008 (199)	Incidence of Doctor diagnosed rhinitis	Crude values	> 6mo					1 (reference)	1067
			3-6 mo					0.86 (0.65-1.14)	3510
			< 3mo					0.83 (0.25-2.73)	56
Cough									
Wilson 1998 (141)	Cough		>/= 15 weeks		Exclusive breast feeding for >/=15 weeks			(10.3 to 11.7)	70
			< 15 weeks		Exclusive breast feeding for >/=15 weeks			(10.3 to 12.6)	71
			>/= 15 weeks		Partial breast feeding (<15 weeks)			(19.3 to 22.7)	44
			< 15 weeks		Partial breast feeding (<15 weeks)			(21.5 to 23.5)	159
			>/= 15 weeks		Bottle feeding			(20.8 to 26.2)	30
			< 15 weeks		Bottle feeding			(23.7 to 25.9)	171
Forsyth 1993 (106)	Persistent cough		<8			18 (43.2%)			
	Persistent cough		8 to 12			102 (44.4%)			
	Persistent cough		>12			68 (36.8%)			
Diarrhea									
Kalanda 2006 (55)	Diarrhoea	Incidence per person (95% CI)	Early: before 3 months of age	162.7 person years				0.87 (0.73, 1.01)	196
		Incidence per person (95% CI)	Late: after 3 months	232.4 person years				0.73 (0.62, 0.84)	262

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
Khadivzadeh 2004 (97)	Diarrhea		EBF (6mo)			11/98			
			CF (4-6mo)			27/95			
Dhami 2020 (166)	Diarrhea		CF < 6mo		National Estimate			1 (reference)	
			6-8mo		National Estimate			1.06 (0.92, 1.21)	
Mondal 1996 (90)	Diarrheal Episodes		</= 3mo	1 year	No episode	98/127			
			</= 3mo		1 episode	12/127			
			</= 3mo		2 episodes	13/127			
			</= 3mo		3+ episodes	4/127			
			>/= 4mo		No episode	18/21			
			>/= 4mo		1 episode	3/21			
			>/= 4mo		2 episodes	0/21			
			>/= 4mo		3+ episodes	0/21			
		Incidence rate ratio						3.02 (95% CI 1.043-8.802)	
Eaton-Evans 1987 (40)	Diarrhea/Vomiting		0-3 mo (no description given on timing)	0-3 mo		Breast milk: 0/23 Mixed: 0/14 Bottle: 3/20 Subtotal: 3/57			
			3-6 mo	3-6 mo		Breast milk: 5/44 Mixed: 1/32 Bottle: 12/34 Subtotal: 18/110			
			6-9 mo	6-9 mo		Breast milk: 2/10 Mixed: 6/43 Bottle: 8/55 Subtotal: 16/108			
			9-12 mo	9-12 mo		Mixed: 8/24 Bottle: 19/71 Subtotal: 27/95			
Brown 1989 (218)	Diarrhea	Incidence of Diarrhea	0-2 mo			3.04 (1777 observations)		RR 1.61	
			3-5 mo			2.63 (9280 observations)		RR 1.79	
			6-8 mo			2.59 (10154 observations)		RR 1.00	
			9-11 mo			2.88 (9450 observations)		RR 1.00	
		Prevalence of Diarrhea	0-2 mo			19.5 (347 days)		RR 2.57	
			3-5 mo			17.1 (1585 days)		RR 3.35	
			6-8mo			14.4 (1467 days)		RR 1.00	
			9-11 mo			14.9 (1411 days)		RR 1.00	
Popkin 1990 (231)	Diarrhea	Diarrheal Morbidity	Breast Milk + Nutritive Foods/Solids at 6 mo	At 6 mo	Urban			RR 10.61 (4.63, 16.60)	

Study Year	Outcome	Definition	Time of CF introduction	Age of outcome assessment	Subgroup	n/N (%) Mean +/- SD	Median (IQR)	OR/RR (95% CI)	n
			Breast Milk + Non-nutritive Liquid	At 6 mo	Urban			RR 3.18 (2.53 3.84)	
			Breast Milk + Nutritive Foods/Solids at 6 mo	At 6 mo	Rural			RR 4.73 (3.95, 5.52)	
			Breast Milk + Non-nutritive Liquid	At 6 mo	Rural			RR 2.21 (2.07 2.35)	
Fever									
Zhao 2016 (31)	Fever		<4mo	At mean age of 20.6 months		108/125			
			4-8 mo			291/412			
			>8mo			52/64			
Non-Communicable Diseases									
Crume 2014 (75)	Mean age of diagnosis of type 1 diabetes		<3 Months	9.4 ± 3.9 years		9.41±0.15			
			3–6 Months			9.42± 0.08			
			7–11 Months			9.38± 0.14			
			12 Months or more						
Savilahti 2009 (201)	Type 1 Diabetes		Introduction of vegetables Before 3.9 mo (< 4mo)	11.5 years		11/2230			
			Introduction of vegetables After 3.9 mo			22/2710			
			Introduction of cereals Before 5.01 mo			17/3008			
			Introduction of cereals After 5.01 mo			13/1671			
Anemia									
Al-Suhiemat 2020 (216)	Anemia	Hb 7–9.9 g/dl	<2 months			0%			
			2			11%			
			4			24%			
			6			12%			

Table 5: Developmental Outcomes from Studies not meta-analysed

Study Year	Outcome	Definition	Time of CF intro	Age of outcome assessment	n/N or Mean SD (n)	Median (IQR)
RCTs						
Gupta 2017 (13)	Neurodevelopment: MoDQ50=motor developmental quotient–50th centile	None	4 mo.	12 months of age	84·0 ± 15·4) (182)	
			6 mo.		83·8 ± 14·0 (184)	
	Neurodevelopment: MoDQ50<70		4 mo.		27/182	
			6 mo.		27/184	
	Neurodevelopment: MoDQ97=motor developmental quotient–97th centile		4 mo.		104·3 ± 18·6 (182)	
			6 mo.		102·6 ± 16·8 (184)	
	Neurodevelopment: MeDQ50 =mental developmental quotient–50th centile		4 mo.		89·0 ± 12·4 (181)	
			6 mo.		89·2 ± 11·5 (184)	
	Neurodevelopment: MeDQ50<70		4 mo.		12/181	
			6 mo.		12/182	
	Neurodevelopment: MeDQ97		4 mo.		108·7 ± 18·4 (181)	
			6 mo.		109·0 ± 14·9 (184)	
Dewey 1998 (2-8)	Raise head	Mean age achieved (mo.)	CF at 6 mo.	6 to 12 months	1.1 ± 0.7 (49)	
			SF at 4 mo.		1.3 ± 0.7 (47)	
			SF-M at 4 mo.		1.2 ± 0.6 (44)	
	Raise head and chest		CF at 6 mo.		1.8 ± 0.8 (49)	
			SF at 4 mo.		2.0 ± 1.0 (47)	
			SF-M at 4 mo.		1.8 ± 0.9 (44)	
	Roll over		CF at 6 mo.		2.9 ± 1.1 (49)	
			SF at 4 mo.		3.4 ± 1.4 (47)	
			SF-M at 4 mo.		2.9 ± 1.1 (44)	
	Crawl		CF at 6 mo.		6.3 ± 1.8 (49)	
			SF at 4 mo.		7.3 ± 1.7 (47)	
			SF-M at 4 mo.		7.2 ± 1.4 (44)	
	Sit, from lying position		CF at 6 mo.		7.0 ± 1.5 (49)	
			SF at 4 mo.		7.0 ± 1.2 (47)	
			SF-M at 4 mo.		6.8 ± 1.1 (44)	
	Stand with assistance		CF at 6 mo.			7.5 (n: 49)
			SF at 4 mo.			7.5 (n: 47)
			SF-M at 4 mo.			7 (n: 44)
	Pull to stand		CF at 6 mo.			8 (n: 49)
			SF at 4 mo.			8 (n: 47)
			SF-M at 4 mo.			8 (n: 44)
	Walk with assistance		CF at 6 mo.			8.5 (n: 49)
			SF at 4 mo.			9.5 (n: 47)
			SF-M at 4 mo.			9 (n: 44)
	Stand alone		CF at 6 mo.			10 (n: 49)
			SF at 4 mo.			10.5 (n: 47)
			SF-M at 4 mo.			10.5 (n: 44)
	Walk by 12 months		CF at 6 mo.	At 12 months of age	28/47	
			SF at 4 mo.		19/46	
			SF-M at 4 mo.		15/41	
Dewey 2004 (LBW) (5, 9-12)	Raise head	Mean age achieved (mo.)	CF at 6 mo.	6-12 months of age	1.0 ± 1.0 (56)	
			SF at 4 mo.		1.0 ± 0.6 (52)	
	Raise head and chest		CF at 6 mo.		1.9 ± 1.6 (56)	
			SF at 4 mo.		1.8 ± 1.3 (52)	
	Roll over		CF at 6 mo.		3.8 ± 2.0 (56)	
			SF at 4 mo.		3.8 ± 1.8 (52)	
	Crawl		CF at 6 mo.		6.8 ± 1.7 (56)	
			SF at 4 mo.		7.4 ± 1.9 (52)	
	Sit, from lying position		CF at 6 mo.		7.4 ± 1.6 (56)	
			SF at 4 mo.		8.0 ± 1.6 (52)	
	Stand with assistance	Median age achieved (mo.)	CF at 6 mo.			8.5 (n: 56)
			SF at 4 mo.			9 (n: 52)

	Pull to stand		CF at 6 mo.			9 (n: 56)
			SF at 4 mo.			9 (n: 52)
	Walk with assistance		CF at 6 mo.			9.5 (n: 56)
			SF at 4 mo.			9.5 (n: 52)
	Stand alone		CF at 6 mo.			11 (n: 56)
			SF at 4 mo.			11 (n: 52)
	Walk by 12 months		CF at 6 mo.	At 12 months of age	9/50	
			SF at 4 mo.		13/49	
Jonsdottir 2014 (14-18)	Parents with concerns according to PEDS at 30–35 months		CF at 4 mo.	at 30–35 months at 30–35 months	14/42	
			EBF at 6 mo.		15/36	
	Brigance Screens-II Total score at 30–35 months		CF at 4 mo.			86.0 (12.5) (n: 35)
			EBF at 6 mo.			86.5 (12.5) (n: 31)
	Brigance Screens-II Total score above cut off value		CF at 4 mo.		2/35	
			EBF at 6 mo.		4/31	
	Brigance Screens-II Score of predictive factors combined above cut off value		CF at 4 mo.		7/35	
			EBF at 6 mo.		3/31	
	Gross motor skills		CF at 4 mo.			6.0 (6.0) (n: 35)
			EBF at 6 mo.			6.0 (4.5) (n: 31)
	Fine motor skills		CF at 4 mo.			19.0 (3.0) (n: 35)
			EBF at 6 mo.			19.0 (3.0)(n: 31)
	Expressive and receptive language		CF at 4 mo.			40.5 (8.0) (n: 35)
			EBF at 6 mo.			42.0 (9.5) (n: 31)
Observational Studies						
Heinig 1993 (36)	Holds self-up on arms	Developmental stages (age in weeks) in Breastfed group	Early Solid < 26 weeks		5.4 ± 4.9	
			Late Solid > 26 weeks		4.4 ± 3.9	
	Rolls over front to back		Early Solid < 26 weeks		16.0 ± 5.6	
			Late Solid > 26 weeks		16.2 ± 5.3	
	Rolls over back to front		Early Solid < 26 weeks		19.6 ± 6.3	
			Late Solid > 26 weeks		24.6 ± 5.9	
	Creeping		Early Solid < 26 weeks		21.0 ± 7.6	
			Late Solid > 26 weeks		27.8 ± 6.7	
	Sits alone		Early Solid < 26 weeks		24.1 ± 3.7	
			Late Solid > 26 weeks		25.7 ± 6.3	
	Crawling		Early Solid < 26 weeks		29.9 ± 5.7	
			Late Solid > 26 weeks		37.9 ± 6.5	
	Sits from lying position		Early Solid < 26 weeks		30.9 ± 5.4	
			Late Solid > 26 weeks		37.2 ± 6.3	
	Pulls to stand		Early Solid < 26 weeks		30.9 ± 4.8	
			Late Solid > 26 weeks		37.2 ± 5.5	
	Cruising		Early Solid < 26 weeks		33.5 ± 5.6	
			Late Solid > 26 weeks		42.1 ± 6.2	

	Stands alone		Early Solid < 26 weeks		41.8 ± 5.8	
			Late Solid > 26 weeks		47.3 ± 5.7	
	Walking		Early Solid < 26 weeks		45.8 ± 4.9	
			Late Solid > 26 weeks		51.5 ± 6.0	
Metwally 2016 (66)	socio-emotional composite scores categories (Below Average)		Before six months		90/201	
			After six months		159/454	
	socio-emotional composite scores categories (Above Average)		Before six months		111/201	
			After six months		295/454	

SF-M: Introduction of solid food with maintenance of pre-intervention breastfeeding frequency; SF: Introduction of solid foods, with ad libitum breastfeeding; PEDS: Parent's Evaluation of Developmental Status questionnaire

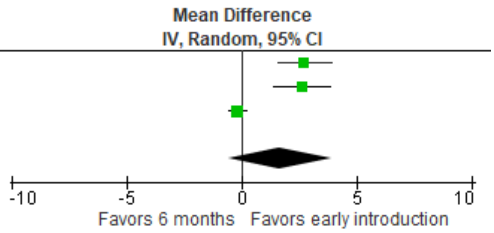
Figures: Forest Plots of Early Initiation of Complementary food

Comparison: Early introduction of CF (≤ four months of age) compared to six months of among normal term Infants (RCTs)

Outcome 1: Length

Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Dewey 1998 (1)	3.9	0.8	12	1.2	1.1	4	32.5%	2.70 [1.53, 3.87]
Dewey 1998 (2)	3.8	0.8	8	1.2	1.1	4	32.3%	2.60 [1.39, 3.81]
Dewey 2004 (3)	4.3	0.9	60	4.5	1.2	59	35.3%	-0.20 [-0.58, 0.18]
Total (95% CI)			**80**			**67**	**100.0%**	**1.64 [-0.59, 3.88]**

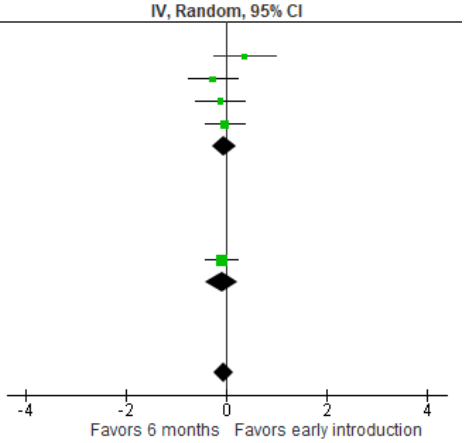
Heterogeneity: Tau² = 3.66; Chi² = 36.61, df = 2 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.44 (P = 0.15)



Footnotes
(1) (length gain (cm) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(2) (length gain (cm) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(3) gain in cm at 4 and 6mo

Outcome 2: Weight

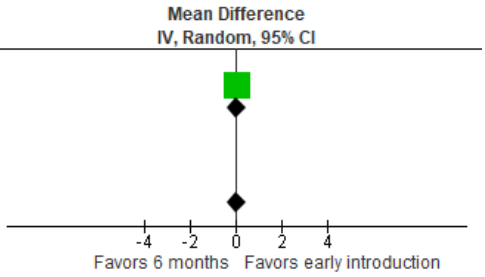
Study or Subgroup	Early introduction Mean	SD	Total	6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 At 4 mo vs. 6 mo								
Bainbridge 1996 (1)	1,360	459	23	1,223	203	18	9.6%	0.36 [-0.26, 0.99]
Dewey 1998 (2)	1,004	302	44	1,092	356	25	15.2%	-0.27 [-0.76, 0.22]
Dewey 1998 (3)	1,051	315	47	1,092	356	25	15.7%	-0.12 [-0.61, 0.36]
Jonsdottir 2014 b (4)	-0.02	0.31	50	-0.01	0.42	50	24.1%	-0.03 [-0.42, 0.37]
Subtotal (95% CI)			**164**			**118**	**64.6%**	**-0.05 [-0.29, 0.19]**
Heterogeneity: Tau² = 0.00; Chi² = 2.56, df = 3 (P = 0.46); I² = 0%								
Test for overall effect: Z = 0.41 (P = 0.68)								
1.2.2 Between 3 to 4 mo vs. 6 mo								
Kattelmann 2001 (5)	9,854	1,086.9	71	9,950	1,124.6	76	35.4%	-0.09 [-0.41, 0.24]
Subtotal (95% CI)			**71**			**76**	**35.4%**	**-0.09 [-0.41, 0.24]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.52 (P = 0.60)								
Total (95% CI)			**235**			**194**	**100.0%**	**-0.06 [-0.26, 0.13]**
Heterogeneity: Tau² = 0.00; Chi² = 2.59, df = 4 (P = 0.63); I² = 0%								
Test for overall effect: Z = 0.64 (P = 0.52)								
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.86), I² = 0%								



Footnotes
(1) Change in weight from 16 to 26 weeks (g)
(2) (weight gain (g) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(3) (weight gain (g) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(4) Weight gain from 4 to 6 mo (z score)
(5) at 12 months (g)

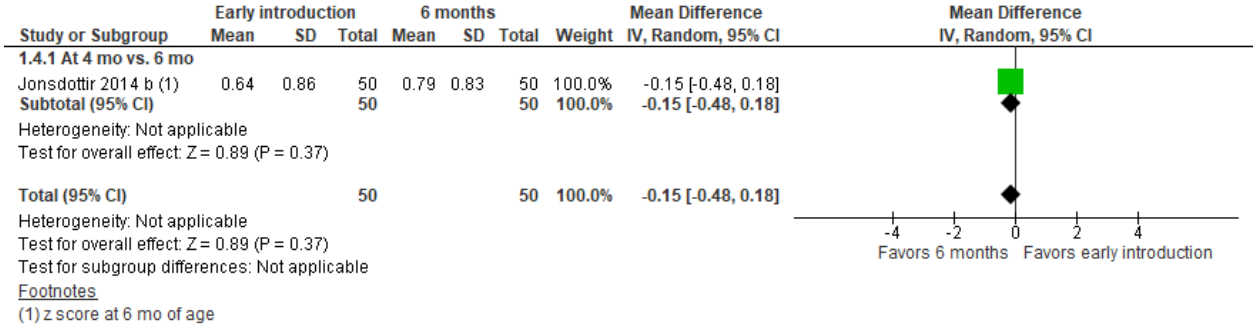
Outcome 3: BMI

Study or Subgroup	Early introduction Mean	SD	Total	6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 At 4 mo vs. 6 mo								
Jonsdottir 2014 b (1)	-0.08	1.14	50	-0.1	1.04	50	100.0%	0.02 [-0.41, 0.45]
Subtotal (95% CI)			**50**			**50**	**100.0%**	**0.02 [-0.41, 0.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.09 (P = 0.93)								
Total (95% CI)			**50**			**50**	**100.0%**	**0.02 [-0.41, 0.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.09 (P = 0.93)								
Test for subgroup differences: Not applicable								

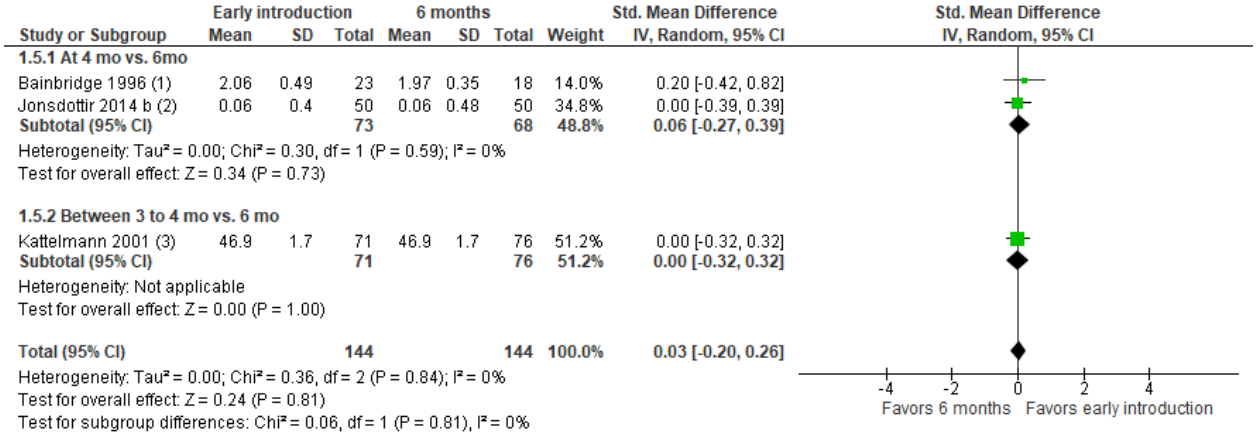


Footnotes
(1) z score at 6 mo of age

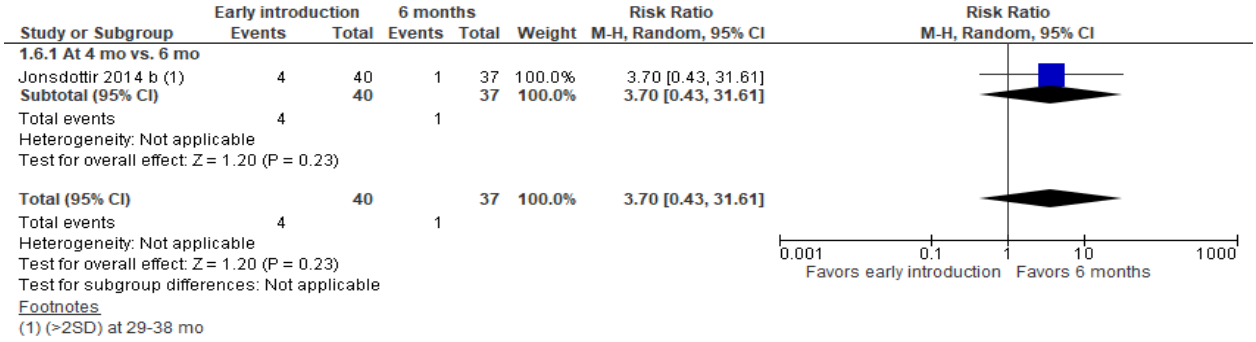
Outcome 4: BMI for age



Outcome 5: Head circumference/occipital frontal circumference (OFC)

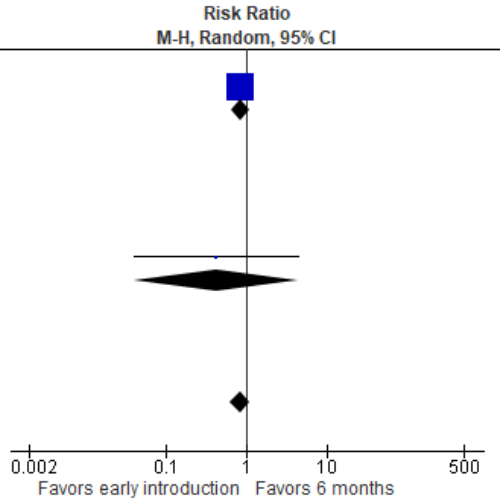


Outcome 6: Overweight



Outcome 7: Anemia

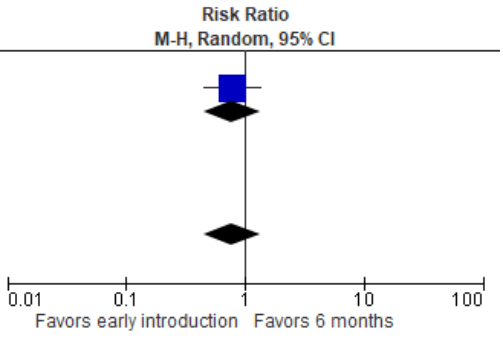
Study or Subgroup	Early introduction Events	Total	6 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 At 4 mo vs. 6 mo						
Dewey 1998 (1)	49	89	33	50	98.7%	0.83 [0.63, 1.10]
Subtotal (95% CI)		**89**		**50**	**98.7%**	**0.83 [0.63, 1.10]**
Total events	49		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						
1.6.2 Between 3 to 4 mo vs. 6 mo						
Kattelmann 2001 (2)	1	42	2	35	1.3%	0.42 [0.04, 4.40]
Subtotal (95% CI)		**42**		**35**	**1.3%**	**0.42 [0.04, 4.40]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						
Total (95% CI)		**131**		**85**	**100.0%**	**0.83 [0.63, 1.08]**
Total events	50		35			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
Test for subgroup differences: Chi² = 0.33, df = 1 (P = 0.57), I² = 0%						



Footnotes
(1) Hb <110g/l
(2) <110g/L at 36 months

Outcome 8: Severe anemia

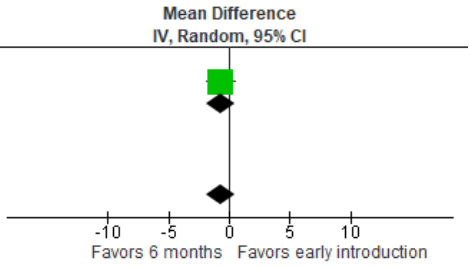
Study or Subgroup	Early introduction Events	Total	6 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 At 4 mo vs. 6 mo						
Dewey 1998 (1)	22	89	16	50	100.0%	0.77 [0.45, 1.33]
Subtotal (95% CI)		**89**		**50**	**100.0%**	**0.77 [0.45, 1.33]**
Total events	22		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)		**89**		**50**	**100.0%**	**0.77 [0.45, 1.33]**
Total events	22		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
Test for subgroup differences: Not applicable						



Footnotes
(1) Hb <103g/l

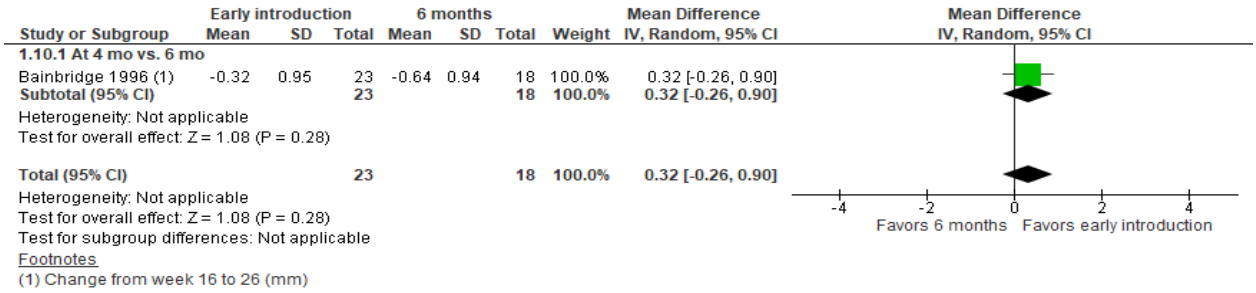
Outcome 9: Skin fold thickness (triceps)

Study or Subgroup	Early introduction Mean	SD	Total	6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.9.1 At 4 mo vs. 6 mo								
Bainbridge 1996 (1)	-0.17	1.69	23	0.55	2.02	18	100.0%	-0.72 [-1.88, 0.44]
Subtotal (95% CI)			**23**			**18**	**100.0%**	**-0.72 [-1.88, 0.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Total (95% CI)			**23**			**18**	**100.0%**	**-0.72 [-1.88, 0.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Test for subgroup differences: Not applicable								

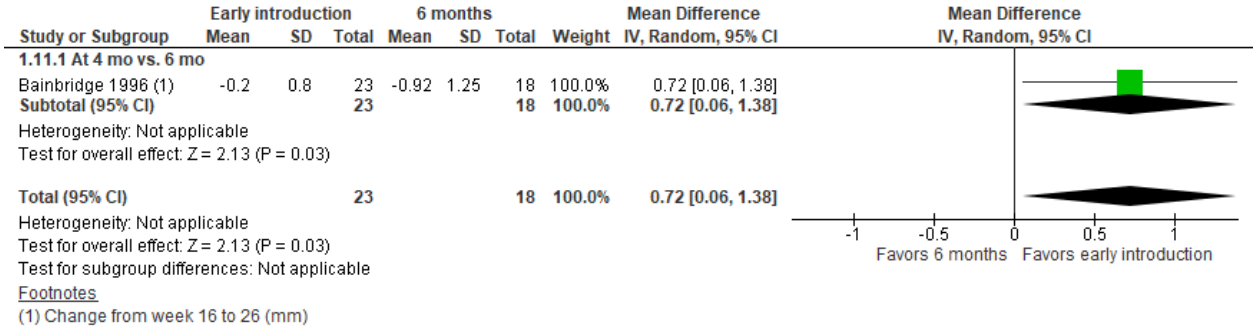


Footnotes
(1) Change from week 16 to 26 (mm)

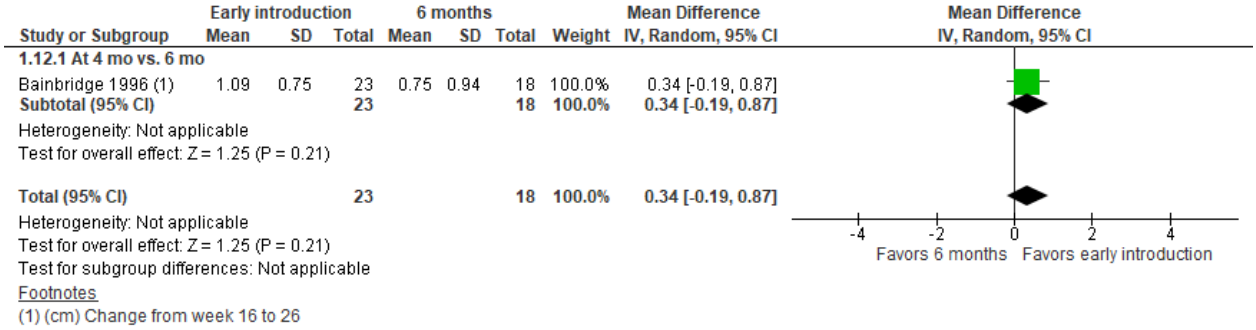
Outcome 10: Skin fold thickness (subscap)



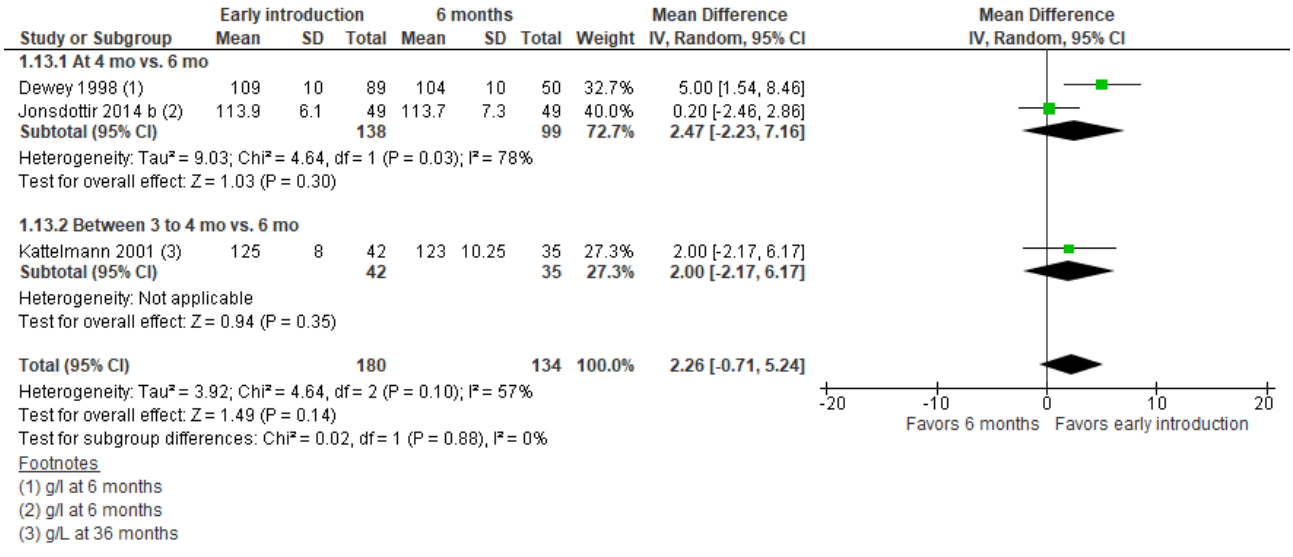
Outcome 11: Skin fold thickness (suprail)



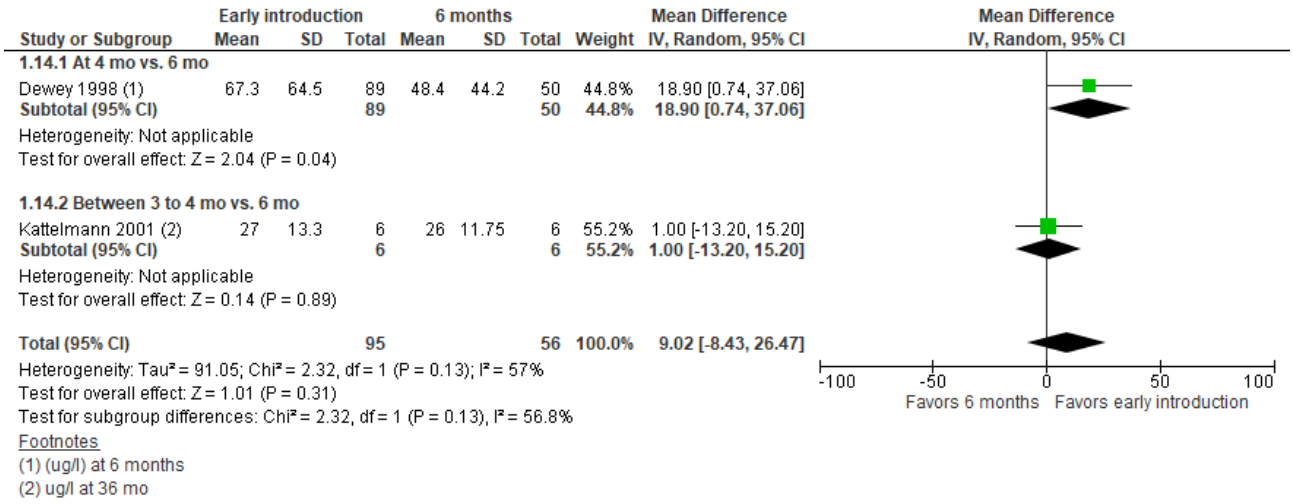
Outcome 12: MUAC



Outcome 13: Hb levels (g/l)



Outcome 14: Serum Ferritin (µg/L)

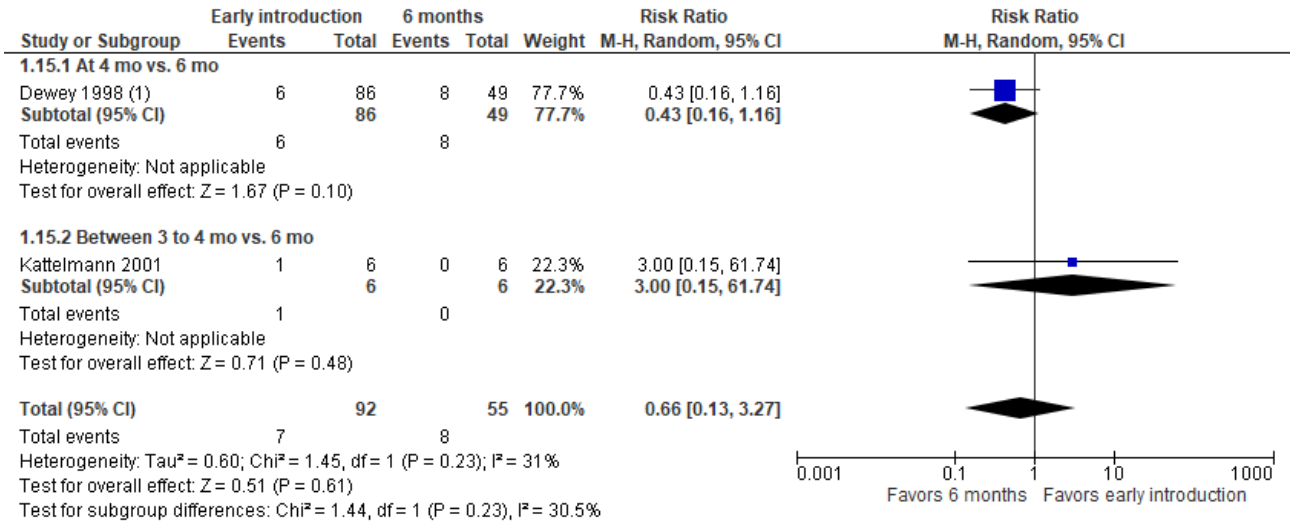


Footnotes

(1) (ug/l) at 6 months

(2) ug/l at 36 mo

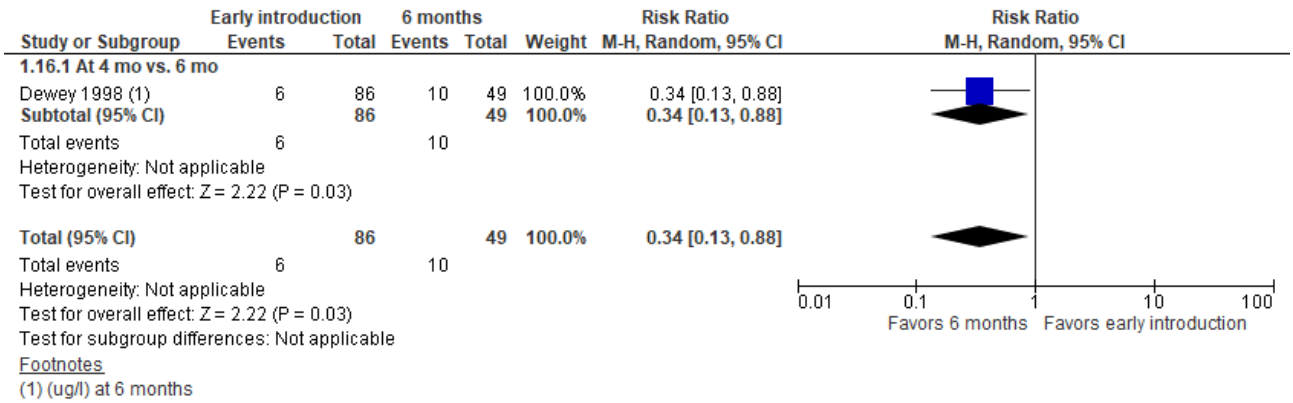
Outcome 15: Ferritin <12 µg/L



Footnotes

(1) (ug/l) at 6 months

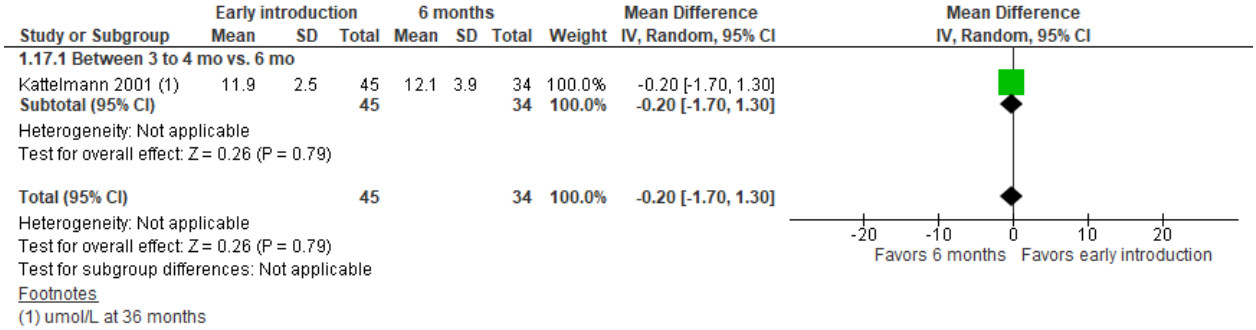
Outcome 16: Ferritin <15 µg/L



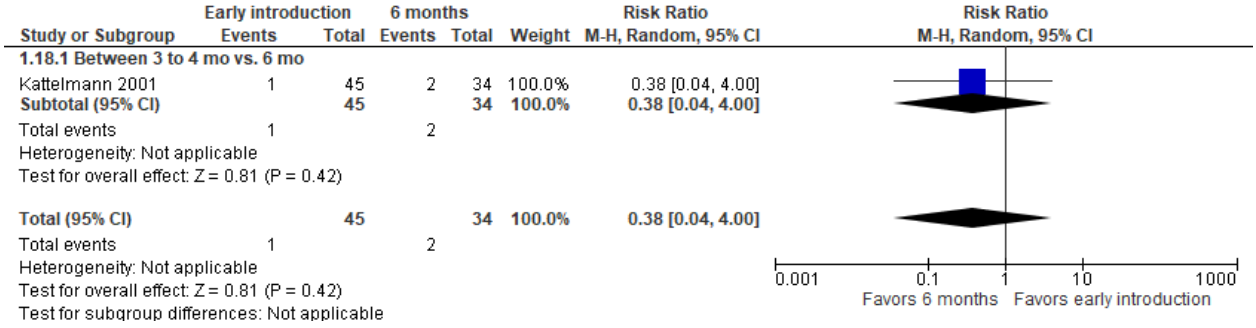
Footnotes

(1) (ug/l) at 6 months

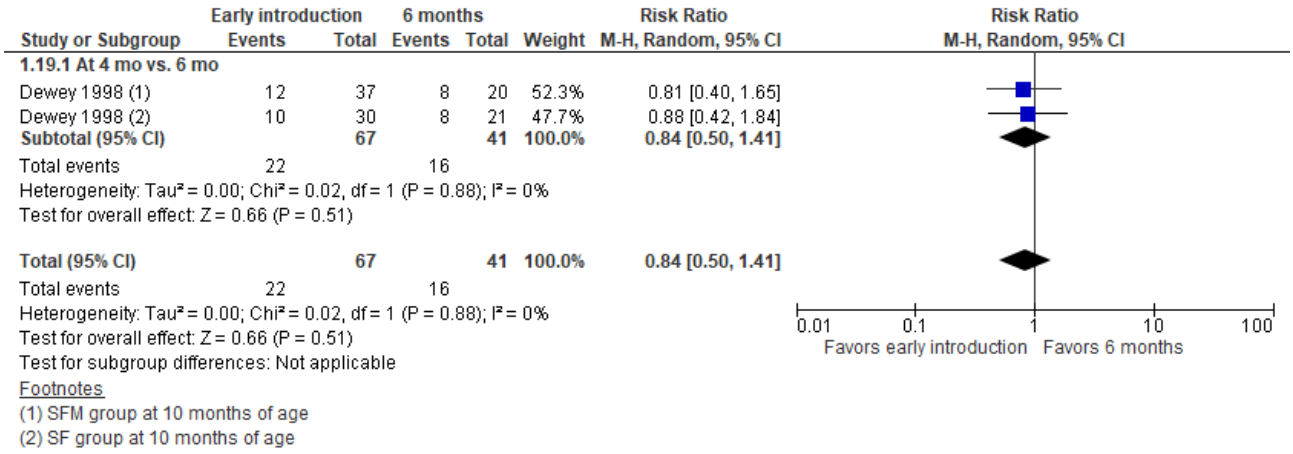
Outcome 17: Serum zinc levels



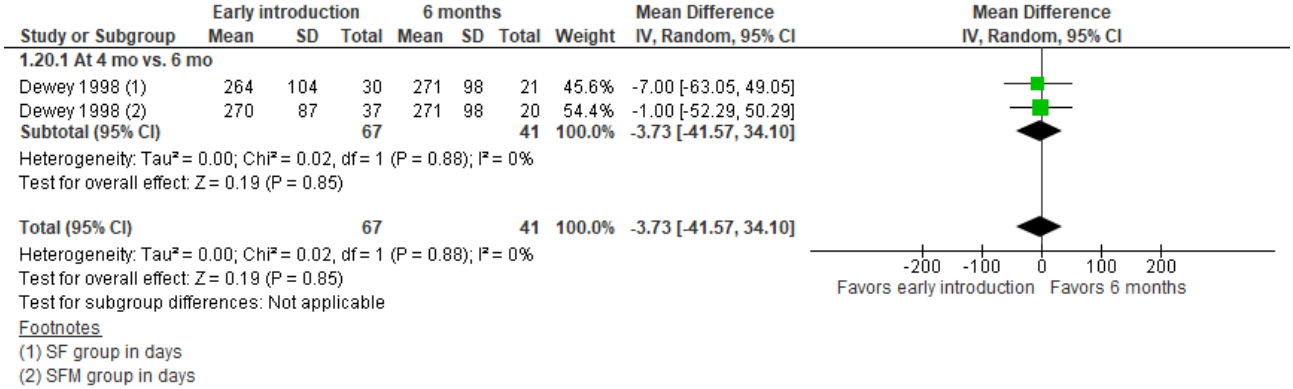
Outcome 18: Serum zinc <9.2 µmol/L



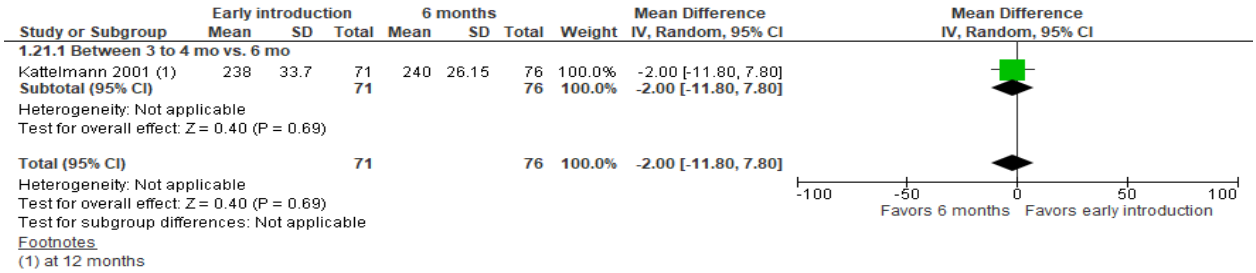
Outcome 19: Amenorrhea



Outcome 20: Duration of lactational amenorrhea

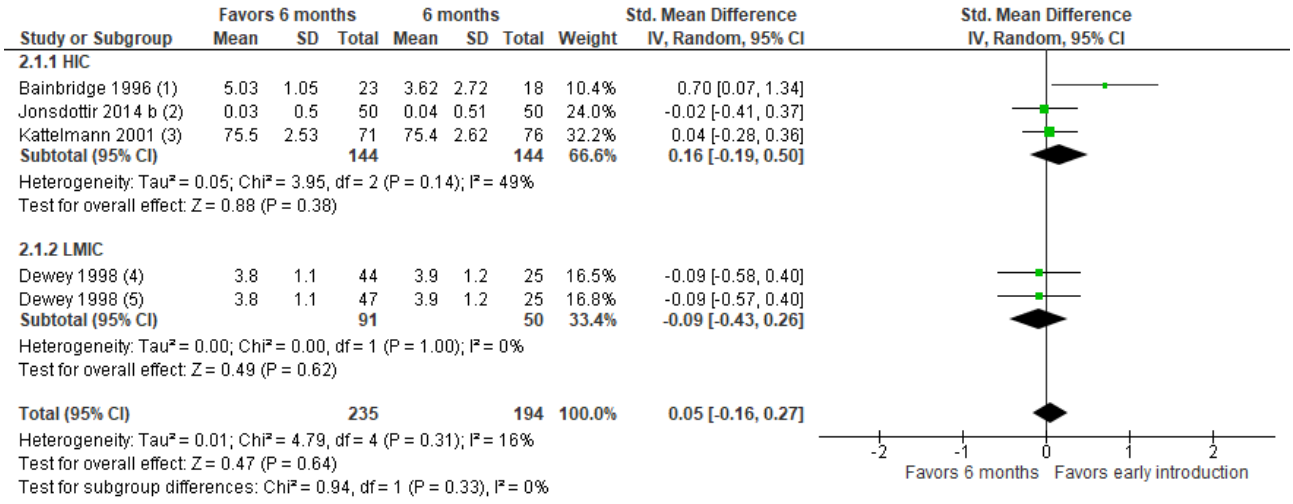


Outcome 21: BMC (g)

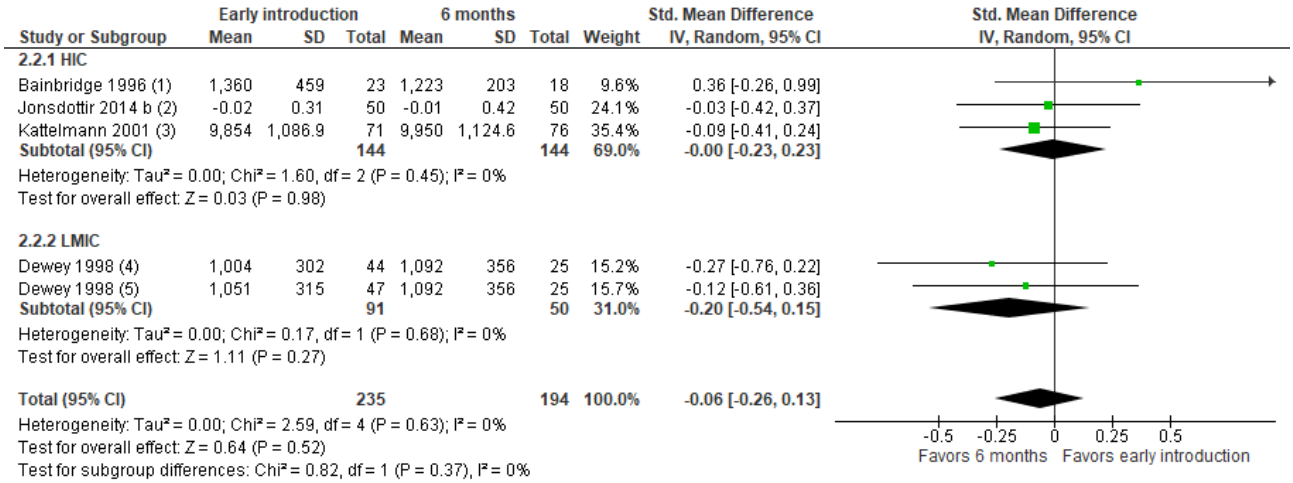


Comparison: Early introduction of CF (<four months of age) compared to six months of age among normal term Infants (RCTs)- subgroup by setting

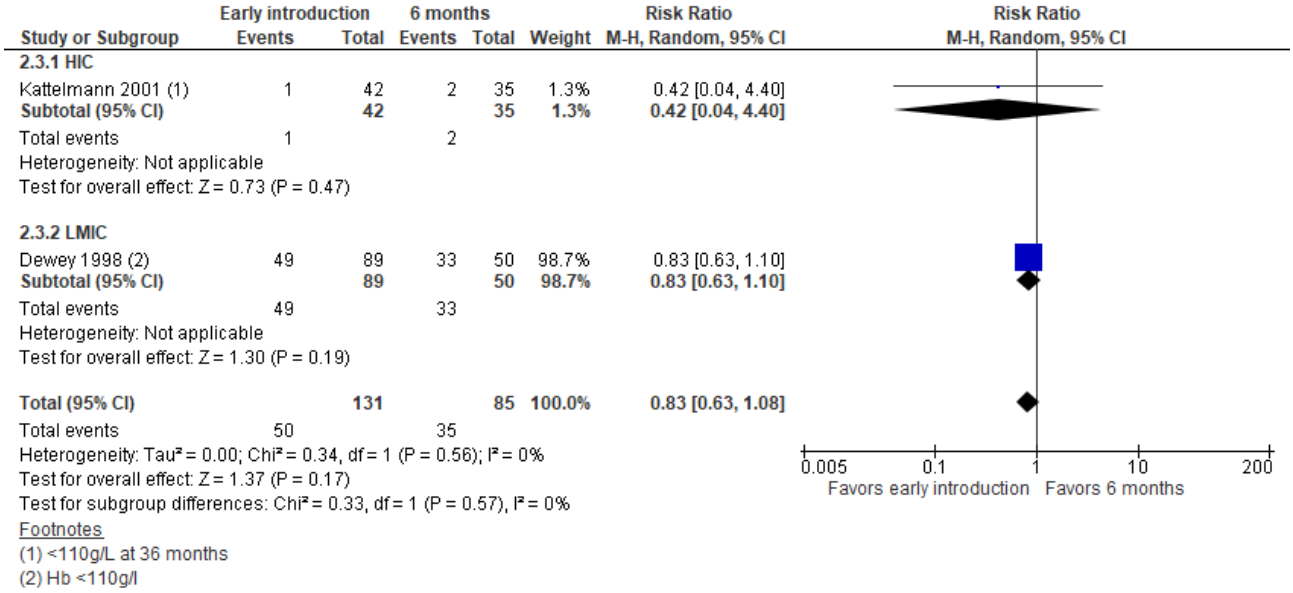
Outcome 1: Length



Outcome 2: Weight

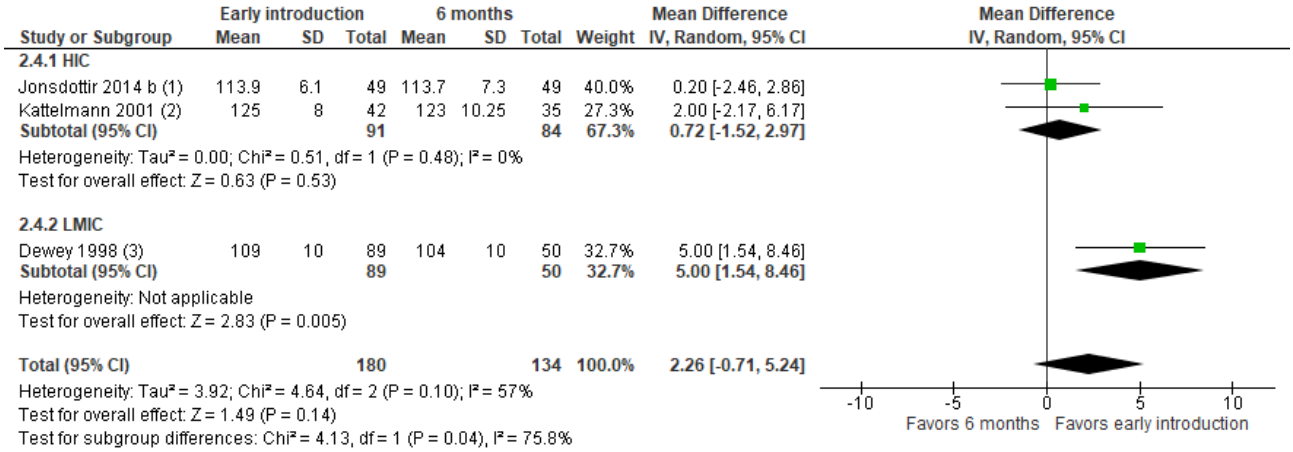


Outcome 3: Anemia



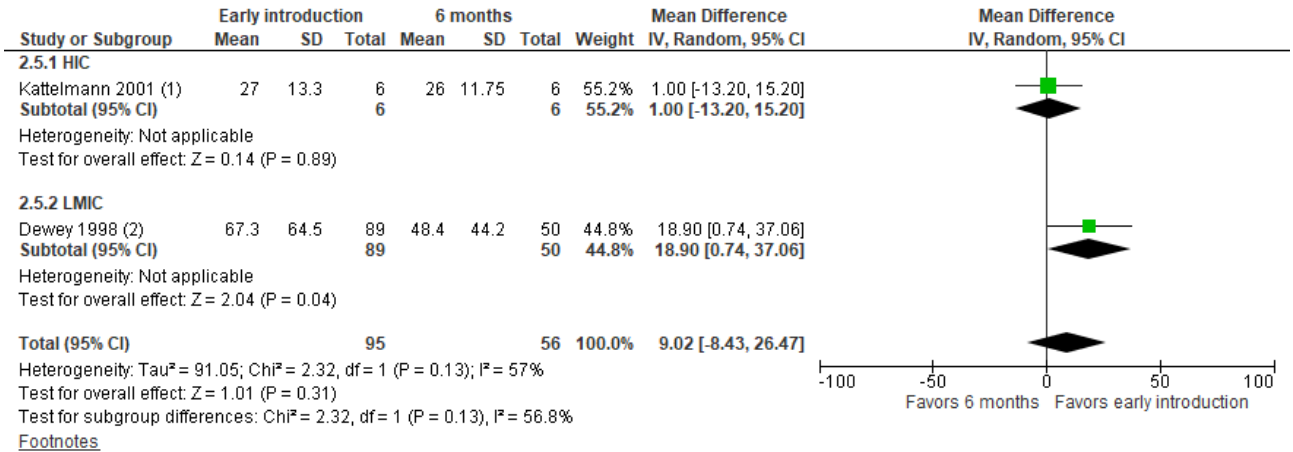
Footnotes
(1) <110g/L at 36 months
(2) Hb <110g/l

Outcome 4: Hb levels (g/l)



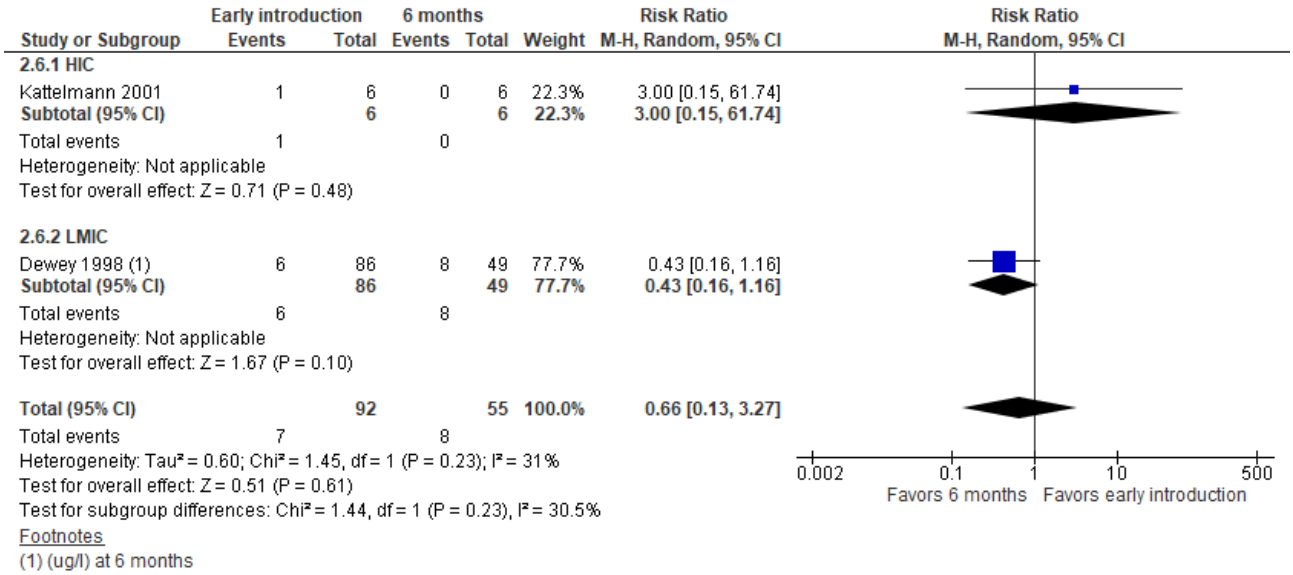
Footnotes
(1) g/l at 6 months
(2) g/L at 36 months
(3) g/l at 6 months

Outcome 5: Serum Ferritin (µg/L)



Footnotes
(1) ug/l at 36 mo
(2) (ug/l) at 6 months

Outcome 6: Ferritin <12 µg/L

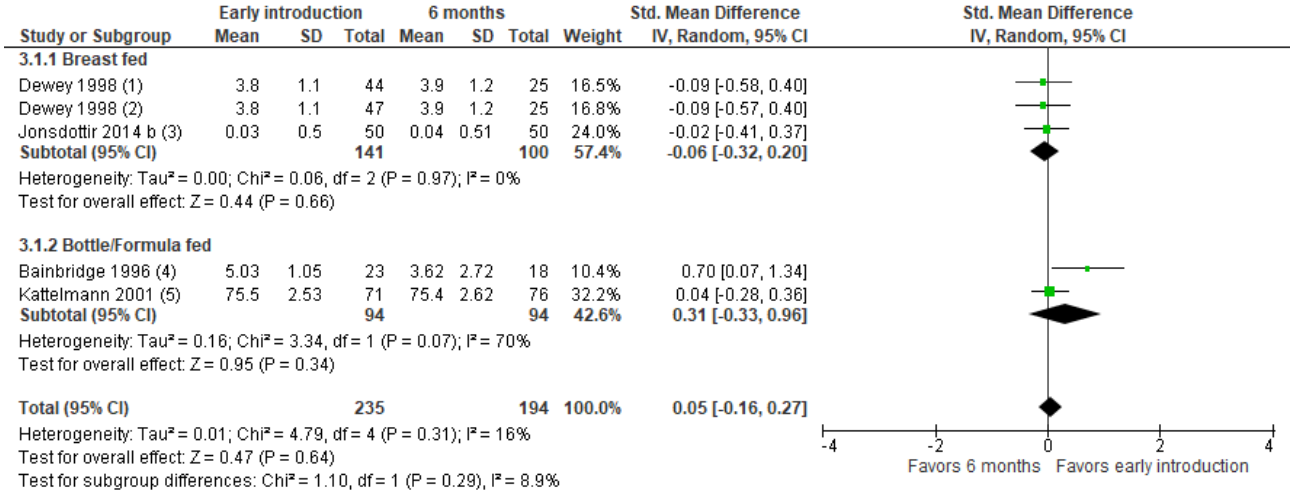


Footnotes

(1) (ug/l) at 6 months

Comparison: Early introduction of CF (≤ four months of age) compared to six months of age among normal term Infants (RCTs) - subgroup by feeding practices

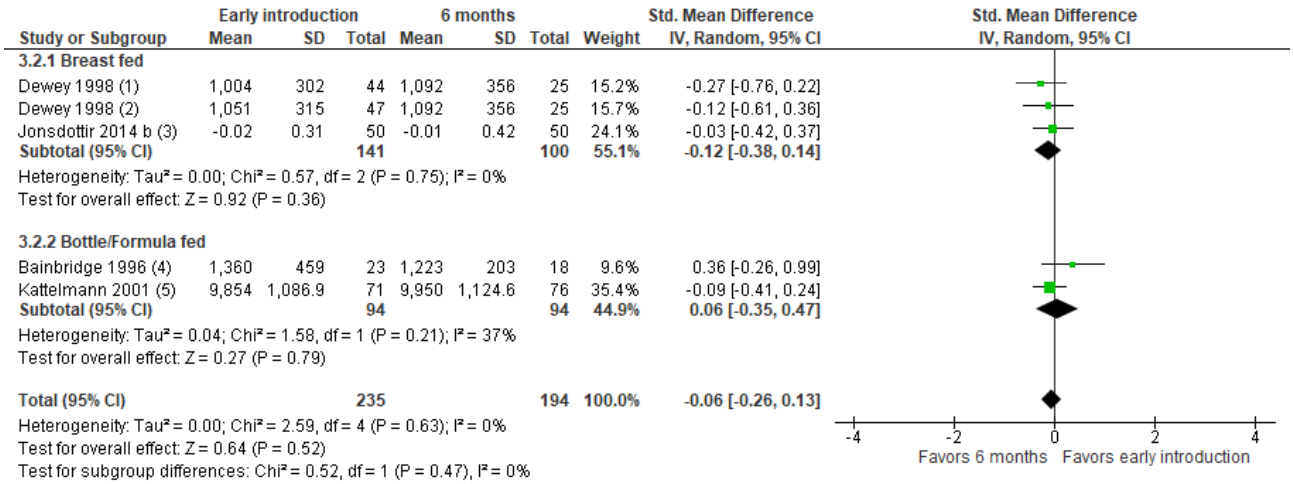
Outcome 1: Length



Footnotes

(1) (length gain (cm) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(2) (length gain (cm) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(3) length gain from 4 to 6 mo (z score)
(4) (change (cm) from 4 to 6mo)
(5) at 12 mo in cm

Outcome 2: Weight

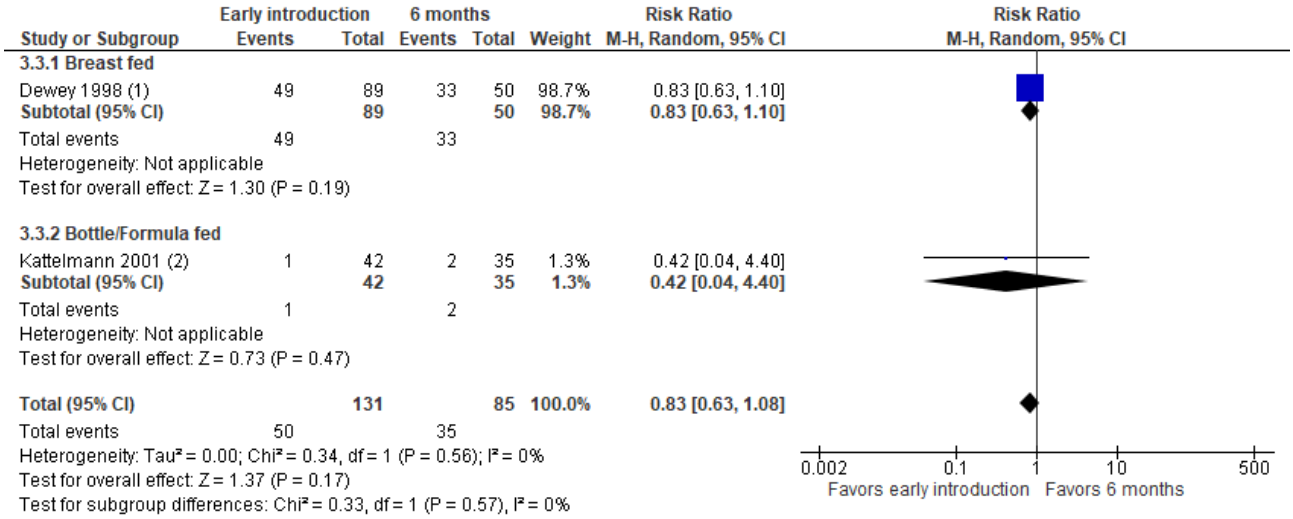


Study or Subgroup	Early introduction Mean	SD	Total	6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.2.1 Breast fed								
Dewey 1998 (1)	1,004	302	44	1,092	356	25	15.2%	-0.27 [-0.76, 0.22]
Dewey 1998 (2)	1,051	315	47	1,092	356	25	15.7%	-0.12 [-0.61, 0.36]
Jonsdottir 2014 b (3)	-0.02	0.31	50	-0.01	0.42	50	24.1%	-0.03 [-0.42, 0.37]
Subtotal (95% CI)			**141**			**100**	**55.1%**	**-0.12 [-0.38, 0.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 2 (P = 0.75); I² = 0%								
Test for overall effect: Z = 0.92 (P = 0.36)								
3.2.2 Bottle/Formula fed								
Bainbridge 1996 (4)	1,360	459	23	1,223	203	18	9.6%	0.36 [-0.26, 0.99]
Kattelmann 2001 (5)	9,854	1,086.9	71	9,950	1,124.6	76	35.4%	-0.09 [-0.41, 0.24]
Subtotal (95% CI)			**94**			**94**	**44.9%**	**0.06 [-0.35, 0.47]**
Heterogeneity: Tau² = 0.04; Chi² = 1.58, df = 1 (P = 0.21); I² = 37%								
Test for overall effect: Z = 0.27 (P = 0.79)								
Total (95% CI)			**235**			**194**	**100.0%**	**-0.06 [-0.26, 0.13]**
Heterogeneity: Tau² = 0.00; Chi² = 2.59, df = 4 (P = 0.63); I² = 0%								
Test for overall effect: Z = 0.64 (P = 0.52)								
Test for subgroup differences: Chi² = 0.52, df = 1 (P = 0.47), I² = 0%								

Footnotes

(1) (weight gain (g) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(2) (weight gain (g) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(3) Weight gain from 4 to 6 mo (z score)
(4) Change in weight from 16 to 26 weeks (g)
(5) at 12 months (g)

Outcome 3: Anemia

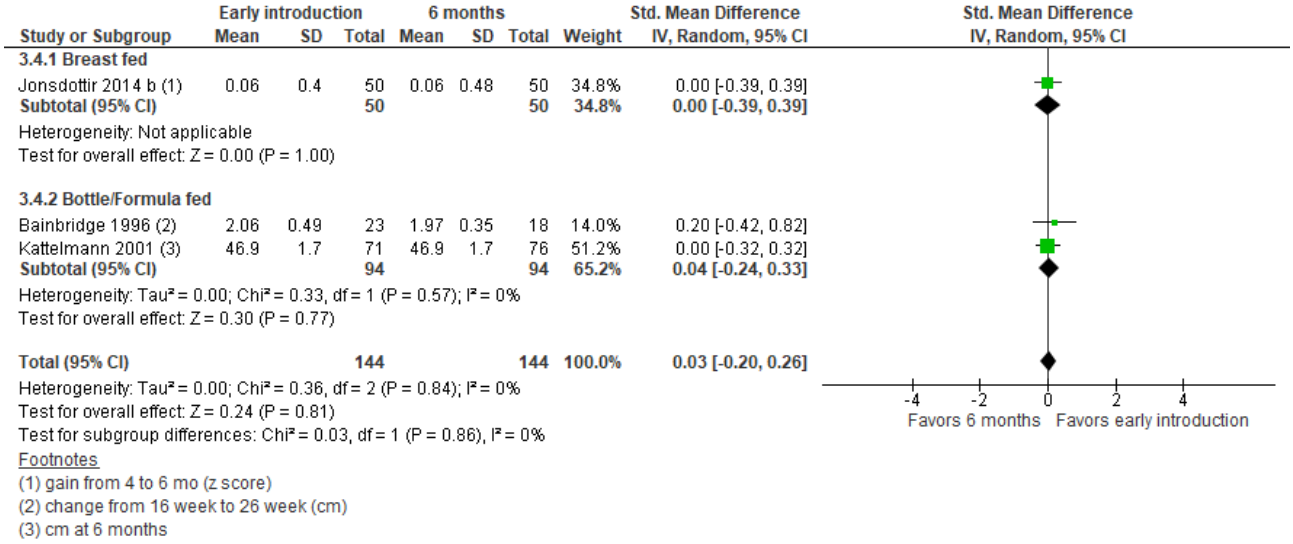


Study or Subgroup	Early introduction Events	Total	6 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.3.1 Breast fed						
Dewey 1998 (1)	49	89	33	50	98.7%	0.83 [0.63, 1.10]
Subtotal (95% CI)		**89**		**50**	**98.7%**	**0.83 [0.63, 1.10]**
Total events	49		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						
3.3.2 Bottle/Formula fed						
Kattelmann 2001 (2)	1	42	2	35	1.3%	0.42 [0.04, 4.40]
Subtotal (95% CI)		**42**		**35**	**1.3%**	**0.42 [0.04, 4.40]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						
Total (95% CI)		**131**		**85**	**100.0%**	**0.83 [0.63, 1.08]**
Total events	50		35			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
Test for subgroup differences: Chi² = 0.33, df = 1 (P = 0.57), I² = 0%						

Footnotes

(1) Hb <110g/l
(2) <110g/L at 36 months

Outcome 4: Head circumference



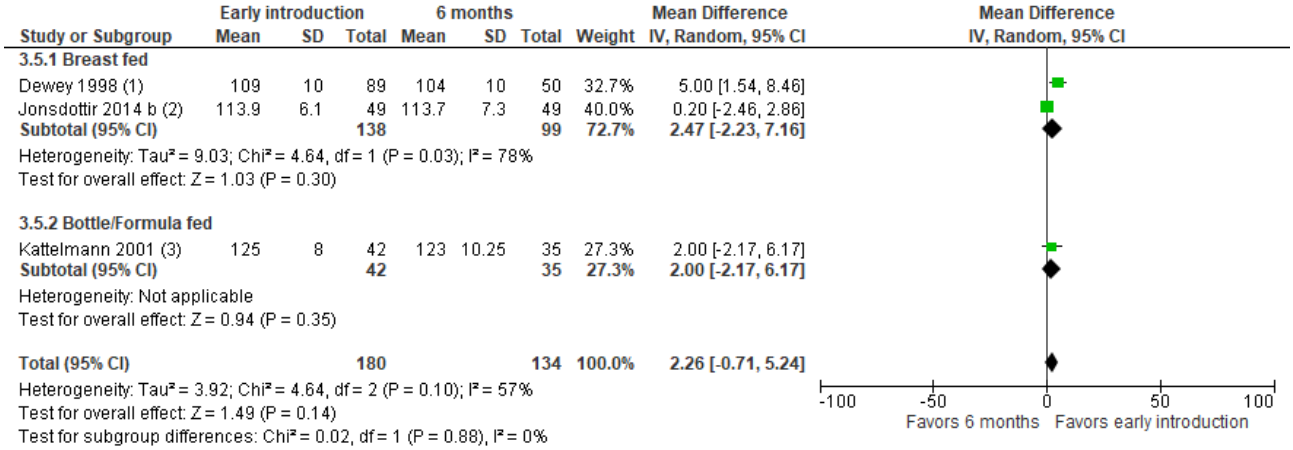
Footnotes

(1) gain from 4 to 6 mo (z score)

(2) change from 16 week to 26 week (cm)

(3) cm at 6 months

Outcome 5: Hb levels



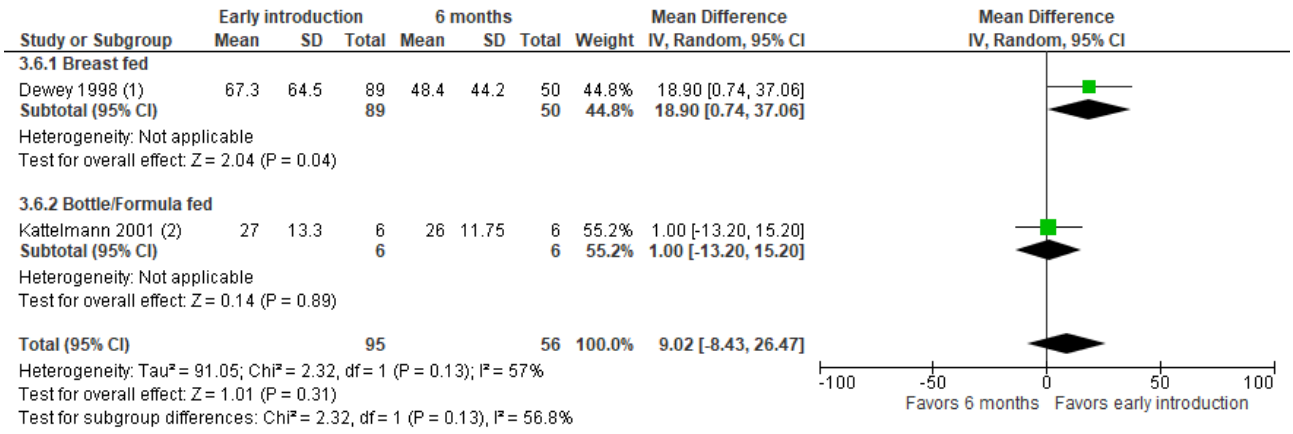
Footnotes

(1) g/l at 6 months

(2) g/l at 6 months

(3) g/L at 36 months

Outcome 6: Serum Ferritin (µg/L)

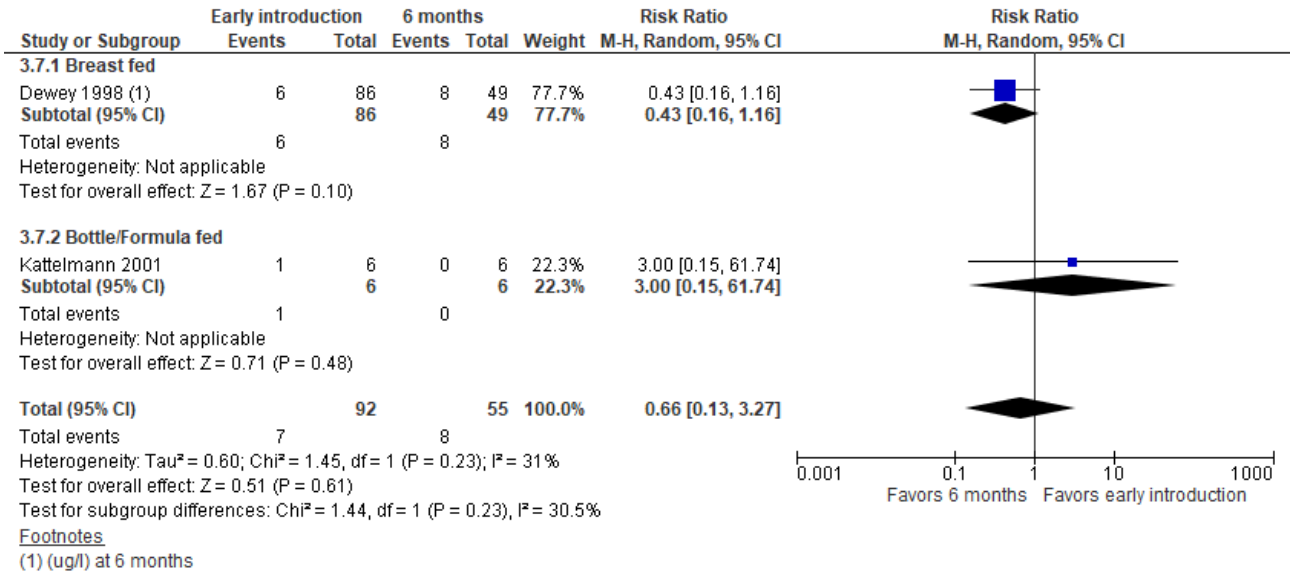


Footnotes

(1) (ug/l) at 6 months

(2) ug/l at 36 mo

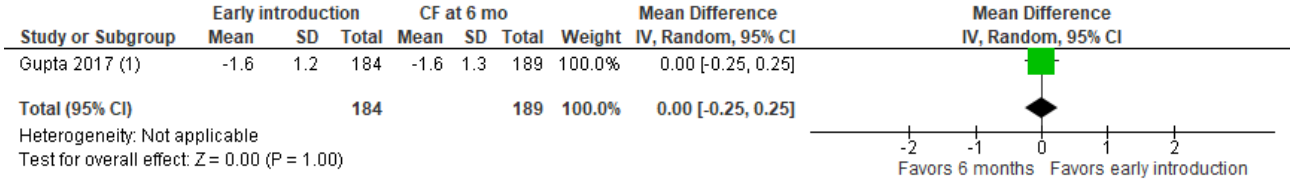
Outcome 6: Ferritin (<12 µg/L)



Footnotes
(1) (ug/l) at 6 months

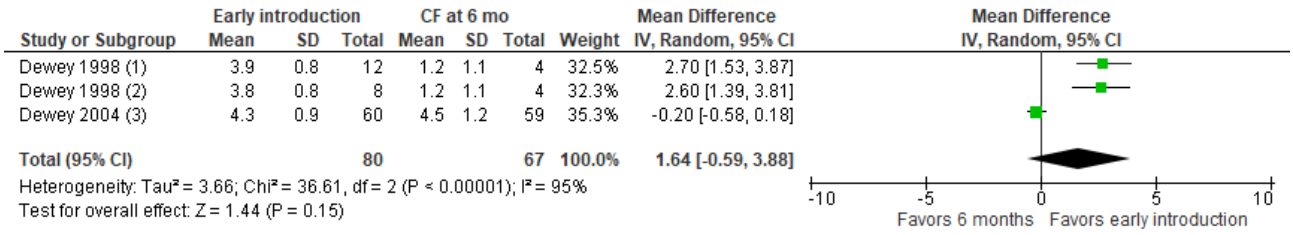
Comparison: Early introduction of CF (at four months of age) compared to six months of age among LBW/Preterm/SGA Infants (RCTs)

Outcome 1: Weight for age Z-score



Footnotes
(1) Based on WHO MGRS growth standards at 12 months of age

Outcome 2: Length

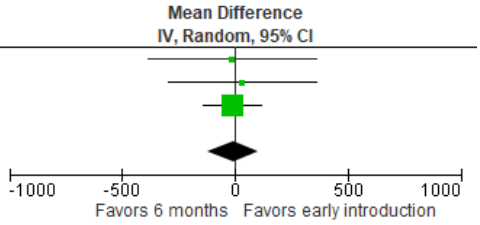


Footnotes
(1) (length gain (cm) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(2) (length gain (cm) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(3) gain in cm at 4 and 6mo

Outcome 3: Weight

Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Dewey 1998 (1)	994	273	8	1,008	326	4	9.4%	-14.00 [-385.28, 357.28]
Dewey 1998 (2)	1,038	134	12	1,008	326	4	12.1%	30.00 [-298.35, 358.35]
Dewey 2004 (3)	1,004	366	60	1,017	350	59	78.5%	-13.00 [-141.66, 115.66]
Total (95% CI)			**80**			**67**	**100.0%**	**-7.91 [-121.91, 106.09]**

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.14 (P = 0.89)

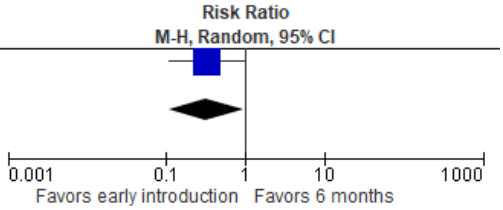


Footnotes
(1) (weight gain (g) 4-6mo of age) SF group: Introduction of solid foods, with ad libitum breastfeeding
(2) (weight gain (g) 4-6mo of age) Introduction of solid foods (SF-M), with maintenance of pre-intervention breastfeeding frequency.
(3) gain in grams at 4 and 6mo

Outcome 4: Severe Anemia

Study or Subgroup	Early introduction Events	Total	CF at 6 mo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Dewey 2004 (1)	4	59	12	57	100.0%	0.32 [0.11, 0.94]
Total (95% CI)		**59**		**57**	**100.0%**	**0.32 [0.11, 0.94]**
Total events	4		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.07 (P = 0.04)

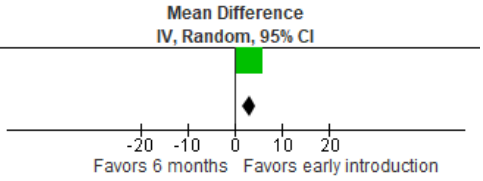


Footnotes
(1) at 4 and 6 mo

Outcome 5: Hb levels

Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Dewey 2004 (1)	111.16	1.5	59	108.08	5.2	57	100.0%	3.08 [1.68, 4.48]
Total (95% CI)			**59**			**57**	**100.0%**	**3.08 [1.68, 4.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.30 (P < 0.0001)

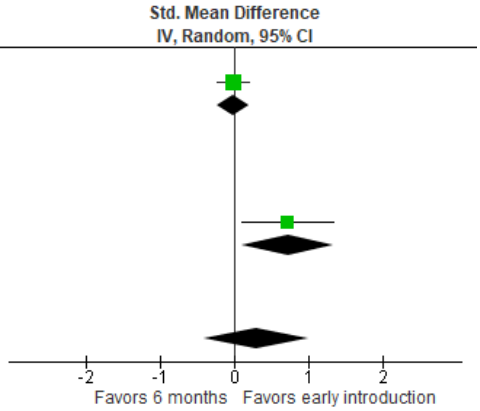


Footnotes
(1) g/l at 4 and 6 mo

Outcome 6: Serum Ferritin (ug/dl)

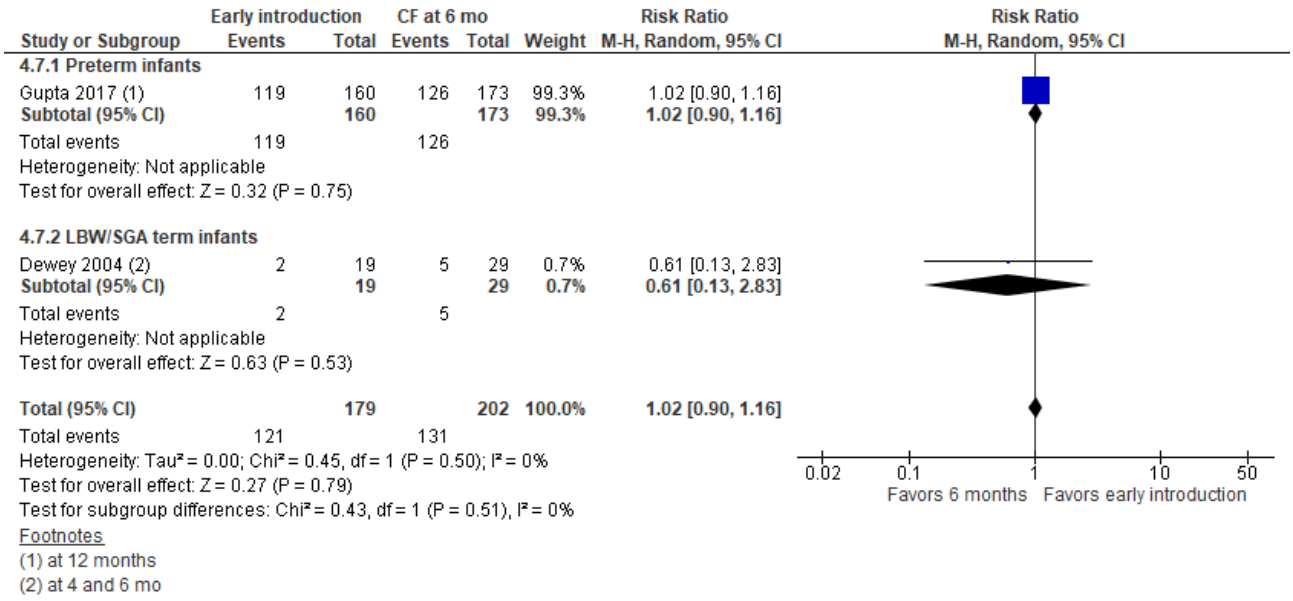
Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.6.1 Preterm infants								
Gupta 2017 (1)	7	6.9	160	7.1	8.07	173	58.1%	-0.01 [-0.23, 0.20]
Subtotal (95% CI)			**160**			**173**	**58.1%**	**-0.01 [-0.23, 0.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.12 (P = 0.90)								
4.6.2 LBW/SGA term infants								
Dewey 2004 (2)	40.93	2.5	18	30.52	18.24	27	41.9%	0.72 [0.10, 1.33]
Subtotal (95% CI)			**18**			**27**	**41.9%**	**0.72 [0.10, 1.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.28 (P = 0.02)								
Total (95% CI)			**178**			**200**	**100.0%**	**0.29 [-0.41, 1.00]**

Heterogeneity: Tau² = 0.21; Chi² = 4.81, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 0.81 (P = 0.42)
Test for subgroup differences: Chi² = 4.81, df = 1 (P = 0.03), I² = 79.2%



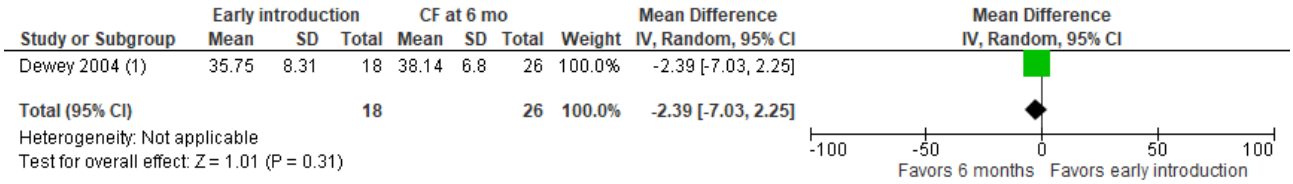
Footnotes
(1) (ug/dl) at 12 months
(2) (ug/l) at 4 and 6 months

Outcome 7: Ferritin <12 µg/L



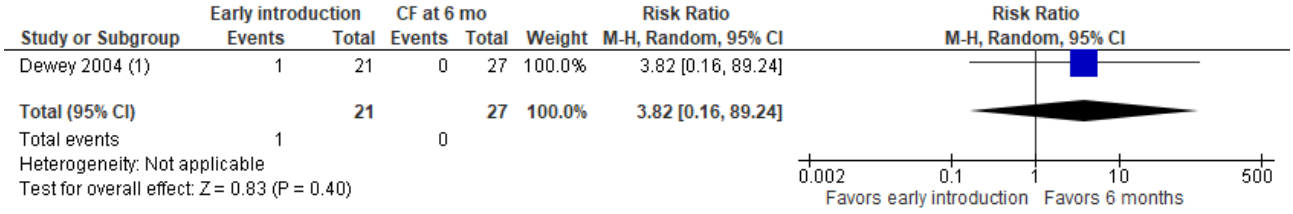
Footnotes
(1) at 12 months
(2) at 4 and 6 mo

Outcome 8: Percentage Transferrin Saturation



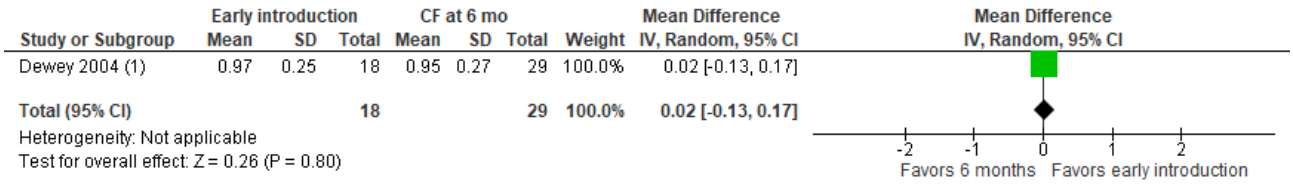
Footnotes
(1) at 4 and 6 mo

Outcome 9: Percentage Transferrin Saturation (<12%)



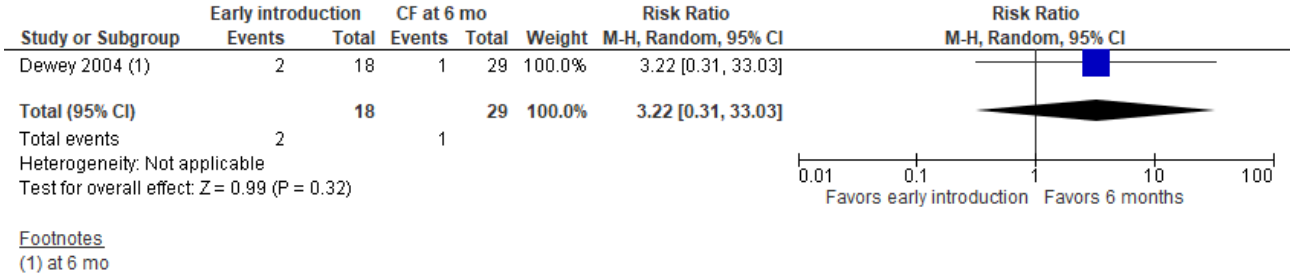
Footnotes
(1) at 4 and 6 mo

Outcome 10: Plasma Vitamin A



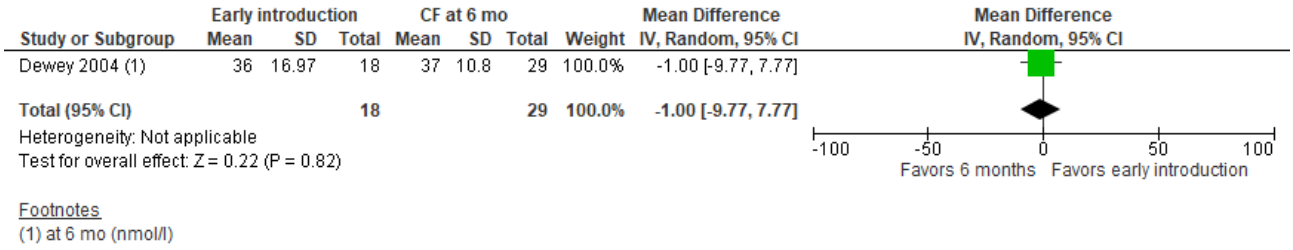
Footnotes
(1) at 6 mo (umol/l)

Outcome 11: Plasma Vitamin A (% <0.7 µmol/l)



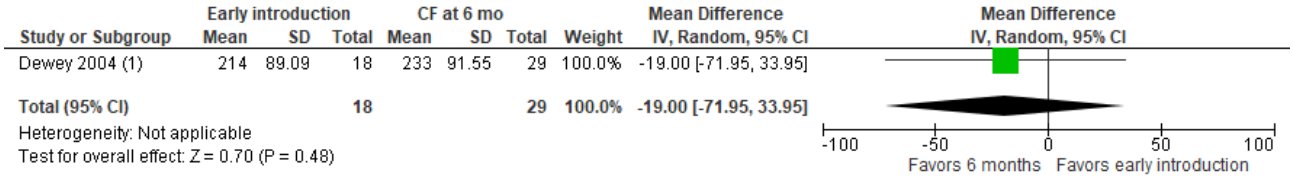
Footnotes
(1) at 6 mo

Outcome 12: Plasma Folate



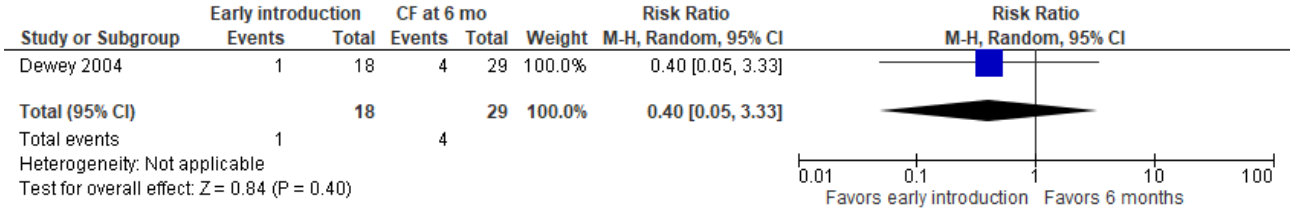
Footnotes
(1) at 6 mo (nmol/l)

Outcome 13: Plasma Vitamin B12

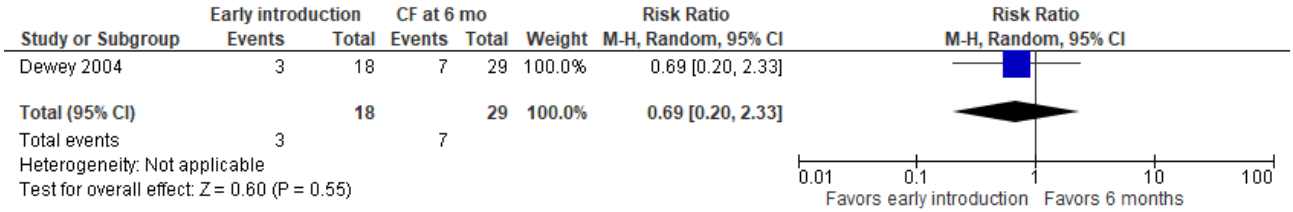


Footnotes
(1) pmol/l at 6 months

Outcome 15: Plasma Vitamin B12 (% <96 pmol/l)



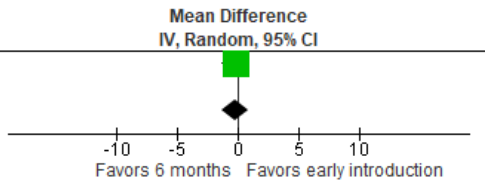
Outcome 16: Plasma Vitamin B12 (% <136 pmol/l)



Outcome 17: Plasma zinc

Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Dewey 2004 (1)	11.4	1.7	18	11.6	2.08	27	100.0%	-0.20 [-1.31, 0.91]
Total (95% CI)			**18**			**27**	**100.0%**	**-0.20 [-1.31, 0.91]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.35 (P = 0.72)

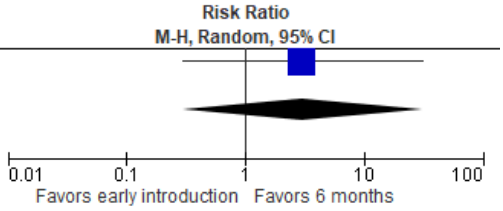


Footnotes
(1) umol/l at 6 months

Outcome 18: Plasma zinc (% <9.2 µmol/l)

Study or Subgroup	Early introduction Events	Total	CF at 6 mo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Dewey 2004 (1)	2	18	1	27	100.0%	3.00 [0.29, 30.69]
Total (95% CI)		**18**		**27**	**100.0%**	**3.00 [0.29, 30.69]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)



Footnotes
(1) at 6 mo

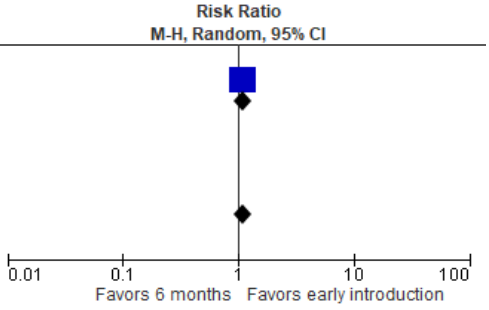
Outcome 19: Acceptable minimum dietary diversity

Study or Subgroup	Early introduction Events	Total	6 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.6.1 At 4 mo vs. 6 mo						
Gupta 2017 (1)	110	183	104	189	100.0%	1.09 [0.92, 1.30]
Subtotal (95% CI)		**183**		**189**	**100.0%**	**1.09 [0.92, 1.30]**
Total events	110		104			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)

Total (95% CI)		**183**		**189**	**100.0%**	**1.09 [0.92, 1.30]**
Total events	110		104			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)
Test for subgroup differences: Not applicable

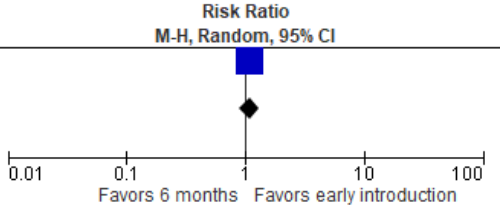


Footnotes
(1) Proportion of infants receiving food from 4 or more food groups

Outcome 20: Acceptable minimum diet

Study or Subgroup	Early introduction Events	Total	CF at 6 mo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gupta 2017 (1)	108	184	103	189	100.0%	1.08 [0.90, 1.29]
Total (95% CI)		**184**		**189**	**100.0%**	**1.08 [0.90, 1.29]**
Total events	108		103			

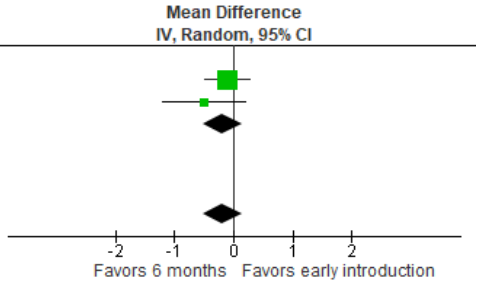
Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)



Footnotes
(1) %

Outcome 21: Meal frequency

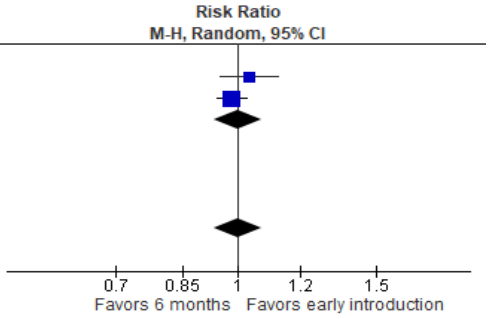
Study or Subgroup	Early introduction Mean	SD	Total	6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.7.1 At 4 mo vs. 6 mo								
Gupta 2017 (1)	4.2	1.4	123	4.3	1.6	118	77.5%	-0.10 [-0.48, 0.28]
Gupta 2017 (2)	8.5	2.1	60	9	2	71	22.5%	-0.50 [-1.21, 0.21]
Subtotal (95% CI)			**183**			**189**	**100.0%**	**-0.19 [-0.52, 0.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 1 (P = 0.33); I² = 0%								
Test for overall effect: Z = 1.11 (P = 0.27)								
Total (95% CI)			**183**			**189**	**100.0%**	**-0.19 [-0.52, 0.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 1 (P = 0.33); I² = 0%								
Test for overall effect: Z = 1.11 (P = 0.27)								
Test for subgroup differences: Not applicable								



Footnotes
(1) Breastfed infants (only liquid feeds)
(2) Non-breastfed infants (including both milk, solid and semisolid feeds)

Outcome 22: Acceptable minimum meal frequency

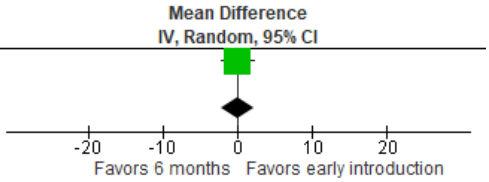
Study or Subgroup	Early introduction Events	Total	6 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.8.1 At 4 mo vs. 6 mo						
Gupta 2017 (1)	112	123	104	118	36.3%	1.03 [0.95, 1.13]
Gupta 2017 (2)	59	60	71	71	63.7%	0.98 [0.94, 1.03]
Subtotal (95% CI)		**183**		**189**	**100.0%**	**1.00 [0.93, 1.07]**
Total events	171		175			
Heterogeneity: Tau² = 0.00; Chi² = 2.13, df = 1 (P = 0.14); I² = 53%						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**183**		**189**	**100.0%**	**1.00 [0.93, 1.07]**
Total events	171		175			
Heterogeneity: Tau² = 0.00; Chi² = 2.13, df = 1 (P = 0.14); I² = 53%						
Test for overall effect: Z = 0.01 (P = 0.99)						
Test for subgroup differences: Not applicable						



Footnotes
(1) Breastfed infants (>=3) who received food from 4 or more food groups and solid, semisolid or soft food atleast 3 times on a previous day
(2) Non-breastfed infants (>=4) who received milk feed, food from 4 or more food groups (not milk) and 4 or more meals on a previous day

Outcome 23: Systolic Blood pressure

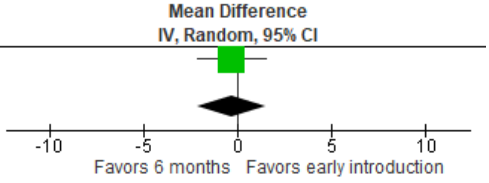
Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Gupta 2017 (1)	80.9	6.6	67	80.9	6.2	74	100.0%	0.00 [-2.12, 2.12]
Total (95% CI)			**67**			**74**	**100.0%**	**0.00 [-2.12, 2.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								



Footnotes
(1) Systolic pressure

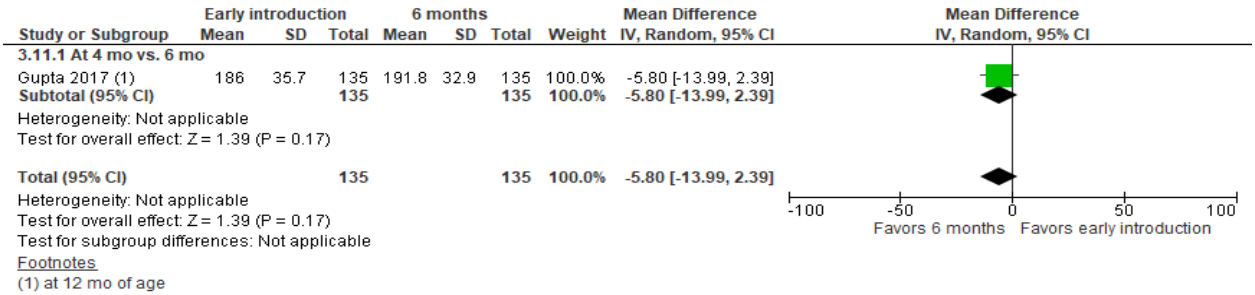
Outcome 24: Diastolic Blood pressure

Study or Subgroup	Early introduction Mean	SD	Total	CF at 6 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Gupta 2017 (1)	50.1	5.8	68	50.4	5.3	75	100.0%	-0.30 [-2.13, 1.53]
Total (95% CI)			**68**			**75**	**100.0%**	**-0.30 [-2.13, 1.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.32 (P = 0.75)								

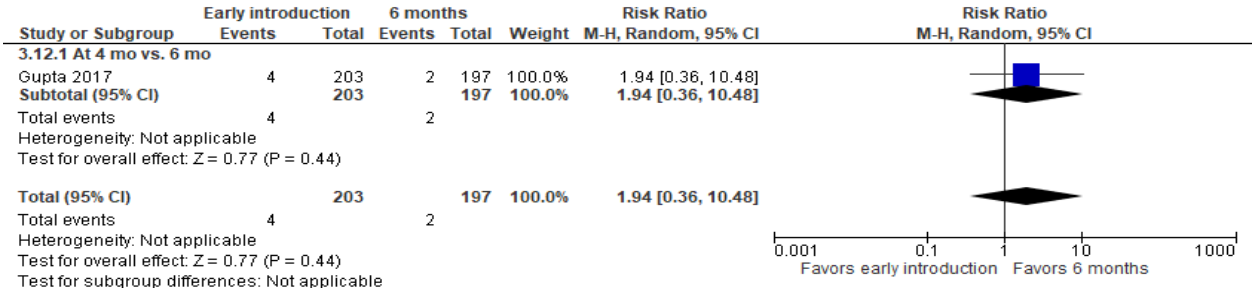


Footnotes
(1) Dystolic pressure

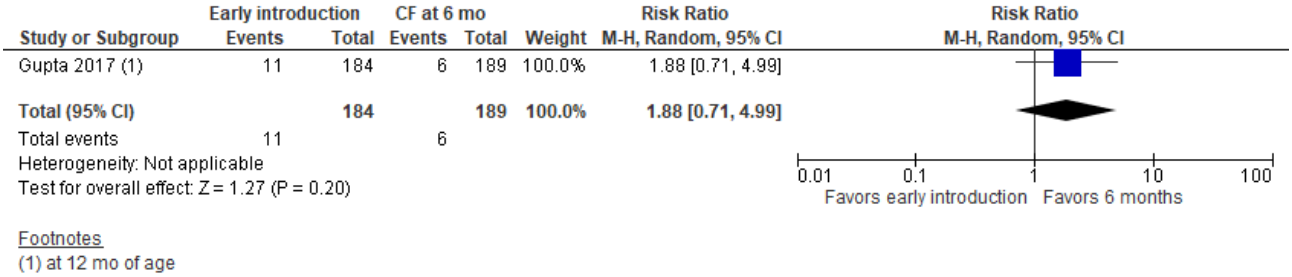
Outcome 25: BMC (g)



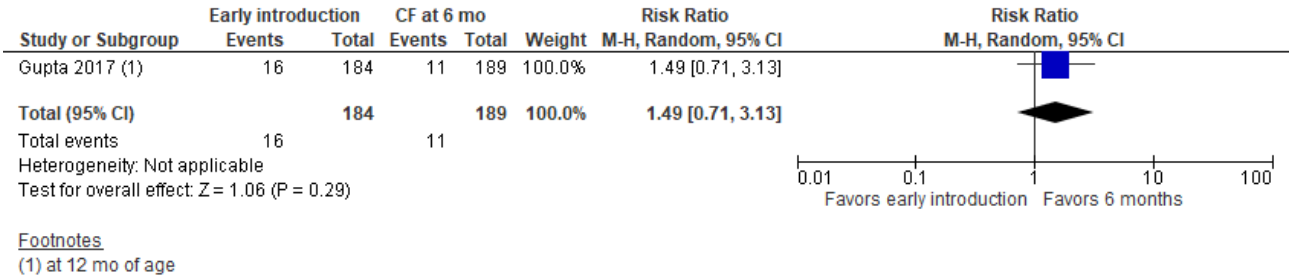
Outcome 26: Infant mortality



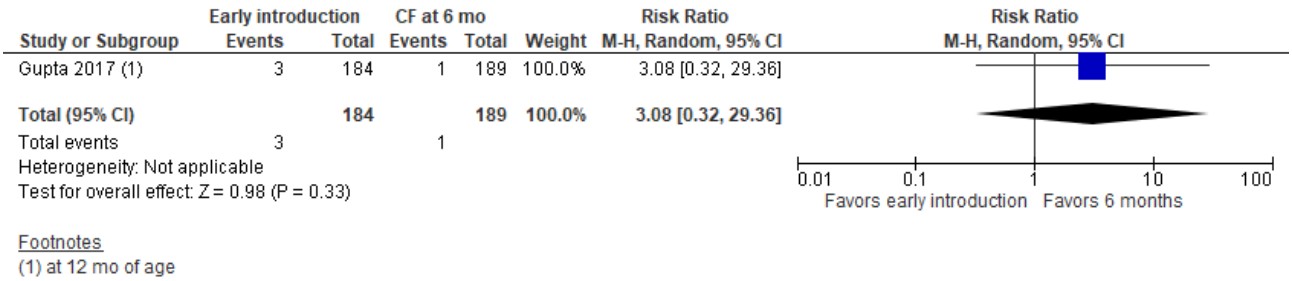
Outcome 27: Diarrhea



Outcome 28: LRTI

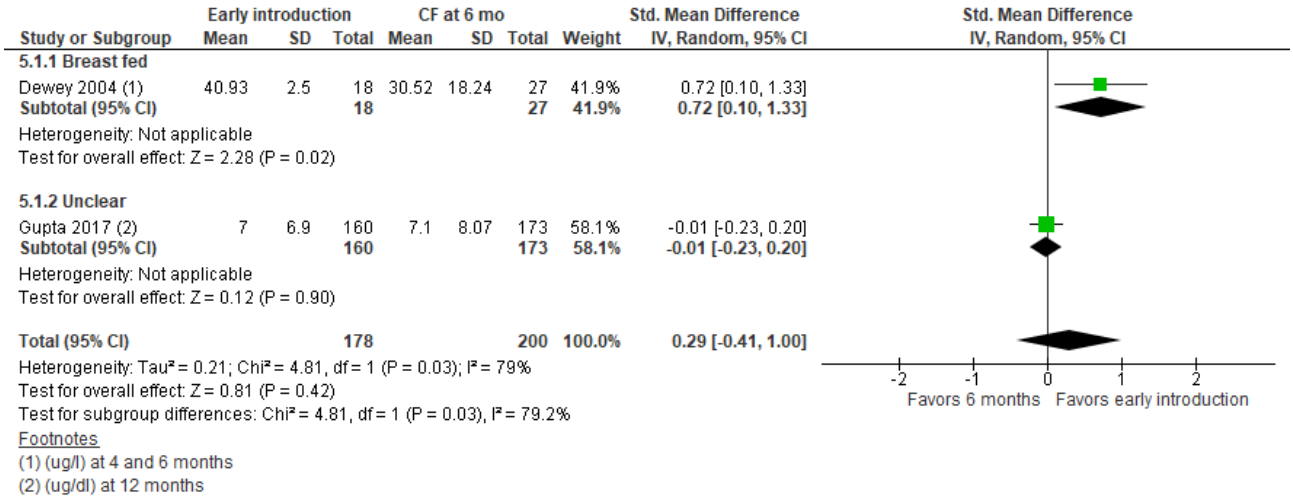


Outcome 29: Sepsis



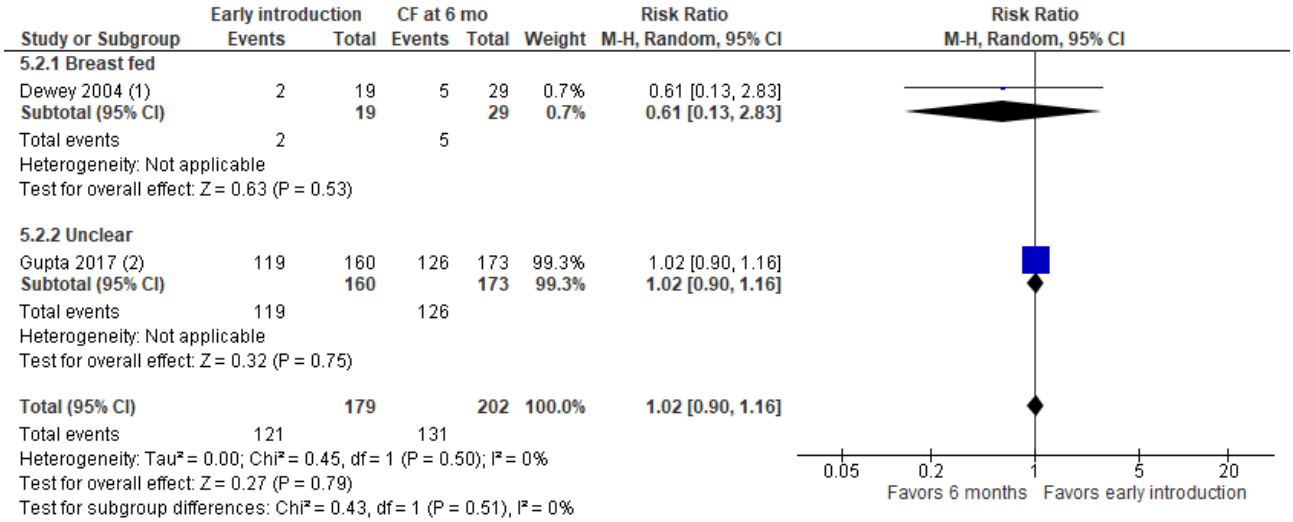
Comparison: Early introduction of CF (at four months of age) compared to six months of age among LBW/Preterm/SGA Infants (RCTs)- subgroup by feeding practices

Outcome 1: Serum Ferritin (µg/l)



Footnotes
(1) (ug/l) at 4 and 6 months
(2) (ug/dl) at 12 months

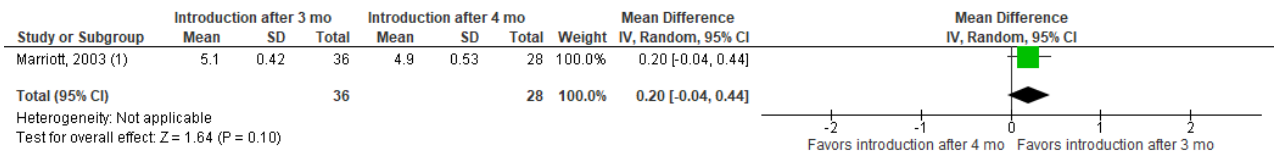
Outcome 2:Ferritin (<12 µg/l)



Footnotes
(1) at 4 and 6 mo
(2) at 12 months

Comparison: Early introduction of CF at three months compared to at four months among preterm/LBW/SGA infants (RCTs)

Outcome 1: Length

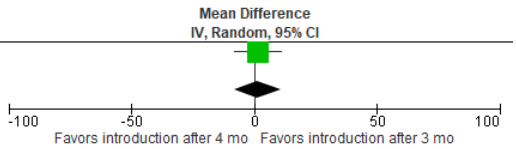


Footnotes
(1) mm/week between 0-12 months of age

Outcome 2: Weight

Study or Subgroup	Introduction after 3 mo Mean	SD	Total	Introduction after 4 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Marriott, 2003 (1)	121	18.6	36	119.6	20.1	28	100.0%	1.40 [-8.21, 11.01]
Total (95% CI)			**36**			**28**	**100.0%**	**1.40 [-8.21, 11.01]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.78)

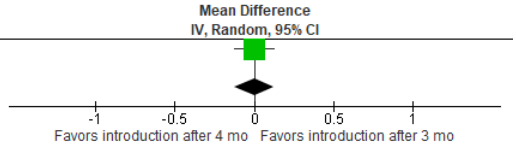


Footnotes
(1) g/week between 0-12 months of age

Outcome 3: Head circumference

Study or Subgroup	Introduction after 3 mo Mean	SD	Total	Introduction after 4 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Marriott, 2003 (1)	2.2	0.3	36	2.2	0.21	28	100.0%	0.00 [-0.13, 0.13]
Total (95% CI)			**36**			**28**	**100.0%**	**0.00 [-0.13, 0.13]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

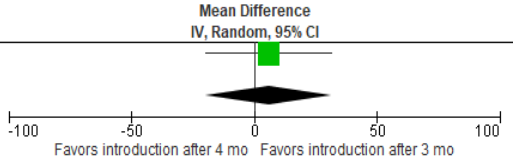


Footnotes
(1) mm/week between 0-12 months of age

Outcome 4: Hb levels (g/l)

Study or Subgroup	Introduction after 3 mo Mean	SD	Total	Introduction after 4 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Marriott, 2003 (1)	120	40.82	34	114	57.16	27	100.0%	6.00 [-19.56, 31.56]
Total (95% CI)			**34**			**27**	**100.0%**	**6.00 [-19.56, 31.56]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)

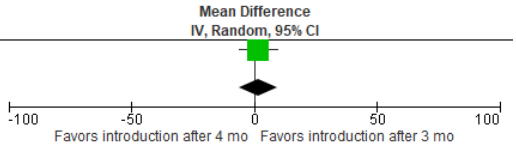


Footnotes
(1) at 6 months of age

Outcome 5: Serum Ferritin (ng/ml)

Study or Subgroup	Introduction after 3 mo Mean	SD	Total	Introduction after 4 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Marriott, 2003 (1)	16.4	13.99	34	14.9	16.62	27	100.0%	1.50 [-6.34, 9.34]
Total (95% CI)			**34**			**27**	**100.0%**	**1.50 [-6.34, 9.34]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.38 (P = 0.71)

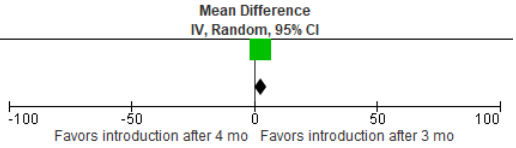


Footnotes
(1) at 6 months of age

Outcome 6: Serum Iron (ng/ml)

Study or Subgroup	Introduction after 3 mo Mean	SD	Total	Introduction after 4 mo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Marriott, 2003 (1)	12.2	3.9	34	9.4	5.6	27	100.0%	2.80 [0.31, 5.29]
Total (95% CI)			**34**			**27**	**100.0%**	**2.80 [0.31, 5.29]**

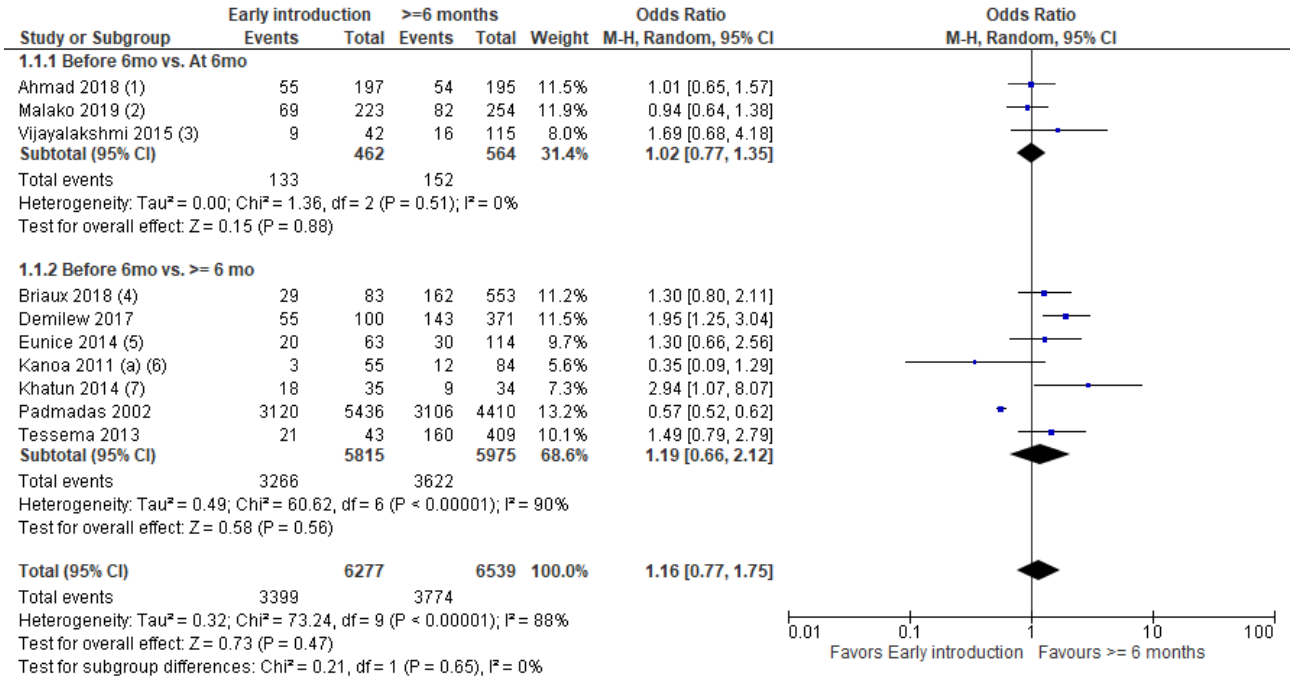
Heterogeneity: Not applicable
Test for overall effect: Z = 2.21 (P = 0.03)



Footnotes
(1) at 6 months of age

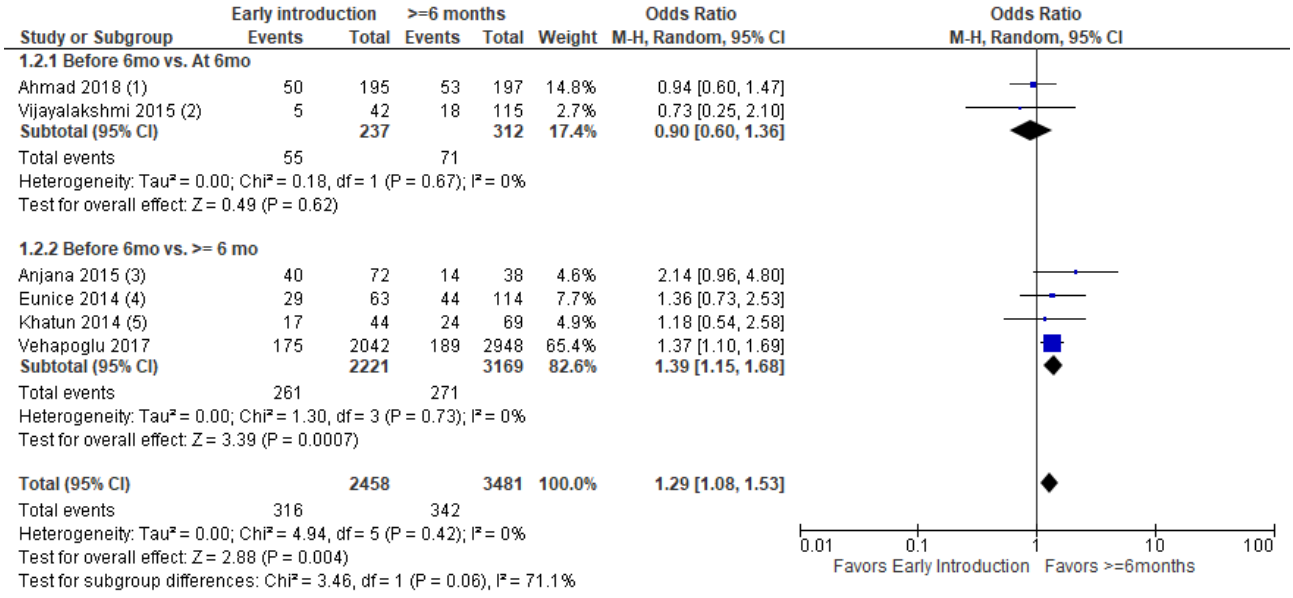
Comparison. Early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies)

Outcome 1: Stunting



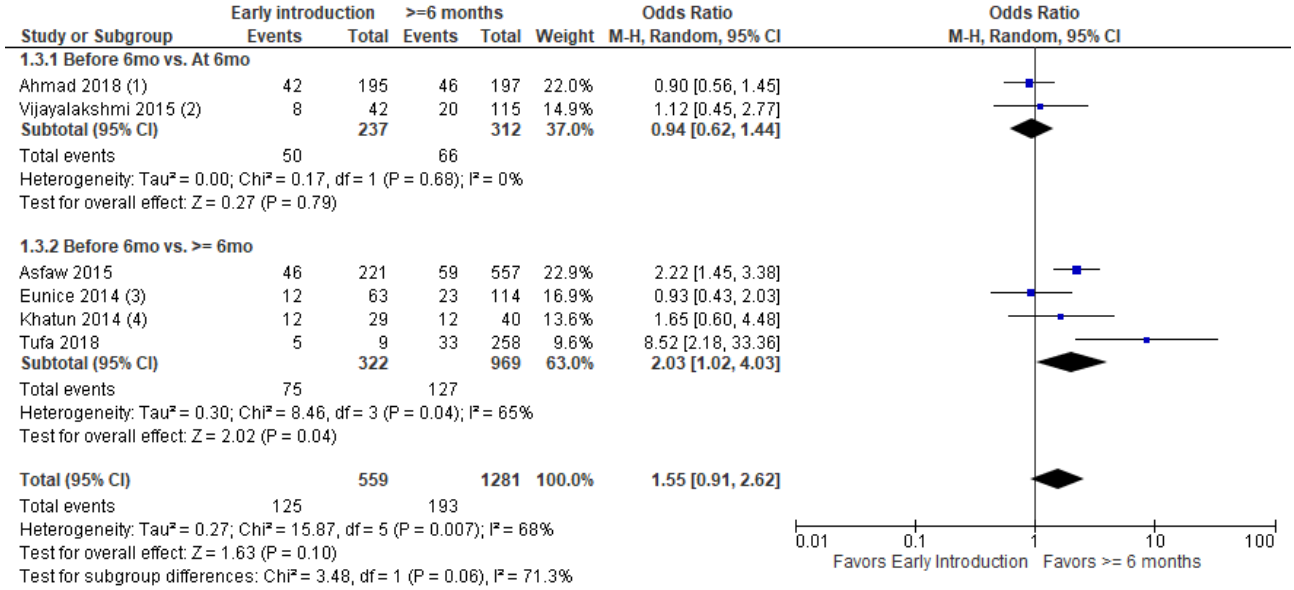
Footnotes
(1) At 6-23mo
(2) at 6-23 mo
(3) at 6-24 mo
(4) at 18-23mo
(5) at 2-5 years
(6) 5-6 year old
(7) child aged between 6-23 months

Outcome 2: Underweight



Footnotes
(1) At 6-23mo
(2) at 6-24 mo
(3) at 7mo to 3 years
(4) at 2-5 years
(5) child aged between 6-23 months

Outcome 3: Wasting



Footnotes

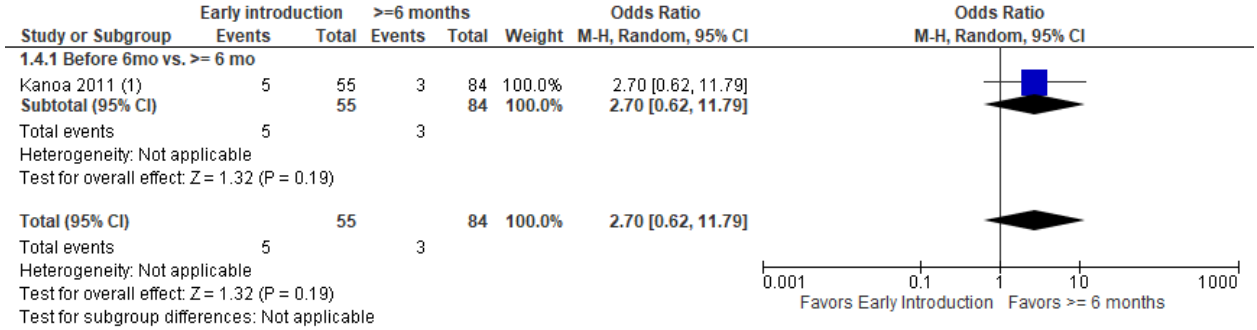
(1) At 6-23mo

(2) at 6-24 mo

(3) at 2-5 years

(4) child aged between 6-23 months

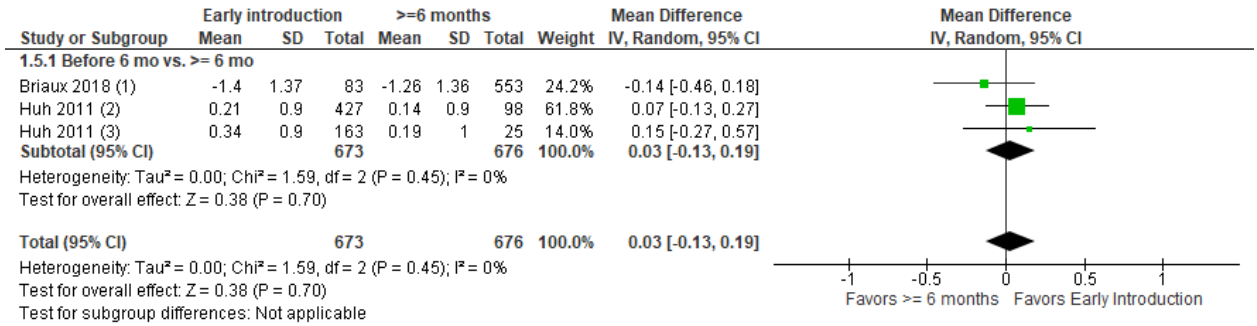
Outcome 4: Thinness



Footnotes

(1) 5-6 year old

Outcome 5: Height for Age Z-Score



Footnotes

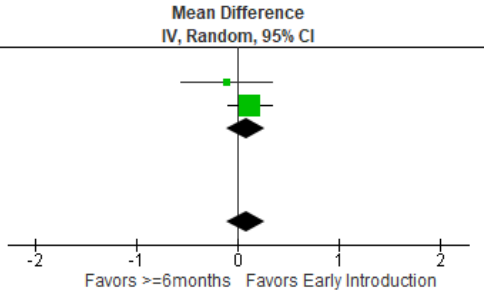
(1) at 18-23 mo

(2) Breastfed group

(3) Formula fed group

Outcome 6: Weight for Age Z-Score

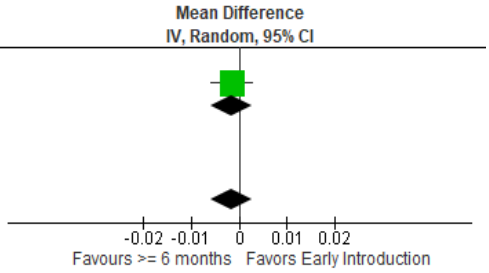
Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.6.1 Before 6 mo vs. >= 6 mo								
Huh 2011 (1)	0.55	0.9	163	0.66	1.1	25	18.5%	-0.11 [-0.56, 0.34]
Huh 2011 (2)	0.42	0.9	427	0.3	1	98	81.5%	0.12 [-0.10, 0.34]
Subtotal (95% CI)			**590**			**123**	**100.0%**	**0.08 [-0.12, 0.27]**
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%								
Test for overall effect: Z = 0.78 (P = 0.44)								
Total (95% CI)			**590**			**123**	**100.0%**	**0.08 [-0.12, 0.27]**
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%								
Test for overall effect: Z = 0.78 (P = 0.44)								
Test for subgroup differences: Not applicable								



Footnotes
(1) Formula fed group at 3 years
(2) Breastfed group at 3 years

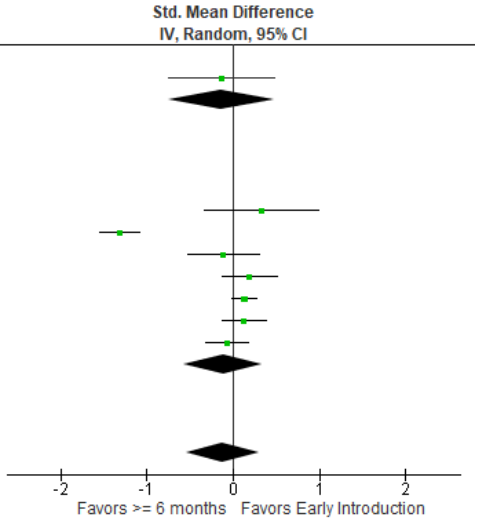
Outcome 7: Weight for Height Z-Score

Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.7.1 Before 6 mo vs. >= 6 mo								
Rossem 2013	-0.0045	0.02	1224	-0.003	0.06	771	100.0%	-0.00 [-0.01, 0.00]
Subtotal (95% CI)			**1224**			**771**	**100.0%**	**-0.00 [-0.01, 0.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								
Total (95% CI)			**1224**			**771**	**100.0%**	**-0.00 [-0.01, 0.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								
Test for subgroup differences: Not applicable								



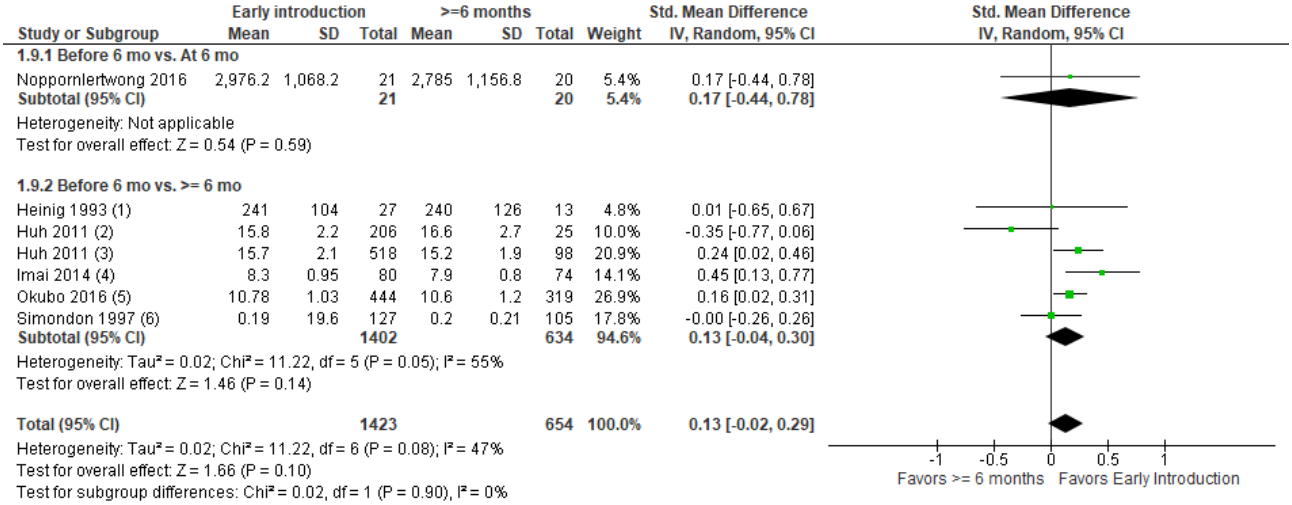
Outcome 8: Length

Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.8.1 Before 6mo vs. At 6mo								
Nopporniertwong 2016 (1)	11.9	2.1	21	12.2	2.2	20	10.8%	-0.14 [-0.75, 0.48]
Subtotal (95% CI)			**21**			**20**	**10.8%**	**-0.14 [-0.75, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.44 (P = 0.66)								
1.8.2 Before 6mo vs.>= 6mo								
Heinig 1993 (2)	1.4	0.3	27	1.3	0.3	13	10.3%	0.33 [-0.34, 0.99]
Huh 2011 (3)	91.1	4.2	470	96.6	4.1	98	13.4%	-1.31 [-1.54, -1.08]
Huh 2011 (4)	98	4.4	254	98.5	5.6	25	12.3%	-0.11 [-0.52, 0.30]
Imai 2014 (5)	68.9	2.15	80	68.5	2.1	74	12.9%	0.19 [-0.13, 0.50]
Okubo 2016 (6)	81.8	2.9	444	81.4	3.2	319	13.7%	0.13 [-0.01, 0.28]
Simondon 1997 (7)	1.3	0.5	127	1.24	0.44	105	13.2%	0.13 [-0.13, 0.38]
Veena 2010 (8)	130.6	5.7	404	131	5.2	78	13.3%	-0.07 [-0.31, 0.17]
Subtotal (95% CI)			**1806**			**712**	**89.2%**	**-0.12 [-0.57, 0.34]**
Heterogeneity: Tau² = 0.34; Chi² = 123.35, df = 6 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 0.51 (P = 0.61)								
Total (95% CI)			**1827**			**732**	**100.0%**	**-0.12 [-0.54, 0.30]**
Heterogeneity: Tau² = 0.33; Chi² = 123.35, df = 7 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 0.56 (P = 0.57)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%								



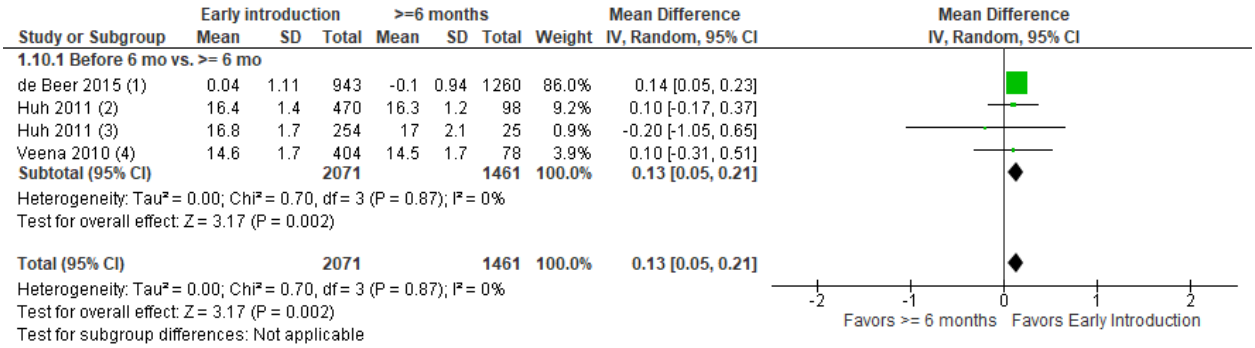
Footnotes
(1) Length increase from enrolment to 12 mo (cm)
(2) 9-12 mo (cm/mo)
(3) Breastfed group
(4) Formula fed group
(5) in cm at 6 months
(6) in cm, at 18 mo
(7) cm/mo at 6-9 mo of age
(8) 9-10 years (height in cm)

Outcome 9: Weight



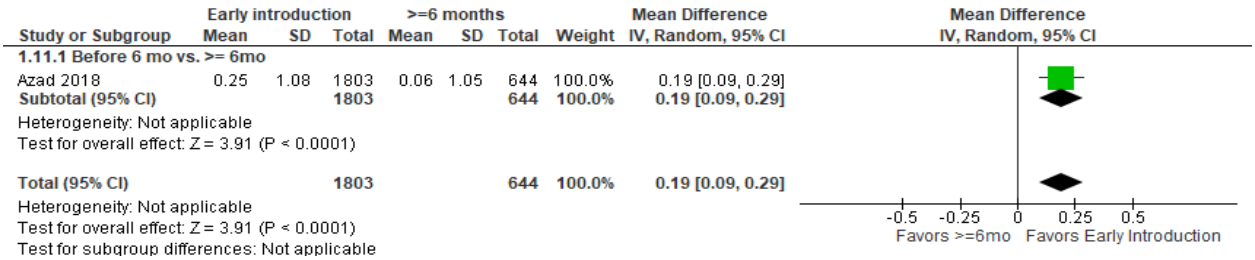
Footnotes
(1) At 9-12 mo (g/mo)
(2) Formula fed group
(3) Breastfed group
(4) kg at 6 mo
(5) in kg at 18 months
(6) kg/mo at 6-9mo of age

Outcome 10: BMI



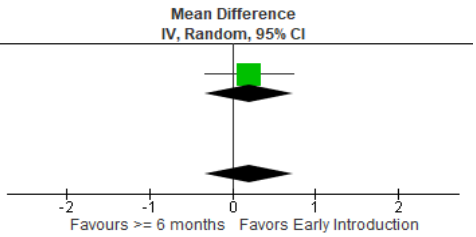
Footnotes
(1) at 5-6 years of age
(2) Breastfed group
(3) Formula fed group
(4) 9-10 years

Outcome 11: BMI Z-score



Outcome 12: Head circumference

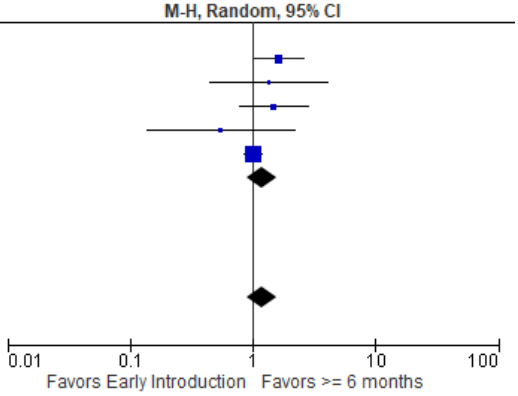
Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.12.1 Before 6 mo vs. At 6mo								
Nopporniertwong 2016 (1)	4.4	1.1	21	4.2	0.6	20	100.0%	0.20 [-0.34, 0.74]
Subtotal (95% CI)			**21**			**20**	**100.0%**	**0.20 [-0.34, 0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.73 (P = 0.47)								
Total (95% CI)			**21**			**20**	**100.0%**	**0.20 [-0.34, 0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.73 (P = 0.47)								
Test for subgroup differences: Not applicable								



Footnotes
(1) increase in cm at 12 mo

Outcome 13: Overweight

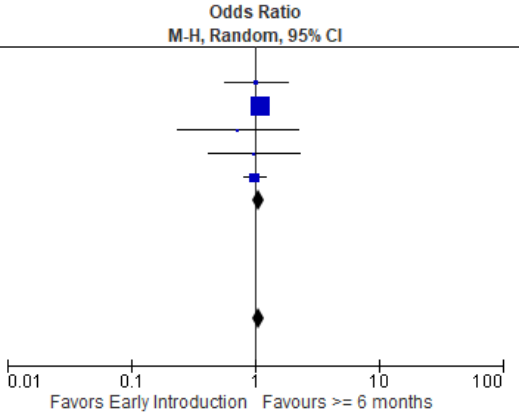
Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.13.1 Before 6mo vs.>= 6 mo						
Azad 2018 (1)	98	1803	22	644	22.6%	1.63 [1.01, 2.60]
Huh 2011 (2)	52	254	4	25	5.6%	1.35 [0.44, 4.11]
Huh 2011 (3)	80	470	12	98	14.1%	1.47 [0.77, 2.82]
Kanoa 2011 (4)	3	55	8	84	3.8%	0.55 [0.14, 2.16]
Vehapoglu 2017	268	2042	386	2948	53.9%	1.00 [0.85, 1.19]
Subtotal (95% CI)		**4624**		**3799**	**100.0%**	**1.17 [0.89, 1.54]**
Total events	501		432			
Heterogeneity: Tau² = 0.03; Chi² = 5.60, df = 4 (P = 0.23); I² = 29%						
Test for overall effect: Z = 1.14 (P = 0.25)						
Total (95% CI)		**4624**		**3799**	**100.0%**	**1.17 [0.89, 1.54]**
Total events	501		432			
Heterogeneity: Tau² = 0.03; Chi² = 5.60, df = 4 (P = 0.23); I² = 29%						
Test for overall effect: Z = 1.14 (P = 0.25)						
Test for subgroup differences: Not applicable						



Footnotes
(1) at 12 mo
(2) Formlafed group at 3 years
(3) Breastfed group at 3 years
(4) defined as greater than or equal to 1 or less than 2 SD (5-6 year old)

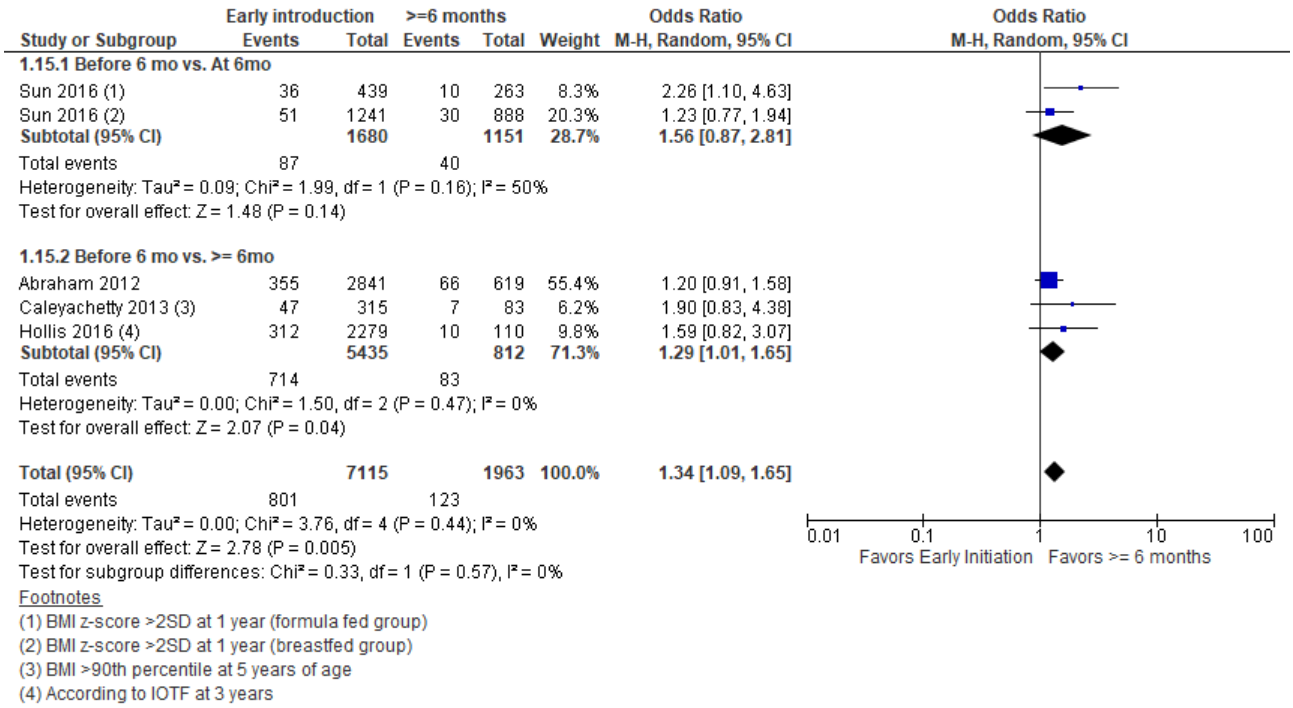
Outcome 14: Obesity

Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.14.1 Before 6mo vs. >= 6mo						
Barrera 2016 (1)	134	1067	14	114	3.5%	1.03 [0.57, 1.85]
Gooze 2011 (2)	812	4550	371	2250	66.6%	1.10 [0.96, 1.26]
Huh 2011 (3)	31	254	4	25	0.9%	0.73 [0.23, 2.27]
Huh 2011 (4)	33	470	7	98	1.7%	0.98 [0.42, 2.29]
Vehapoglu 2017 (5)	159	2043	230	2947	27.3%	1.00 [0.81, 1.23]
Subtotal (95% CI)		**8384**		**5434**	**100.0%**	**1.06 [0.95, 1.19]**
Total events	1169		626			
Heterogeneity: Tau² = 0.00; Chi² = 1.08, df = 4 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.08 (P = 0.28)						
Total (95% CI)		**8384**		**5434**	**100.0%**	**1.06 [0.95, 1.19]**
Total events	1169		626			
Heterogeneity: Tau² = 0.00; Chi² = 1.08, df = 4 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.08 (P = 0.28)						
Test for subgroup differences: Not applicable						

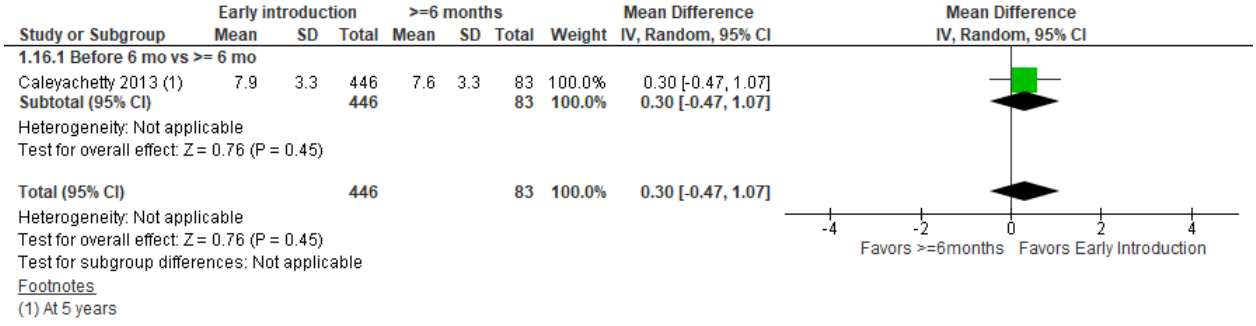


Footnotes
(1) BMI >/=95 percentile (At 6 years)
(2) BMI >/=95 percentile (5.5 years)
(3) Formula fed group (BMI >95 percentile) at 3 years
(4) Breastfed group (BMI >95 percentile) at 3 years
(5) BMI >95 percentile (2-14 years)

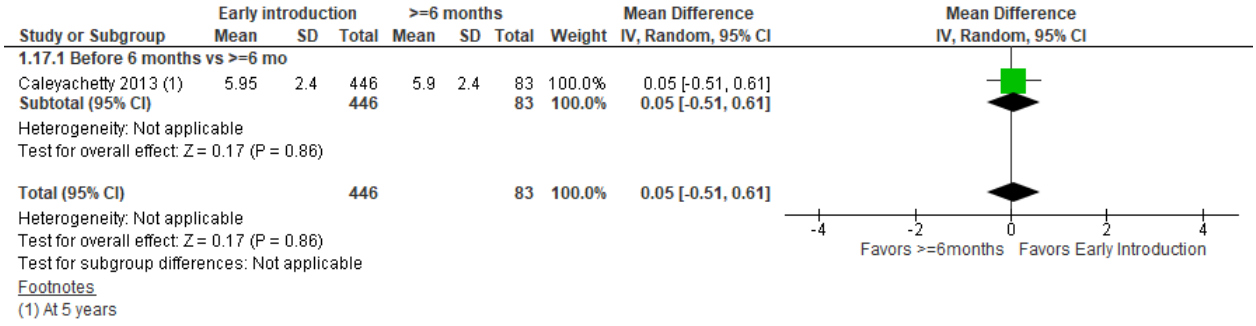
Outcome 15: Overweight and obesity



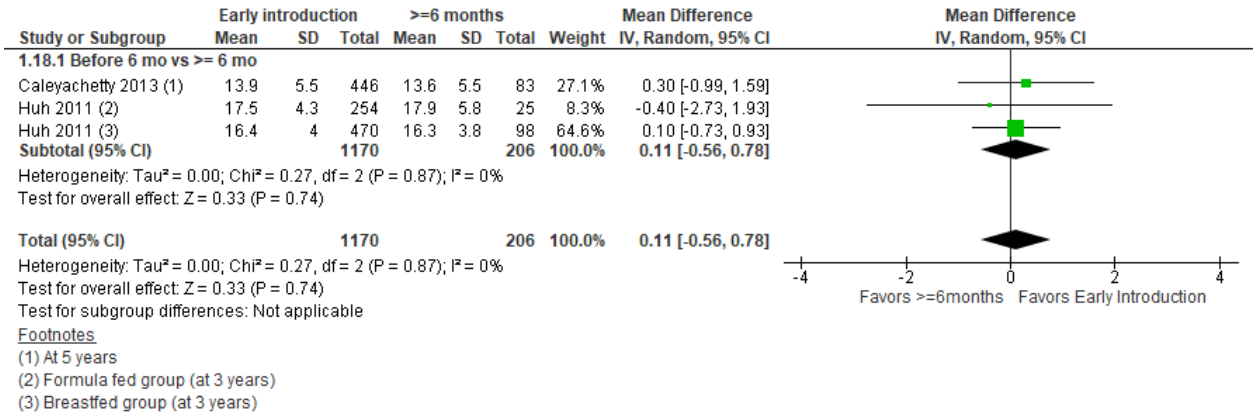
Outcome 16: Skinfold thickness (triceps)



Outcome 17: Skinfold thickness (subscapular)



Outcome 18: Skinfold thickness (triceps+ subscapular)



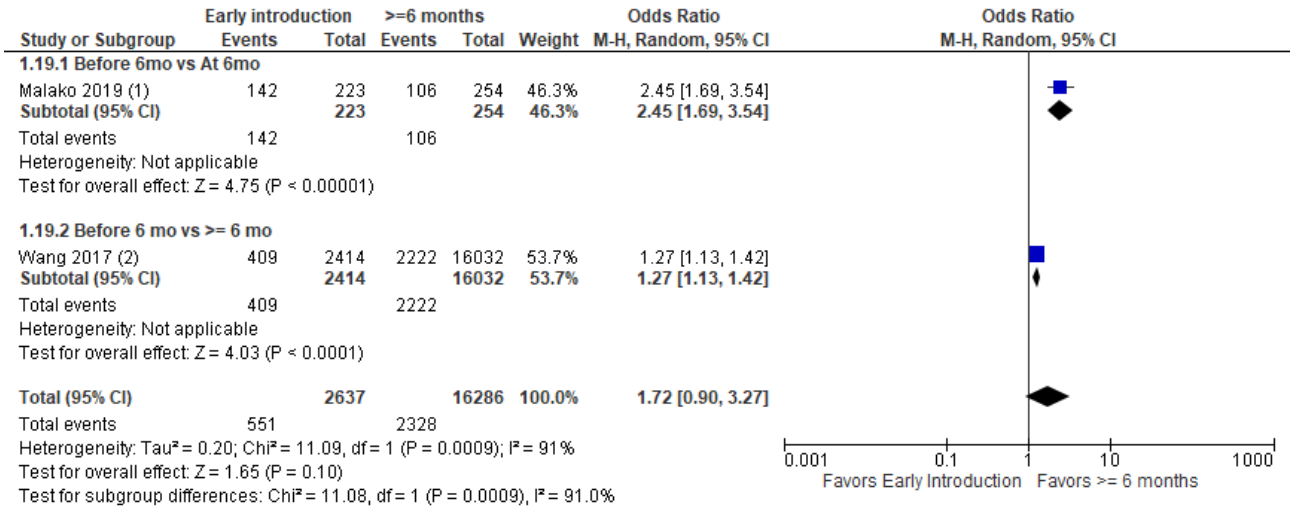
Footnotes

(1) At 5 years

(2) Formula fed group (at 3 years)

(3) Breastfed group (at 3 years)

Outcome 19: Anemia

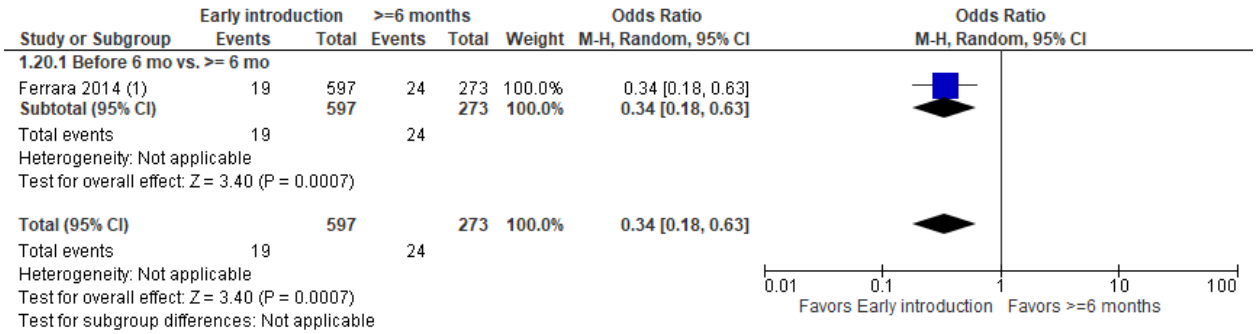


Footnotes

(1) Hb <110g/l (at 6-23mo)

(2) Hb conc <110g/l (at 4-6 years)

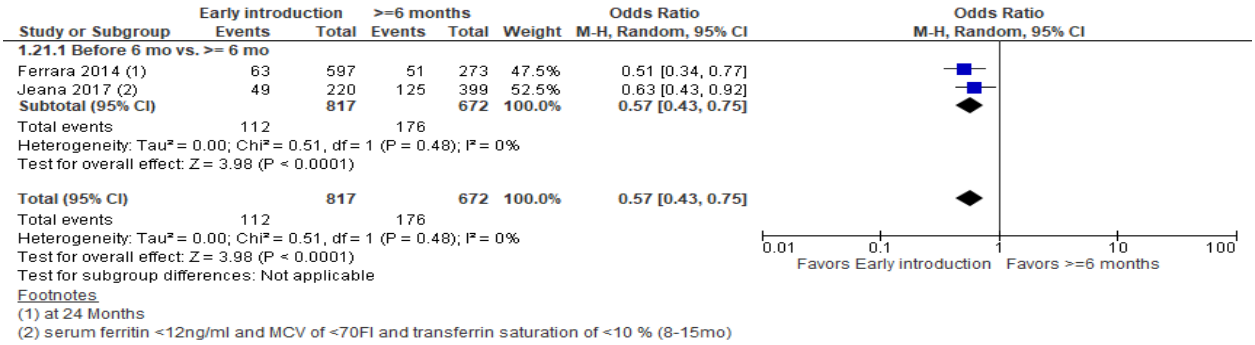
Outcome 20: Iron deficiency anemia



Footnotes

(1) at 24 months

Outcome 21: Iron deficiency

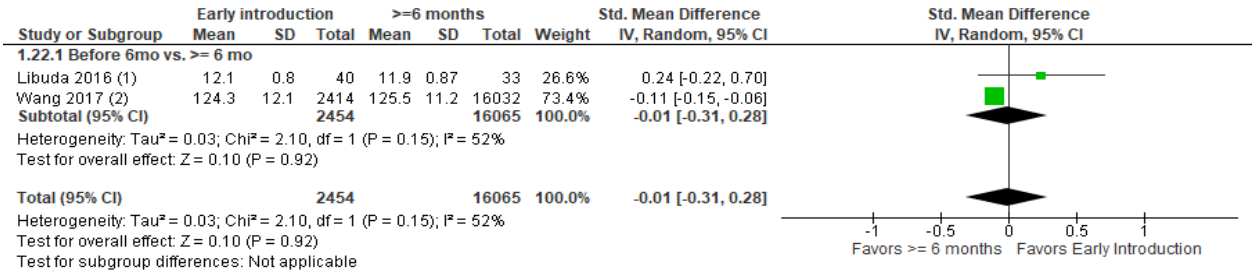


Footnotes

(1) at 24 Months

(2) serum ferritin <12ng/ml and MCV of <70Fl and transferrin saturation of <10 % (8-15mo)

Outcome 22: Hb levels

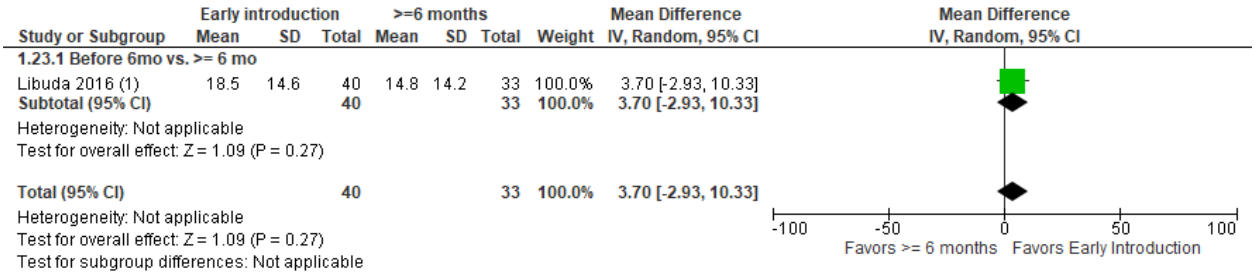


Footnotes

(1) g/dl (at 10 mo)

(2) g/l (at 4-6 years)

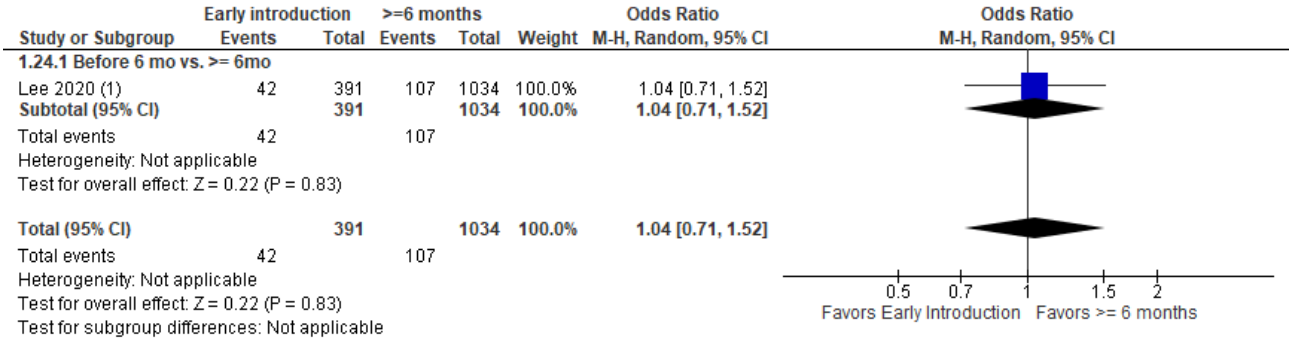
Outcome 23: Serum ferritin



Footnotes

(1) ng/ml (at 10 mo)

Outcome 24: Atopic dermatitis

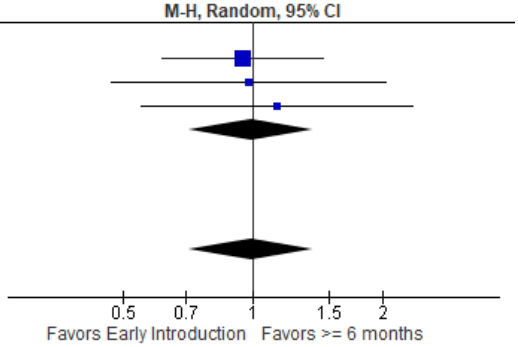


Footnotes

(1) Between 1-3 years

Outcome 25: Asthma

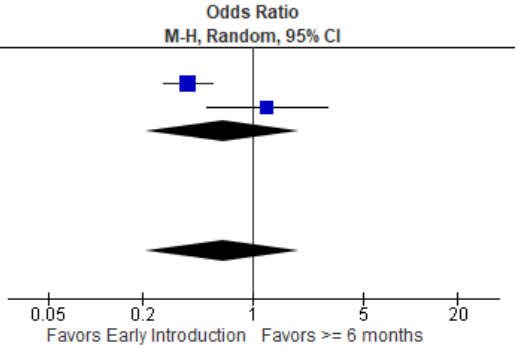
Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.25.1 Before 6 mo vs. >= 6mo						
Ekelund 2021 (1)	75	1699	30	644	58.7%	0.95 [0.61, 1.46]
Lee 2020 (2)	10	391	27	1034	20.4%	0.98 [0.47, 2.04]
Lossius 2018 (3)	50	972	9	198	20.9%	1.14 [0.55, 2.36]
Subtotal (95% CI)		**3062**		**1876**	**100.0%**	**0.99 [0.71, 1.38]**
Total events	135		66			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 0.06 (P = 0.95)						
Total (95% CI)		**3062**		**1876**	**100.0%**	**0.99 [0.71, 1.38]**
Total events	135		66			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 0.06 (P = 0.95)						
Test for subgroup differences: Not applicable						



Footnotes
(1) at 2 and 6 years
(2) Between 1-3 years
(3) at 7 years

Outcome 26: Diarrhea

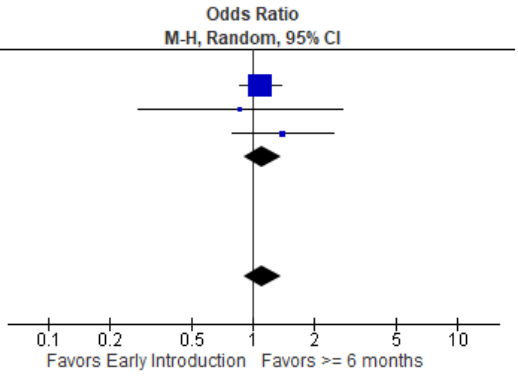
Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.26.1 Before 6 mo vs. >= 6mo						
Ogbo 2018 (1)	42	355	237	920	56.5%	0.39 [0.27, 0.55]
Quigley 2008	166	102340	5	3792	43.5%	1.23 [0.51, 3.00]
Subtotal (95% CI)		**102695**		**4712**	**100.0%**	**0.64 [0.21, 1.97]**
Total events	208		242			
Heterogeneity: Tau² = 0.55; Chi² = 5.61, df = 1 (P = 0.02); I² = 82%						
Test for overall effect: Z = 0.78 (P = 0.44)						
Total (95% CI)		**102695**		**4712**	**100.0%**	**0.64 [0.21, 1.97]**
Total events	208		242			
Heterogeneity: Tau² = 0.55; Chi² = 5.61, df = 1 (P = 0.02); I² = 82%						
Test for overall effect: Z = 0.78 (P = 0.44)						
Test for subgroup differences: Not applicable						



Footnotes
(1) 0-23 mo of age

Outcome 27: LRTI

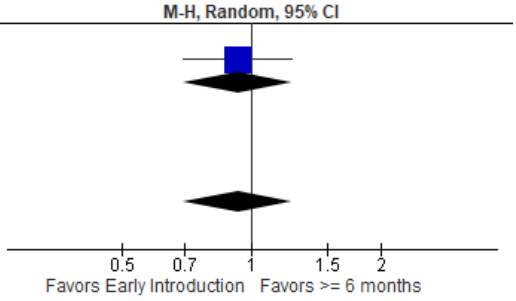
Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.27.1 Before 6 mo vs. >= 6mo						
Ekelund 2021 (1)	307	2809	101	992	82.4%	1.08 [0.85, 1.37]
Nirmolia 2018 (2)	13	76	5	26	3.6%	0.87 [0.28, 2.72]
Quigley 2008 (3)	453	102340	12	3792	14.1%	1.40 [0.79, 2.49]
Subtotal (95% CI)		**105225**		**4810**	**100.0%**	**1.11 [0.90, 1.38]**
Total events	773		118			
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 0.98 (P = 0.33)						
Total (95% CI)		**105225**		**4810**	**100.0%**	**1.11 [0.90, 1.38]**
Total events	773		118			
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 0.98 (P = 0.33)						
Test for subgroup differences: Not applicable						



Footnotes
(1) within 1st year of life
(2) Pneumonia
(3) among children less than or equal to 8 mo

Outcome 28: Wheeze

Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.28.1 Before 6 mo vs. >= 6mo						
Ekelund 2021 (1)	173	1683	70	637	100.0%	0.93 [0.69, 1.25]
Subtotal (95% CI)		**1683**		**637**	**100.0%**	**0.93 [0.69, 1.25]**
Total events	173		70			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
Total (95% CI)		**1683**		**637**	**100.0%**	**0.93 [0.69, 1.25]**
Total events	173		70			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
Test for subgroup differences: Not applicable						

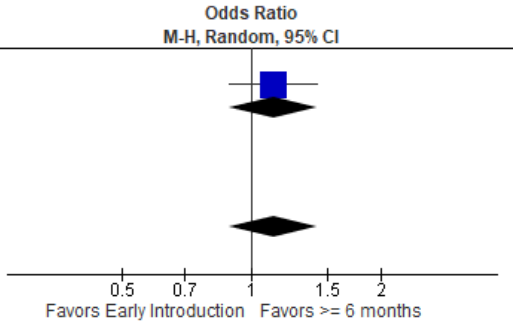


Footnotes

(1) at 6 years (wheeze currently)

Outcome 29: Eczema

Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.29.1 Before 6 mo vs. >= 6mo						
Ekelund 2021 (1)	328	1661	113	629	100.0%	1.12 [0.89, 1.42]
Subtotal (95% CI)		**1661**		**629**	**100.0%**	**1.12 [0.89, 1.42]**
Total events	328		113			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.33)						
Total (95% CI)		**1661**		**629**	**100.0%**	**1.12 [0.89, 1.42]**
Total events	328		113			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.33)						
Test for subgroup differences: Not applicable						

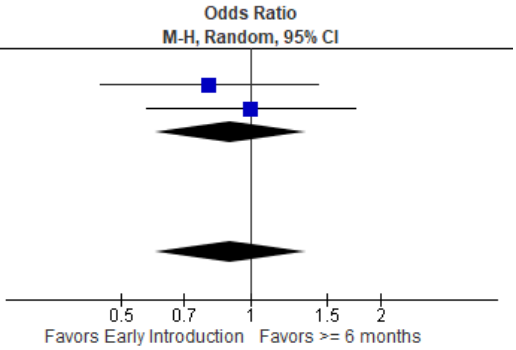


Footnotes

(1) ever had eczema (6 years)

Outcome 30: Food Allergy

Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.30.1 Before 6 mo vs. >= 6mo						
Kim 2011 (1)	16	354	45	803	48.2%	0.80 [0.44, 1.43]
Luccioli 2014 (2)	68	1003	16	236	51.8%	1.00 [0.57, 1.76]
Subtotal (95% CI)		**1357**		**1039**	**100.0%**	**0.90 [0.60, 1.35]**
Total events	84		61			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.30$, df = 1 (P = 0.58); $I^2 = 0\%$						
Test for overall effect: Z = 0.53 (P = 0.60)						
Total (95% CI)		**1357**		**1039**	**100.0%**	**0.90 [0.60, 1.35]**
Total events	84		61			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.30$, df = 1 (P = 0.58); $I^2 = 0\%$						
Test for overall effect: Z = 0.53 (P = 0.60)						
Test for subgroup differences: Not applicable						



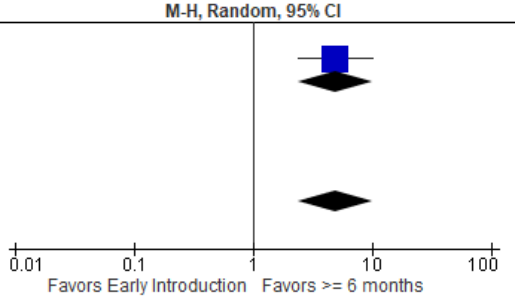
Footnotes

(1) At 12 mo

(2) Total probable food allergy (at 6 years)

Outcome 31: Malnutrition

Study or Subgroup	Early introduction Events	Total	>=6 months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.31.1 Before 6 mo vs. >= 6mo						
Werdani 2019 (1)	40	80	14	82	100.0%	4.86 [2.36, 10.01]
Subtotal (95% CI)		**80**		**82**	**100.0%**	**4.86 [2.36, 10.01]**
Total events	40		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.28 (P < 0.0001)						
Total (95% CI)		**80**		**82**	**100.0%**	**4.86 [2.36, 10.01]**
Total events	40		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.28 (P < 0.0001)						
Test for subgroup differences: Not applicable						

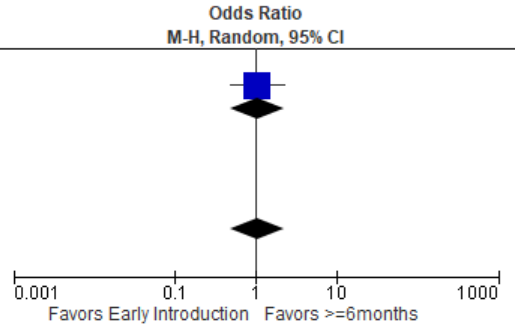


Footnotes

(1) among children under five years of age

Outcome 32: Gastrointestinal illness

Study or Subgroup	Early Introduction Events	Total	>=6months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.32.1 Before 6 mo vs. >=6 mo						
Kanoa 2011 (b) (1)	41	186	10	47	100.0%	1.05 [0.48, 2.28]
Subtotal (95% CI)		**186**		**47**	**100.0%**	**1.05 [0.48, 2.28]**
Total events	41		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.11 (P = 0.91)						
Total (95% CI)		**186**		**47**	**100.0%**	**1.05 [0.48, 2.28]**
Total events	41		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.11 (P = 0.91)						
Test for subgroup differences: Not applicable						

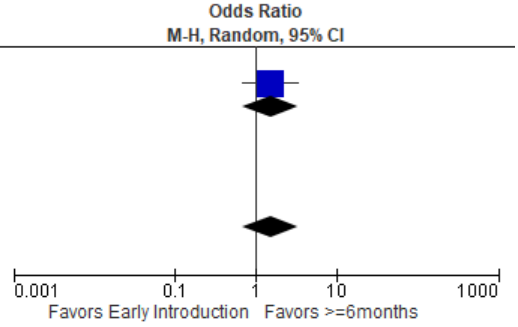


Footnotes

(1) among children upto 2 years

Outcome 33: Respiratory illness

Study or Subgroup	Early Introduction Events	Total	>=6months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.33.1 Before 6 mo vs. >=6 mo						
Kanoa 2011 (b) (1)	49	186	9	47	100.0%	1.51 [0.68, 3.35]
Subtotal (95% CI)		**186**		**47**	**100.0%**	**1.51 [0.68, 3.35]**
Total events	49		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
Total (95% CI)		**186**		**47**	**100.0%**	**1.51 [0.68, 3.35]**
Total events	49		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
Test for subgroup differences: Not applicable						

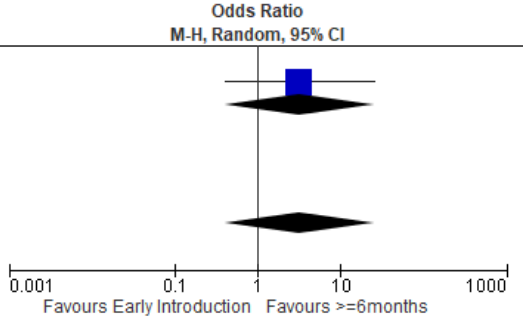


Footnotes

(1) among children upto 2 years

Outcome 34: Rickets

Study or Subgroup	Early Introduction Events	Total	>=6months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.34.1 Before 6 mo vs. >=6 mo						
Kanoa 2011 (b) (1)	12	186	1	47	100.0%	3.17 [0.40, 25.03]
Subtotal (95% CI)		**186**		**47**	**100.0%**	**3.17 [0.40, 25.03]**
Total events	12		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
Total (95% CI)		**186**		**47**	**100.0%**	**3.17 [0.40, 25.03]**
Total events	12		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
Test for subgroup differences: Not applicable						

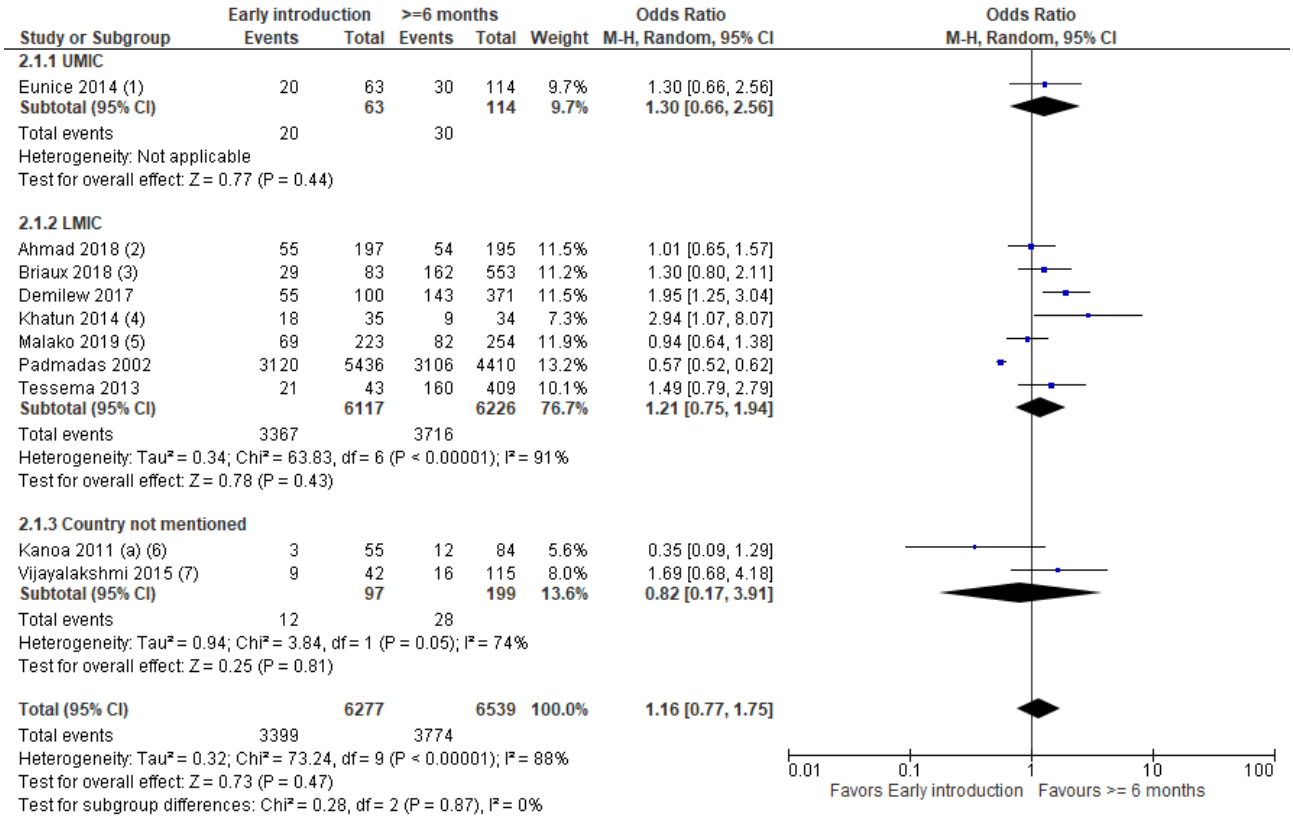


Footnotes

(1) among children upto 2 years

Comparison 1d. Early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies) – subgroup by setting

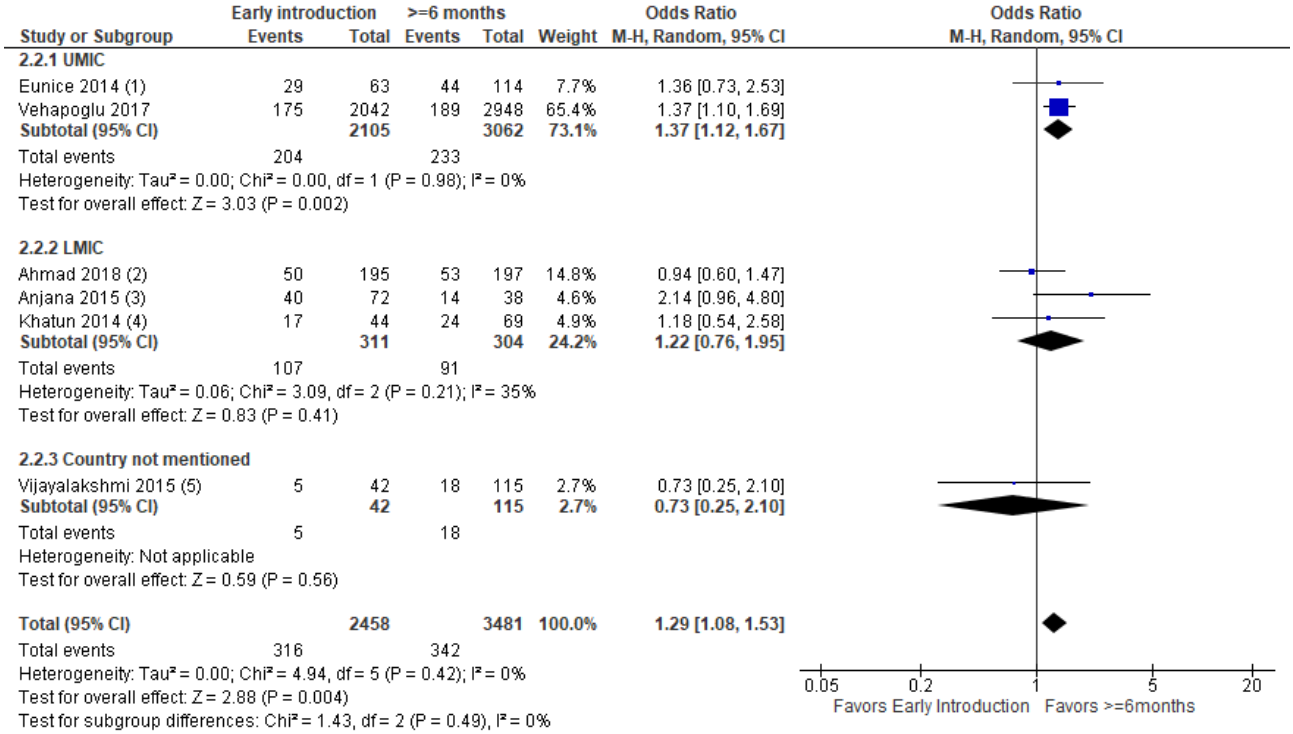
Outcome 1: Stunting



Footnotes

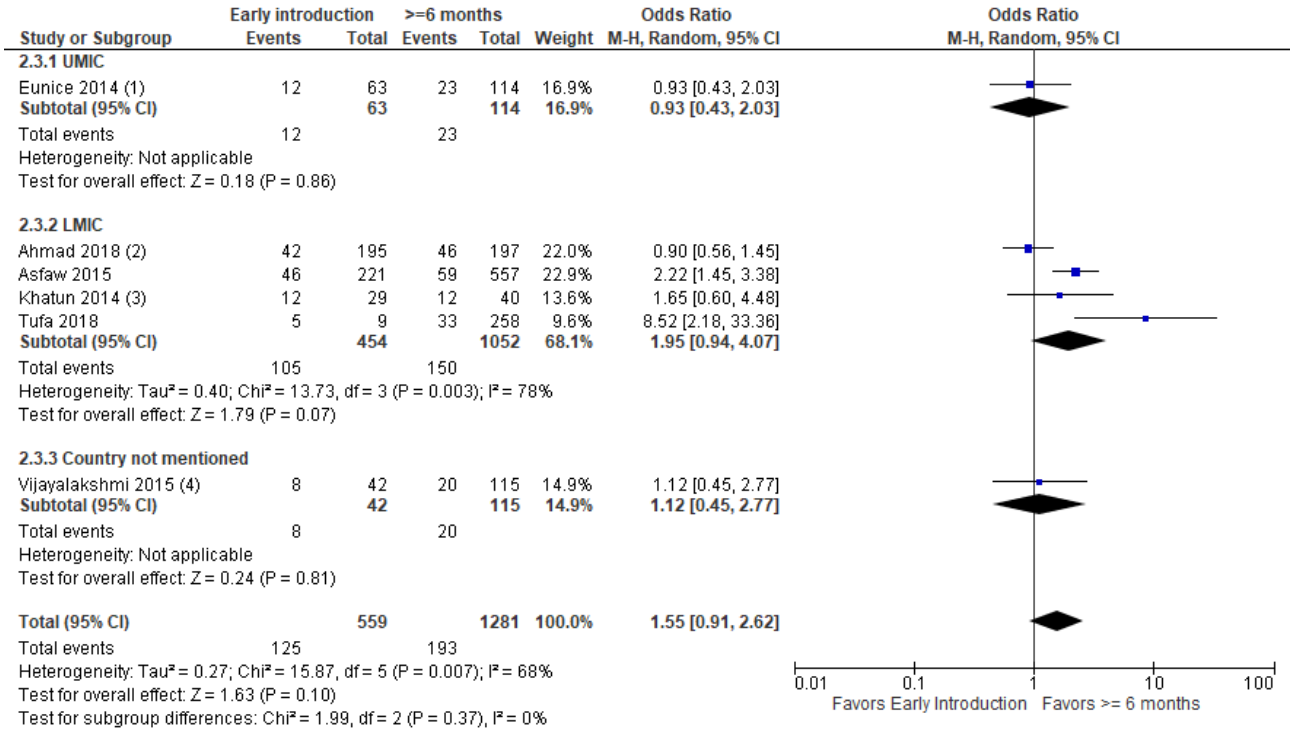
(1) at 2-5 years
(2) At 6-23mo
(3) at 18-23mo
(4) child aged between 6-23 months
(5) at 6-23 mo
(6) 5-6 year old
(7) at 6-24 mo

Outcome 2: Underweight



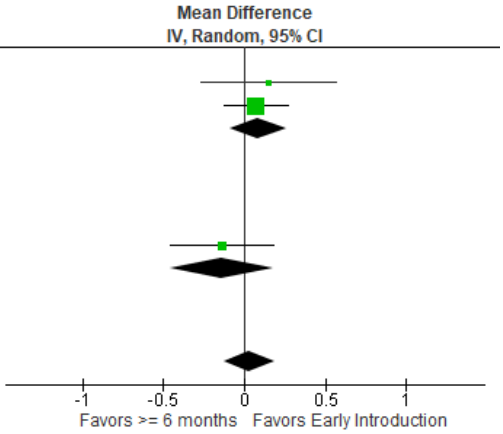
Footnotes
(1) at 2-5 years
(2) At 6-23mo
(3) at 7mo to 3 years
(4) child aged between 6-23 months
(5) at 6-24 mo

Outcome 3: Wasting



Footnotes
(1) at 2-5 years
(2) At 6-23mo
(3) child aged between 6-23 months
(4) at 6-24 mo

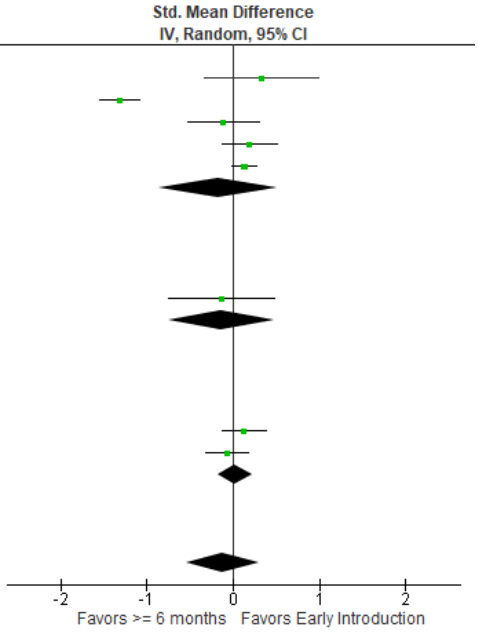
Outcome 4: Height for age Z-score



Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.4.1 HIC								
Huh 2011 (1)	0.34	0.9	163	0.19	1	25	14.0%	0.15 [-0.27, 0.57]
Huh 2011 (2)	0.21	0.9	427	0.14	0.9	98	61.8%	0.07 [-0.13, 0.27]
Subtotal (95% CI)			**590**			**123**	**75.8%**	**0.08 [-0.09, 0.26]**
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%								
Test for overall effect: Z = 0.93 (P = 0.35)								
2.4.2 LMIC								
Briaux 2018 (3)	-1.4	1.37	83	-1.26	1.36	553	24.2%	-0.14 [-0.46, 0.18]
Subtotal (95% CI)			**83**			**553**	**24.2%**	**-0.14 [-0.46, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.38)								
Total (95% CI)			**673**			**676**	**100.0%**	**0.03 [-0.13, 0.19]**
Heterogeneity: Tau² = 0.00; Chi² = 1.59, df = 2 (P = 0.45); I² = 0%								
Test for overall effect: Z = 0.38 (P = 0.70)								
Test for subgroup differences: Chi² = 1.47, df = 1 (P = 0.22), I² = 32.2%								

Footnotes
(1) Formula fed group
(2) Breastfed group
(3) at 18-23 mo

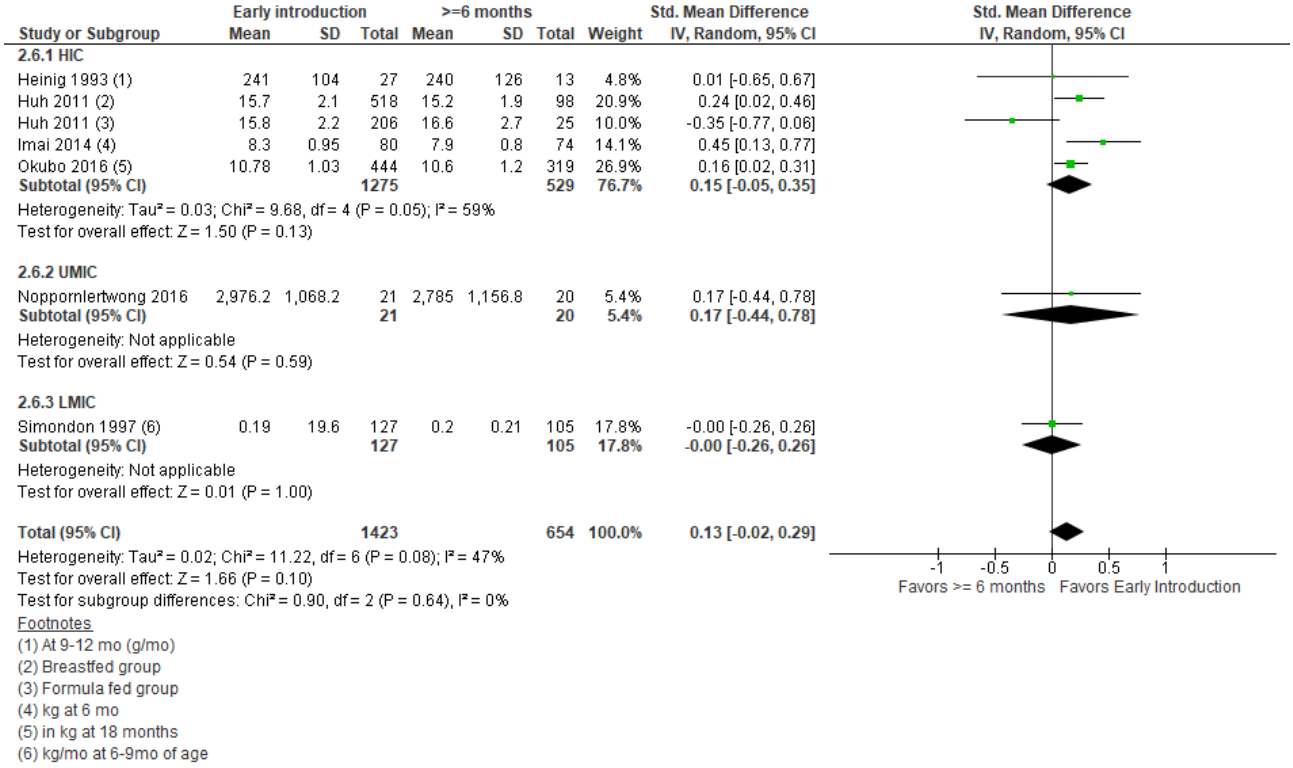
Outcome 5: Length



Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.5.1 HIC								
Heinig 1993 (1)	1.4	0.3	27	1.3	0.3	13	10.3%	0.33 [-0.34, 0.99]
Huh 2011 (2)	91.1	4.2	470	96.6	4.1	98	13.4%	-1.31 [-1.54, -1.08]
Huh 2011 (3)	98	4.4	254	98.5	5.6	25	12.3%	-0.11 [-0.52, 0.30]
Imai 2014 (4)	68.9	2.15	80	68.5	2.1	74	12.9%	0.19 [-0.13, 0.50]
Okubo 2016 (5)	81.8	2.9	444	81.4	3.2	319	13.7%	0.13 [-0.01, 0.28]
Subtotal (95% CI)			**1275**			**529**	**62.7%**	**-0.17 [-0.86, 0.51]**
Heterogeneity: Tau² = 0.57; Chi² = 118.10, df = 4 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.49 (P = 0.62)								
2.5.2 UMIC								
Nopporniertwong 2016 (6)	11.9	2.1	21	12.2	2.2	20	10.8%	-0.14 [-0.75, 0.48]
Subtotal (95% CI)			**21**			**20**	**10.8%**	**-0.14 [-0.75, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.44 (P = 0.66)								
2.5.3 LMIC								
Simondon 1997 (7)	1.3	0.5	127	1.24	0.44	105	13.2%	0.13 [-0.13, 0.38]
Veena 2010 (8)	130.6	5.7	404	131	5.2	78	13.3%	-0.07 [-0.31, 0.17]
Subtotal (95% CI)			**531**			**183**	**26.6%**	**0.02 [-0.17, 0.22]**
Heterogeneity: Tau² = 0.00; Chi² = 1.19, df = 1 (P = 0.28); I² = 16%								
Test for overall effect: Z = 0.23 (P = 0.82)								
Total (95% CI)			**1827**			**732**	**100.0%**	**-0.12 [-0.54, 0.30]**
Heterogeneity: Tau² = 0.33; Chi² = 123.35, df = 7 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 0.56 (P = 0.57)								
Test for subgroup differences: Chi² = 0.48, df = 2 (P = 0.79), I² = 0%								

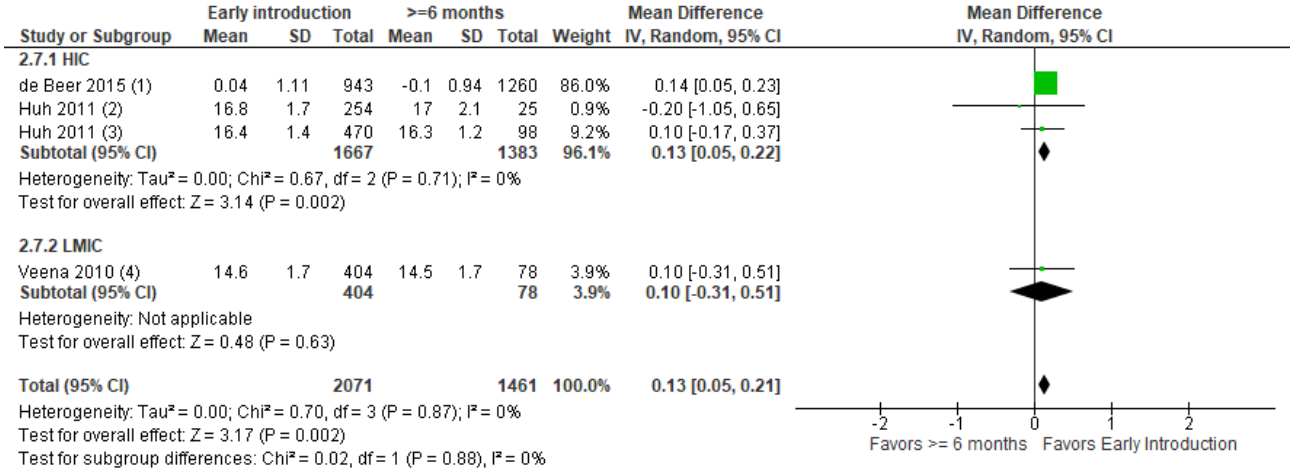
Footnotes
(1) 9-12 mo (cm/mo)
(2) Breastfed group
(3) Formula fed group
(4) in cm at 6 months
(5) in cm, at 18 mo
(6) Length increase from enrolment to 12 mo (cm)
(7) cm/mo at 6-9 mo of age
(8) 9-10 years (height in cm)

Outcome 6: Weight



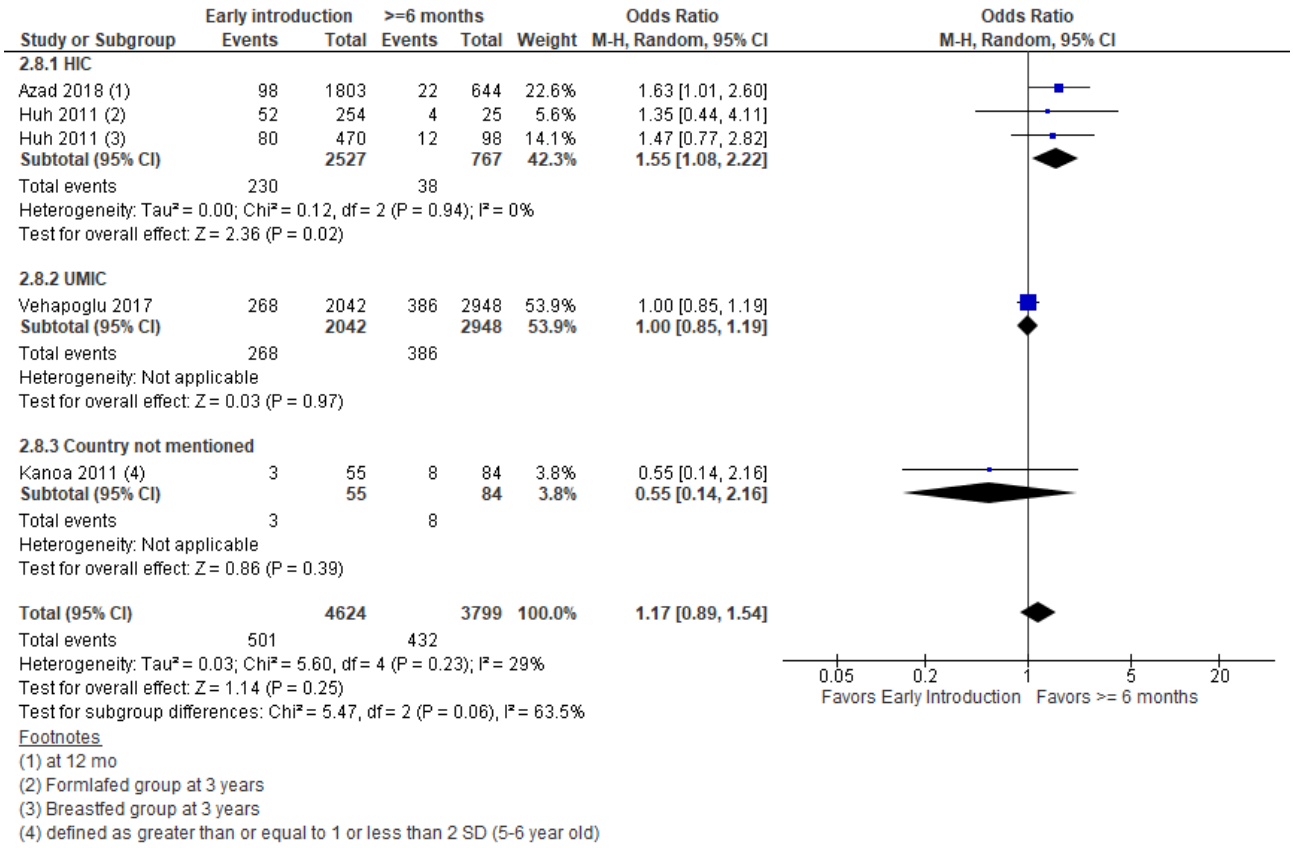
Footnotes
(1) At 9-12 mo (g/mo)
(2) Breastfed group
(3) Formula fed group
(4) kg at 6 mo
(5) in kg at 18 months
(6) kg/mo at 6-9mo of age

Outcome 7: BMI



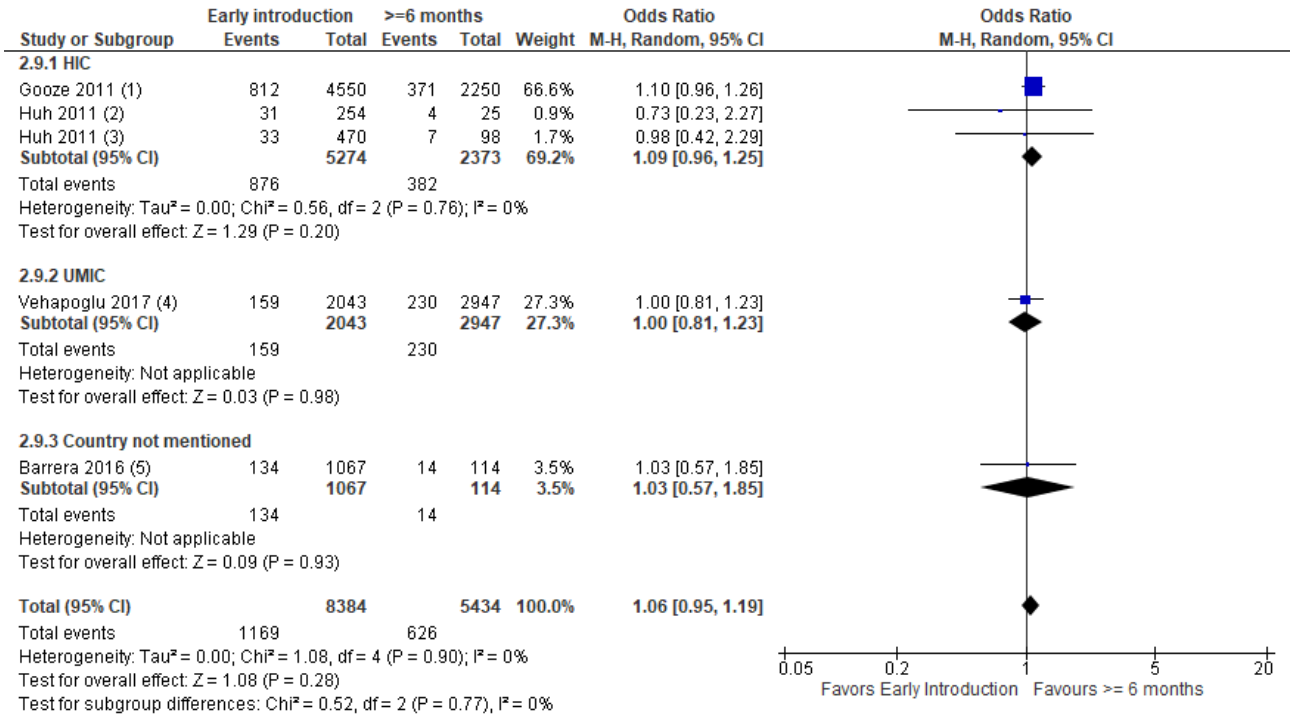
Footnotes
(1) at 5-6 years of age
(2) Formula fed group
(3) Breastfed group
(4) 9-10 years

Outcome 8: Overweight



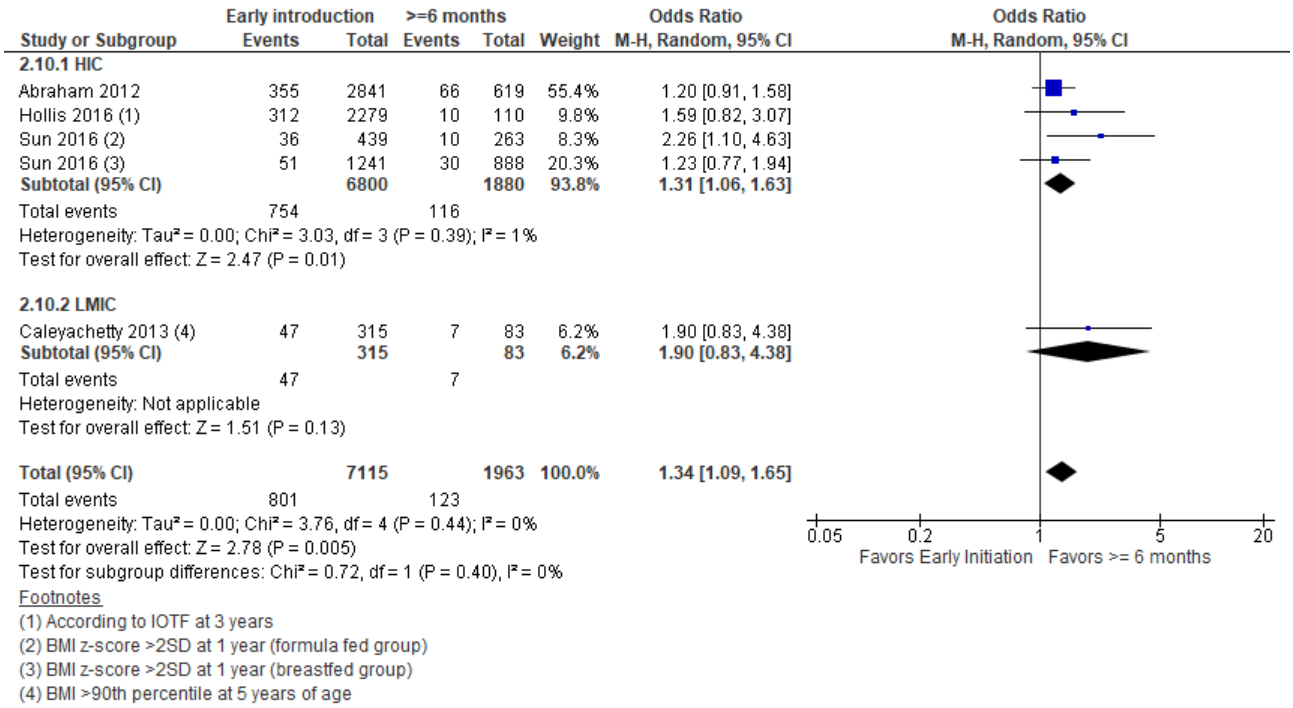
Footnotes
(1) at 12 mo
(2) Formlafed group at 3 years
(3) Breastfed group at 3 years
(4) defined as greater than or equal to 1 or less than 2 SD (5-6 year old)

Outcome 9: Obesity



Footnotes
(1) BMI >/=95 percentile (5.5 years)
(2) Formula fed group (BMI >95 percentile) at 3 years
(3) Breastfed group (BMI >95 percentile) at 3 years
(4) BMI >95 percentile (2-14 years)
(5) BMI >/=95 percentile (At 6 years)

Outcome 10: Overweight and obesity



Footnotes

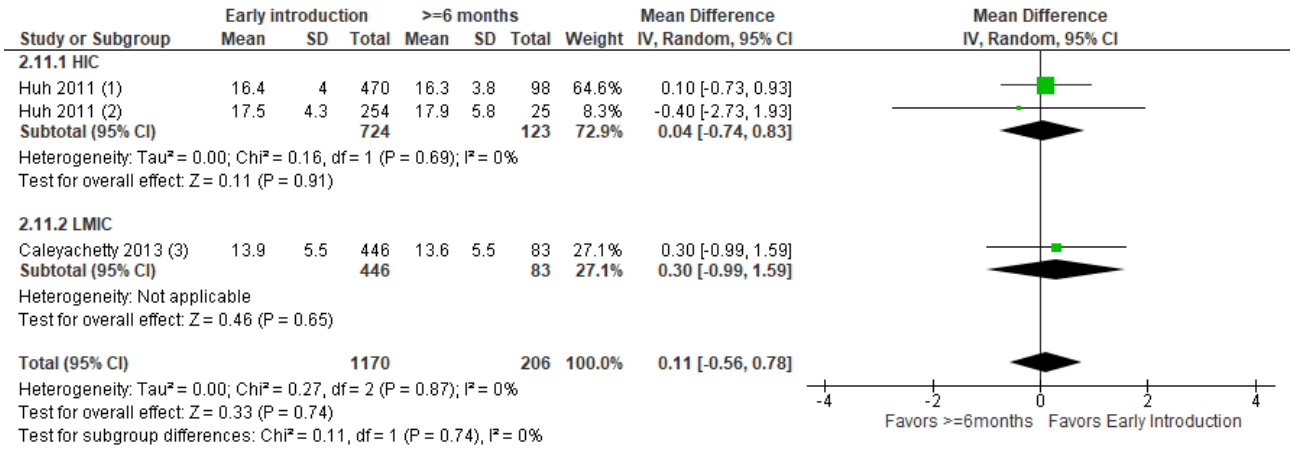
(1) According to IOTF at 3 years

(2) BMI z-score >2SD at 1 year (formula fed group)

(3) BMI z-score >2SD at 1 year (breastfed group)

(4) BMI >90th percentile at 5 years of age

Outcome 11: Skinfold Thickness (triceps + subscapular)



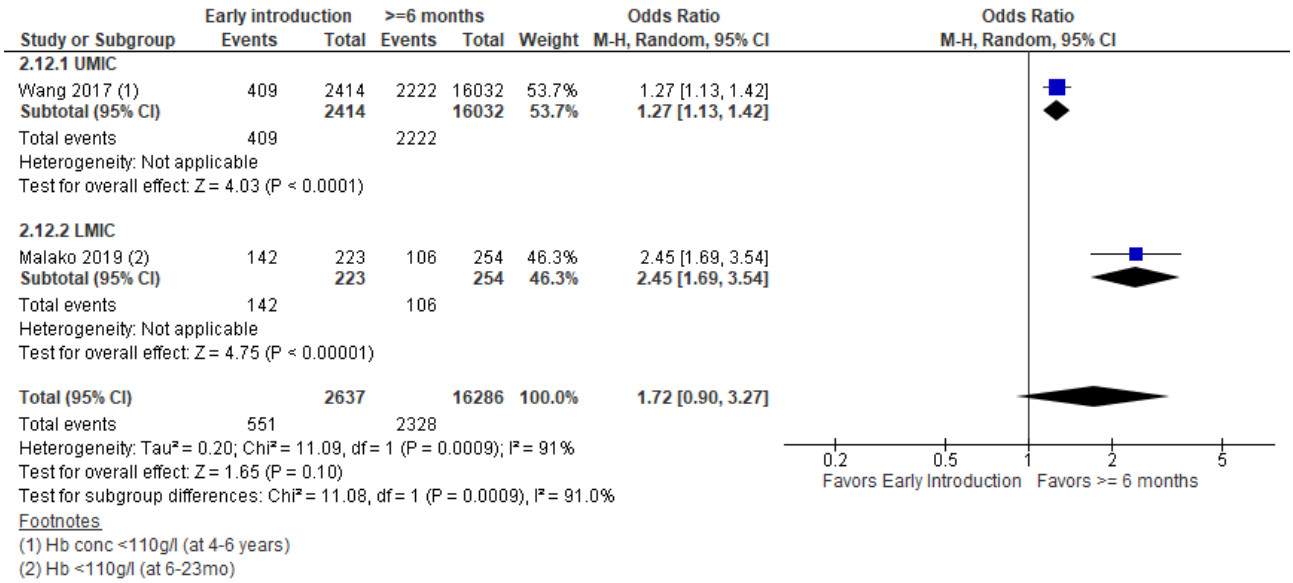
Footnotes

(1) Breastfed group (at 3 years)

(2) Formula fed group (at 3 years)

(3) At 5 years

Outcome 12: Anemia

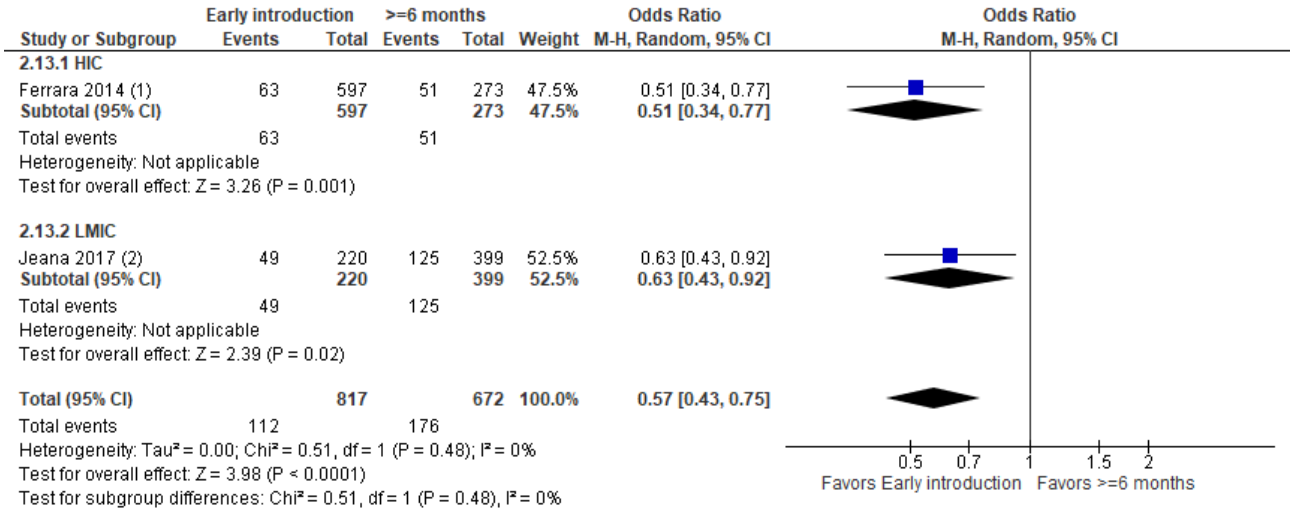


Footnotes

(1) Hb conc <110g/l (at 4-6 years)

(2) Hb <110g/l (at 6-23mo)

Outcome 13: Iron Deficiency

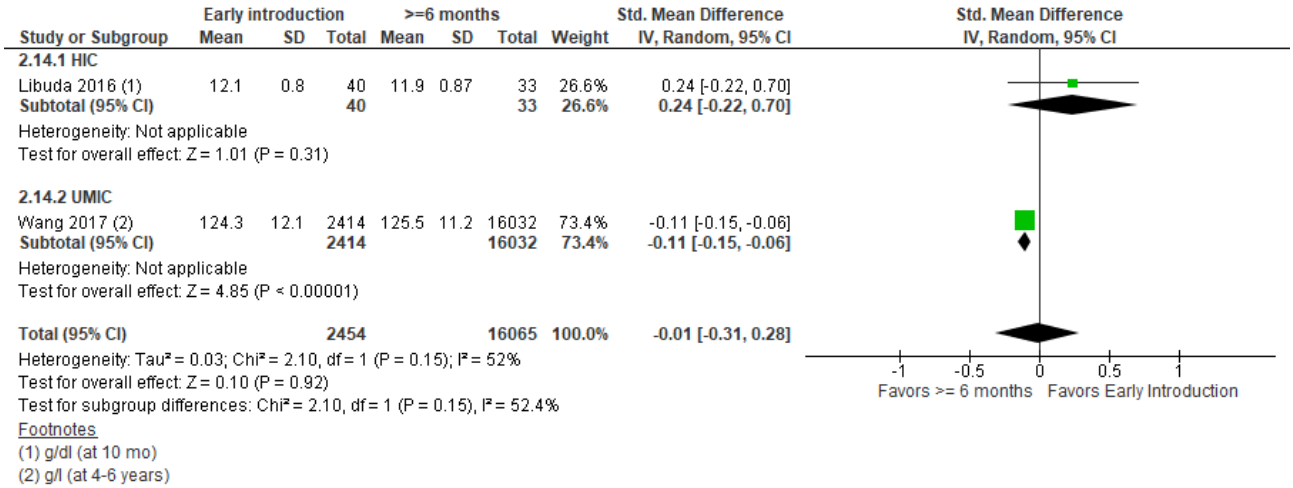


Footnotes

(1) at 24 Months

(2) serum ferritin <12ng/ml and MCV of <70Fl and transferrin saturation of <10 % (8-15mo)

Outcome 14: Hb levels

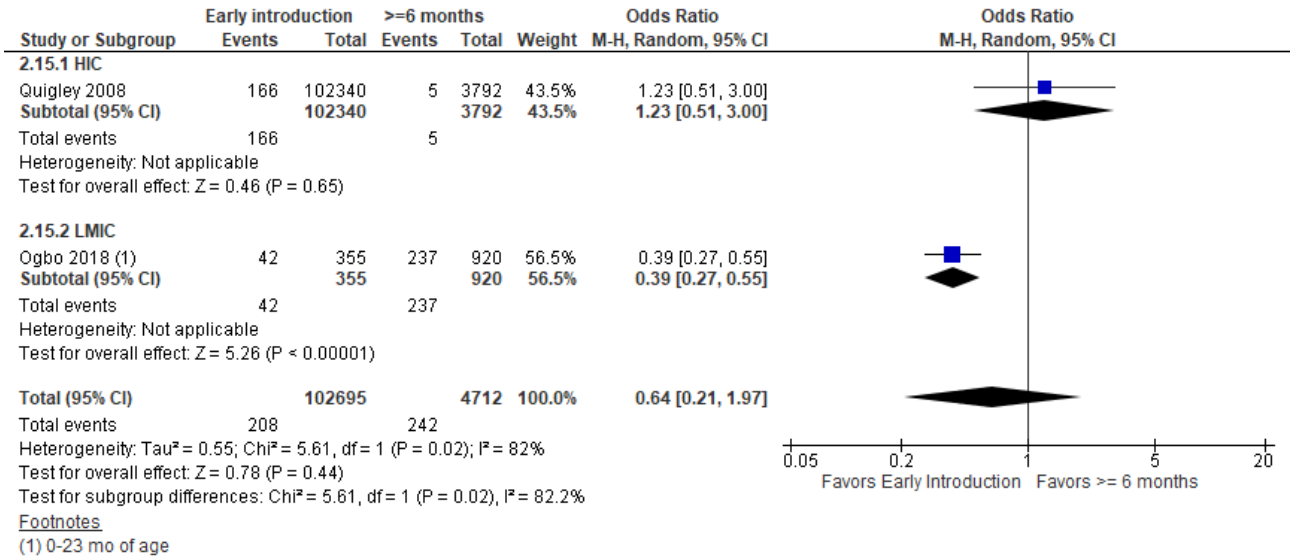


Footnotes

(1) g/dl (at 10 mo)

(2) g/l (at 4-6 years)

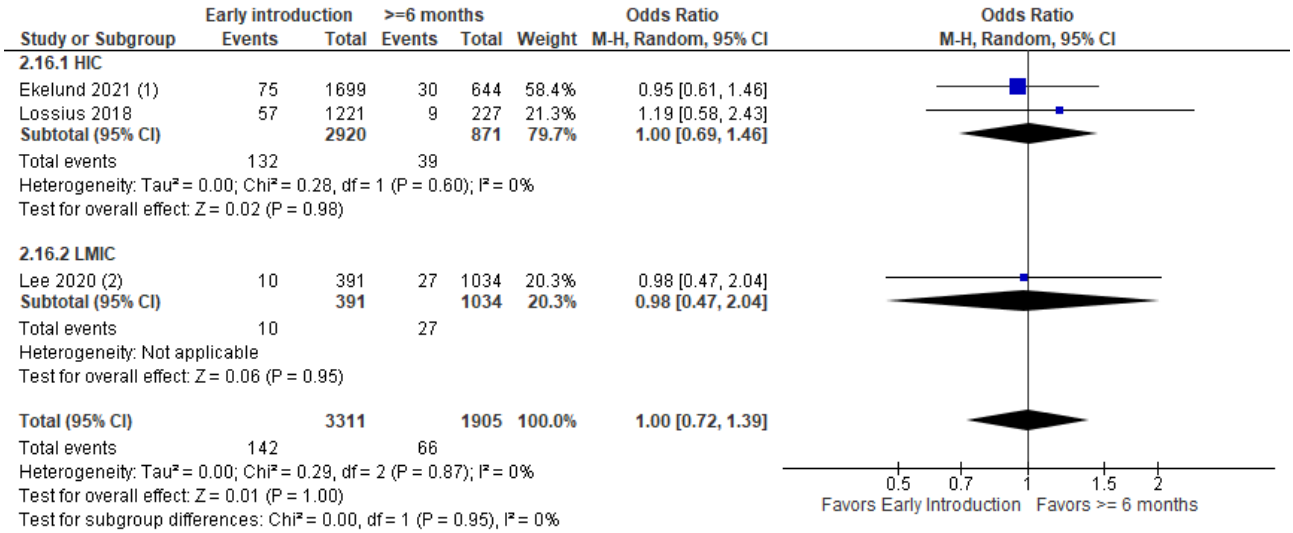
Outcome 15:Diarrhea



Footnotes

(1) 0-23 mo of age

Outcome 16:Asthma

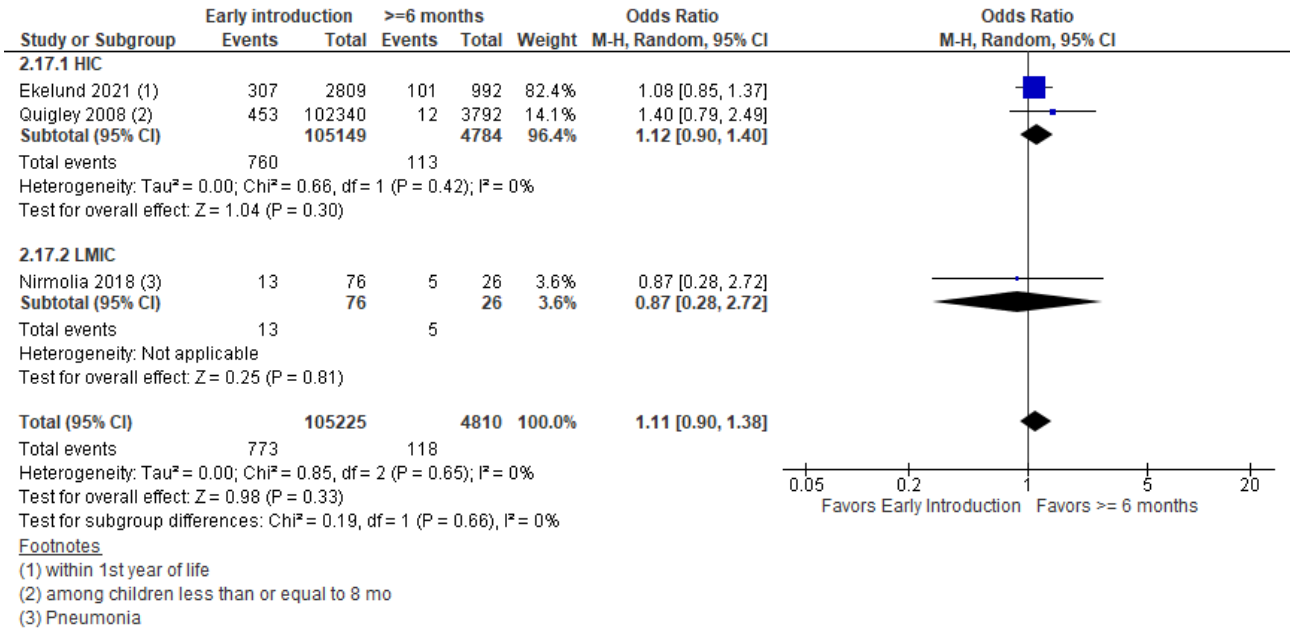


Footnotes

(1) at 2 and 6 years

(2) Between 1-3 years

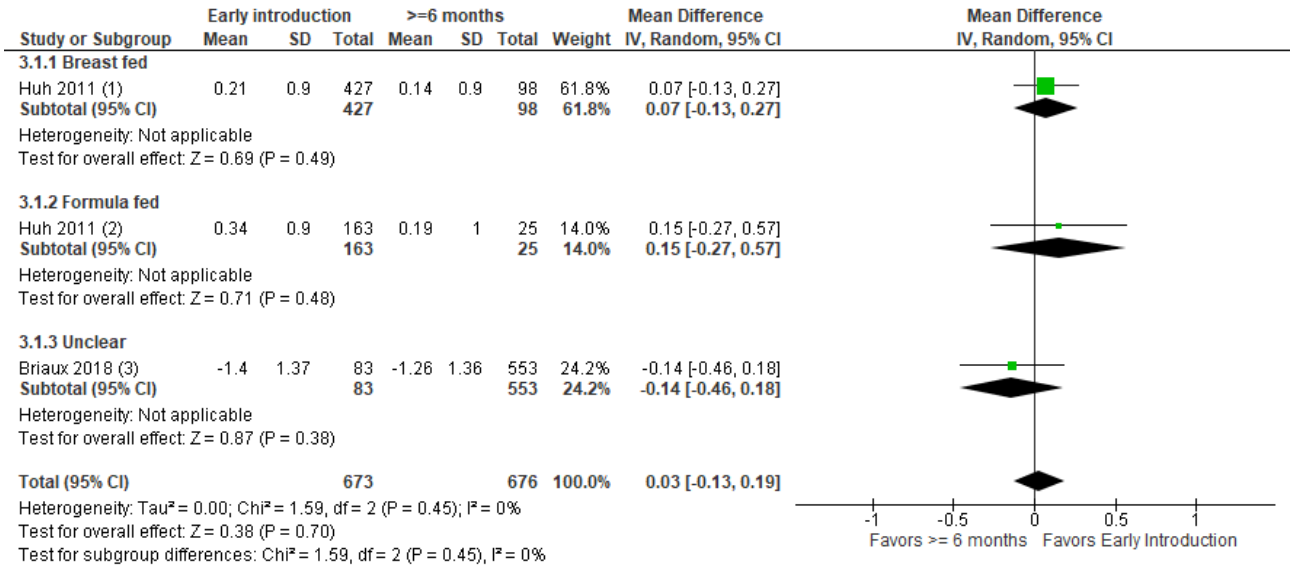
Outcome 17:LRTI



Footnotes
(1) within 1st year of life
(2) among children less than or equal to 8 mo
(3) Pneumonia

Comparison. Early introduction of CF (< six months of age) compared to ≥ six months of age among normal term infants (Observational studies) – subgroup by feeding practices

Outcome 1: HAZ

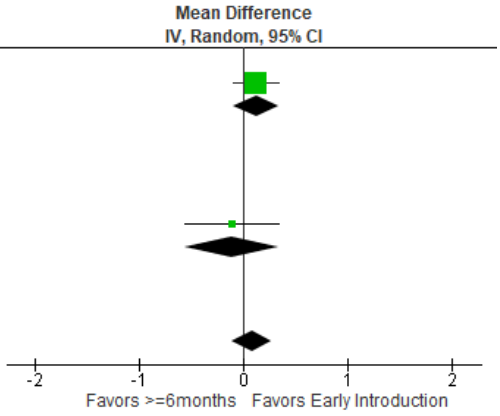


Footnotes
(1) Breastfed group
(2) Formula fed group
(3) at 18-23 mo

Outcome 2: WAZ

Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.2.1 Breast fed								
Huh 2011 (1)	0.42	0.9	427	0.3	1	98	81.5%	0.12 [-0.10, 0.34]
Subtotal (95% CI)			**427**			**98**	**81.5%**	**0.12 [-0.10, 0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.28)								
3.2.2 Formula fed								
Huh 2011 (2)	0.55	0.9	163	0.66	1.1	25	18.5%	-0.11 [-0.56, 0.34]
Subtotal (95% CI)			**163**			**25**	**18.5%**	**-0.11 [-0.56, 0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.48 (P = 0.63)								
Total (95% CI)			**590**			**123**	**100.0%**	**0.08 [-0.12, 0.27]**

Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.44)
Test for subgroup differences: Chi² = 0.81, df = 1 (P = 0.37), I² = 0%

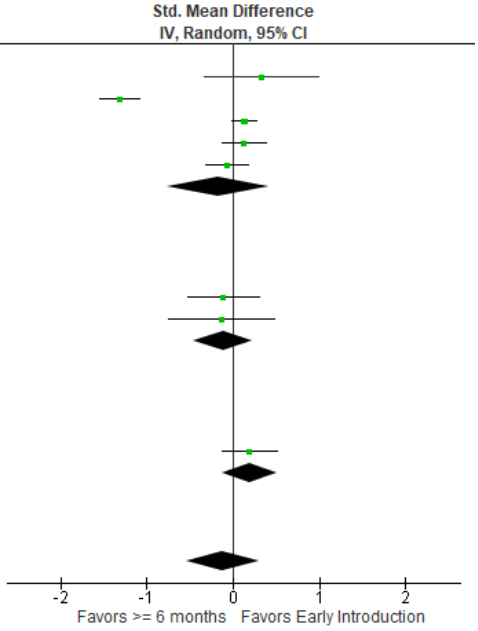


Footnotes
(1) Breastfed group at 3 years
(2) Formula fed group at 3 years

Outcome 3: Height

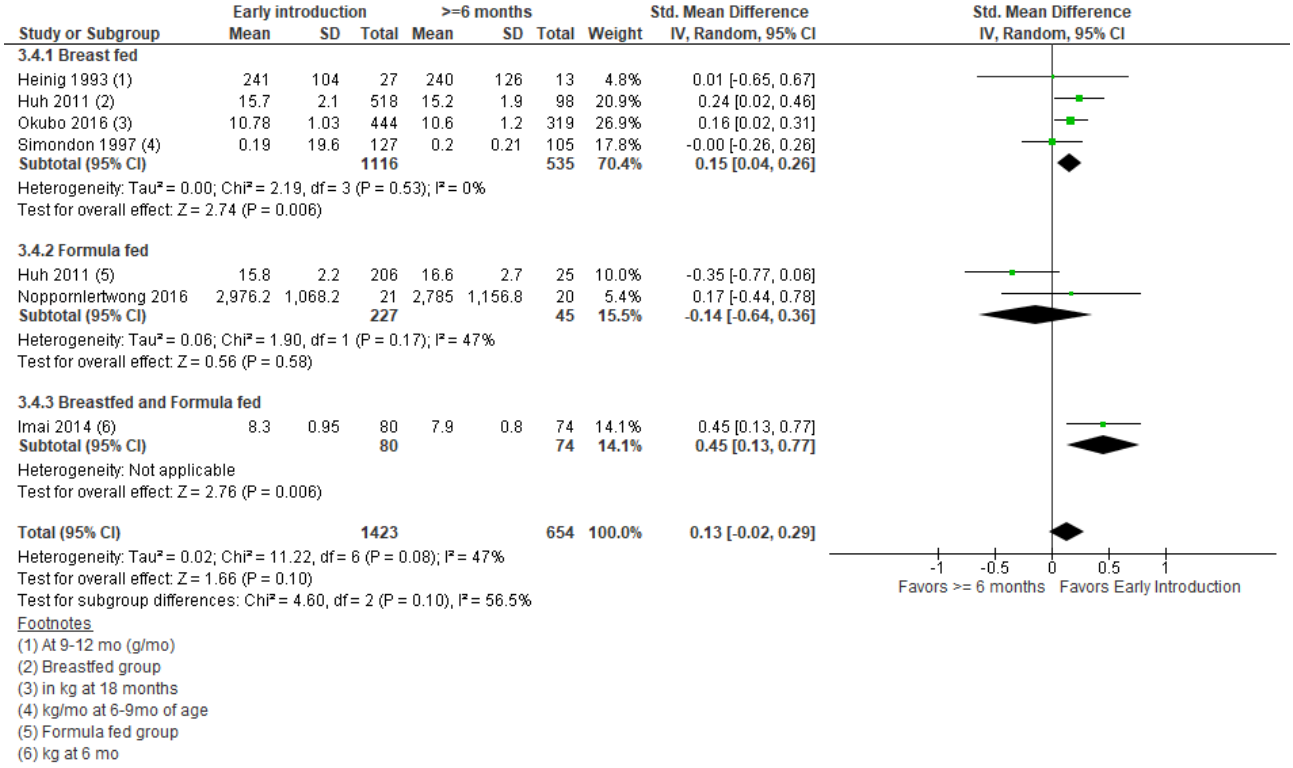
Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.3.1 Breast fed								
Heinig 1993 (1)	1.4	0.3	27	1.3	0.3	13	10.3%	0.33 [-0.34, 0.99]
Huh 2011 (2)	91.1	4.2	470	96.6	4.1	98	13.4%	-1.31 [-1.54, -1.08]
Okubo 2016 (3)	81.8	2.9	444	81.4	3.2	319	13.7%	0.13 [-0.01, 0.28]
Simondon 1997 (4)	1.3	0.5	127	1.24	0.44	105	13.2%	0.13 [-0.13, 0.38]
Veena 2010 (5)	130.6	5.7	404	131	5.2	78	13.3%	-0.07 [-0.31, 0.17]
Subtotal (95% CI)			**1472**			**613**	**64.0%**	**-0.18 [-0.77, 0.42]**
Heterogeneity: Tau² = 0.43; Chi² = 118.97, df = 4 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.59 (P = 0.56)								
3.3.2 Formula fed								
Huh 2011 (6)	98	4.4	254	98.5	5.6	25	12.3%	-0.11 [-0.52, 0.30]
Nopporniertwong 2016 (7)	11.9	2.1	21	12.2	2.2	20	10.8%	-0.14 [-0.75, 0.48]
Subtotal (95% CI)			**275**			**45**	**23.1%**	**-0.12 [-0.46, 0.22]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.94); I² = 0%								
Test for overall effect: Z = 0.68 (P = 0.50)								
3.3.3 Breastfed and Formula fed								
Imai 2014 (8)	68.9	2.15	80	68.5	2.1	74	12.9%	0.19 [-0.13, 0.50]
Subtotal (95% CI)			**80**			**74**	**12.9%**	**0.19 [-0.13, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.16 (P = 0.25)								
Total (95% CI)			**1827**			**732**	**100.0%**	**-0.12 [-0.54, 0.30]**

Heterogeneity: Tau² = 0.33; Chi² = 123.35, df = 7 (P < 0.00001); I² = 94%
Test for overall effect: Z = 0.56 (P = 0.57)
Test for subgroup differences: Chi² = 2.13, df = 2 (P = 0.35), I² = 6.0%



Footnotes
(1) 9-12 mo (cm/mo)
(2) Breastfed group
(3) in cm, at 18 mo
(4) cm/mo at 6-9 mo of age
(5) 9-10 years (height in cm)
(6) Formula fed group
(7) Length increase from enrolment to 12 mo (cm)
(8) in cm at 6 months

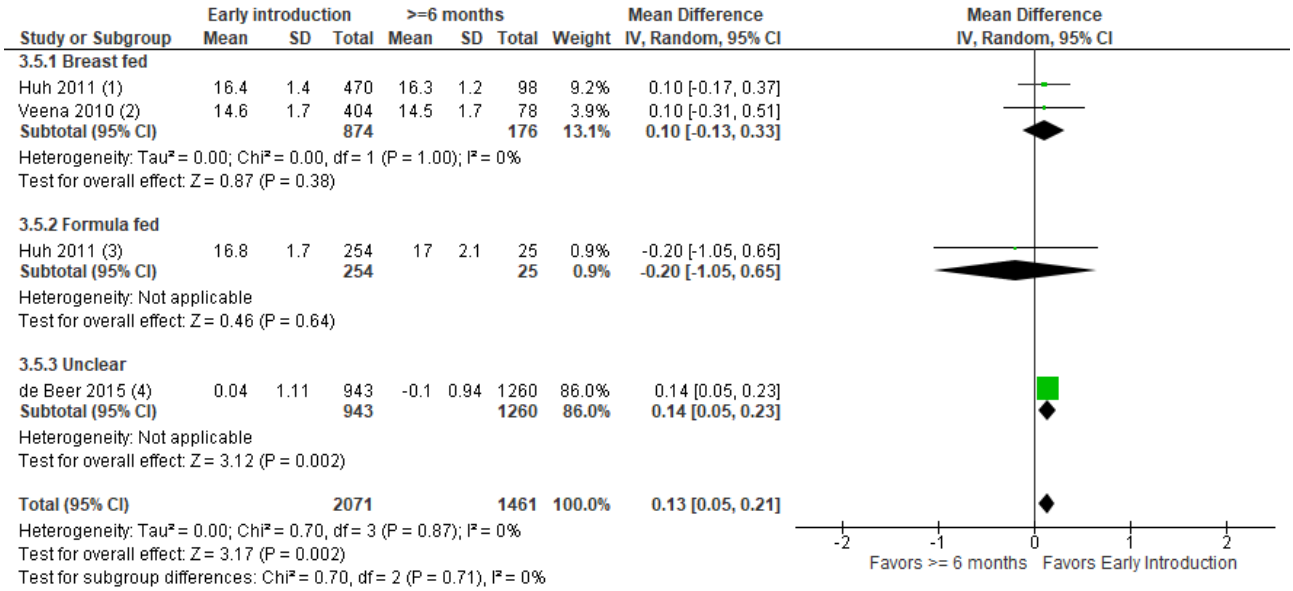
Outcome 4: Weight



Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.4.1 Breast fed								
Heinig 1993 (1)	241	104	27	240	126	13	4.8%	0.01 [-0.65, 0.67]
Huh 2011 (2)	15.7	2.1	518	15.2	1.9	98	20.9%	0.24 [0.02, 0.46]
Okubo 2016 (3)	10.78	1.03	444	10.6	1.2	319	26.9%	0.16 [0.02, 0.31]
Simondon 1997 (4)	0.19	19.6	127	0.2	0.21	105	17.8%	-0.00 [-0.26, 0.26]
Subtotal (95% CI)			**1116**			**535**	**70.4%**	**0.15 [0.04, 0.26]**
Heterogeneity: Tau² = 0.00; Chi² = 2.19, df = 3 (P = 0.53); I² = 0%								
Test for overall effect: Z = 2.74 (P = 0.006)								
3.4.2 Formula fed								
Huh 2011 (5)	15.8	2.2	206	16.6	2.7	25	10.0%	-0.35 [-0.77, 0.06]
Nopporniertwong 2016	2,976.2	1,068.2	21	2,785	1,156.8	20	5.4%	0.17 [-0.44, 0.78]
Subtotal (95% CI)			**227**			**45**	**15.5%**	**-0.14 [-0.64, 0.36]**
Heterogeneity: Tau² = 0.06; Chi² = 1.90, df = 1 (P = 0.17); I² = 47%								
Test for overall effect: Z = 0.56 (P = 0.58)								
3.4.3 Breastfed and Formula fed								
Imai 2014 (6)	8.3	0.95	80	7.9	0.8	74	14.1%	0.45 [0.13, 0.77]
Subtotal (95% CI)			**80**			**74**	**14.1%**	**0.45 [0.13, 0.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.76 (P = 0.006)								
Total (95% CI)			**1423**			**654**	**100.0%**	**0.13 [-0.02, 0.29]**
Heterogeneity: Tau² = 0.02; Chi² = 11.22, df = 6 (P = 0.08); I² = 47%								
Test for overall effect: Z = 1.66 (P = 0.10)								
Test for subgroup differences: Chi² = 4.60, df = 2 (P = 0.10), I² = 56.5%								

Footnotes
(1) At 9-12 mo (g/mo)
(2) Breastfed group
(3) in kg at 18 months
(4) kg/mo at 6-9mo of age
(5) Formula fed group
(6) kg at 6 mo

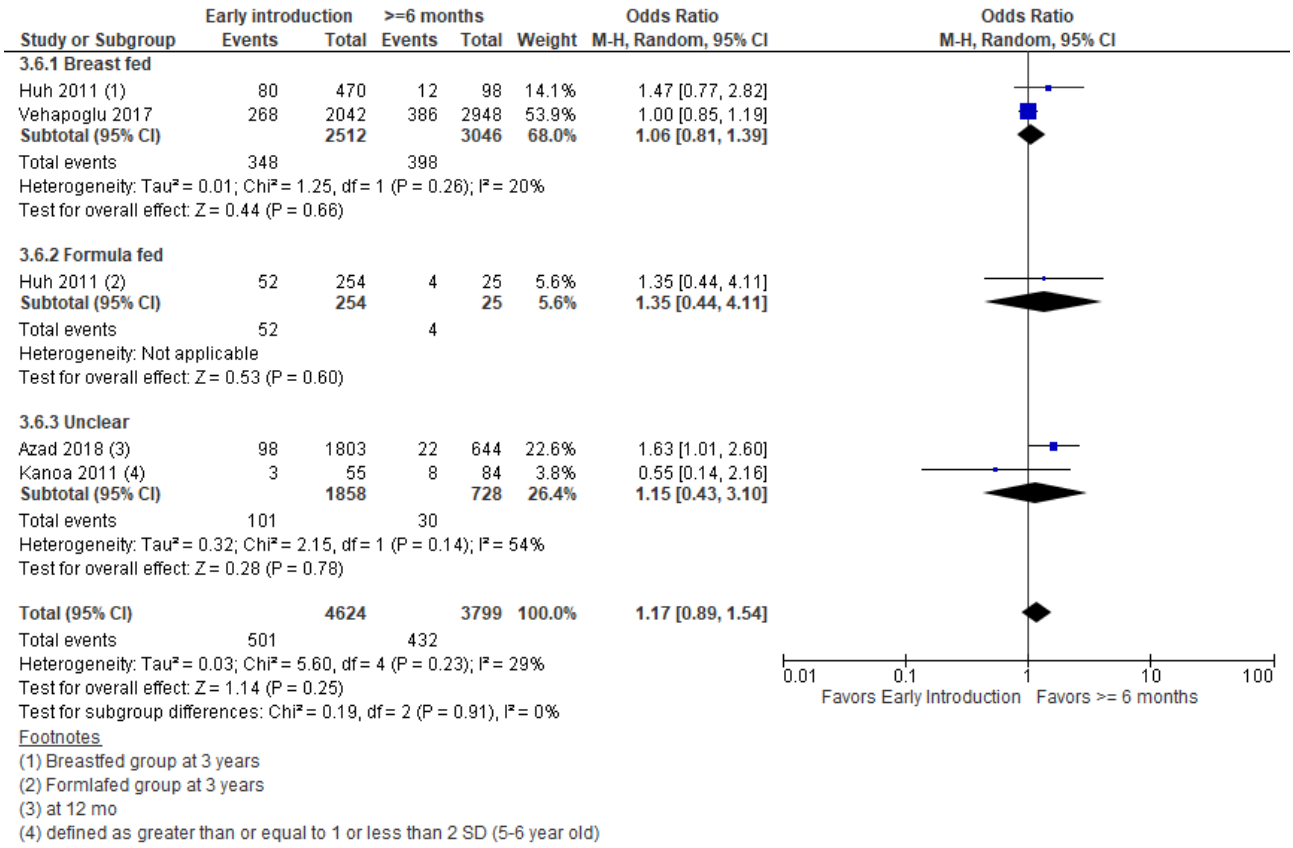
Outcome 5: BMI



Study or Subgroup	Early introduction Mean	SD	Total	>=6 months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.5.1 Breast fed								
Huh 2011 (1)	16.4	1.4	470	16.3	1.2	98	9.2%	0.10 [-0.17, 0.37]
Veena 2010 (2)	14.6	1.7	404	14.5	1.7	78	3.9%	0.10 [-0.31, 0.51]
Subtotal (95% CI)			**874**			**176**	**13.1%**	**0.10 [-0.13, 0.33]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%								
Test for overall effect: Z = 0.87 (P = 0.38)								
3.5.2 Formula fed								
Huh 2011 (3)	16.8	1.7	254	17	2.1	25	0.9%	-0.20 [-1.05, 0.65]
Subtotal (95% CI)			**254**			**25**	**0.9%**	**-0.20 [-1.05, 0.65]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.46 (P = 0.64)								
3.5.3 Unclear								
de Beer 2015 (4)	0.04	1.11	943	-0.1	0.94	1260	86.0%	0.14 [0.05, 0.23]
Subtotal (95% CI)			**943**			**1260**	**86.0%**	**0.14 [0.05, 0.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.12 (P = 0.002)								
Total (95% CI)			**2071**			**1461**	**100.0%**	**0.13 [0.05, 0.21]**
Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 3 (P = 0.87); I² = 0%								
Test for overall effect: Z = 3.17 (P = 0.002)								
Test for subgroup differences: Chi² = 0.70, df = 2 (P = 0.71), I² = 0%								

Footnotes
(1) Breastfed group
(2) 9-10 years
(3) Formula fed group
(4) at 5-6 years of age

Outcome 6: Overweight



Footnotes

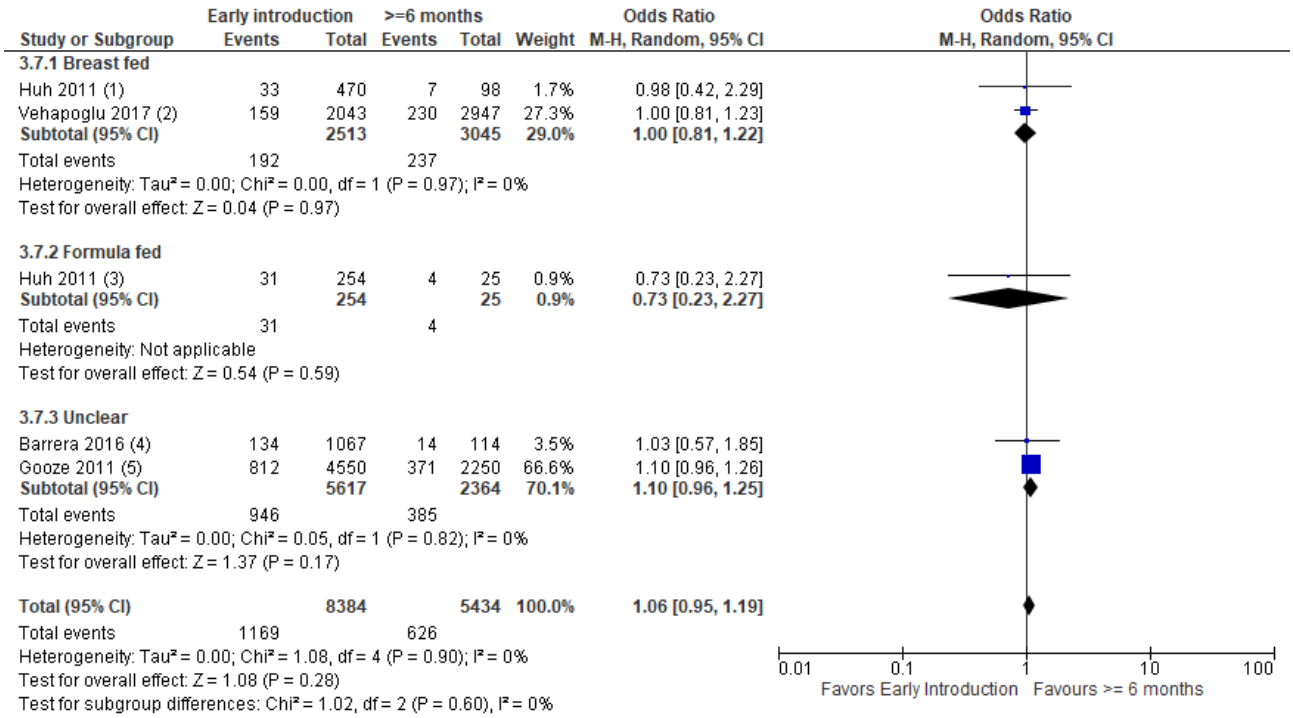
(1) Breastfed group at 3 years

(2) Formlafed group at 3 years

(3) at 12 mo

(4) defined as greater than or equal to 1 or less than 2 SD (5-6 year old)

Outcome 7: Obesity



Footnotes

(1) Breastfed group (BMI >95 percentile) at 3 years

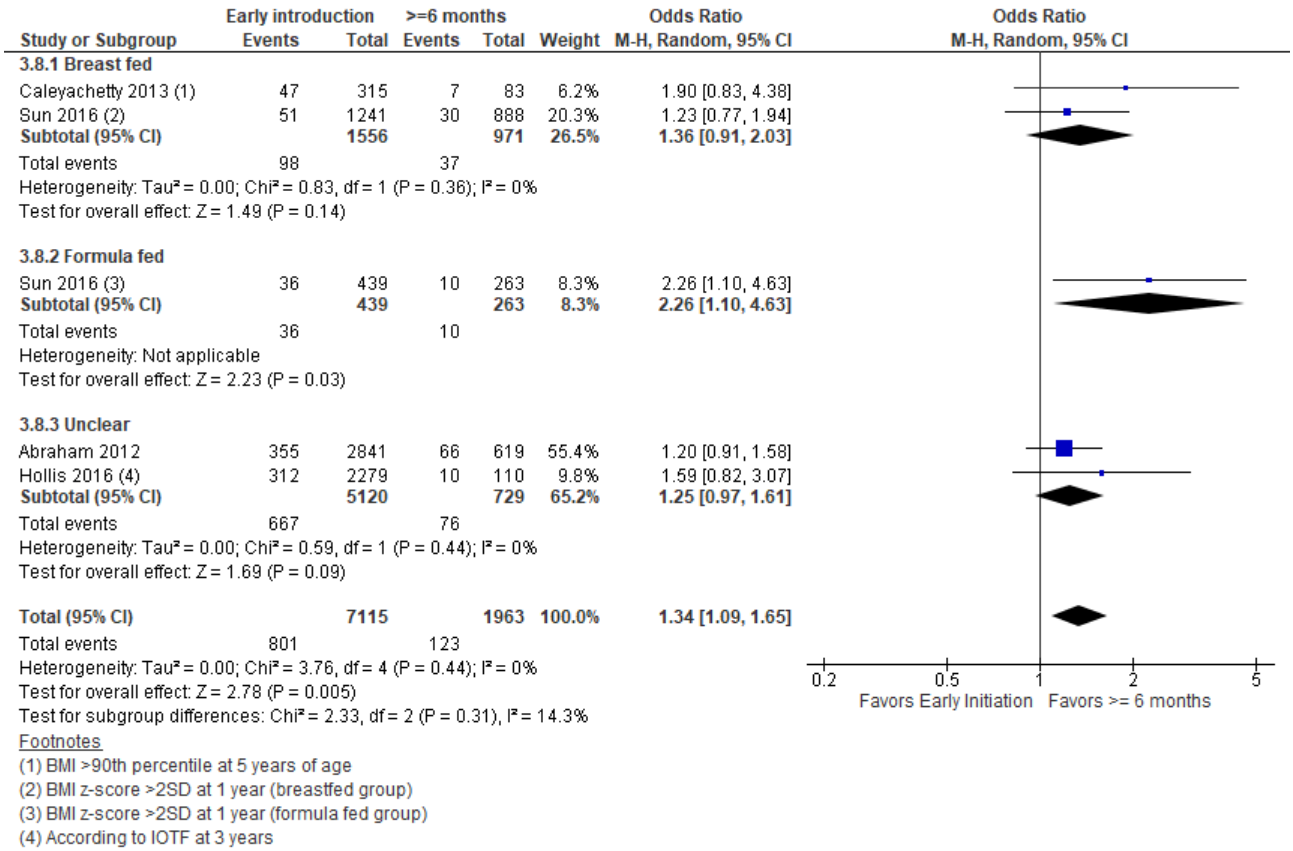
(2) BMI >95 percentile (2-14 years)

(3) Formula fed group (BMI >95 percentile) at 3 years

(4) BMI >/=95 percentile (At 6 years)

(5) BMI >/=95 percentile (5.5 years)

Outcome 8: Overweight and Obesity



Footnotes

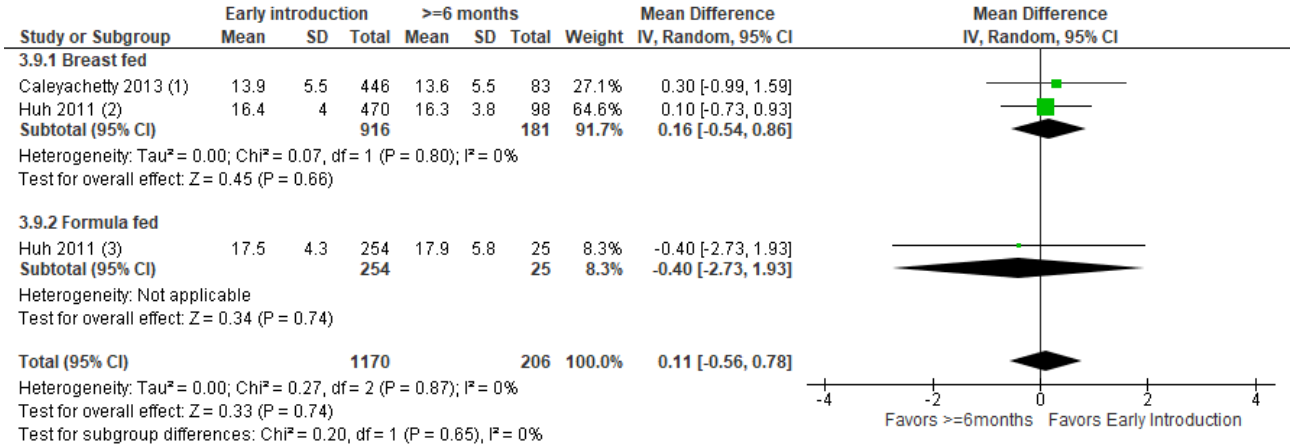
(1) BMI >90th percentile at 5 years of age

(2) BMI z-score >2SD at 1 year (breastfed group)

(3) BMI z-score >2SD at 1 year (formula fed group)

(4) According to IOTF at 3 years

Outcome 9: Skinfold Thickness (triceps + subscapular)



Footnotes

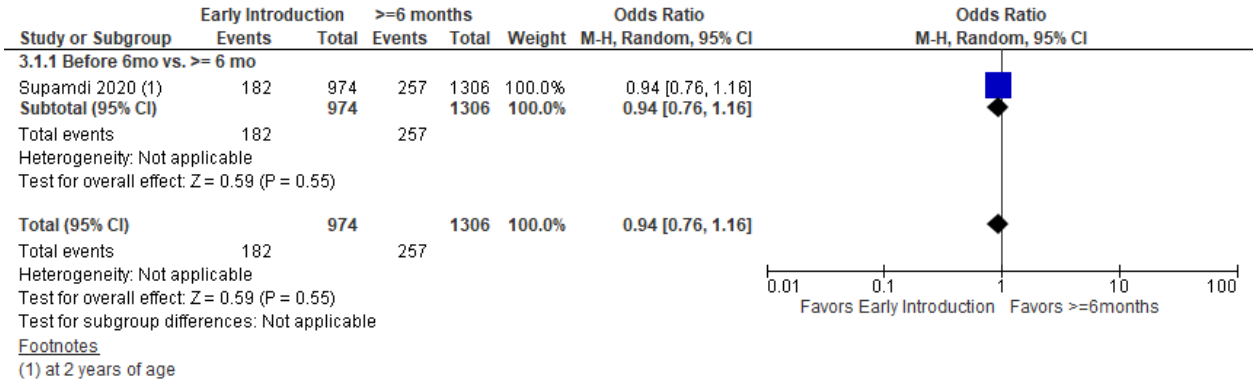
(1) At 5 years

(2) Breastfed group (at 3 years)

(3) Formula fed group (at 3 years)

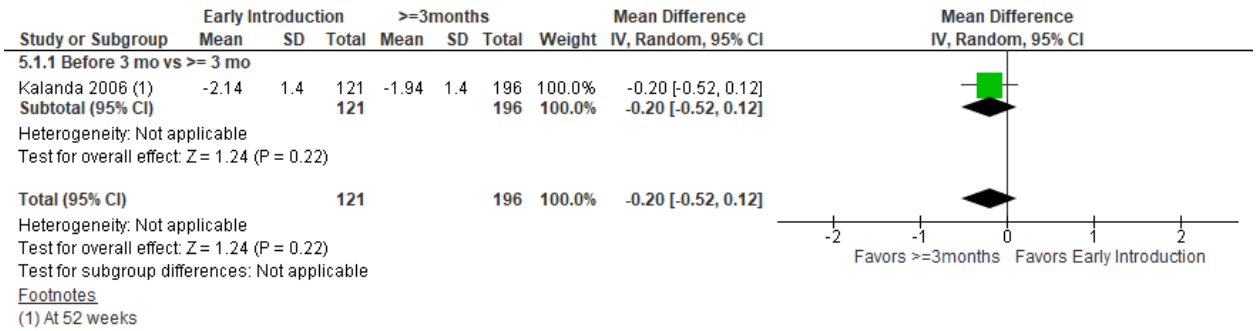
Comparison. Early introduction of CF (< six months of age) compared to ≥ six months of age among preterm infants (Observational studies)

Outcome 1: Underweight

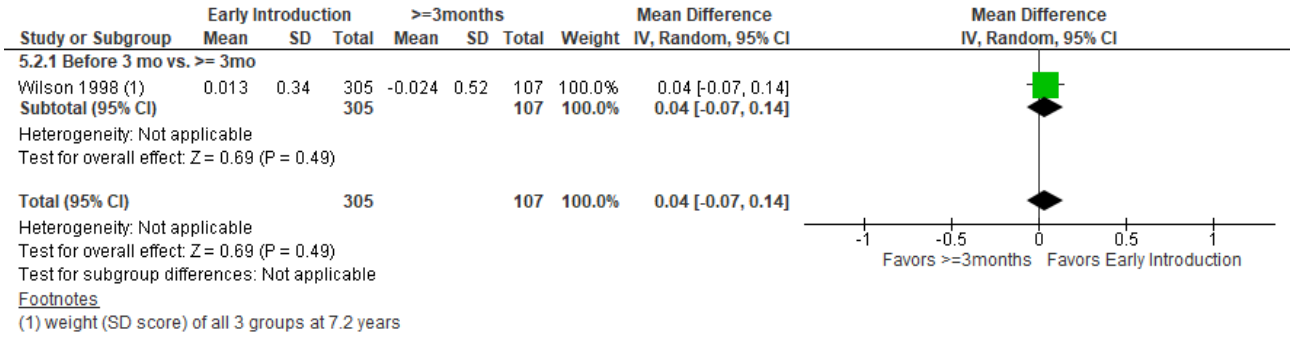


Comparison. Early introduction of CF (< three months of age) compared to ≥ three months of age among normal term infants (Observational studies)

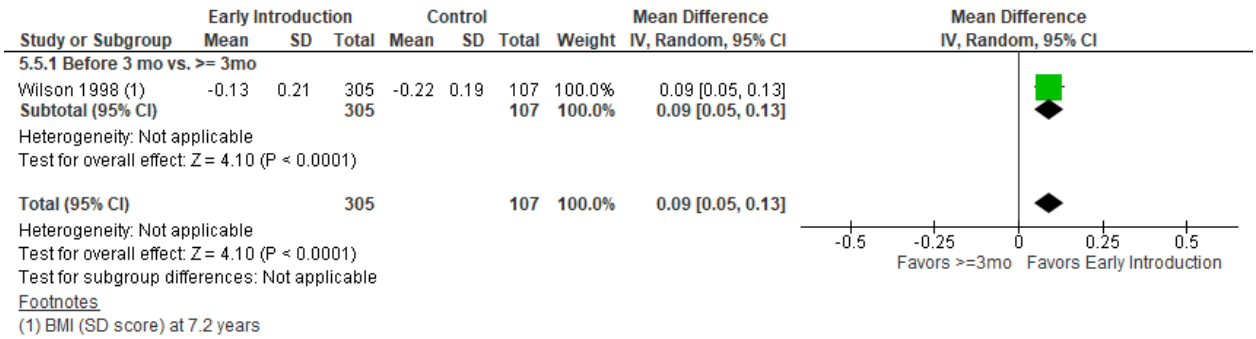
Outcome 1: Weight for age Z-score



Outcome 2: Weight

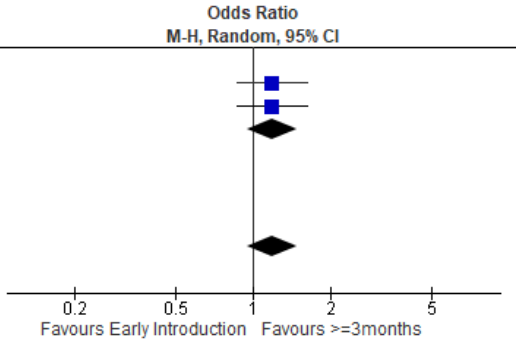


Outcome 3: BMI



Outcome 4:Diarrhea

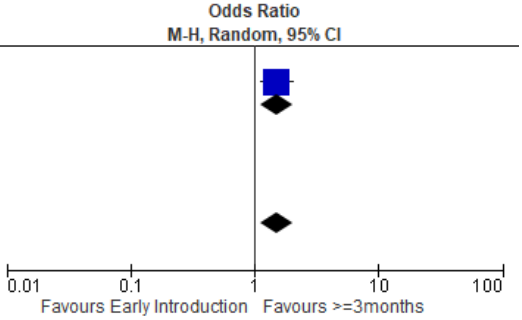
Study or Subgroup	Early Introduction Events	Total	>=3months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
5.4.1 Before 3 mo vs. >=3 mo						
Quigley 2008 (1)	61	33734	110	72392	50.0%	1.19 [0.87, 1.63]
Wright 2004 (2)	61	33734	110	72398	50.0%	1.19 [0.87, 1.63]
Subtotal (95% CI)		**67468**		**144790**	**100.0%**	**1.19 [0.95, 1.49]**
Total events	122		220			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
Total (95% CI)		**67468**		**144790**	**100.0%**	**1.19 [0.95, 1.49]**
Total events	122		220			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
Test for subgroup differences: Not applicable						



Footnotes
(1) among children less than or equal to 8 mo
(2) between age 6 week to 4 months

Outcome 5: LRTI

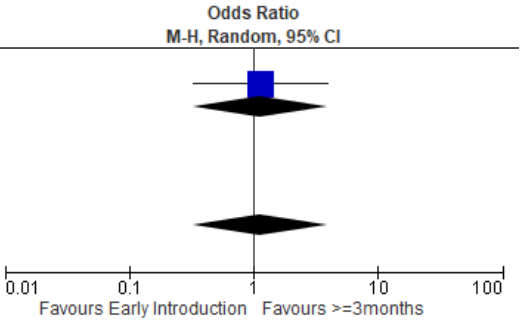
Study or Subgroup	Early Introduction Events	Total	>=3months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
5.5.1 Before 3 mo vs. >=3 mo						
Quigley 2008 (1)	49	7712	416	98420	100.0%	1.51 [1.12, 2.03]
Subtotal (95% CI)		**7712**		**98420**	**100.0%**	**1.51 [1.12, 2.03]**
Total events	49		416			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.70 (P = 0.007)						
Total (95% CI)		**7712**		**98420**	**100.0%**	**1.51 [1.12, 2.03]**
Total events	49		416			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.70 (P = 0.007)						
Test for subgroup differences: Not applicable						



Footnotes
(1) among children less than or equal to 8 mo

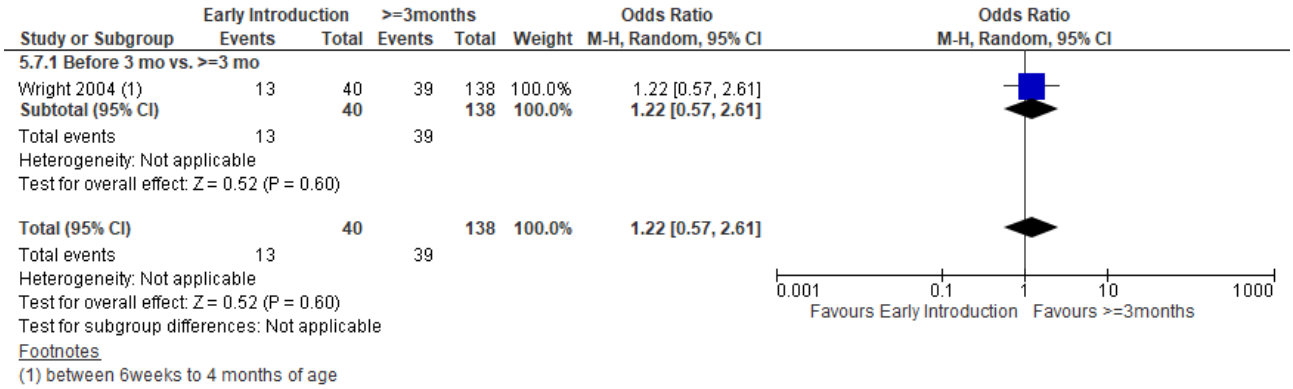
Outcome 6: Chest Infection

Study or Subgroup	Early Introduction Events	Total	>=3months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
5.6.1 Before 3 mo vs. >=3 mo						
Wright 2004 (1)	4	24	11	73	100.0%	1.13 [0.32, 3.94]
Subtotal (95% CI)		**24**		**73**	**100.0%**	**1.13 [0.32, 3.94]**
Total events	4		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						
Total (95% CI)		**24**		**73**	**100.0%**	**1.13 [0.32, 3.94]**
Total events	4		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						
Test for subgroup differences: Not applicable						

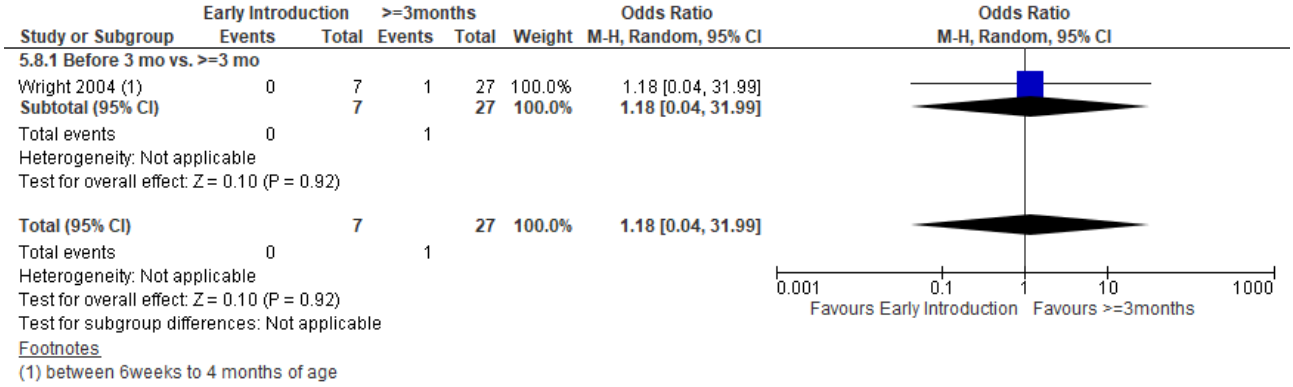


Footnotes
(1) between 6weeks to 4 months of age

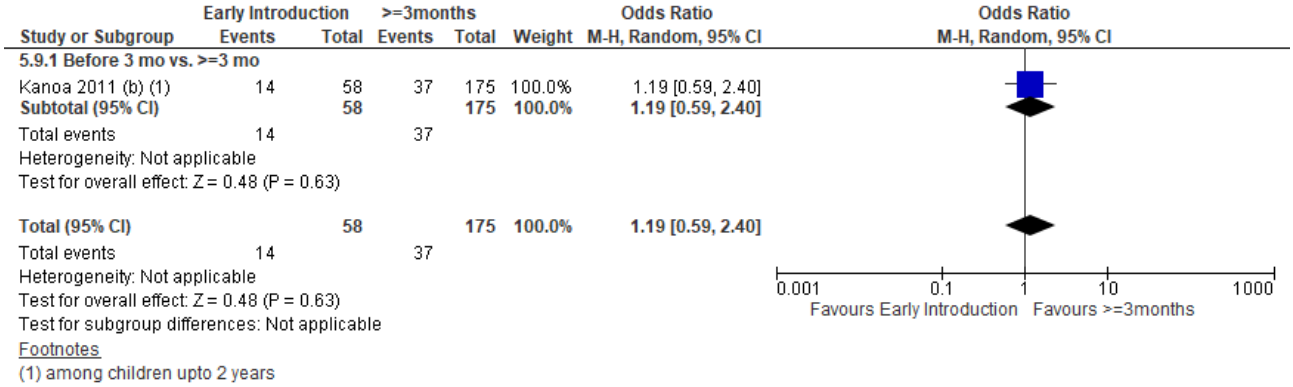
Outcome 7: Eczema



Outcome 8: Ear Infection

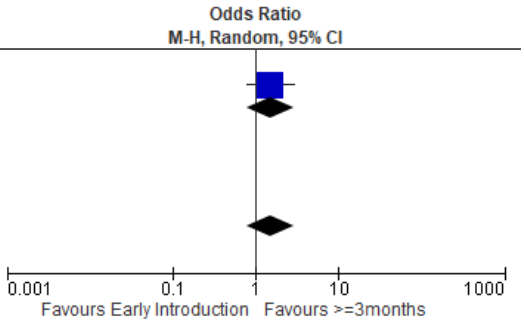


Outcome 9: Gastrointestinal illness



Outcome 10: Respiratory illness

Study or Subgroup	Early Introduction Events	Total	>=3months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
5.10.1 Before 3 mo vs. >=3 mo						
Kanoa 2011 (b) (1)	18	58	40	175	100.0%	1.52 [0.79, 2.93]
Subtotal (95% CI)		**58**		**175**	**100.0%**	**1.52 [0.79, 2.93]**
Total events	18		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.24 (P = 0.21)						
Total (95% CI)		**58**		**175**	**100.0%**	**1.52 [0.79, 2.93]**
Total events	18		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.24 (P = 0.21)						
Test for subgroup differences: Not applicable						

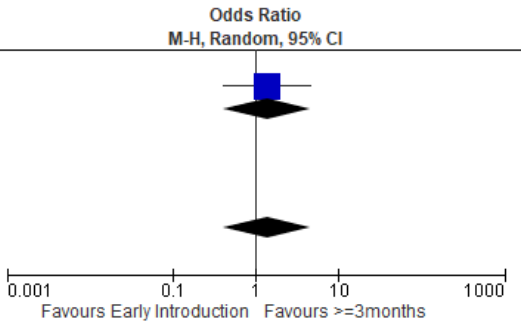


Footnotes

(1) among children upto 2 years

Outcome 11: Rickets

Study or Subgroup	Early Introduction Events	Total	>=3months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
5.11.1 Before 3 mo vs. >=3 mo						
Kanoa 2011 (b) (1)	4	58	9	175	100.0%	1.37 [0.40, 4.61]
Subtotal (95% CI)		**58**		**175**	**100.0%**	**1.37 [0.40, 4.61]**
Total events	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
Total (95% CI)		**58**		**175**	**100.0%**	**1.37 [0.40, 4.61]**
Total events	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						
Test for subgroup differences: Not applicable						

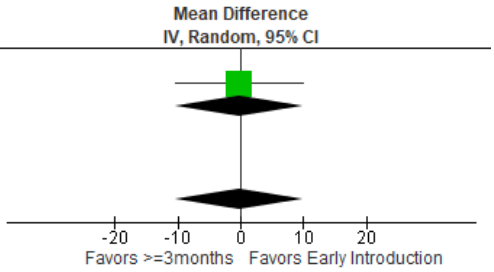


Footnotes

(1) among children upto 2 years

Outcome 12: Systolic Blood Pressure

Study or Subgroup	Early Introduction Mean	SD	Total	>=3months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.9.1 Before 3 mo vs. >= 3mo								
Wilson 1998 (1)	91.72	4.16	26	91.93	19.21	14	100.0%	-0.21 [-10.40, 9.98]
Subtotal (95% CI)			**26**			**14**	**100.0%**	**-0.21 [-10.40, 9.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.04 (P = 0.97)								
Total (95% CI)			**26**			**14**	**100.0%**	**-0.21 [-10.40, 9.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.04 (P = 0.97)								
Test for subgroup differences: Not applicable								

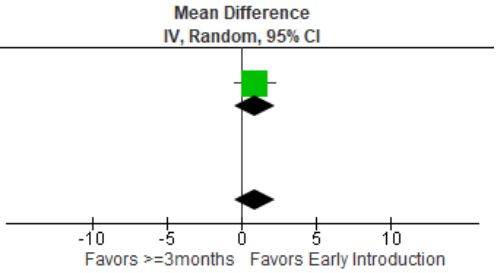


Footnotes

(1) mm of Hg at 7.2 years

Outcome 13: Diastolic Blood Pressure

Study or Subgroup	Early Introduction Mean	SD	Total	>=3months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.10.1 Before 3 mo vs. >= 3mo								
Wilson 1998 (1)	57.27	2.5	26	56.41	1.91	14	100.0%	0.86 [-0.53, 2.25]
Subtotal (95% CI)			**26**			**14**	**100.0%**	**0.86 [-0.53, 2.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Total (95% CI)			**26**			**14**	**100.0%**	**0.86 [-0.53, 2.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Test for subgroup differences: Not applicable								

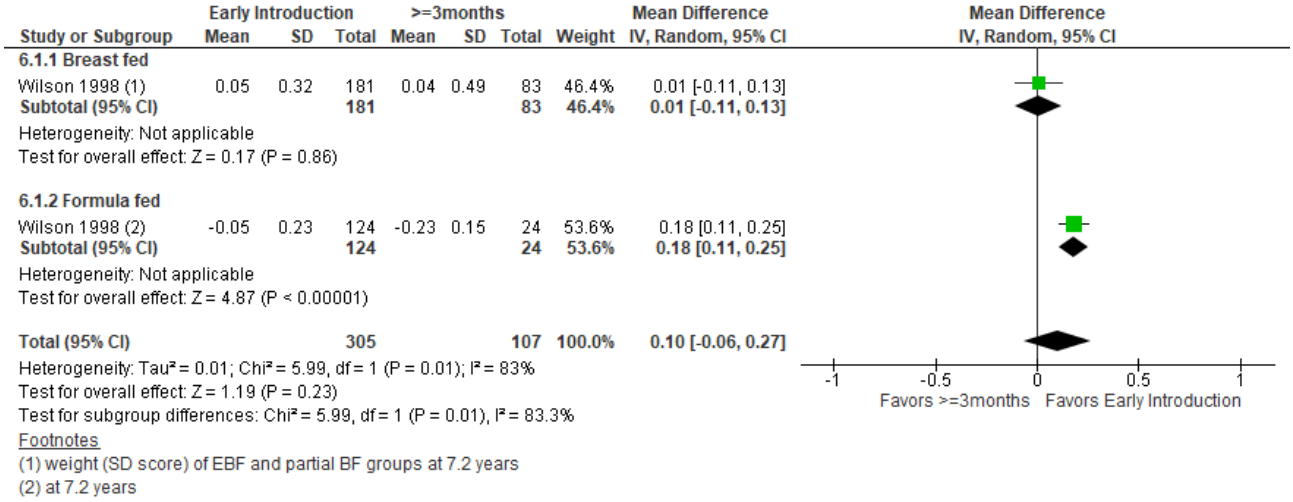


Footnotes

(1) mm of Hg at 7.2 years

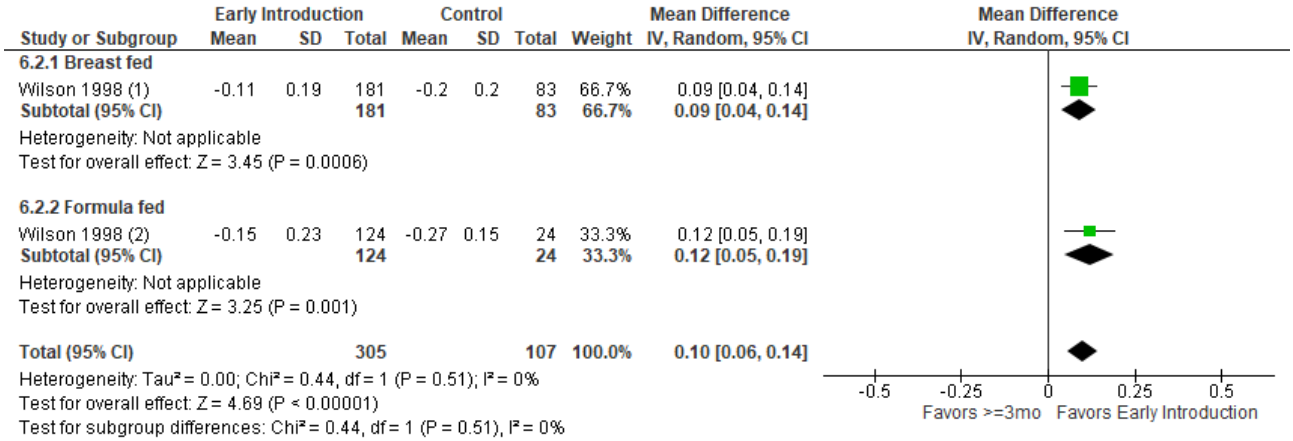
Comparison. Early introduction of CF (< three months of age) compared to ≥ three months of age (among normal term infants (Observational studies) – subgroup by feeding practices

Outcome 1: Weight



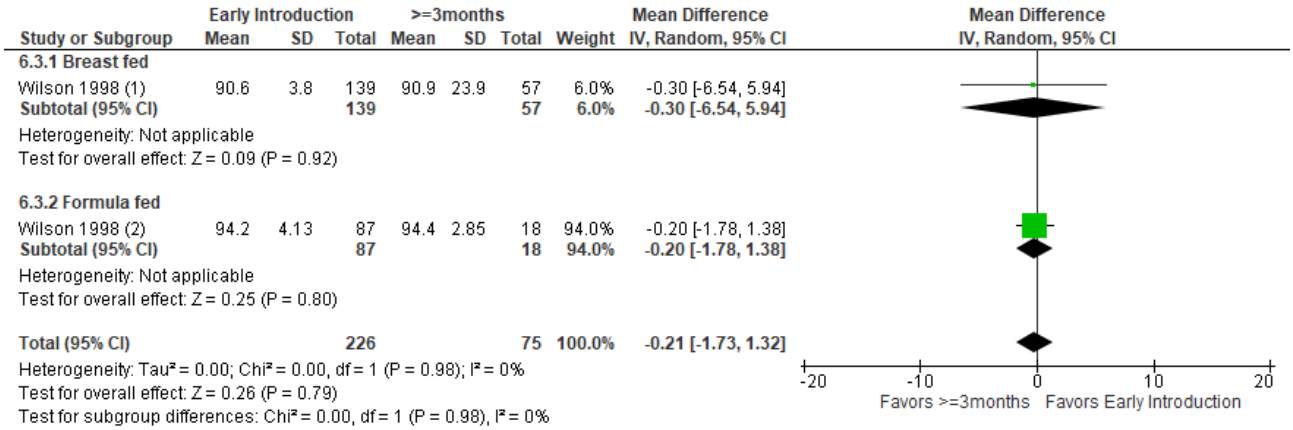
Footnotes
(1) weight (SD score) of EBF and partial BF groups at 7.2 years
(2) at 7.2 years

Outcome 2: BMI



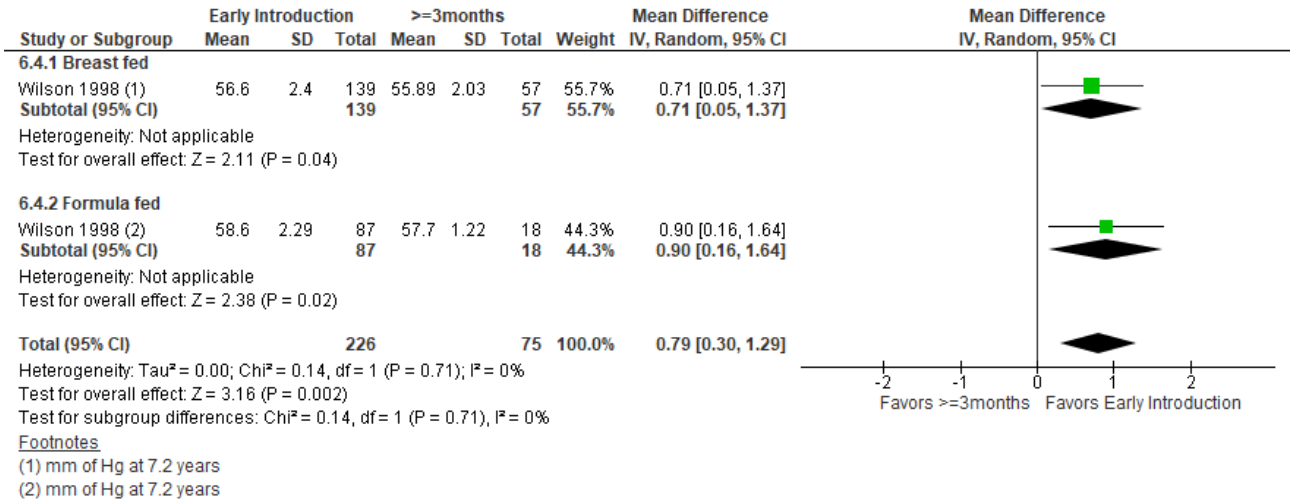
Footnotes
(1) BMI (SD score) EBP plus partially BF group at 7.2 years
(2) BMI (SD score) at 7.2 years

Outcome 3: Systolic Blood Pressure



Footnotes
(1) mm of Hg at 7.2 years
(2) mm of Hg at 7.2 years

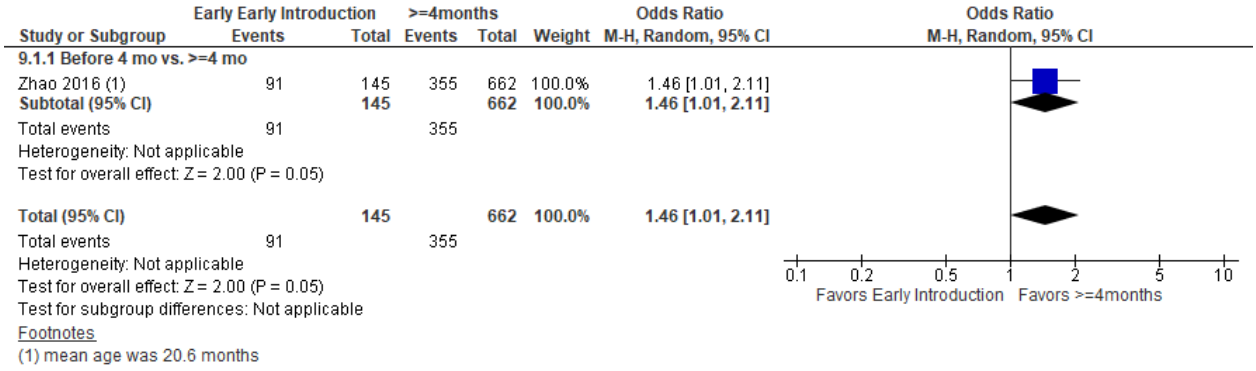
Outcome 4: Diastolic Blood Pressure



Footnotes
(1) mm of Hg at 7.2 years
(2) mm of Hg at 7.2 years

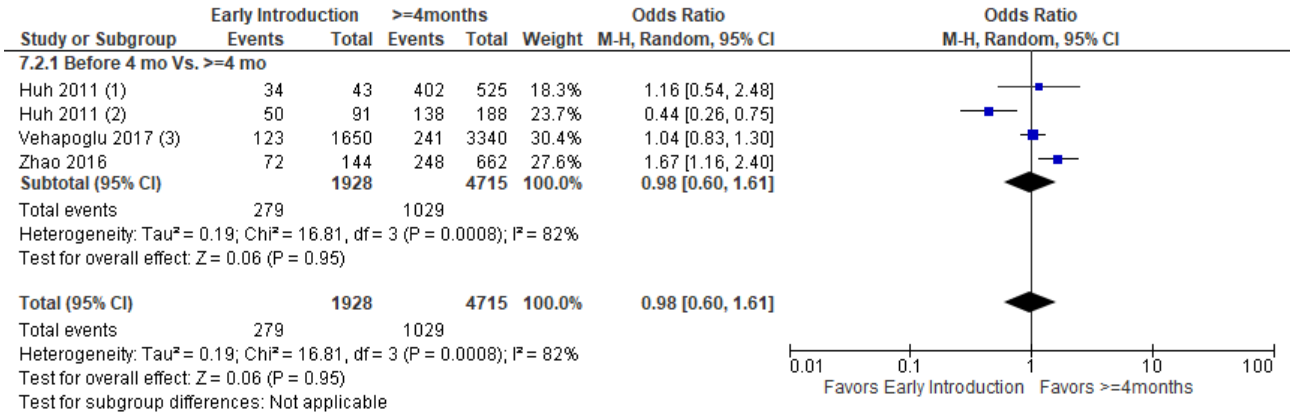
Comparison. Early introduction of CF (< four months of age) compared to ≥ four months of age among normal term infants (Observational studies)

Outcome 1: Stunting



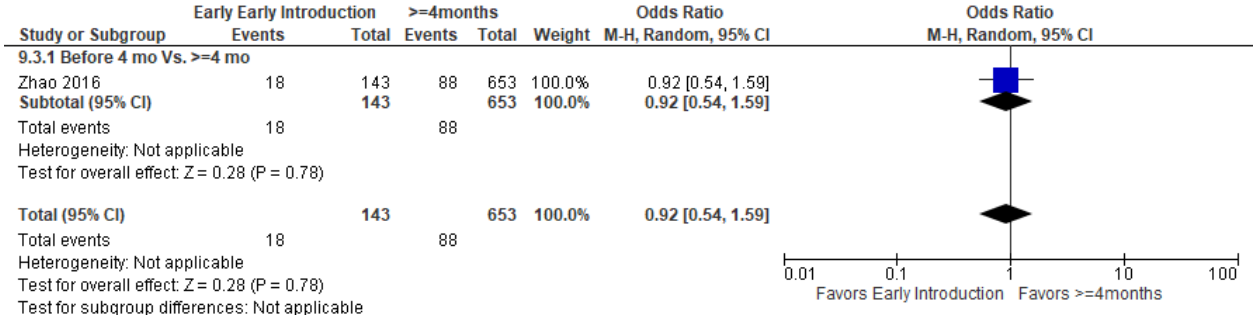
Footnotes
(1) mean age was 20.6 months

Outcome 2: Underweight

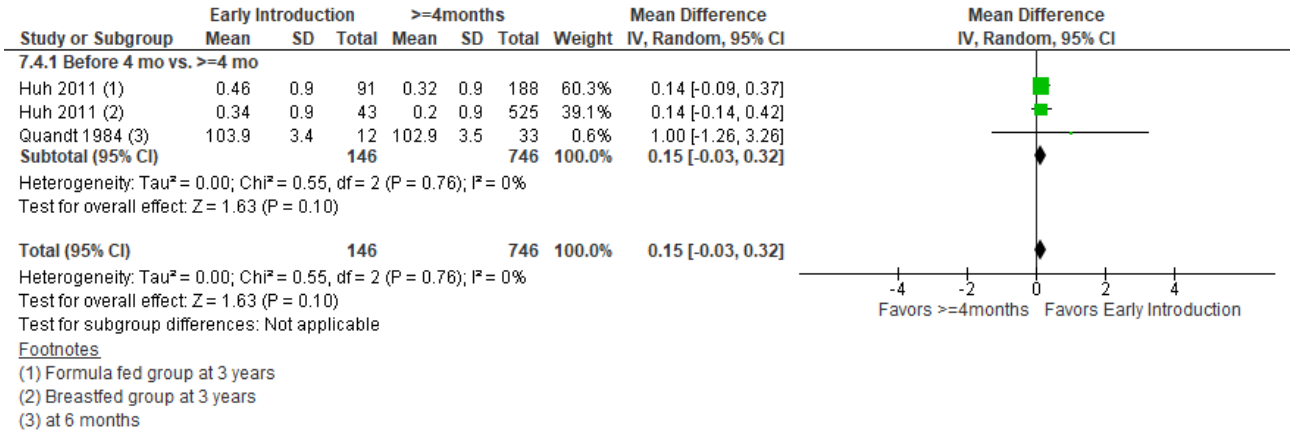


Footnotes
(1) Breastfed group at 3 years
(2) Formula fed group at 3 years
(3) 2-14years

Outcome 3: Wasting

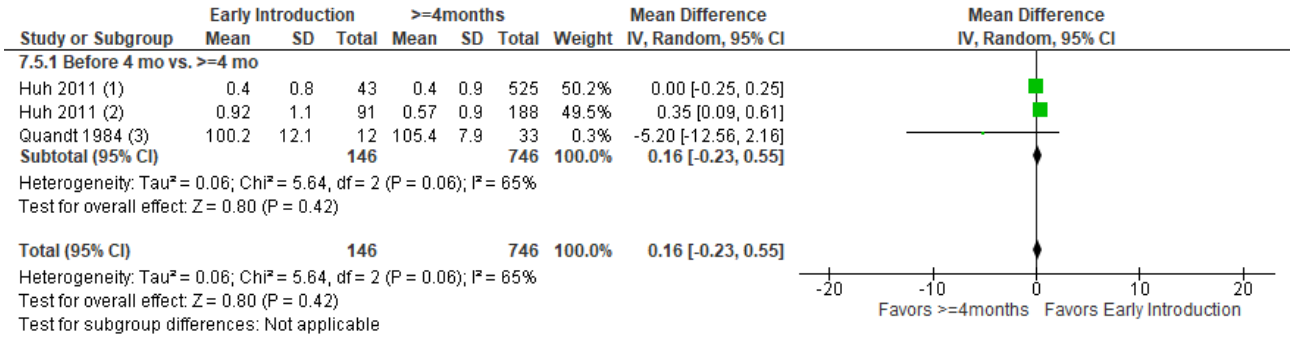


Outcome 4: Height for age Z-score



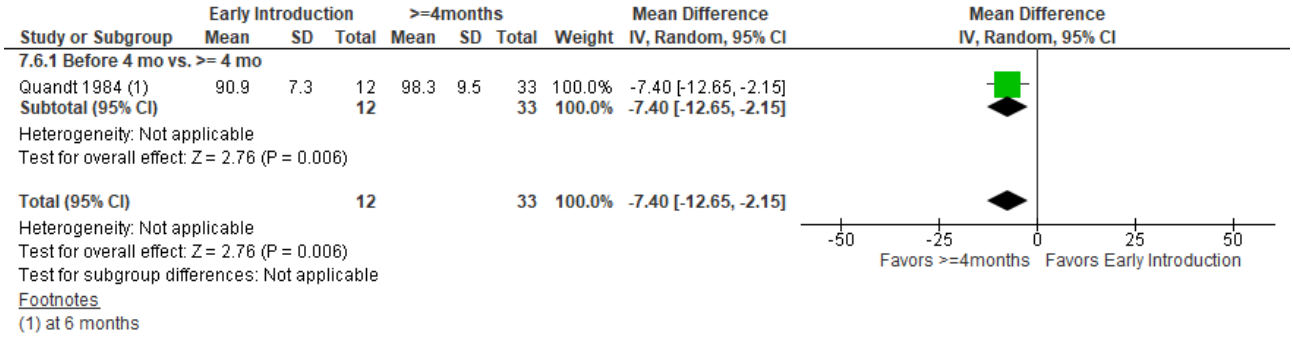
Footnotes
(1) Formula fed group at 3 years
(2) Breastfed group at 3 years
(3) at 6 months

Outcome 5: Weight for age Z-score

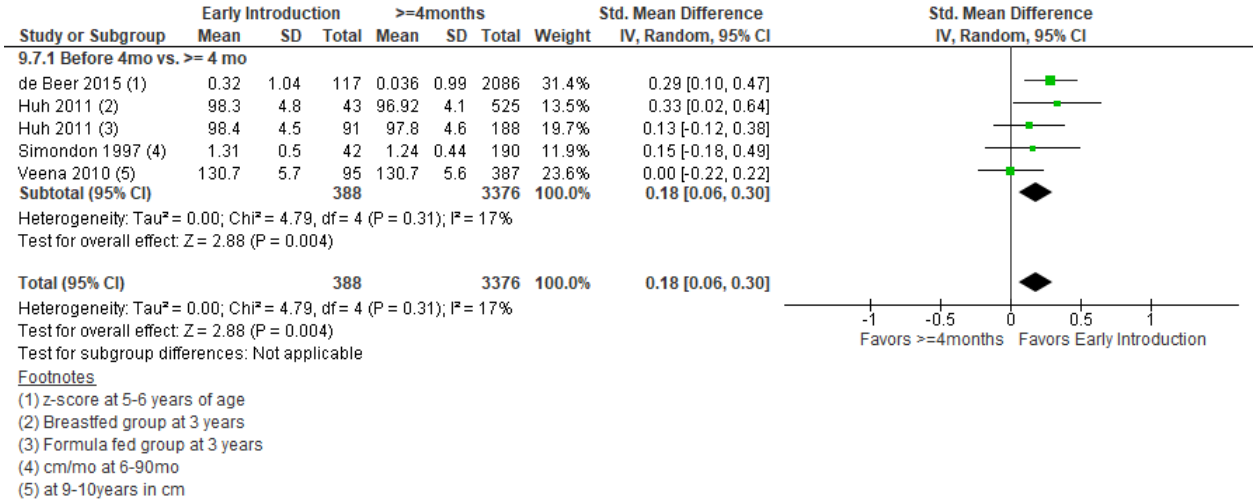


Footnotes
(1) Breastfed group at 3 years
(2) Formula fed group at 3 years
(3) at 6 months

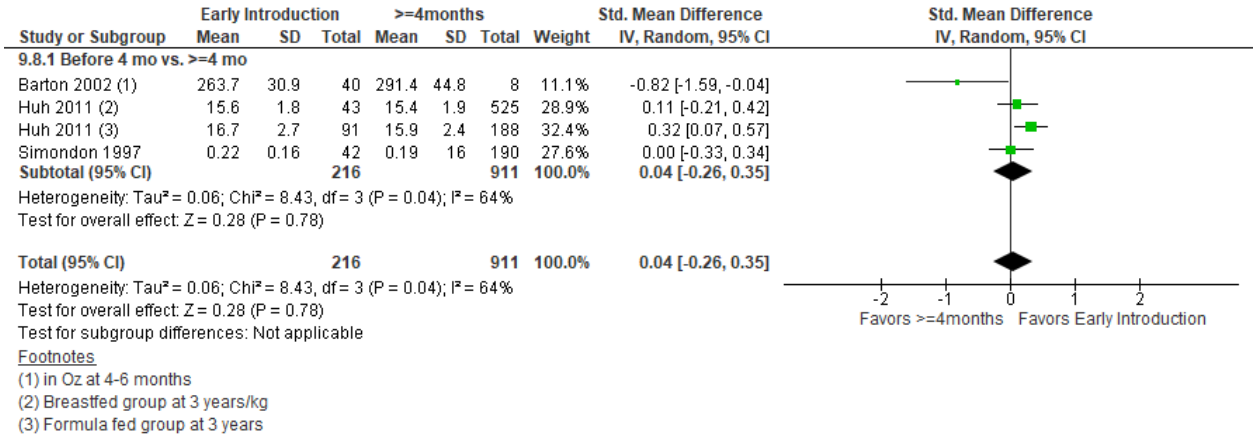
Outcome 6: Weight for height Z-score



Outcome 7: Length

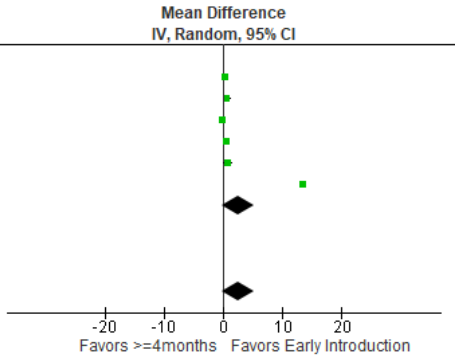


Outcome 8: Weight



Outcome 9: BMI

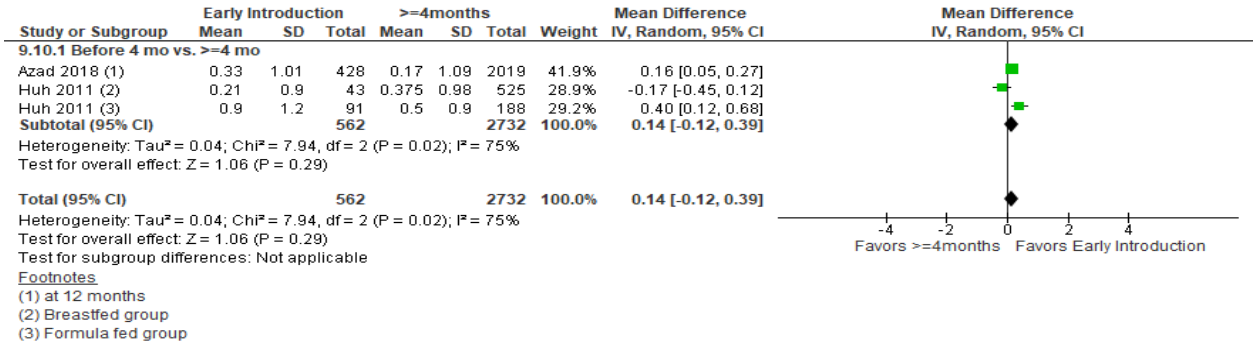
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.9.1 Before 4 mo Vs. >=4 mo								
de Beer 2015 (1)	0.18	1.18	117	-0.052	1.007	2086	16.7%	0.23 [0.01, 0.45]
Huh 2011 (2)	17.2	1.9	91	16.6	1.6	188	16.7%	0.60 [0.15, 1.05]
Huh 2011 (3)	16.2	1.1	43	16.4	1.4	525	16.7%	-0.20 [-0.55, 0.15]
Morgen 2018 (4)	17.8	2.6	1643	17.3	2.4	20940	16.7%	0.50 [0.37, 0.63]
Rodriguez-Cano 2020 (5)	17.4	1.4	28	16.7	1.4	78	16.6%	0.70 [0.10, 1.30]
Veena 2010 (6)	14.9	2.3	95	1.5	1.7	387	16.6%	13.40 [12.91, 13.89]
Subtotal (95% CI)			**2017**			**24204**	**100.0%**	**2.53 [-0.16, 5.23]**
Heterogeneity: Tau² = 11.28; Chi² = 2586.45, df = 5 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 1.85 (P = 0.07)								
Total (95% CI)			**2017**			**24204**	**100.0%**	**2.53 [-0.16, 5.23]**
Heterogeneity: Tau² = 11.28; Chi² = 2586.45, df = 5 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 1.85 (P = 0.07)								
Test for subgroup differences: Not applicable								



Footnotes

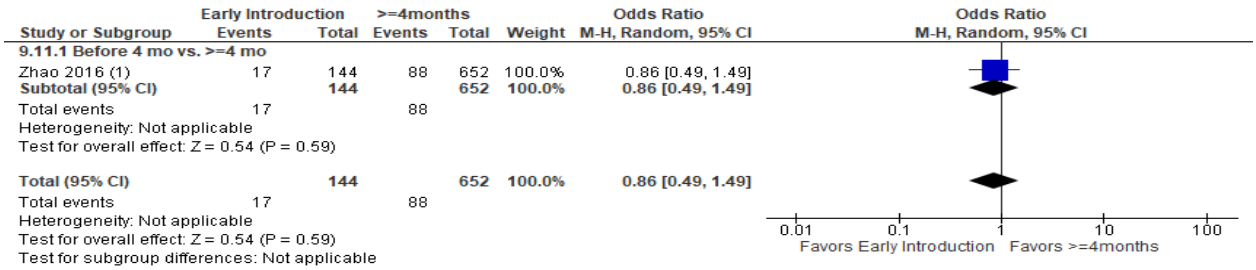
(1) at 5-6 years of age
(2) Formula fed group at 3 years
(3) Breastfed group at 3 years
(4) At 11 years of age
(5) At 12 months
(6) at 9-10years

Outcome 10: BMI Z-score



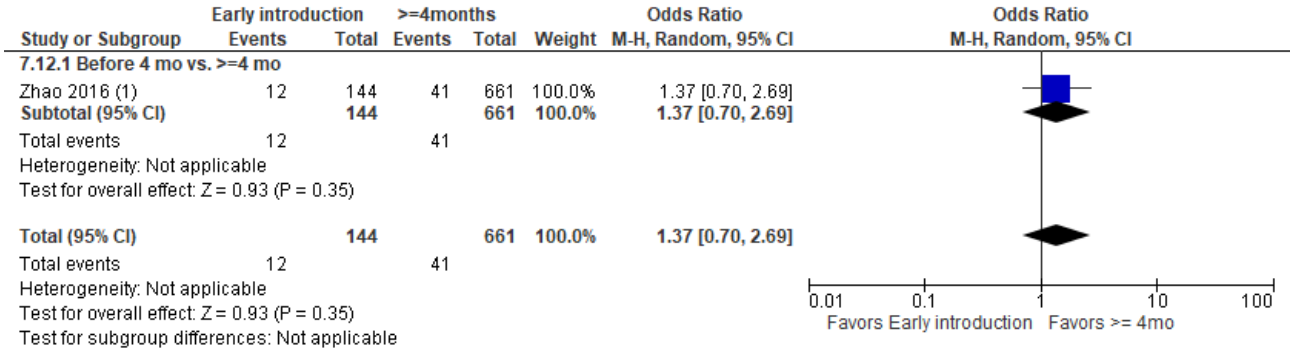
Footnotes
(1) at 12 months
(2) Breastfed group
(3) Formula fed group

Outcome 11: Head circumference <-2 Z-score



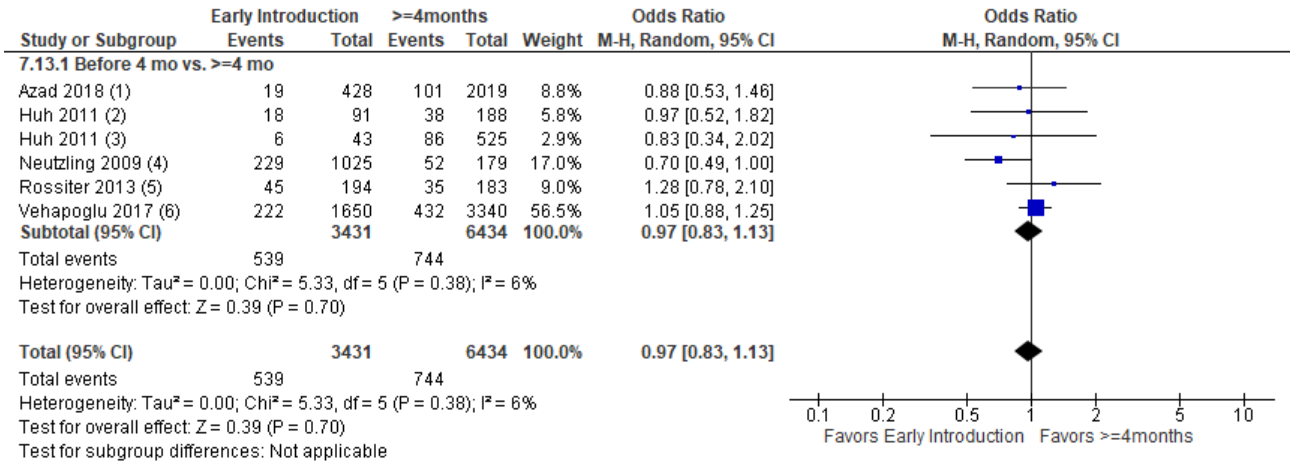
Footnotes
(1) mean age was 20.6 months

Outcome 12: MUAC <-2 Z-score



Footnotes
(1) children older than 16 months

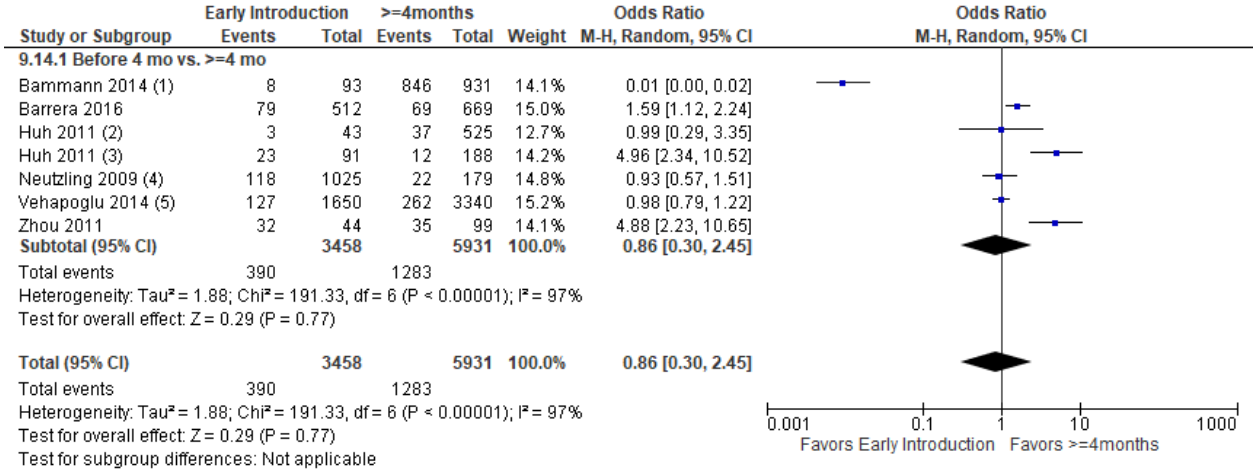
Outcome 13: Overweight



Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.13.1 Before 4 mo vs. >=4 mo						
Azad 2018 (1)	19	428	101	2019	8.8%	0.88 [0.53, 1.46]
Huh 2011 (2)	18	91	38	188	5.8%	0.97 [0.52, 1.82]
Huh 2011 (3)	6	43	86	525	2.9%	0.83 [0.34, 2.02]
Neutzling 2009 (4)	229	1025	52	179	17.0%	0.70 [0.49, 1.00]
Rossiter 2013 (5)	45	194	35	183	9.0%	1.28 [0.78, 2.10]
Vehapoglu 2017 (6)	222	1650	432	3340	56.5%	1.05 [0.88, 1.25]
Subtotal (95% CI)		**3431**		**6434**	**100.0%**	**0.97 [0.83, 1.13]**
Total events	539		744			
Heterogeneity: Tau² = 0.00; Chi² = 5.33, df = 5 (P = 0.38); I² = 6%						
Test for overall effect: Z = 0.39 (P = 0.70)						
Total (95% CI)		**3431**		**6434**	**100.0%**	**0.97 [0.83, 1.13]**
Total events	539		744			
Heterogeneity: Tau² = 0.00; Chi² = 5.33, df = 5 (P = 0.38); I² = 6%						
Test for overall effect: Z = 0.39 (P = 0.70)						
Test for subgroup differences: Not applicable						

Footnotes
(1) at 12 mo
(2) Formula fed group at 3 years
(3) Breastfed group at 3 years
(4) BMI>= 85th percentile of children 11 years old
(5) Defined as BMI above 85 and below 95 percentile (at 48 months of age)
(6) 2-14years

Outcome 14: Obesity

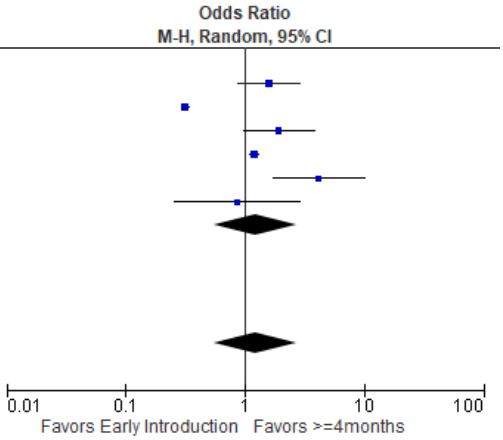


Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
9.14.1 Before 4 mo vs. >=4 mo						
Bammann 2014 (1)	8	93	846	931	14.1%	0.01 [0.00, 0.02]
Barrera 2016	79	512	69	669	15.0%	1.59 [1.12, 2.24]
Huh 2011 (2)	3	43	37	525	12.7%	0.99 [0.29, 3.35]
Huh 2011 (3)	23	91	12	188	14.2%	4.96 [2.34, 10.52]
Neutzling 2009 (4)	118	1025	22	179	14.8%	0.93 [0.57, 1.51]
Vehapoglu 2014 (5)	127	1650	262	3340	15.2%	0.98 [0.79, 1.22]
Zhou 2011	32	44	35	99	14.1%	4.88 [2.23, 10.65]
Subtotal (95% CI)		**3458**		**5931**	**100.0%**	**0.86 [0.30, 2.45]**
Total events	390		1283			
Heterogeneity: Tau² = 1.88; Chi² = 191.33, df = 6 (P < 0.00001); I² = 97%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Total (95% CI)		**3458**		**5931**	**100.0%**	**0.86 [0.30, 2.45]**
Total events	390		1283			
Heterogeneity: Tau² = 1.88; Chi² = 191.33, df = 6 (P < 0.00001); I² = 97%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Test for subgroup differences: Not applicable						

Footnotes
(1) at 7-8 years (by definition of IOTF)
(2) Breastfed group at 3 years
(3) Formula fed group at 3 years
(4) at 11 years
(5) 2-14years

Outcome 15: Overweight and obesity

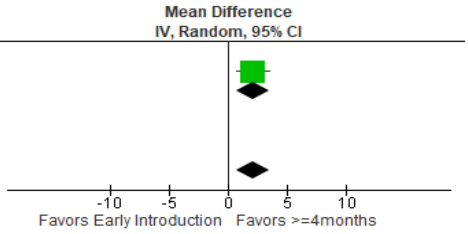
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.15.1 Before 4 mo vs. >=4 mo						
Caleyachetty 2013 (1)	36	301	18	228	17.1%	1.58 [0.87, 2.87]
Hawkins 2009 (2)	1668	4633	5468	8544	18.9%	0.32 [0.29, 0.34]
Hollis 2016 (3)	103	642	10	110	16.6%	1.91 [0.96, 3.78]
Massion 2016 (4)	1299	4176	2087	7588	18.9%	1.19 [1.10, 1.29]
Sun 2016 (5)	6	46	76	2171	15.3%	4.13 [1.70, 10.05]
Sun 2016 (6)	3	49	49	690	13.2%	0.85 [0.26, 2.84]
Subtotal (95% CI)		**9847**		**19331**	**100.0%**	**1.22 [0.55, 2.71]**
Total events	3115		7708			
Heterogeneity: Tau² = 0.88; Chi² = 586.22, df = 5 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 0.49 (P = 0.63)						
Total (95% CI)		**9847**		**19331**	**100.0%**	**1.22 [0.55, 2.71]**
Total events	3115		7708			
Heterogeneity: Tau² = 0.88; Chi² = 586.22, df = 5 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 0.49 (P = 0.63)						
Test for subgroup differences: Not applicable						



Footnotes
(1) at 5 years
(2) According to IOTF at 3 years of age
(3) According to IOTF at 3 years
(4) at 11 years
(5) BMI z-score >2SD at 1 year (breastfed group)
(6) BMI z-score >2SD at 1 year (formula fed group)

Outcome 16: Waist circumference

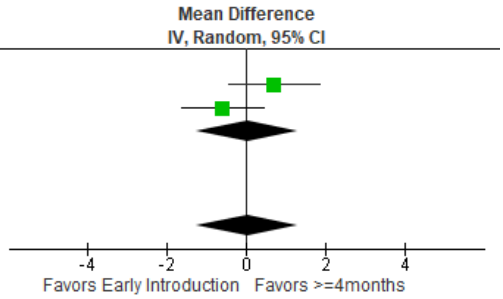
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.16.1 Before 4 mo vs. >=4 mo								
Rodriguez-Cano 2020 (1)	43	3.5	28	40.9	2.7	78	100.0%	2.10 [0.67, 3.53]
Subtotal (95% CI)			**28**			**78**	**100.0%**	**2.10 [0.67, 3.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.88 (P = 0.004)								
Total (95% CI)			**28**			**78**	**100.0%**	**2.10 [0.67, 3.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.88 (P = 0.004)								
Test for subgroup differences: Not applicable								



Footnotes
(1) in cm at 12 months of age

Outcome 17: Skinfold Thickness (triceps + subscapular)

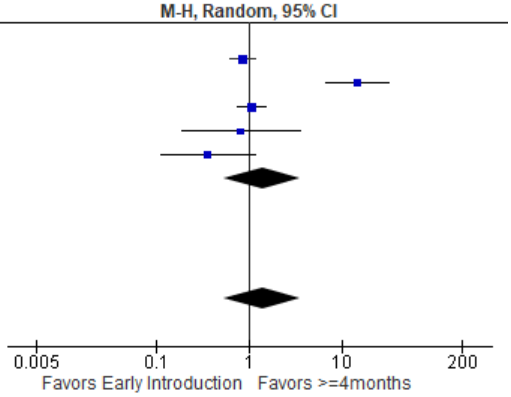
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.17.1 Before 4 mo vs. >=4 mo								
Huh 2011 (1)	18	4.8	91	17.3	4.3	188	48.0%	0.70 [-0.46, 1.86]
Huh 2011 (2)	15.9	3.3	43	16.5	4	525	52.0%	-0.60 [-1.64, 0.44]
Subtotal (95% CI)			**134**			**713**	**100.0%**	**0.02 [-1.25, 1.30]**
Heterogeneity: Tau² = 0.53; Chi² = 2.66, df = 1 (P = 0.10); I² = 62%								
Test for overall effect: Z = 0.04 (P = 0.97)								
Total (95% CI)			**134**			**713**	**100.0%**	**0.02 [-1.25, 1.30]**
Heterogeneity: Tau² = 0.53; Chi² = 2.66, df = 1 (P = 0.10); I² = 62%								
Test for overall effect: Z = 0.04 (P = 0.97)								
Test for subgroup differences: Not applicable								



Footnotes
(1) formula group at 3 years of age
(2) Breastfed group at 3 years of age

Outcome 18: Atopic dermatitis

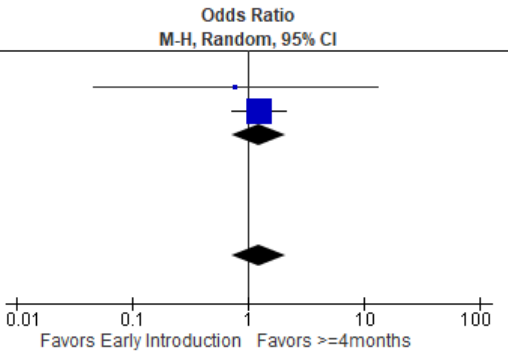
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.18.1 Before 4 mo vs. >=4 mo						
Chuang 2011 (1)	41	847	1009	17926	23.4%	0.85 [0.62, 1.17]
Dunlop 2006 (2)	357	632	7	86	20.6%	14.65 [6.66, 32.24]
Joseph 2011 (3)	66	236	96	358	23.2%	1.06 [0.73, 1.53]
Lee 2020 (4)	2	23	147	1402	15.3%	0.81 [0.19, 3.50]
Snijders 2008 (5)	3	55	106	767	17.5%	0.36 [0.11, 1.17]
Subtotal (95% CI)		**1793**		**20539**	**100.0%**	**1.38 [0.53, 3.54]**
Total events	469		1365			
Heterogeneity: Tau² = 0.97; Chi² = 49.55, df = 4 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Total (95% CI)		**1793**		**20539**	**100.0%**	**1.38 [0.53, 3.54]**
Total events	469		1365			
Heterogeneity: Tau² = 0.97; Chi² = 49.55, df = 4 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Not applicable						



Footnotes
(1) (at 6-18mo)
(2) At 1 year of age
(3) at or before 2 years of age
(4) Between 1-3 years
(5) at the age of 2 years

Outcome 19: Asthma

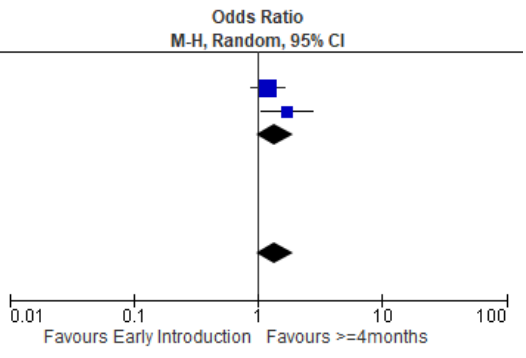
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.19.1 Before 4 mo vs. >=4 mo						
Lee 2020 (1)	0	23	37	1402	3.6%	0.77 [0.05, 13.00]
Lossius 2018 (2)	22	381	37	789	96.4%	1.25 [0.72, 2.14]
Subtotal (95% CI)		**404**		**2191**	**100.0%**	**1.22 [0.72, 2.09]**
Total events	22		74			
Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.75 (P = 0.46)						
Total (95% CI)		**404**		**2191**	**100.0%**	**1.22 [0.72, 2.09]**
Total events	22		74			
Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.75 (P = 0.46)						
Test for subgroup differences: Not applicable						



Footnotes
(1) Between 1-3 years
(2) at 7 years

Outcome 20: Diarrhea

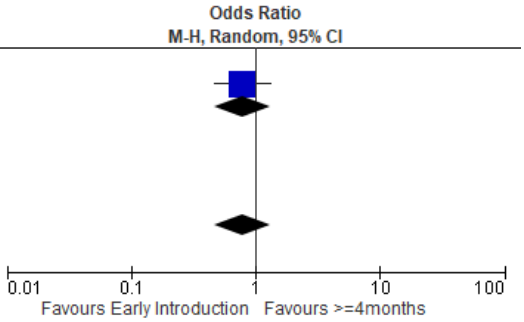
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.20.1 Before 4 mo vs. >=4 mo						
Quigley 2008 (1)	61	33734	110	72398	63.3%	1.19 [0.87, 1.63]
Zhao 2016 (2)	85	111	285	434	36.7%	1.71 [1.06, 2.77]
Subtotal (95% CI)		**33845**		**72832**	**100.0%**	**1.36 [0.97, 1.91]**
Total events	146		395			
Heterogeneity: Tau² = 0.02; Chi² = 1.52, df = 1 (P = 0.22); I² = 34%						
Test for overall effect: Z = 1.76 (P = 0.08)						
Total (95% CI)		**33845**		**72832**	**100.0%**	**1.36 [0.97, 1.91]**
Total events	146		395			
Heterogeneity: Tau² = 0.02; Chi² = 1.52, df = 1 (P = 0.22); I² = 34%						
Test for overall effect: Z = 1.76 (P = 0.08)						
Test for subgroup differences: Not applicable						



Footnotes
(1) among children less than or equal to 8 mo
(2) At 20.6 mo

Outcome 21: Wheeze

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.21.1 Before 4 mo vs. >=4 mo						
Snijders 2008 (1)	17	153	242	1741	100.0%	0.77 [0.46, 1.31]
Subtotal (95% CI)		**153**		**1741**	**100.0%**	**0.77 [0.46, 1.31]**
Total events	17		242			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.34)						
Total (95% CI)		**153**		**1741**	**100.0%**	**0.77 [0.46, 1.31]**
Total events	17		242			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.34)						
Test for subgroup differences: Not applicable						

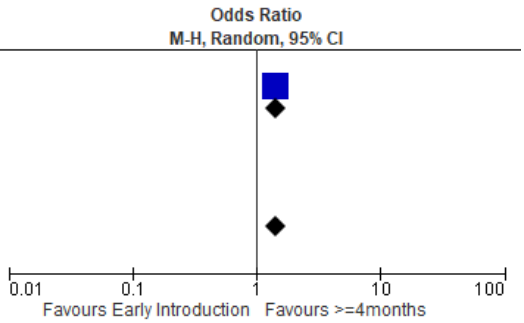


Footnotes

(1) At the age of 2 years

Outcome 22: LRTI

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.22.1 Before 4 mo vs. >=4 mo						
Quigley 2008 (1)	186	33734	279	72398	100.0%	1.43 [1.19, 1.73]
Subtotal (95% CI)		**33734**		**72398**	**100.0%**	**1.43 [1.19, 1.73]**
Total events	186		279			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.79 (P = 0.0001)						
Total (95% CI)		**33734**		**72398**	**100.0%**	**1.43 [1.19, 1.73]**
Total events	186		279			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.79 (P = 0.0001)						
Test for subgroup differences: Not applicable						

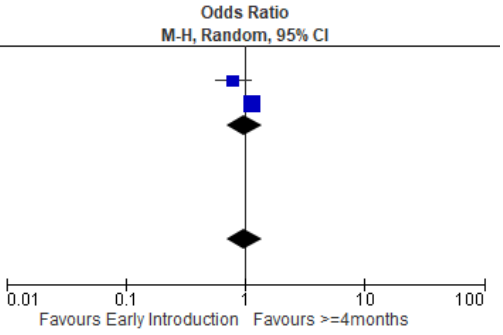


Footnotes

(1) among children less than or equal to 8 mo

Outcome 23: Eczema

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.23.1 Before 4 mo vs. >=4 mo						
Snijders 2008 (1)	51	191	732	2319	39.6%	0.79 [0.57, 1.10]
Taylor-Robinson 2016 (2)	1877	5100	3169	9349	60.4%	1.14 [1.06, 1.22]
Subtotal (95% CI)		**5291**		**11668**	**100.0%**	**0.98 [0.69, 1.39]**
Total events	1928		3901			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 4.39$, df = 1 (P = 0.04); $I^2 = 77\%$						
Test for overall effect: Z = 0.09 (P = 0.93)						
Total (95% CI)		**5291**		**11668**	**100.0%**	**0.98 [0.69, 1.39]**
Total events	1928		3901			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 4.39$, df = 1 (P = 0.04); $I^2 = 77\%$						
Test for overall effect: Z = 0.09 (P = 0.93)						
Test for subgroup differences: Not applicable						



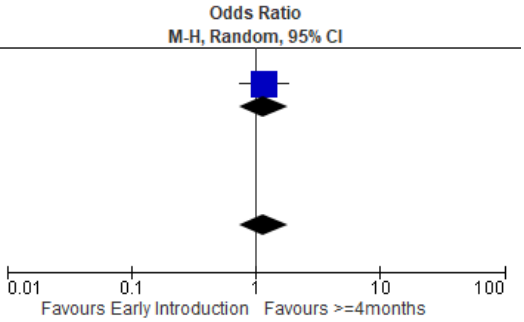
Footnotes

(1) At the age of 2 years

(2) at 5 years

Outcome 24: Food Allergy

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
7.24.1 Before 4 mo vs. >=4 mo						
Luccioli 2014 (1)	34	461	50	778	100.0%	1.16 [0.74, 1.82]
Subtotal (95% CI)		**461**		**778**	**100.0%**	**1.16 [0.74, 1.82]**
Total events	34		50			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						
Total (95% CI)		**461**		**778**	**100.0%**	**1.16 [0.74, 1.82]**
Total events	34		50			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						
Test for subgroup differences: Not applicable						

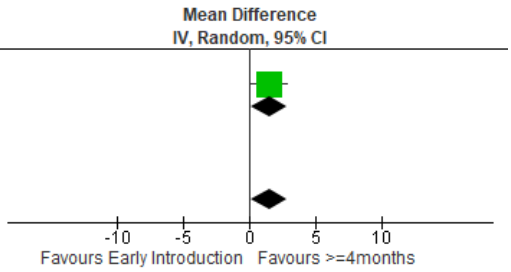


Footnotes

(1) Total probable food allergy (at 6 years)

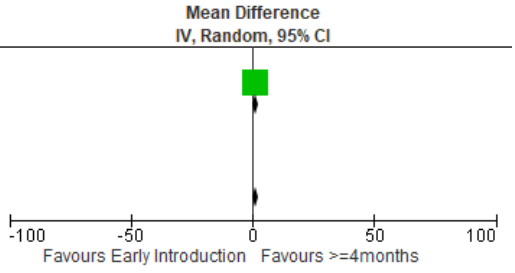
Outcome 25: Systolic Blood Pressure

Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.25.1 Before 4 mo vs. >=4 mo								
de Beer 2016	100.4	7.5	117	98.9	7.02	2086	100.0%	1.50 [0.11, 2.89]
Subtotal (95% CI)			**117**			**2086**	**100.0%**	**1.50 [0.11, 2.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.11 (P = 0.03)								
Total (95% CI)			**117**			**2086**	**100.0%**	**1.50 [0.11, 2.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.11 (P = 0.03)								
Test for subgroup differences: Not applicable								



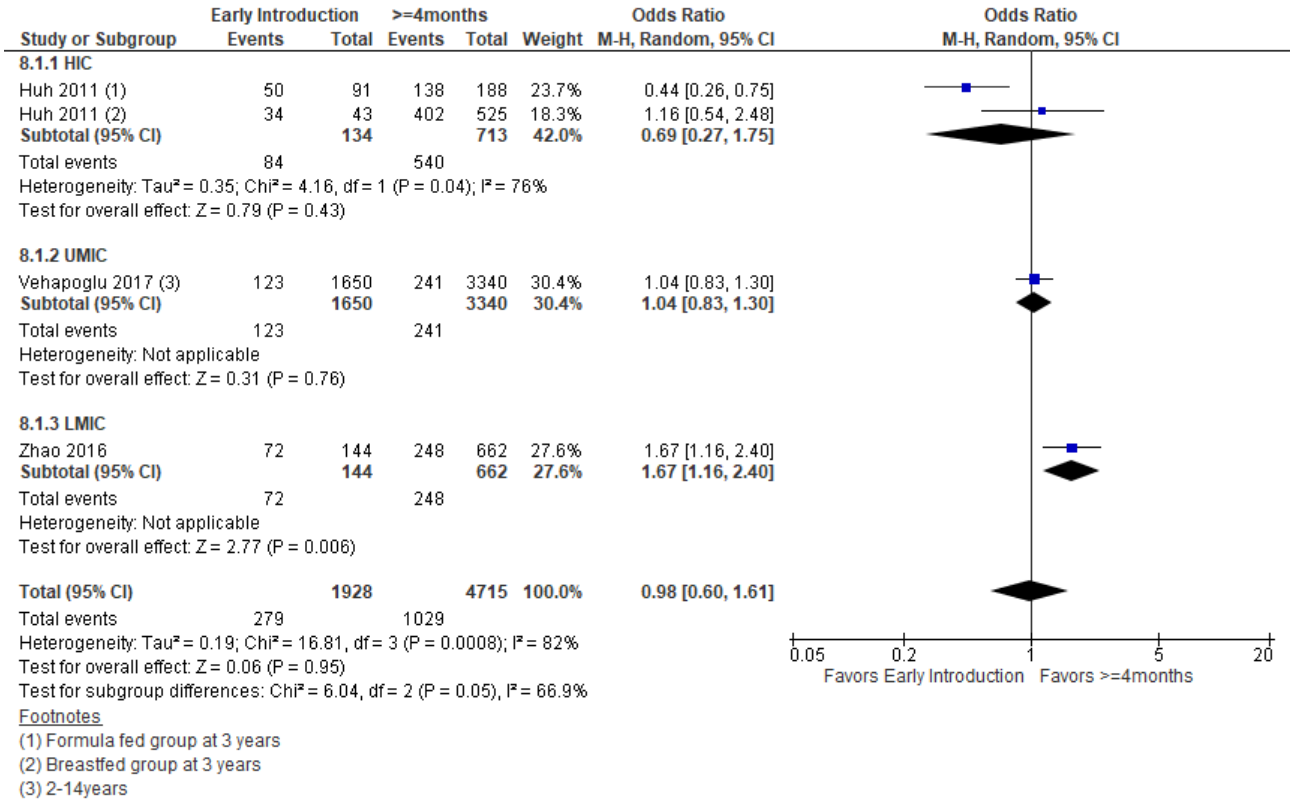
Outcome 26: Diastolic Blood Pressure

Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.26.1 Before 4 mo vs. >=4 mo								
de Beer 2016	58.2	5.5	117	56.9	5.9	2086	100.0%	1.30 [0.27, 2.33]
Subtotal (95% CI)			**117**			**2086**	**100.0%**	**1.30 [0.27, 2.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.48 (P = 0.01)								
Total (95% CI)			**117**			**2086**	**100.0%**	**1.30 [0.27, 2.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.48 (P = 0.01)								
Test for subgroup differences: Not applicable								



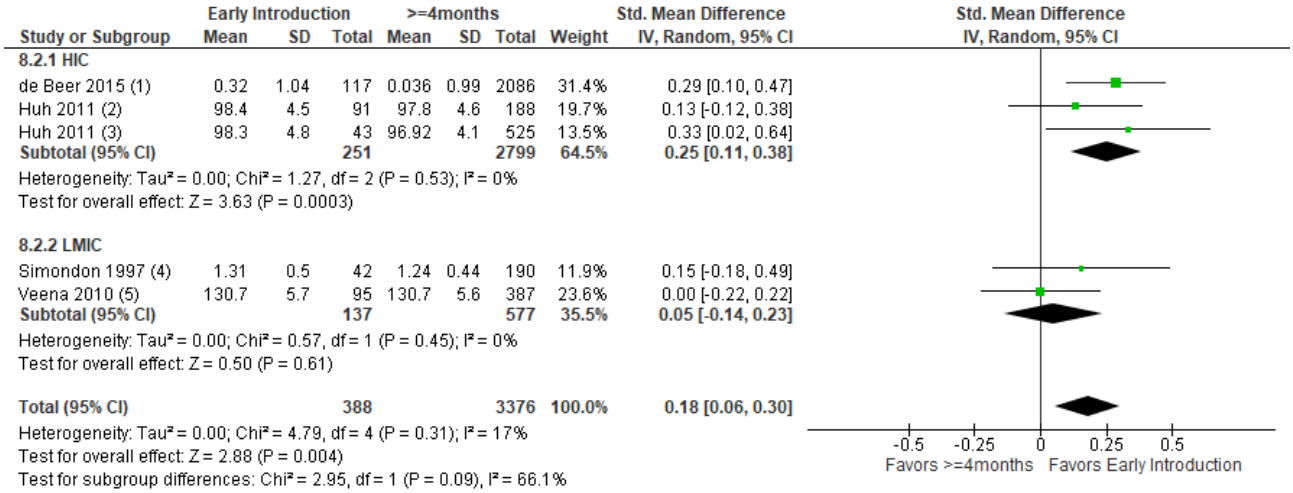
Comparison. Early introduction of CF (< four months of age) compared to ≥ four months of age (among normal term infants (Observational studies) – subgroup by setting

Outcome 1: Underweight



Footnotes
(1) Formula fed group at 3 years
(2) Breastfed group at 3 years
(3) 2-14years

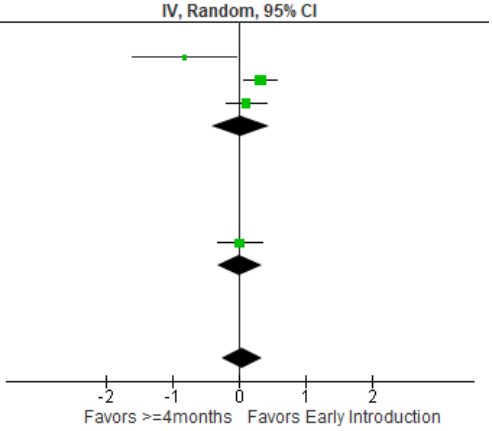
Outcome 2: Length



Footnotes
(1) z-score at 5-6 years of age
(2) Formula fed group at 3 years
(3) Breastfed group at 3 years
(4) cm/mo at 6-90mo
(5) at 9-10years in cm

Outcome 3: Weight

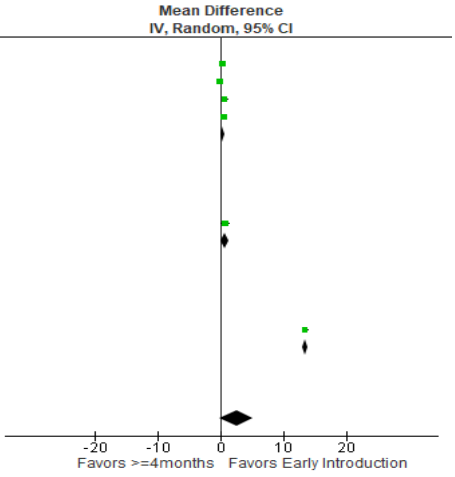
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.3.1 HIC								
Barton 2002 (1)	263.7	30.9	40	291.4	44.8	8	11.1%	-0.82 [-1.59, -0.04]
Huh 2011 (2)	16.7	2.7	91	15.9	2.4	188	32.4%	0.32 [0.07, 0.57]
Huh 2011 (3)	15.6	1.8	43	15.4	1.9	525	28.9%	0.11 [-0.21, 0.42]
Subtotal (95% CI)			**174**			**721**	**72.4%**	**0.02 [-0.41, 0.45]**
Heterogeneity: Tau² = 0.10; Chi² = 7.68, df = 2 (P = 0.02); I² = 74%								
Test for overall effect: Z = 0.09 (P = 0.93)								
8.3.2 LMIC								
Simondon 1997	0.22	0.16	42	0.19	16	190	27.6%	0.00 [-0.33, 0.34]
Subtotal (95% CI)			**42**			**190**	**27.6%**	**0.00 [-0.33, 0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.01 (P = 0.99)								
Total (95% CI)			**216**			**911**	**100.0%**	**0.04 [-0.26, 0.35]**
Heterogeneity: Tau² = 0.06; Chi² = 8.43, df = 3 (P = 0.04); I² = 64%								
Test for overall effect: Z = 0.28 (P = 0.78)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%								



Footnotes
(1) in Oz at 4-6 months
(2) Formula fed group at 3 years
(3) Breastfed group at 3 years/kg

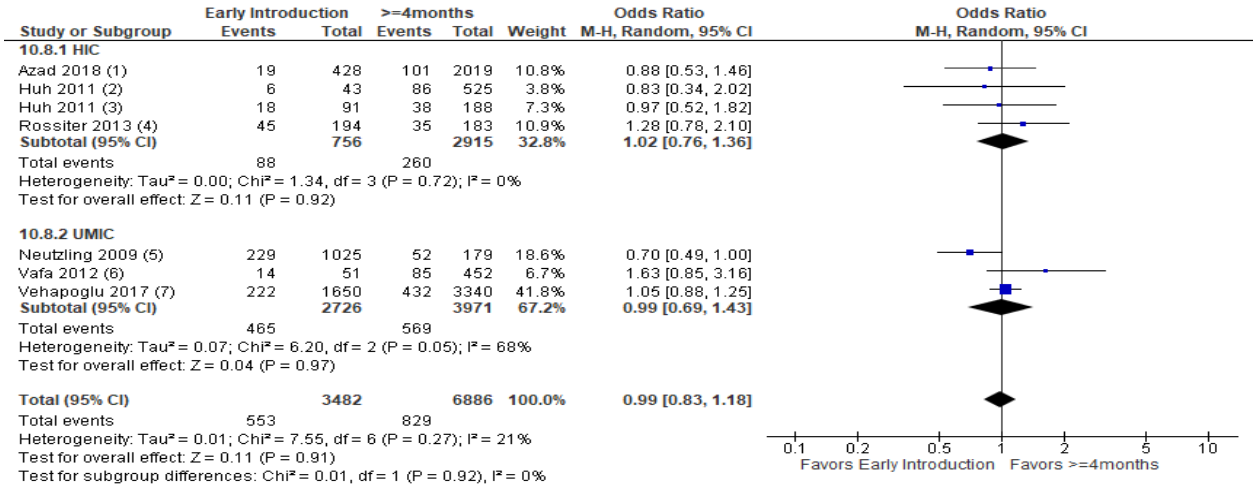
Outcome 4: BMI

Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
10.7.1 HIC								
de Beer 2015 (1)	0.18	1.18	117	-0.052	1.007	2086	16.7%	0.23 [0.01, 0.45]
Huh 2011 (2)	16.2	1.1	43	16.4	1.4	525	16.7%	-0.20 [-0.55, 0.15]
Huh 2011 (3)	17.2	1.9	91	16.6	1.6	188	16.7%	0.60 [0.15, 1.05]
Morgen 2018 (4)	17.8	2.6	1643	17.3	2.4	20940	16.7%	0.50 [0.37, 0.63]
Subtotal (95% CI)			**1894**			**23739**	**66.8%**	**0.29 [-0.01, 0.58]**
Heterogeneity: Tau² = 0.07; Chi² = 16.51, df = 3 (P = 0.0009); I² = 82%								
Test for overall effect: Z = 1.88 (P = 0.06)								
10.7.2 UMIC								
Rodriguez-Cano 2020 (5)	17.4	1.4	28	16.7	1.4	78	16.6%	0.70 [0.10, 1.30]
Subtotal (95% CI)			**28**			**78**	**16.6%**	**0.70 [0.10, 1.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.27 (P = 0.02)								
10.7.3 LMIC								
Veena 2010 (6)	14.9	2.3	95	1.5	1.7	387	16.6%	13.40 [12.91, 13.89]
Subtotal (95% CI)			**95**			**387**	**16.6%**	**13.40 [12.91, 13.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 53.32 (P < 0.00001)								
Total (95% CI)			**2017**			**24204**	**100.0%**	**2.53 [-0.16, 5.23]**
Heterogeneity: Tau² = 11.28; Chi² = 2586.45, df = 5 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 1.85 (P = 0.07)								
Test for subgroup differences: Chi² = 2080.19, df = 2 (P < 0.00001), I² = 99.9%								



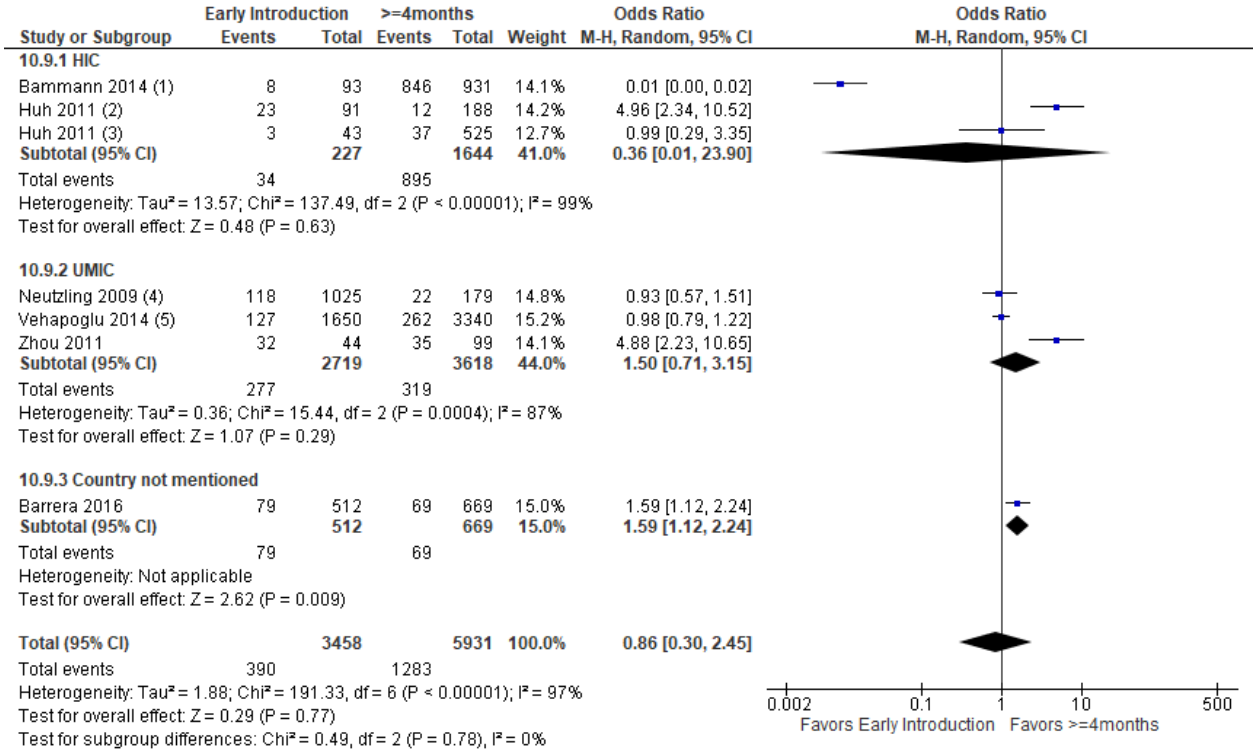
Footnotes
(1) at 5-6 years of age
(2) Breastfed group at 3 years
(3) Formula fed group at 3 years
(4) At 11 years of age
(5) At 12 months
(6) at 9-10years

Outcome 5: Overweight



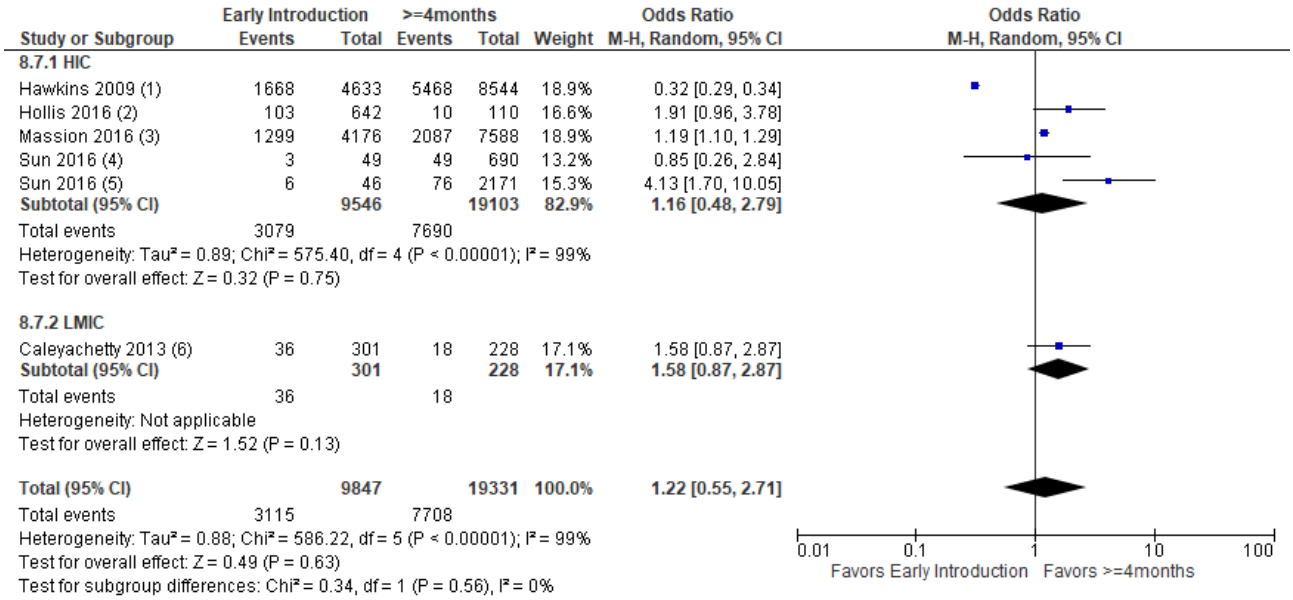
Footnotes
(1) at 12 mo
(2) Breastfed group at 3 years
(3) Formula fed group at 3 years
(4) Defined as BMI above 85 and below 95 percentile (at 48 months of age)
(5) BMI>= 85th percentile of children 11 years old
(6) at 7 years
(7) 2-14years

Outcome 6: Obesity



Footnotes
(1) at 7-8 years (by definition of IOTF)
(2) Formula fed group at 3 years
(3) Breastfed group at 3 years
(4) at 11 years
(5) 2-14years

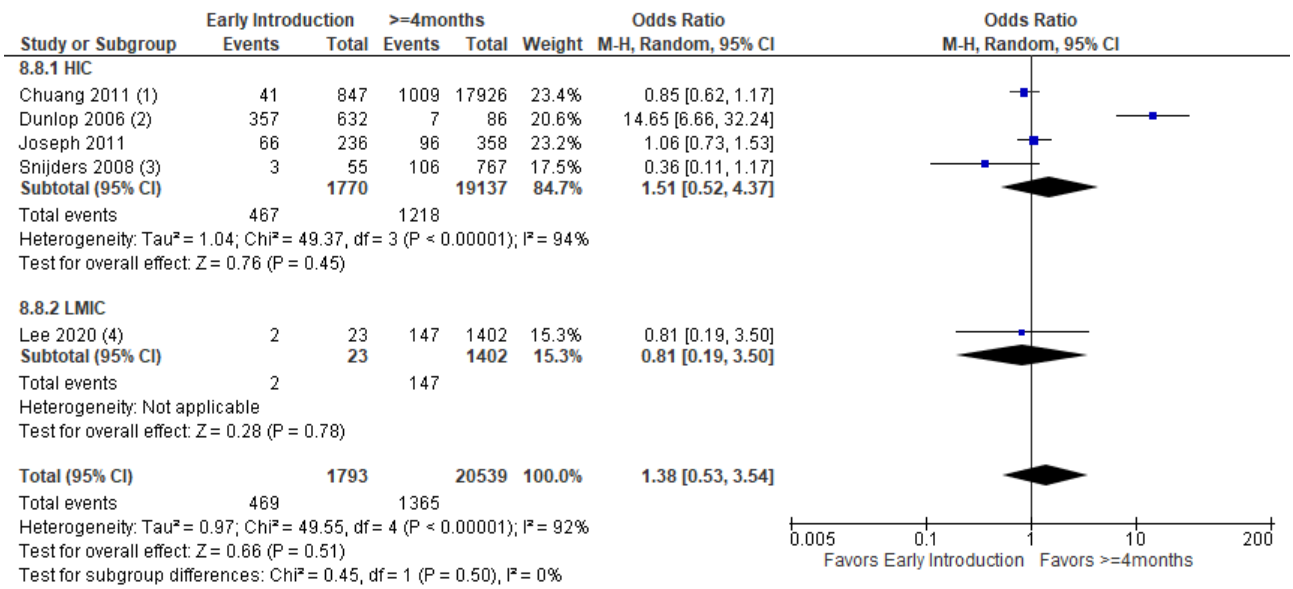
Outcome 7: Overweight and obesity



Footnotes

(1) According to IOTF at 3 years of age
(2) According to IOTF at 3 years
(3) at 11 years
(4) BMI z-score >2SD at 1 year (formula fed group)
(5) BMI z-score >2SD at 1 year (breastfed group)
(6) at 5 years

Outcome 8: Atopic dermatitis

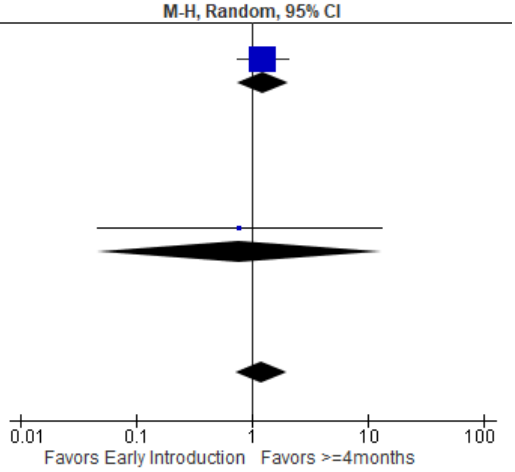


Footnotes

(1) (at 6-18mo)
(2) At 1 year of age
(3) at the age of 2 years
(4) Between 1-3 years

Outcome 9: Asthma

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
8.9.1 HIC						
Lossius 2018	24	463	42	985	96.8%	1.23 [0.73, 2.05]
Subtotal (95% CI)		**463**		**985**	**96.8%**	**1.23 [0.73, 2.05]**
Total events	24		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.43)						
8.9.2 LMIC						
Lee 2020 (1)	0	23	37	1402	3.2%	0.77 [0.05, 13.00]
Subtotal (95% CI)		**23**		**1402**	**3.2%**	**0.77 [0.05, 13.00]**
Total events	0		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.18 (P = 0.86)						
Total (95% CI)		**486**		**2387**	**100.0%**	**1.21 [0.73, 2.01]**
Total events	24		79			
Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Test for subgroup differences: Chi² = 0.10, df = 1 (P = 0.75), I² = 0%						

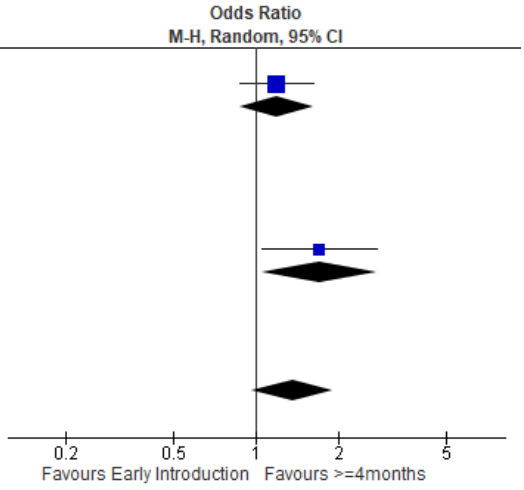


Footnotes

(1) Between 1-3 years

Outcome 10: Diarrhea

Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
8.10.1 HIC						
Quigley 2008 (1)	61	33734	110	72398	63.3%	1.19 [0.87, 1.63]
Subtotal (95% CI)		**33734**		**72398**	**63.3%**	**1.19 [0.87, 1.63]**
Total events	61		110			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.28)						
8.10.2 LMIC						
Zhao 2016 (2)	85	111	285	434	36.7%	1.71 [1.06, 2.77]
Subtotal (95% CI)		**111**		**434**	**36.7%**	**1.71 [1.06, 2.77]**
Total events	85		285			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.18 (P = 0.03)						
Total (95% CI)		**33845**		**72832**	**100.0%**	**1.36 [0.97, 1.91]**
Total events	146		395			
Heterogeneity: Tau² = 0.02; Chi² = 1.52, df = 1 (P = 0.22); I² = 34%						
Test for overall effect: Z = 1.76 (P = 0.08)						
Test for subgroup differences: Chi² = 1.52, df = 1 (P = 0.22), I² = 34.3%						



Footnotes

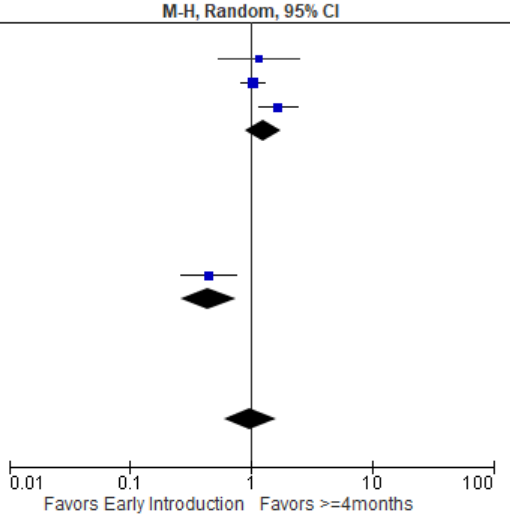
(1) among children less than or equal to 8 mo

(2) At 20.6 mo

Comparison. Early introduction of CF (< four months of age) compared to ≥ four months of age among normal term infants (Observational studies) – subgroup by feeding practices

Outcome 1: Underweight

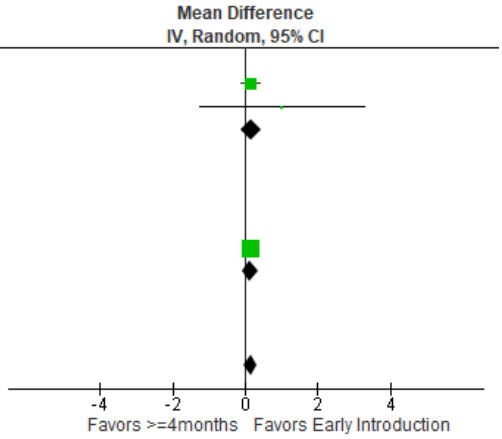
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
9.1.1 Breast fed						
Huh 2011 (1)	34	43	402	525	18.3%	1.16 [0.54, 2.48]
Vehapoglu 2017 (2)	123	1650	241	3340	30.4%	1.04 [0.83, 1.30]
Zhao 2016	72	144	248	662	27.6%	1.67 [1.16, 2.40]
Subtotal (95% CI)		**1837**		**4527**	**76.3%**	**1.25 [0.88, 1.78]**
Total events	229		891			
Heterogeneity: Tau² = 0.05; Chi² = 4.80, df = 2 (P = 0.09); I² = 58%						
Test for overall effect: Z = 1.26 (P = 0.21)						
9.1.2 Formula fed						
Huh 2011 (3)	50	91	138	188	23.7%	0.44 [0.26, 0.75]
Subtotal (95% CI)		**91**		**188**	**23.7%**	**0.44 [0.26, 0.75]**
Total events	50		138			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.05 (P = 0.002)						
Total (95% CI)		**1928**		**4715**	**100.0%**	**0.98 [0.60, 1.61]**
Total events	279		1029			
Heterogeneity: Tau² = 0.19; Chi² = 16.81, df = 3 (P = 0.0008); I² = 82%						
Test for overall effect: Z = 0.06 (P = 0.95)						
Test for subgroup differences: Chi² = 10.49, df = 1 (P = 0.001), I² = 90.5%						



Footnotes
(1) Breastfed group at 3 years
(2) 2-14years
(3) Formula fed group at 3 years

Outcome 2: HAZ

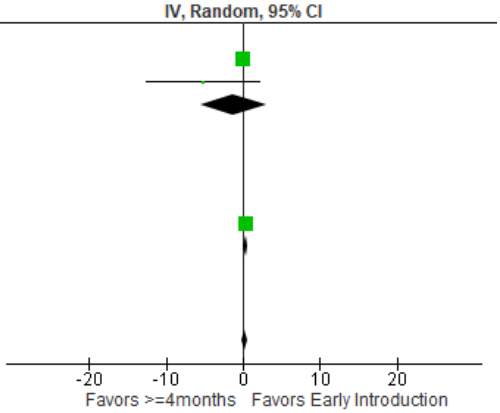
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.2.1 Breast fed								
Huh 2011 (1)	0.34	0.9	43	0.2	0.9	525	39.1%	0.14 [-0.14, 0.42]
Quandt 1984 (2)	103.9	3.4	12	102.9	3.5	33	0.6%	1.00 [-1.26, 3.26]
Subtotal (95% CI)			**55**			**558**	**39.7%**	**0.15 [-0.12, 0.43]**
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%								
Test for overall effect: Z = 1.08 (P = 0.28)								
9.2.2 Formula fed								
Huh 2011 (3)	0.46	0.9	91	0.32	0.9	188	60.3%	0.14 [-0.09, 0.37]
Subtotal (95% CI)			**91**			**188**	**60.3%**	**0.14 [-0.09, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Total (95% CI)			**146**			**746**	**100.0%**	**0.15 [-0.03, 0.32]**
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 2 (P = 0.76); I² = 0%								
Test for overall effect: Z = 1.63 (P = 0.10)								
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%								



Footnotes
(1) Breastfed group at 3 years
(2) at 6 months
(3) Formula fed group at 3 years

Outcome 3: WAZ

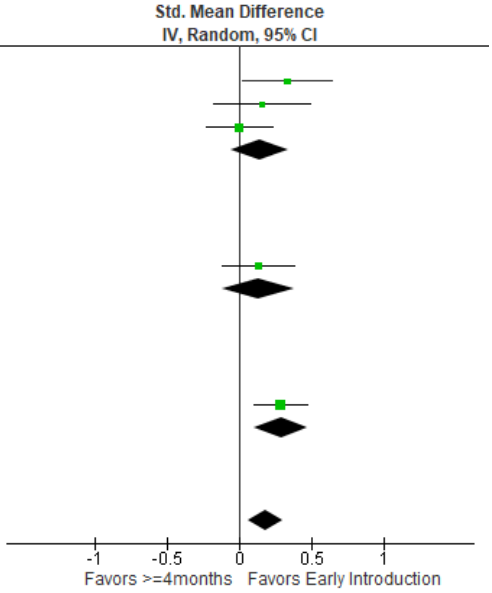
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.3.1 Breast fed								
Huh 2011 (1)	0.4	0.8	43	0.4	0.9	525	50.2%	0.00 [-0.25, 0.25]
Quandt 1984 (2)	100.2	12.1	12	105.4	7.9	33	0.3%	-5.20 [-12.56, 2.16]
Subtotal (95% CI)			55			558	50.5%	**-1.25 [-5.60, 3.10]**
Heterogeneity: Tau² = 6.47; Chi² = 1.92, df = 1 (P = 0.17); I² = 48%								
Test for overall effect: Z = 0.56 (P = 0.57)								
9.3.2 Formula fed								
Huh 2011 (3)	0.92	1.1	91	0.57	0.9	188	49.5%	0.35 [0.09, 0.61]
Subtotal (95% CI)			**91**			**188**	**49.5%**	**0.35 [0.09, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.64 (P = 0.008)								
Total (95% CI)			**146**			**746**	**100.0%**	**0.16 [-0.23, 0.55]**
Heterogeneity: Tau² = 0.06; Chi² = 5.64, df = 2 (P = 0.06); I² = 65%								
Test for overall effect: Z = 0.80 (P = 0.42)								
Test for subgroup differences: Chi² = 0.52, df = 1 (P = 0.47), I² = 0%								



Footnotes
(1) Breastfed group at 3 years
(2) at 6 months
(3) Formula fed group at 3 years

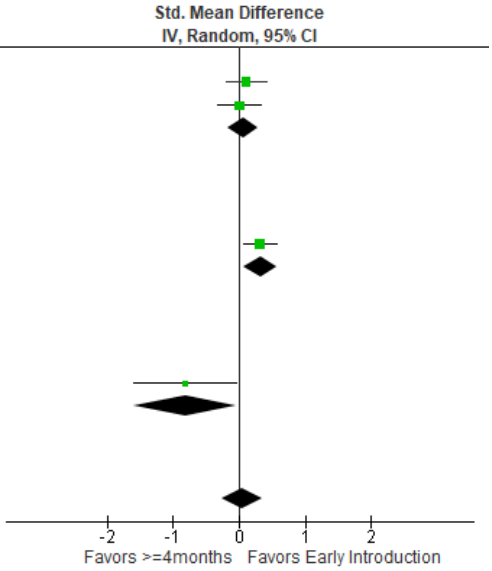
Outcome 4: Height

Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.4.1 Breast fed								
Huh 2011 (1)	98.3	4.8	43	96.92	4.1	525	13.5%	0.33 [0.02, 0.64]
Simondon 1997 (2)	1.31	0.5	42	1.24	0.44	190	11.9%	0.15 [-0.18, 0.49]
Veena 2010 (3)	130.7	5.7	95	130.7	5.6	387	23.6%	0.00 [-0.22, 0.22]
Subtotal (95% CI)			**180**			**1102**	**49.0%**	**0.14 [-0.06, 0.34]**
Heterogeneity: Tau² = 0.01; Chi² = 2.91, df = 2 (P = 0.23); I² = 31%								
Test for overall effect: Z = 1.36 (P = 0.17)								
9.4.2 Formula fed								
Huh 2011 (4)	98.4	4.5	91	97.8	4.6	188	19.7%	0.13 [-0.12, 0.38]
Subtotal (95% CI)			**91**			**188**	**19.7%**	**0.13 [-0.12, 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.02 (P = 0.31)								
9.4.3 Unclear								
de Beer 2015 (5)	0.32	1.04	117	0.036	0.99	2086	31.4%	0.29 [0.10, 0.47]
Subtotal (95% CI)			**117**			**2086**	**31.4%**	**0.29 [0.10, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.01 (P = 0.003)								
Total (95% CI)			**388**			**3376**	**100.0%**	**0.18 [0.06, 0.30]**
Heterogeneity: Tau² = 0.00; Chi² = 4.79, df = 4 (P = 0.31); I² = 17%								
Test for overall effect: Z = 2.88 (P = 0.004)								
Test for subgroup differences: Chi² = 1.49, df = 2 (P = 0.47), I² = 0%								



Footnotes
(1) Breastfed group at 3 years
(2) cm/mo at 6-90mo
(3) at 9-10years in cm
(4) Formula fed group at 3 years
(5) z-score at 5-6 years of age

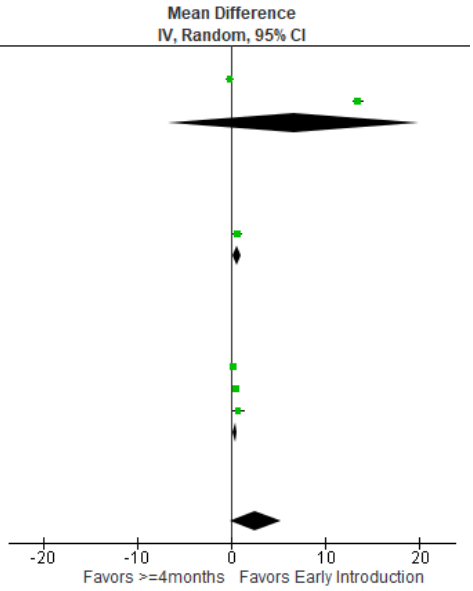
Outcome 5: Weight



Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
9.5.1 Breast fed								
Huh 2011 (1)	15.6	1.8	43	15.4	1.9	525	28.9%	0.11 [-0.21, 0.42]
Simondon 1997	0.22	0.16	42	0.19	16	190	27.6%	0.00 [-0.33, 0.34]
Subtotal (95% CI)			**85**			**715**	**56.6%**	**0.06 [-0.17, 0.29]**
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.66); I² = 0%								
Test for overall effect: Z = 0.50 (P = 0.62)								
9.5.2 Formula fed								
Huh 2011 (2)	16.7	2.7	91	15.9	2.4	188	32.4%	0.32 [0.07, 0.57]
Subtotal (95% CI)			**91**			**188**	**32.4%**	**0.32 [0.07, 0.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.48 (P = 0.01)								
9.5.3 Unclear								
Barton 2002 (3)	263.7	30.9	40	291.4	44.8	8	11.1%	-0.82 [-1.59, -0.04]
Subtotal (95% CI)			**40**			**8**	**11.1%**	**-0.82 [-1.59, -0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.06 (P = 0.04)								
Total (95% CI)			**216**			**911**	**100.0%**	**0.04 [-0.26, 0.35]**
Heterogeneity: Tau² = 0.06; Chi² = 8.43, df = 3 (P = 0.04); I² = 64%								
Test for overall effect: Z = 0.28 (P = 0.78)								
Test for subgroup differences: Chi² = 8.23, df = 2 (P = 0.02), I² = 75.7%								

Footnotes
(1) Breastfed group at 3 years/kg
(2) Formula fed group at 3 years
(3) in Oz at 4-6 months

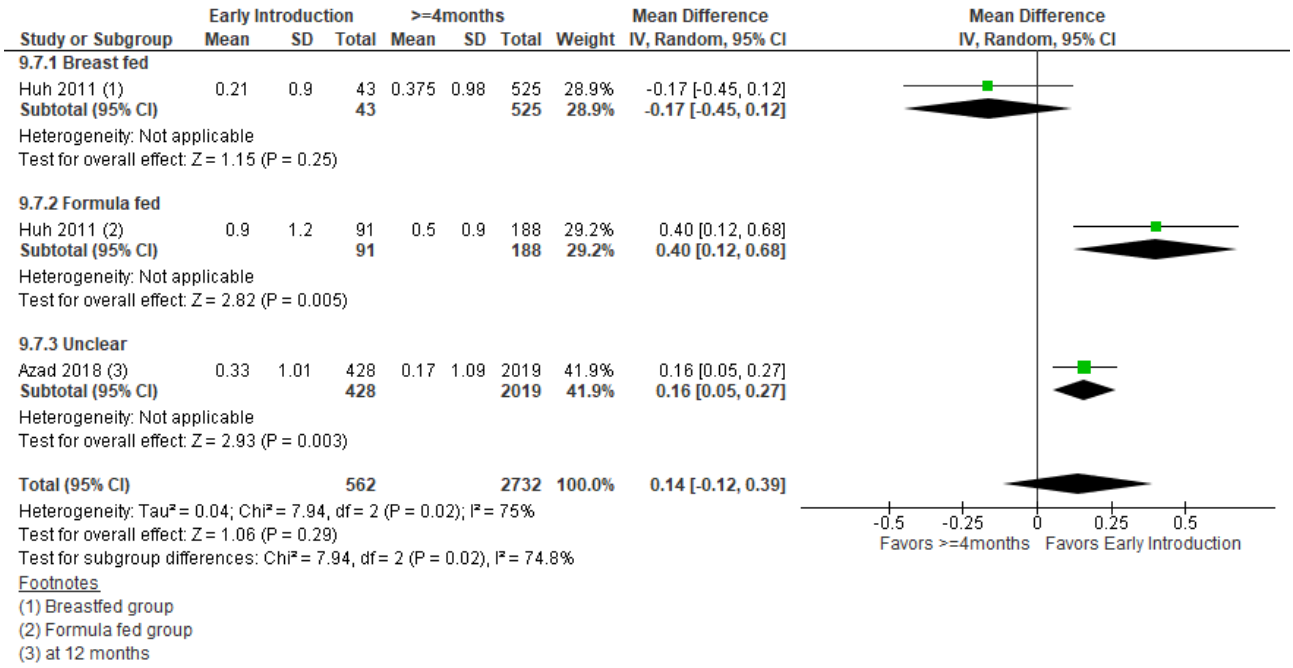
Outcome 6: BMI



Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.6.1 Breast fed								
Huh 2011 (1)	16.2	1.1	43	16.4	1.4	525	16.7%	-0.20 [-0.55, 0.15]
Veena 2010 (2)	14.9	2.3	95	1.5	1.7	387	16.6%	13.40 [12.91, 13.89]
Subtotal (95% CI)			**138**			**912**	**33.3%**	**6.60 [-6.73, 19.93]**
Heterogeneity: Tau² = 92.43; Chi² = 1946.44, df = 1 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 0.97 (P = 0.33)								
9.6.2 Formula fed								
Huh 2011 (3)	17.2	1.9	91	16.6	1.6	188	16.7%	0.60 [0.15, 1.05]
Subtotal (95% CI)			**91**			**188**	**16.7%**	**0.60 [0.15, 1.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.60 (P = 0.009)								
9.6.3 Unclear								
de Beer 2015 (4)	0.18	1.18	117	-0.052	1.007	2086	16.7%	0.23 [0.01, 0.45]
Morgen 2018 (5)	17.8	2.6	1643	17.3	2.4	20940	16.7%	0.50 [0.37, 0.63]
Rodriguez-Cano 2020 (6)	17.4	1.4	28	16.7	1.4	78	16.6%	0.70 [0.10, 1.30]
Subtotal (95% CI)			**1788**			**23104**	**50.0%**	**0.42 [0.19, 0.65]**
Heterogeneity: Tau² = 0.02; Chi² = 5.02, df = 2 (P = 0.08); I² = 60%								
Test for overall effect: Z = 3.63 (P = 0.0003)								
Total (95% CI)			**2017**			**24204**	**100.0%**	**2.53 [-0.16, 5.23]**
Heterogeneity: Tau² = 11.28; Chi² = 2586.45, df = 5 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 1.85 (P = 0.07)								
Test for subgroup differences: Chi² = 1.30, df = 2 (P = 0.52), I² = 0%								

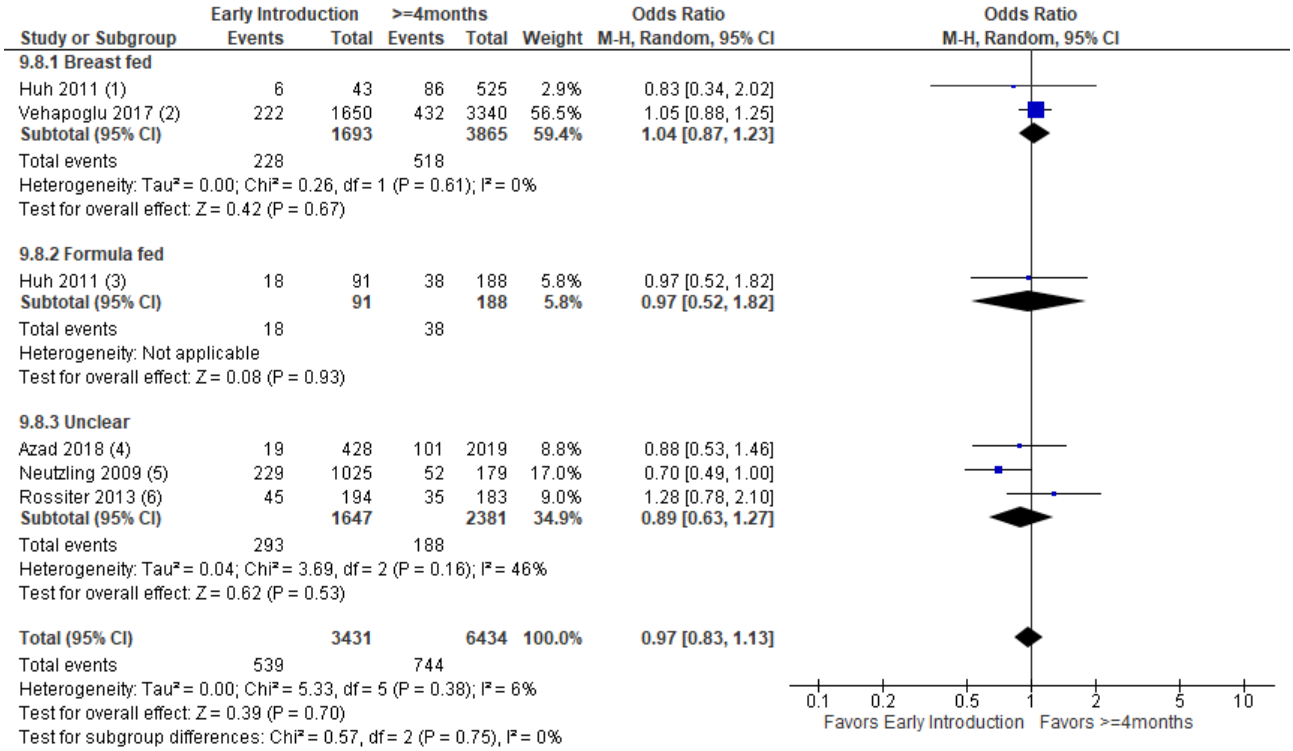
Footnotes
(1) Breastfed group at 3 years
(2) at 9-10years
(3) Formula fed group at 3 years
(4) at 5-6 years of age
(5) At 11 years of age
(6) At 12 months

Outcome 7: BMI z-score



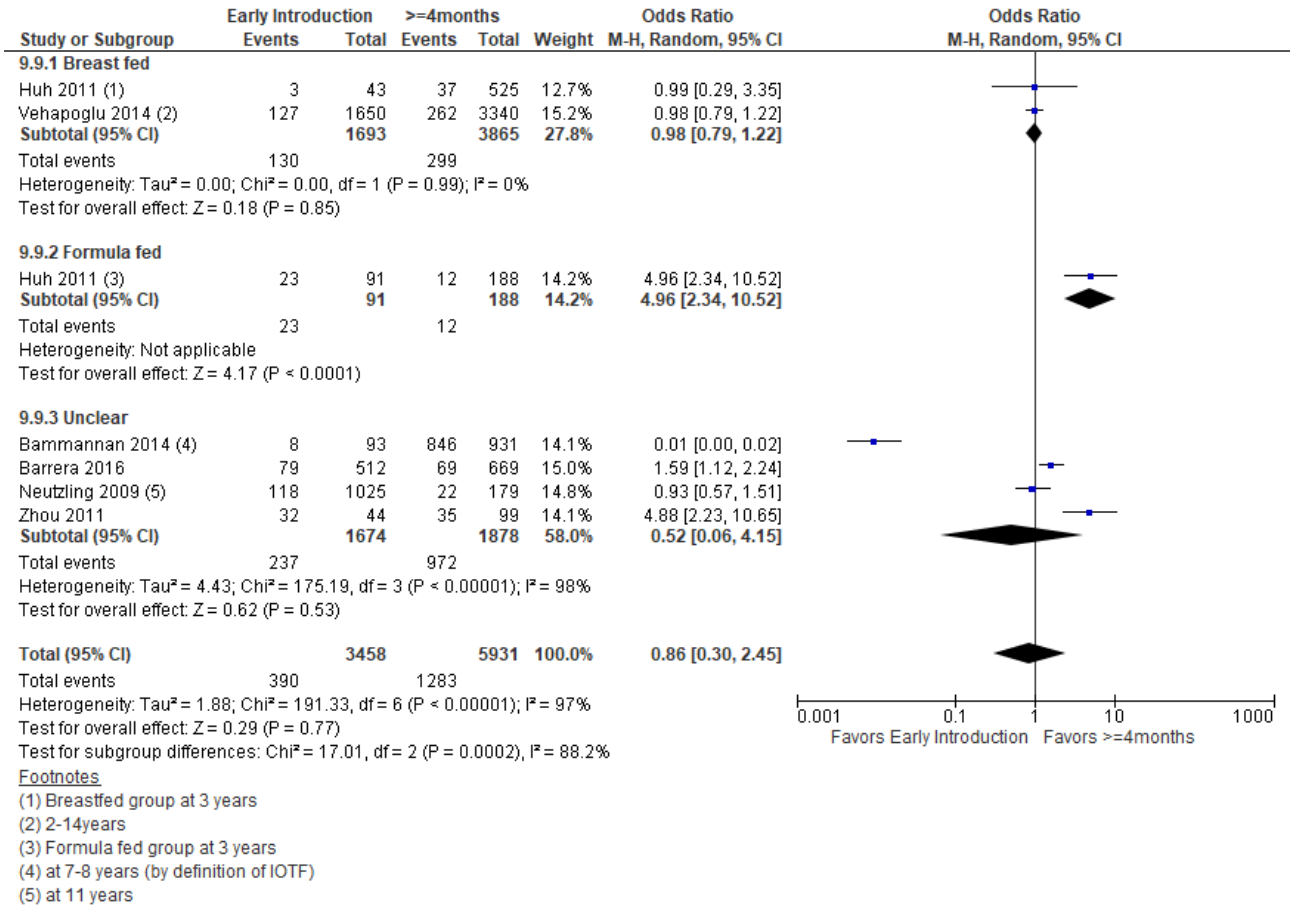
Footnotes
(1) Breastfed group
(2) Formula fed group
(3) at 12 months

Outcome 8: Overweight



Footnotes
(1) Breastfed group at 3 years
(2) 2-14years
(3) Formula fed group at 3 years
(4) at 12 mo
(5) BMI>= 85th percentile of children 11 years old
(6) Defined as BMI above 85 and below 95 percentile (at 48 months of age)

Outcome 9: Obesity

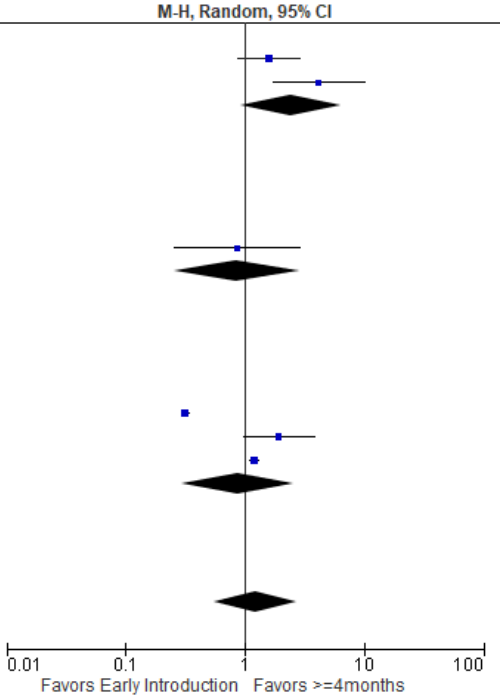


Footnotes

(1) Breastfed group at 3 years
(2) 2-14years
(3) Formula fed group at 3 years
(4) at 7-8 years (by definition of IOTF)
(5) at 11 years

Outcome 10: Overweight and Obesity

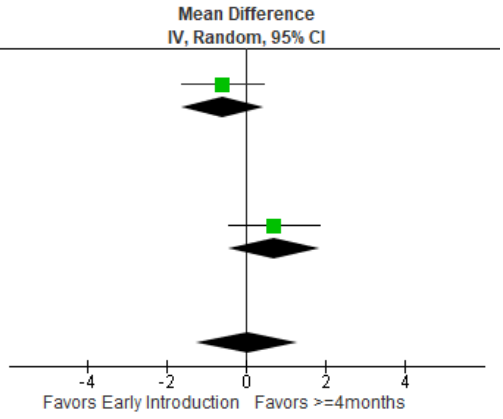
Study or Subgroup	Early Introduction Events	Total	>=4months Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
9.10.1 Breast fed						
Caleyachetty 2013 (1)	36	301	18	228	17.1%	1.58 [0.87, 2.87]
Sun 2016 (2)	6	46	76	2171	15.3%	4.13 [1.70, 10.05]
Subtotal (95% CI)		**347**		**2399**	**32.4%**	**2.42 [0.93, 6.31]**
Total events	42		94			
Heterogeneity: Tau² = 0.34; Chi² = 3.26, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 1.81 (P = 0.07)						
9.10.2 Formula fed						
Sun 2016 (3)	3	49	49	690	13.2%	0.85 [0.26, 2.84]
Subtotal (95% CI)		**49**		**690**	**13.2%**	**0.85 [0.26, 2.84]**
Total events	3		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.80)						
9.10.3 Unclear						
Hawkins 2009 (4)	1668	4633	5468	8544	18.9%	0.32 [0.29, 0.34]
Hollis 2016 (5)	103	642	10	110	16.6%	1.91 [0.96, 3.78]
Massion 2016 (6)	1299	4176	2087	7588	18.9%	1.19 [1.10, 1.29]
Subtotal (95% CI)		**9451**		**16242**	**54.3%**	**0.87 [0.29, 2.56]**
Total events	3070		7565			
Heterogeneity: Tau² = 0.88; Chi² = 556.21, df = 2 (P < 0.00001); I² = 100%						
Test for overall effect: Z = 0.26 (P = 0.80)						
Total (95% CI)		**9847**		**19331**	**100.0%**	**1.22 [0.55, 2.71]**
Total events	3115		7708			
Heterogeneity: Tau² = 0.88; Chi² = 586.22, df = 5 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 0.49 (P = 0.63)						
Test for subgroup differences: Chi² = 2.62, df = 2 (P = 0.27), I² = 23.6%						



Footnotes
(1) at 5 years
(2) BMI z-score >2SD at 1 year (breastfed group)
(3) BMI z-score >2SD at 1 year (formula fed group)
(4) According to IOTF at 3 years of age
(5) According to IOTF at 3 years
(6) at 11 years

Outcome 11: Skinfold thickness (tricep and subscapular)

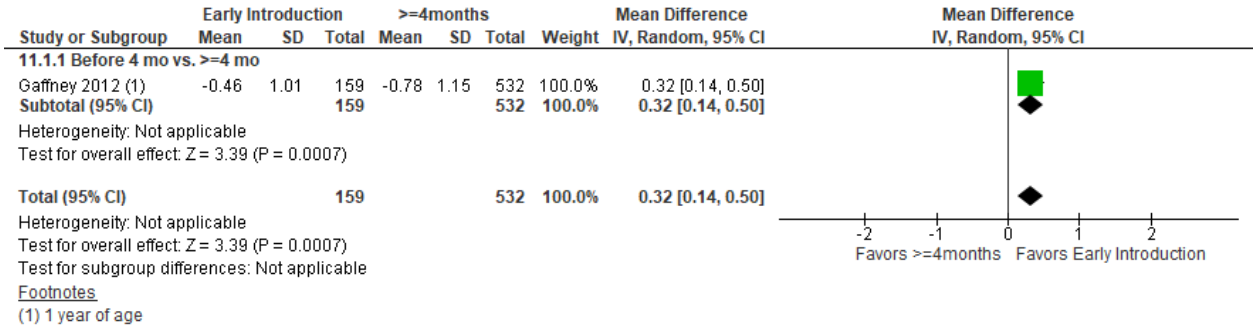
Study or Subgroup	Early Introduction Mean	SD	Total	>=4months Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.11.1 Breast fed								
Huh 2011 (1)	15.9	3.3	43	16.5	4	525	52.0%	-0.60 [-1.64, 0.44]
Subtotal (95% CI)			**43**			**525**	**52.0%**	**-0.60 [-1.64, 0.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.13 (P = 0.26)								
9.11.2 Formula fed								
Huh 2011 (2)	18	4.8	91	17.3	4.3	188	48.0%	0.70 [-0.46, 1.86]
Subtotal (95% CI)			**91**			**188**	**48.0%**	**0.70 [-0.46, 1.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.18 (P = 0.24)								
Total (95% CI)			**134**			**713**	**100.0%**	**0.02 [-1.25, 1.30]**
Heterogeneity: Tau² = 0.53; Chi² = 2.66, df = 1 (P = 0.10); I² = 62%								
Test for overall effect: Z = 0.04 (P = 0.97)								
Test for subgroup differences: Chi² = 2.66, df = 1 (P = 0.10), I² = 62.4%								



Footnotes
(1) Breastfed group at 3 years of age
(2) formula group at 3 years of age

Comparison. Early introduction of CF (< four months of age) compared to ≥ four months of age among preterm infants (Observation studies)

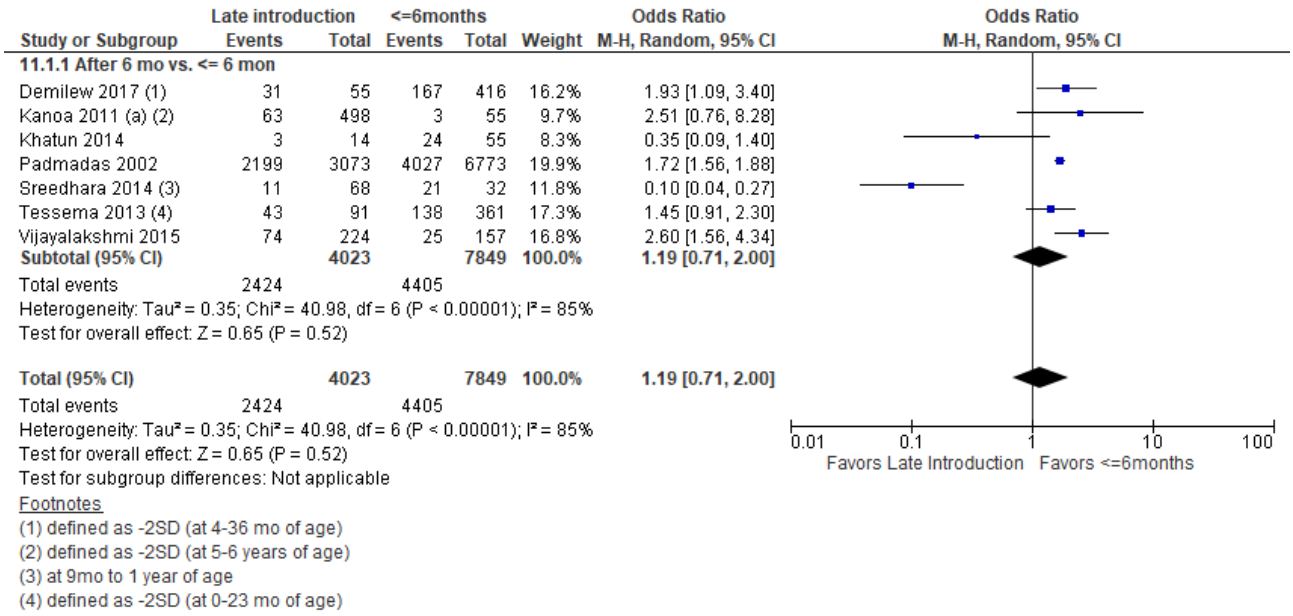
Outcome 1: Weight for age Z-score



Annex 2: Forest Plots of Late Initiation of Complementary food

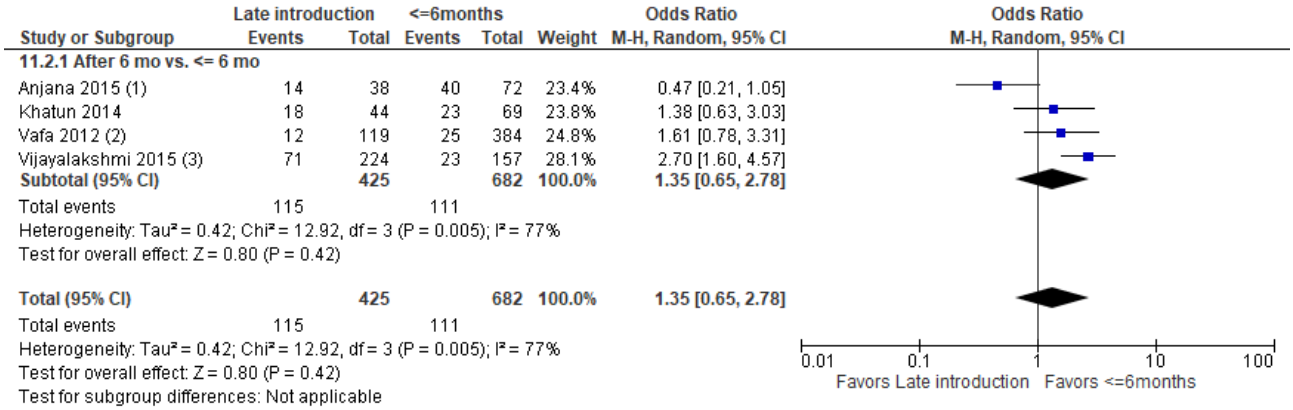
Comparison. Late introduction of CF (> six months) compared to ≤ six months of age among normal term infants (Observational studies)

Outcome 1: Stunting



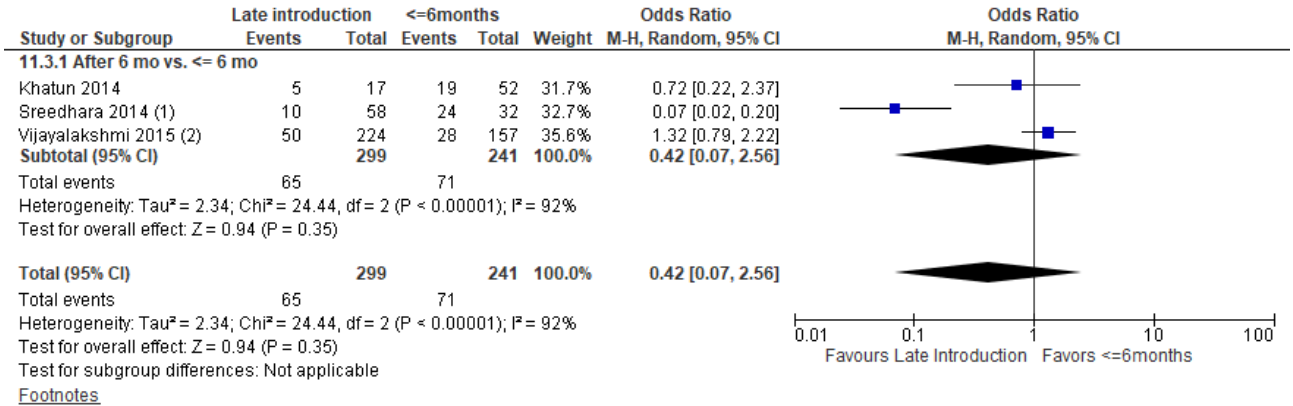
Footnotes
(1) defined as -2SD (at 4-36 mo of age)
(2) defined as -2SD (at 5-6 years of age)
(3) at 9mo to 1 year of age
(4) defined as -2SD (at 0-23 mo of age)

Outcome 2: Underweight



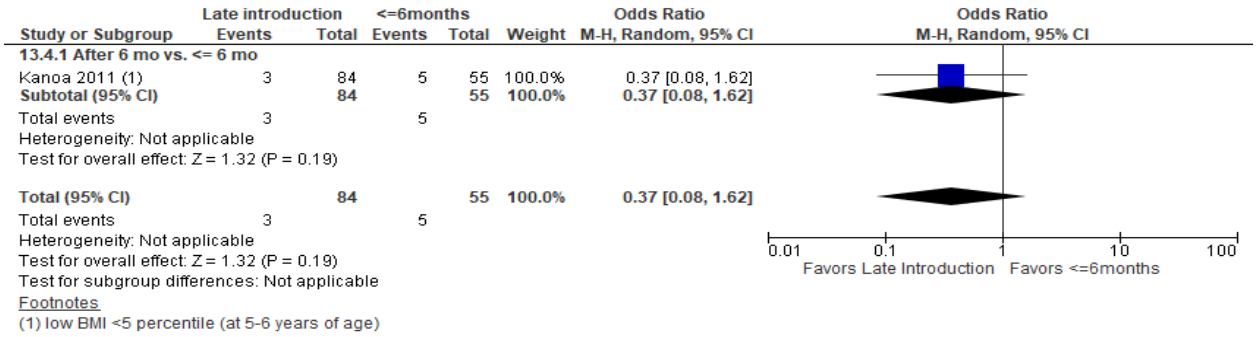
Footnotes
(1) at 7 mo to 3 years
(2) <18.5 at 7 years
(3) at 6-24 mo

Outcome 3: Wasting

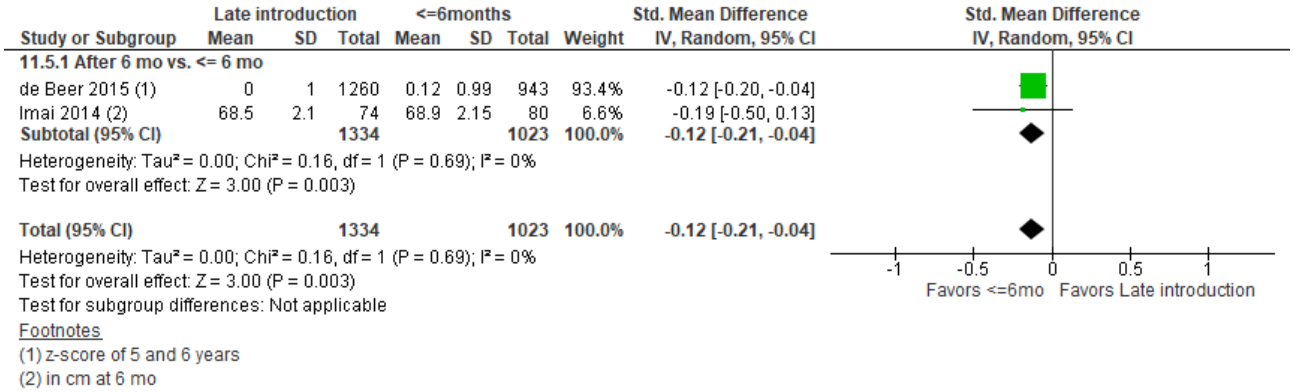


Footnotes
(1) at 9mo to 1 year of age
(2) at 6-24 mo

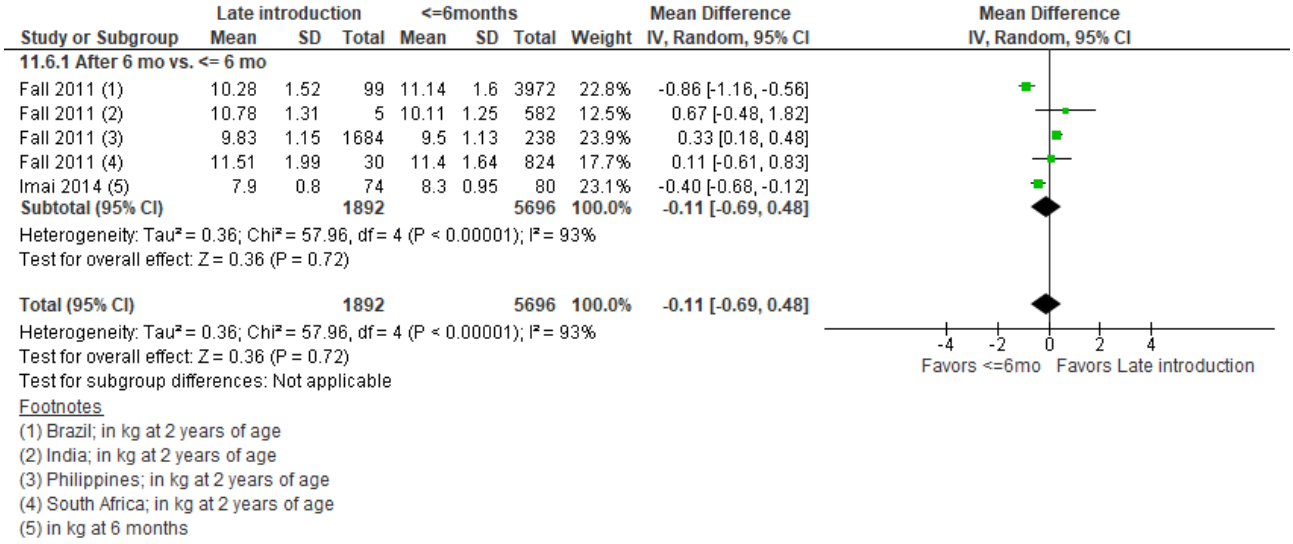
Outcome 4: Thinness



Outcome 5: Length



Outcome 6: Weight



Footnotes

(1) Brazil; in kg at 2 years of age

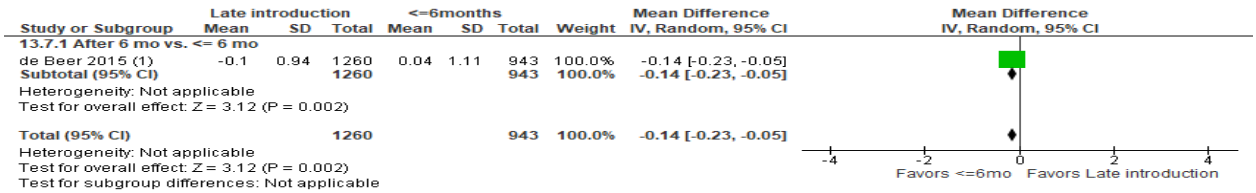
(2) India; in kg at 2 years of age

(3) Philippines; in kg at 2 years of age

(4) South Africa; in kg at 2 years of age

(5) in kg at 6 months

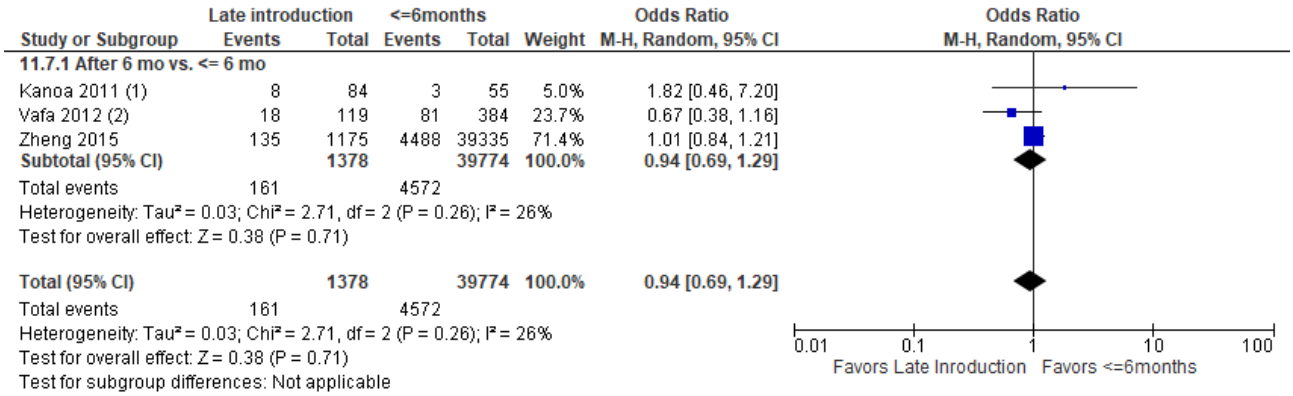
Outcome 7: BMI



Footnotes

(1) of 5 and 6 years

Outcome 8: Overweight

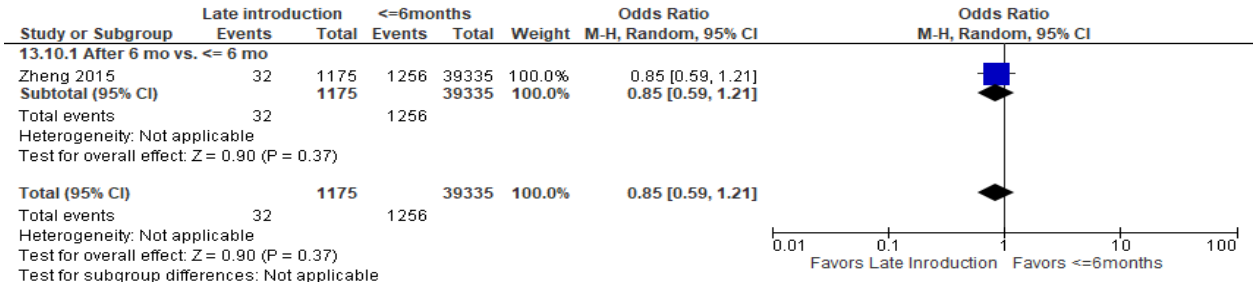


Footnotes

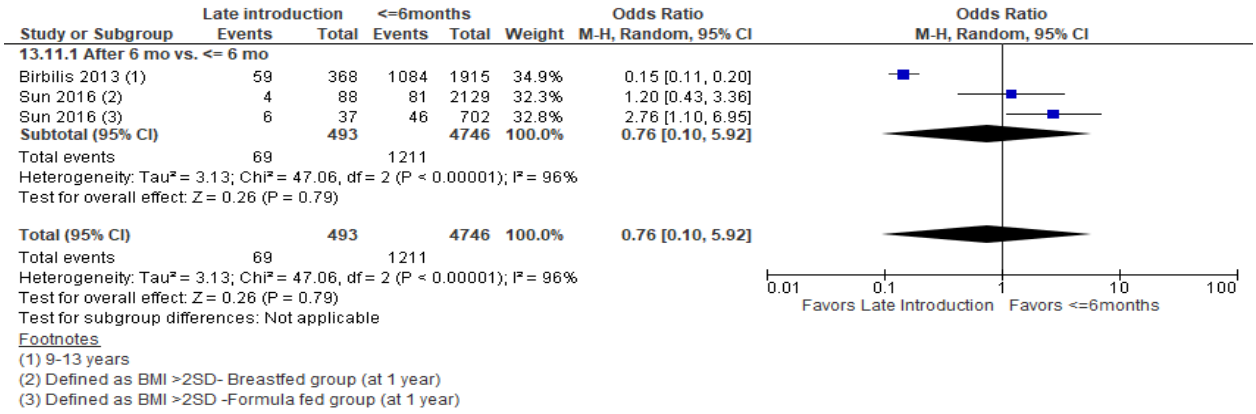
(1) Between >1 to <2SD (at 5-6 years of age)

(2) BMI 25 to 29.9

Outcome 9: Obesity



Outcome 10: Overweight and obesity



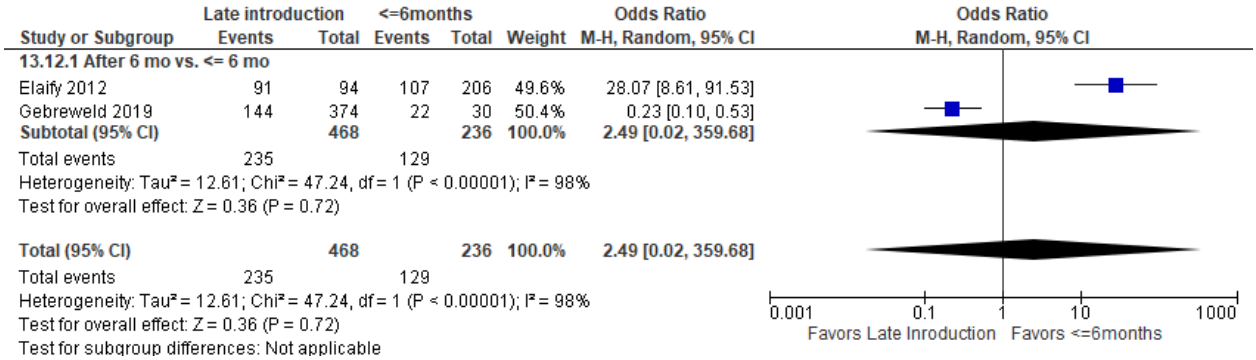
Footnotes

(1) 9-13 years

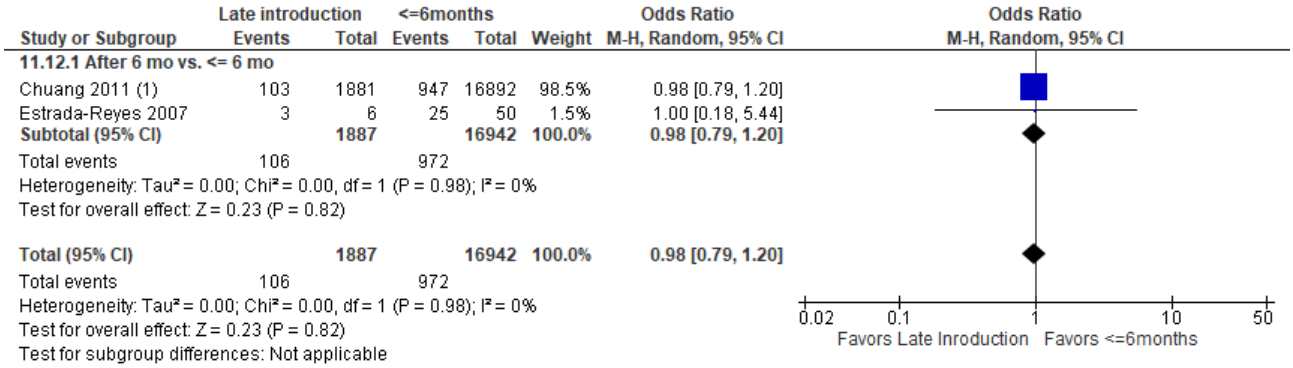
(2) Defined as BMI >2SD- Breastfed group (at 1 year)

(3) Defined as BMI >2SD -Formula fed group (at 1 year)

Outcome 11: Anemia



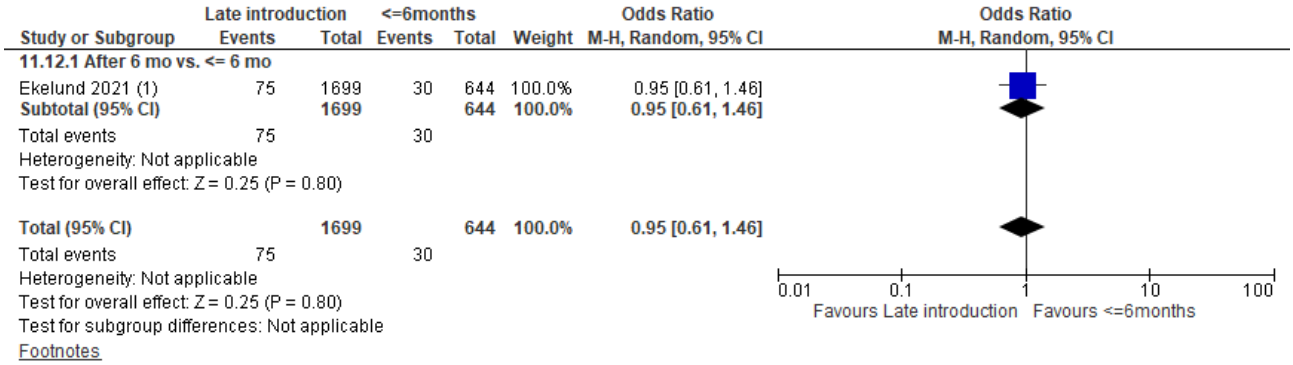
Outcome 12: Atopic dermatitis



Footnotes

(1) children under 5 years

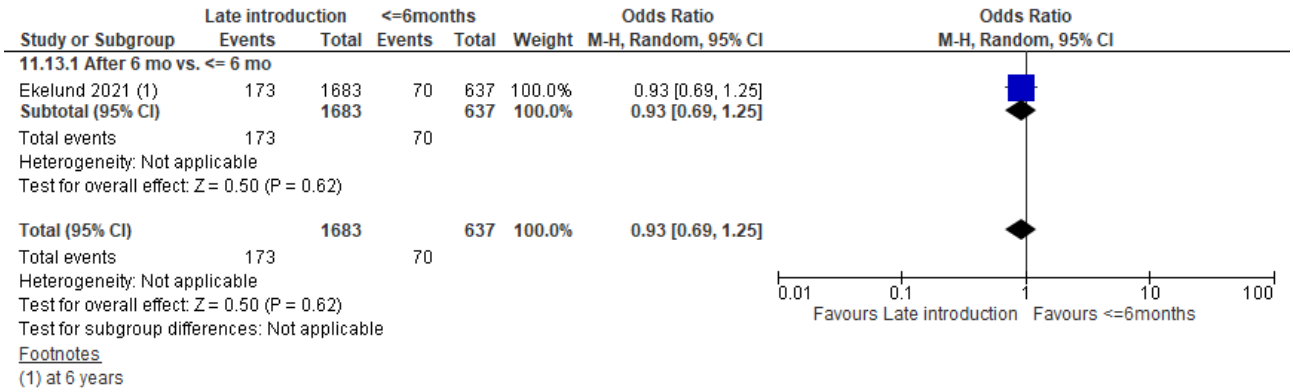
Outcome 13: Asthma



Footnotes

(1) at 6 years

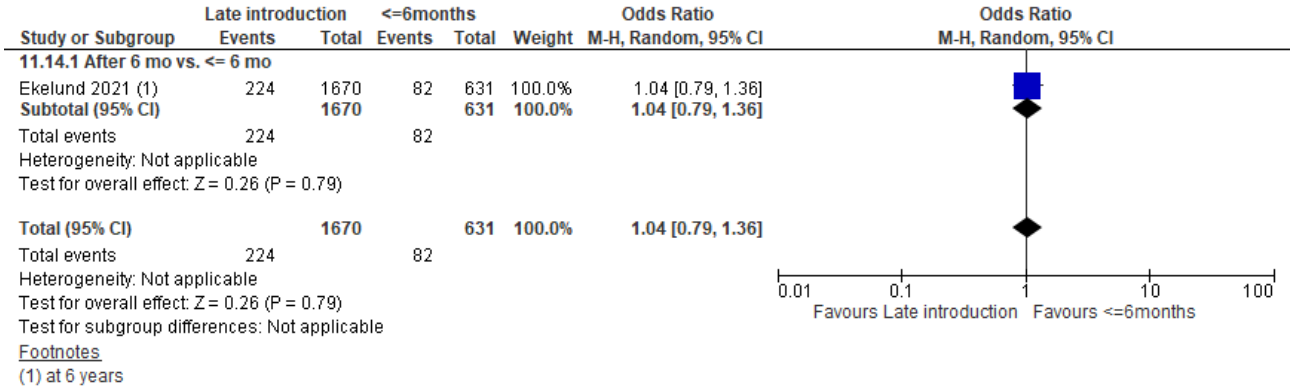
Outcome 14: Wheeze



Footnotes

(1) at 6 years

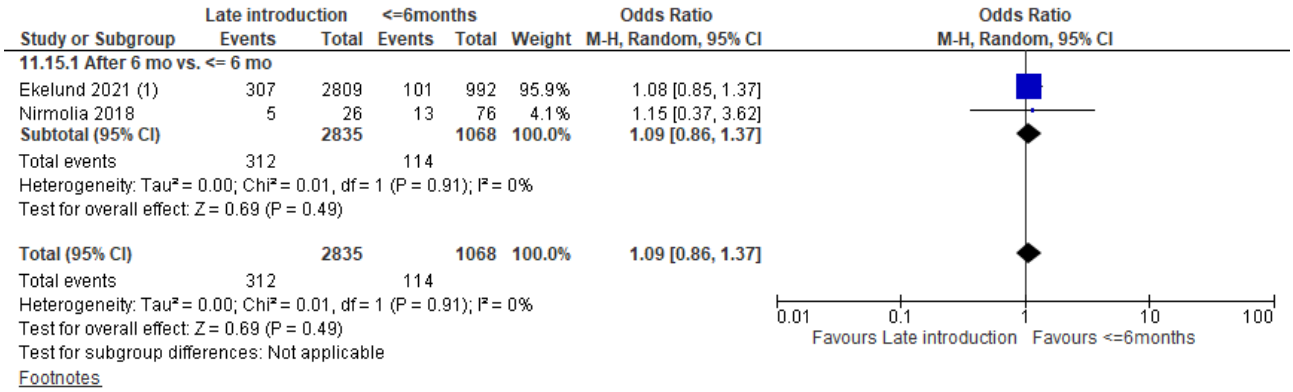
Outcome 15: Eczema



Footnotes

(1) at 6 years

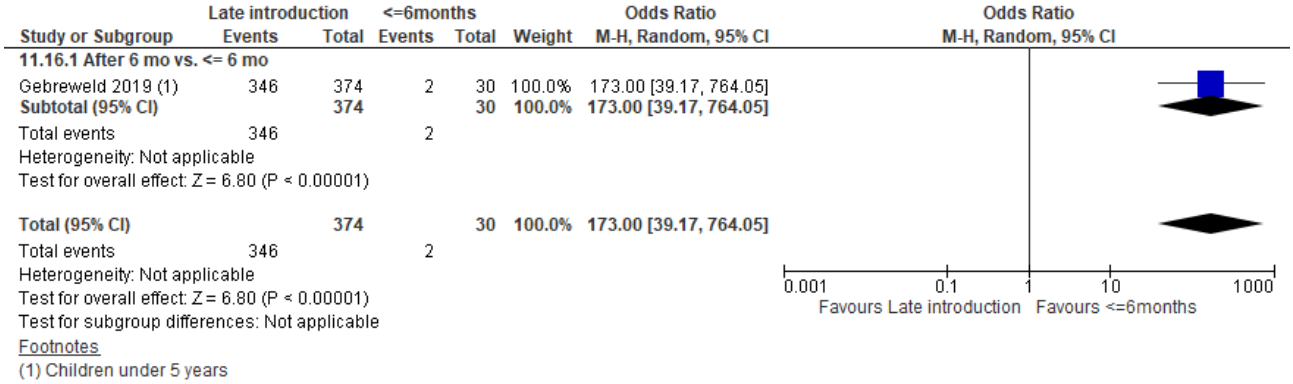
Outcome 16: LRTI



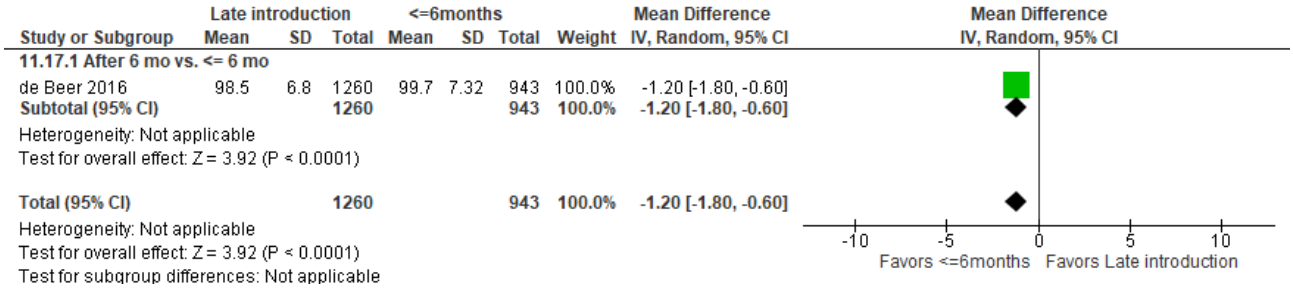
Footnotes

(1) within 1st year of life

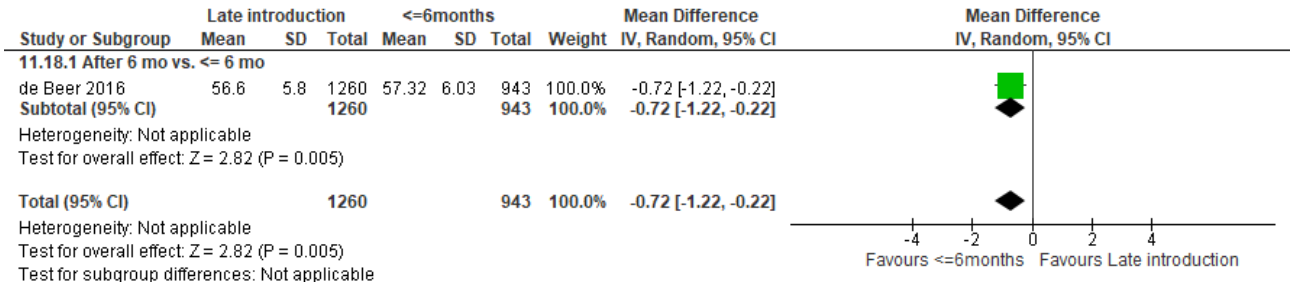
Outcome 17: Intestinal Helminth Infection



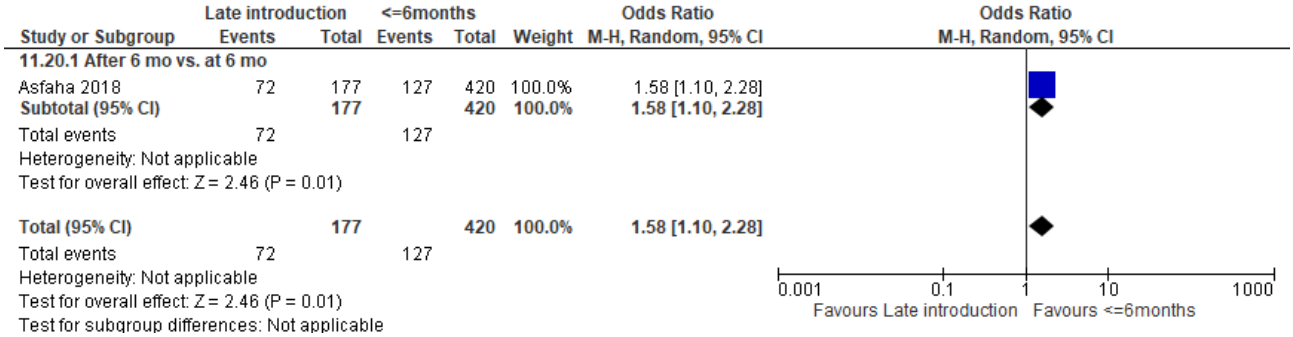
Outcome 18: Systolic Blood Pressure



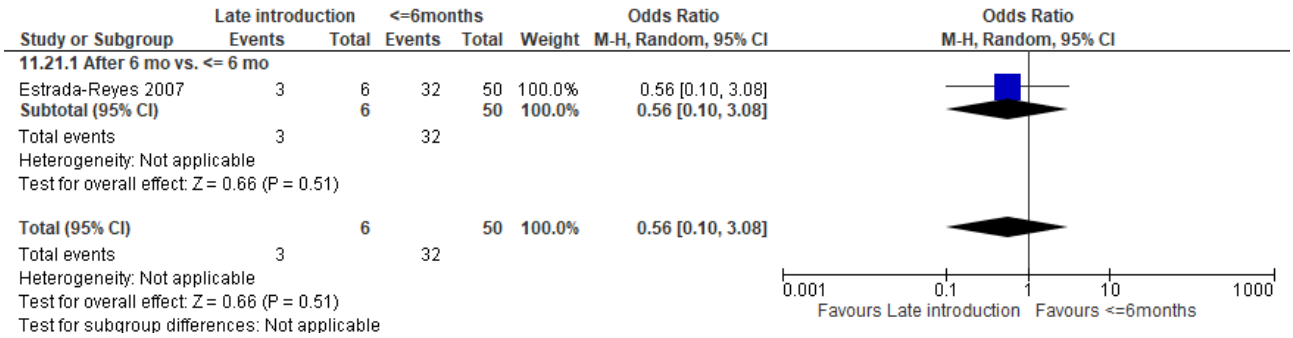
Outcome 19: Diastolic Blood Pressure



Outcome 20: Diarrhea

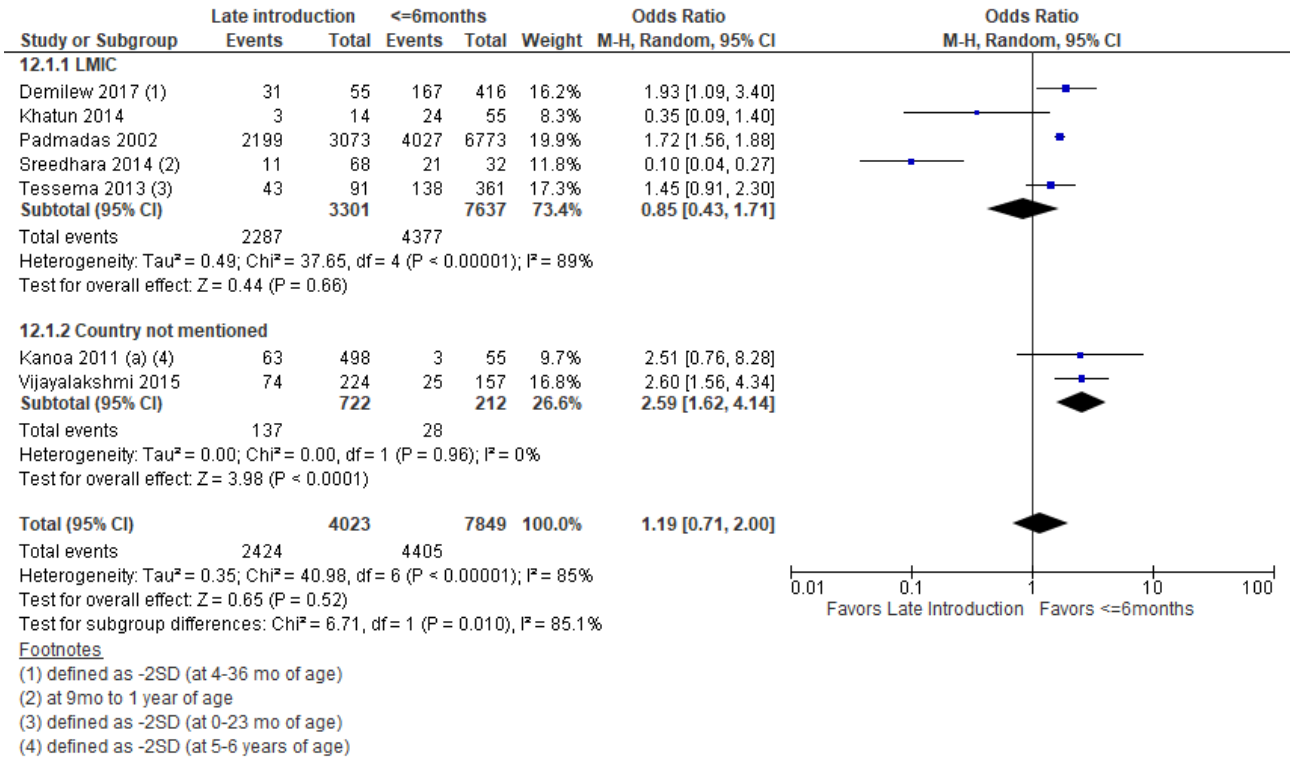


Outcome 21: Food hypersensitivity



Comparison. Late introduction of CF (> six months) compared to ≤ six months of age among normal term infants (Observational studies) - subgroup by setting

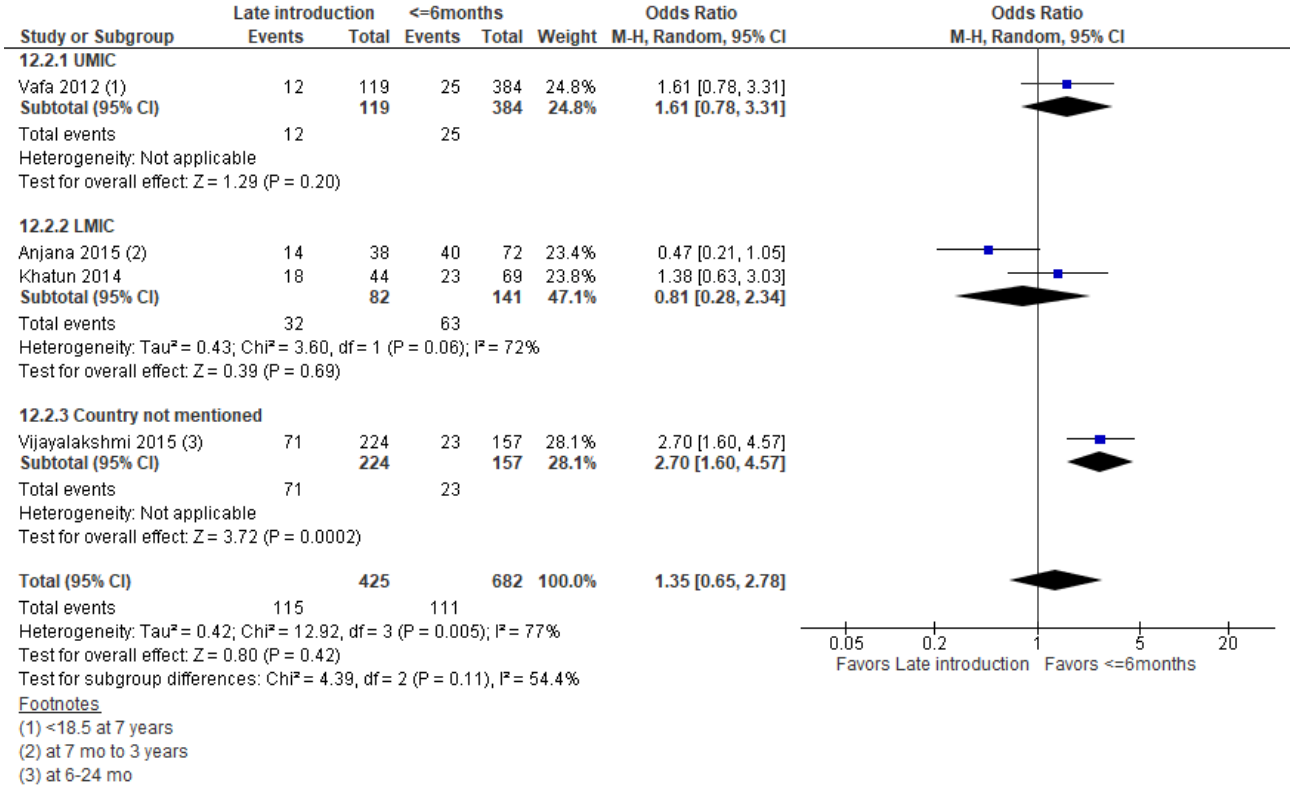
Outcome 1: Stunting



Footnotes

(1) defined as -2SD (at 4-36 mo of age)
(2) at 9mo to 1 year of age
(3) defined as -2SD (at 0-23 mo of age)
(4) defined as -2SD (at 5-6 years of age)

Outcome 2: Underweight



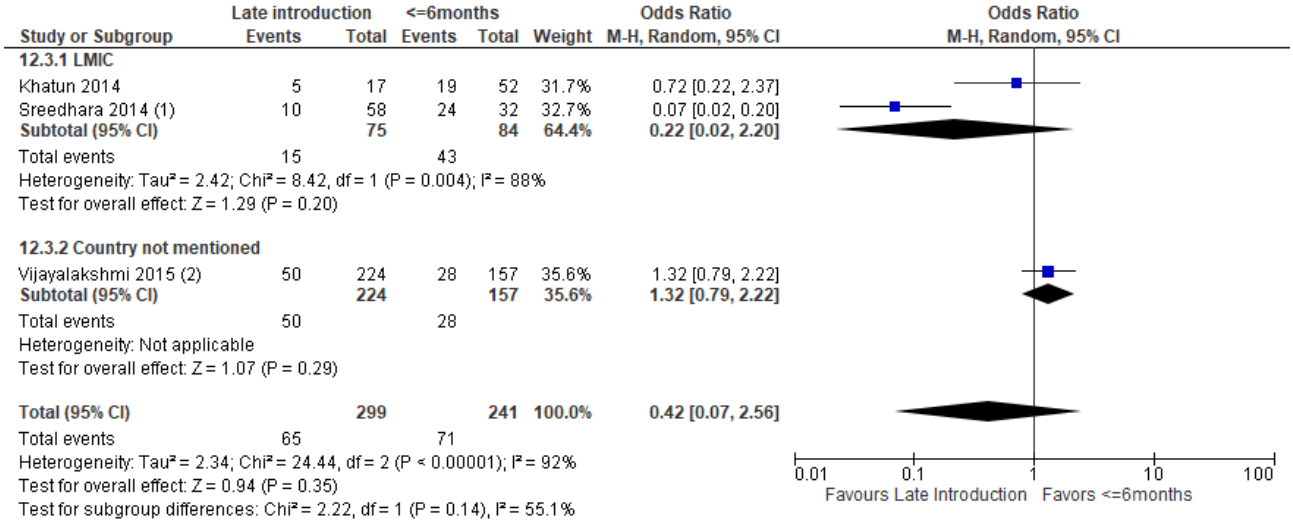
Footnotes

(1) <18.5 at 7 years

(2) at 7 mo to 3 years

(3) at 6-24 mo

Outcome 3: Wasting

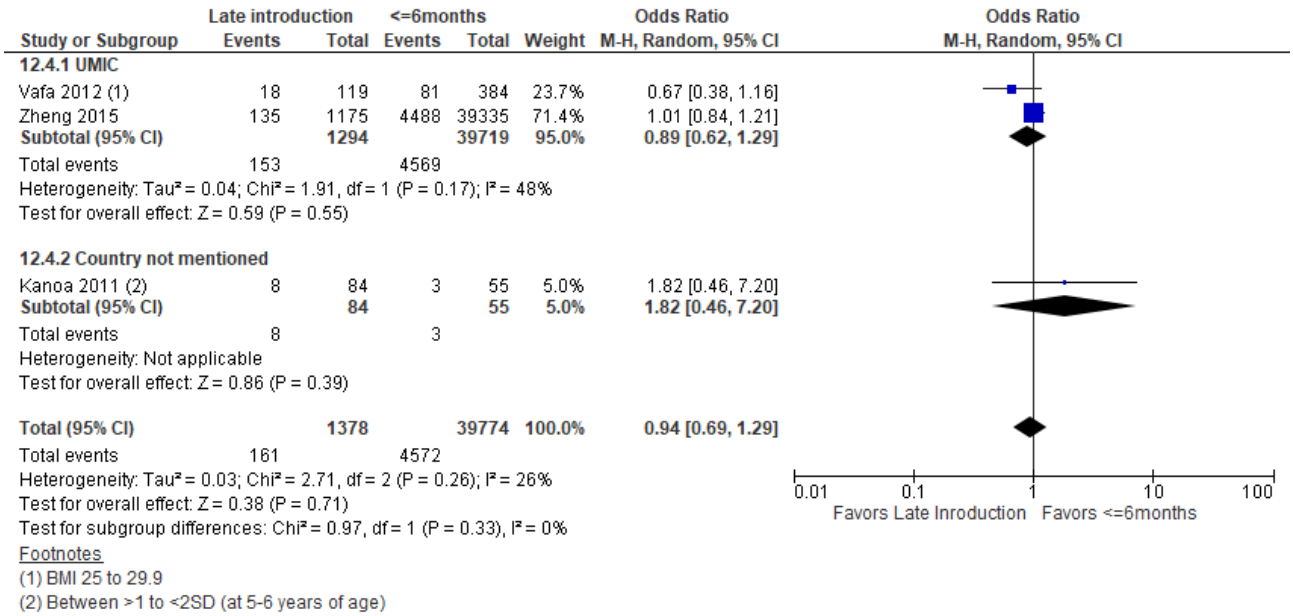


Footnotes

(1) at 9mo to 1 year of age

(2) at 6-24 mo

Outcome 4: Overweight

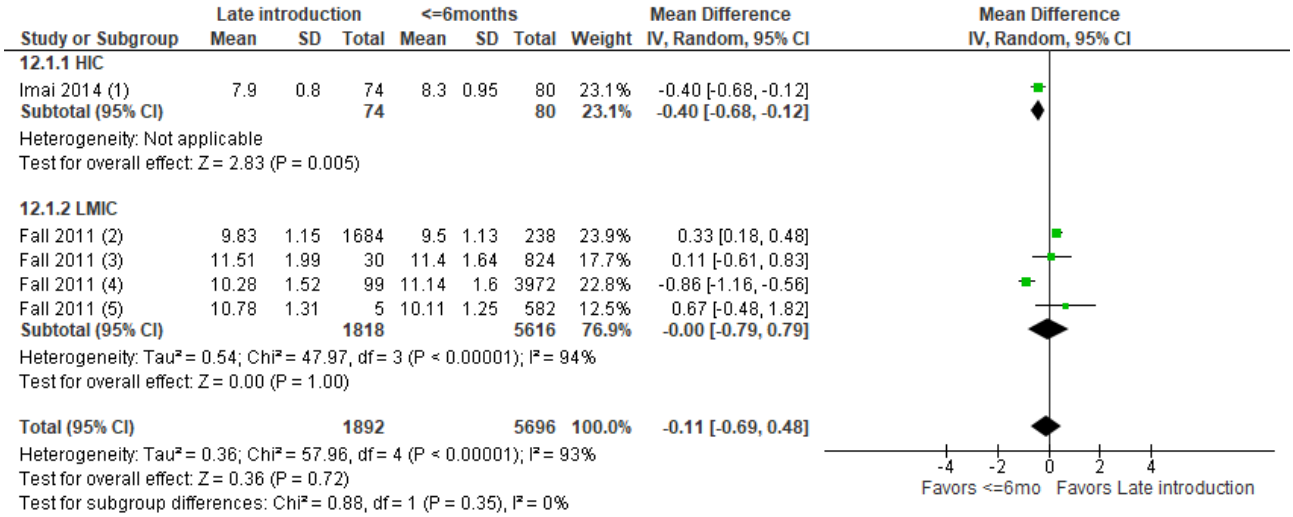


Footnotes

(1) BMI 25 to 29.9

(2) Between >1 to <2SD (at 5-6 years of age)

Outcome 5: Weight



Footnotes

(1) in kg at 6 months

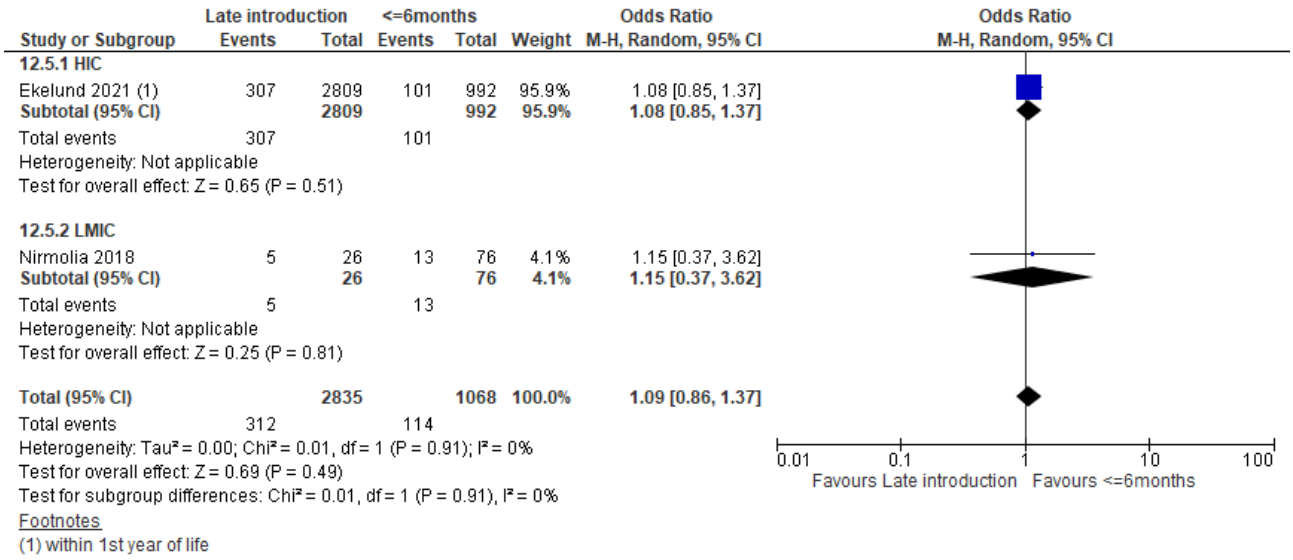
(2) Philippines; in kg at 2 years of age

(3) South Africa; in kg at 2 years of age

(4) Brazil; in kg at 2 years of age

(5) India; in kg at 2 years of age

Outcome 6: LRTI

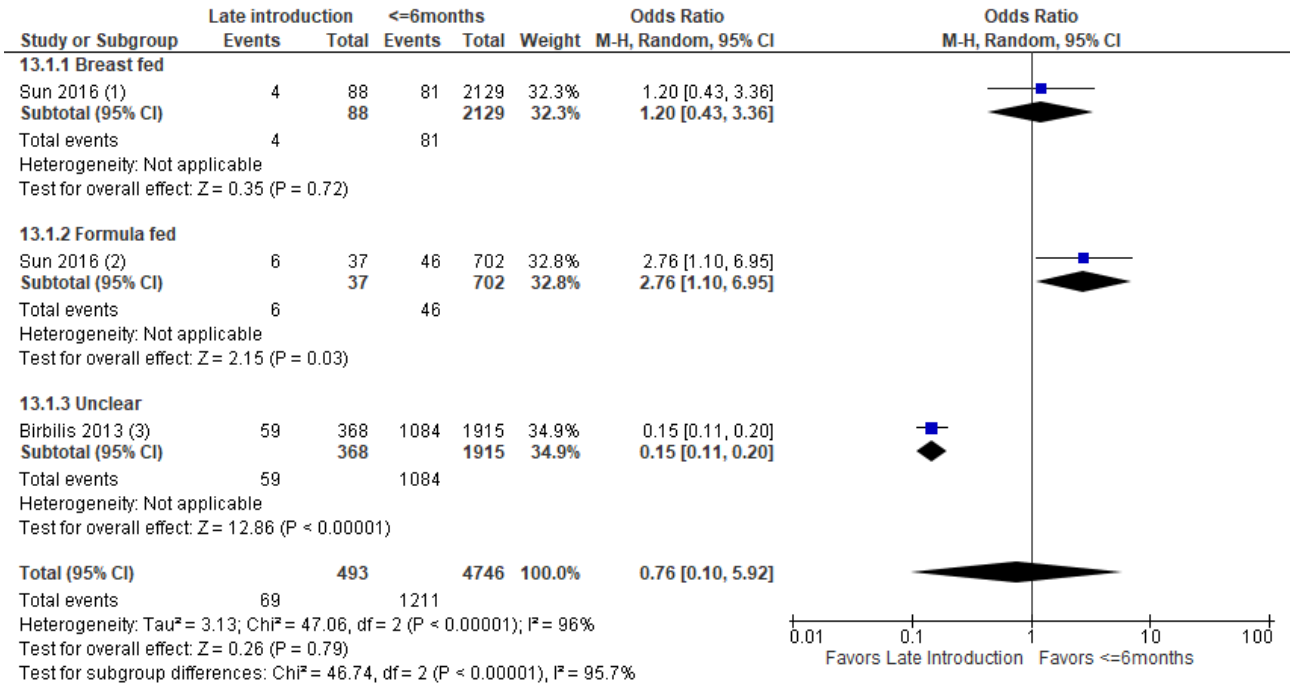


Footnotes

(1) within 1st year of life

Comparison. Late introduction of CF (> six months) compared to ≤ six months of age among normal term infants (Observational studies) - subgroup by feeding practices

Outcome 1: Overweight and Obesity



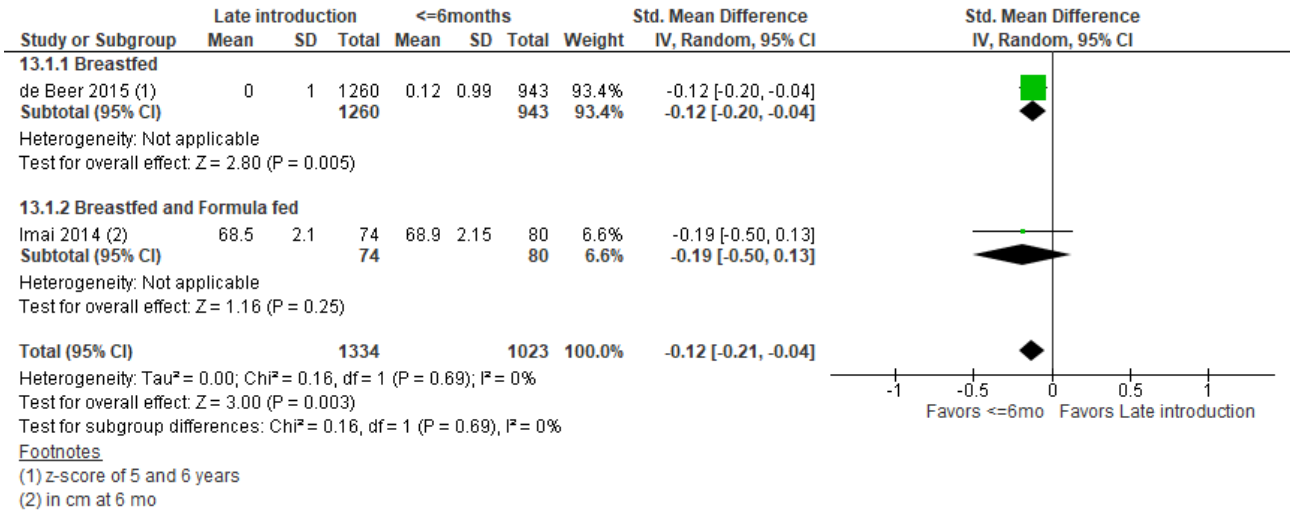
Footnotes

(1) Defined as BMI >2SD- Breastfed group (at 1 year)

(2) Defined as BMI >2SD -Formula fed group (at 1 year)

(3) 9-13 years

Outcome 2: Height



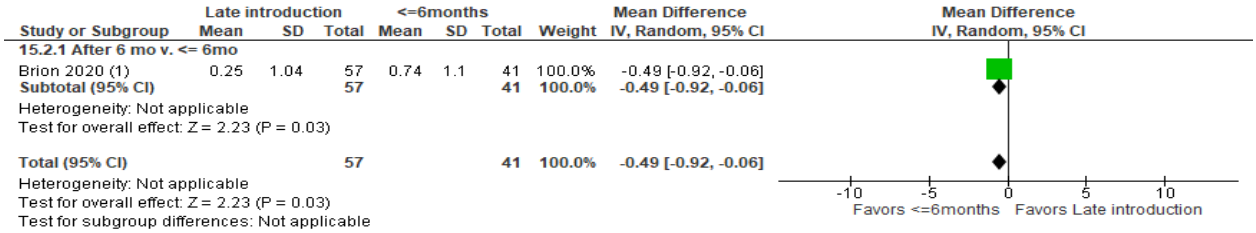
Footnotes

(1) z-score of 5 and 6 years

(2) in cm at 6 mo

Comparison. Late introduction of CF (> six months) compared to ≤ six months of age among preterm infants (Observational studies)

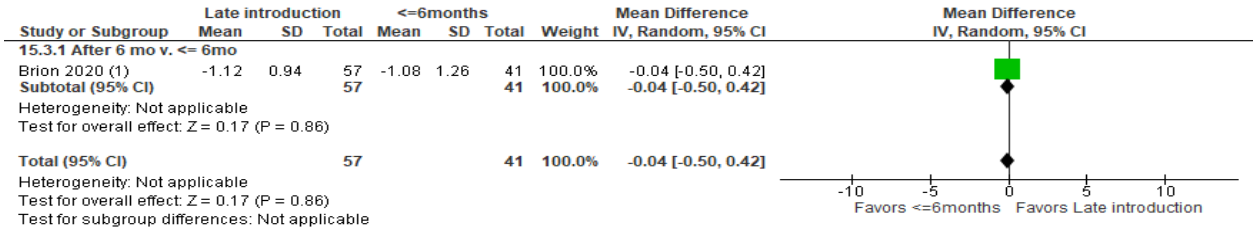
Outcome 1: Weight for age Z-score



Footnotes

(1) at 1 year of age

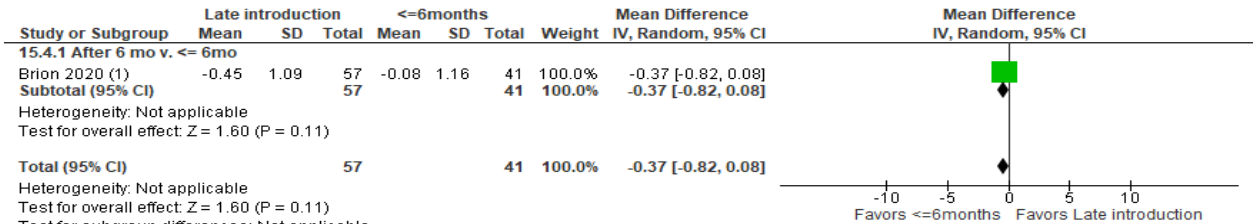
Outcome 2: Length



Footnotes

(1) Z-score at 1 year of age

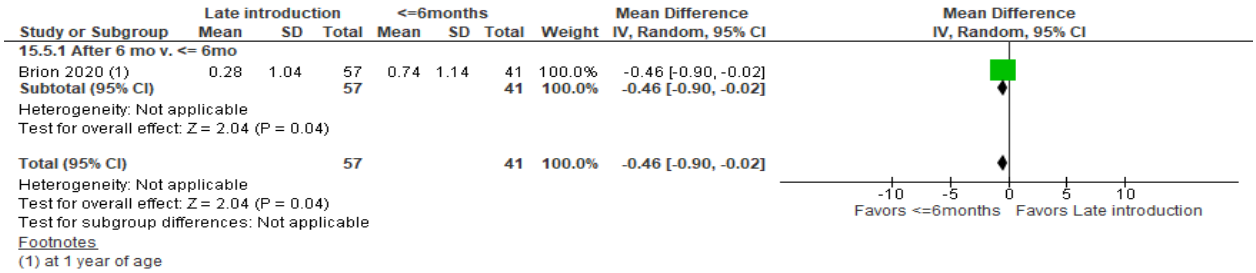
Outcome 3: Weight



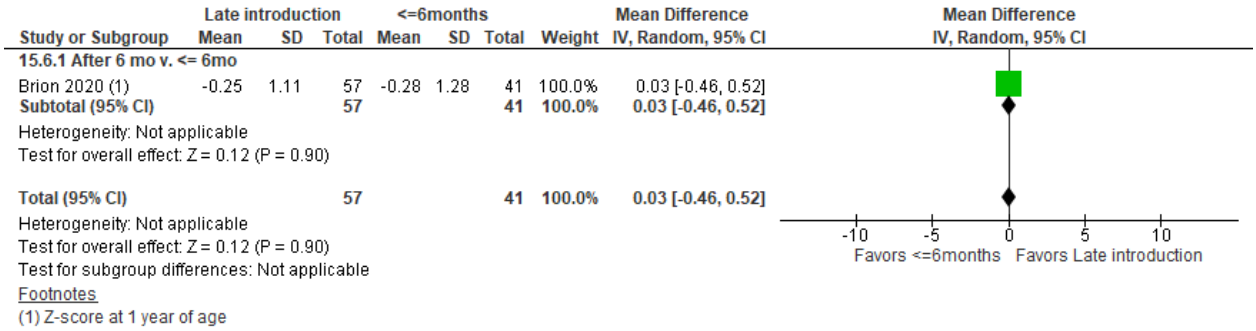
Footnotes

(1) Z-score at 1 year of age

Outcome 4: BMI Z-score

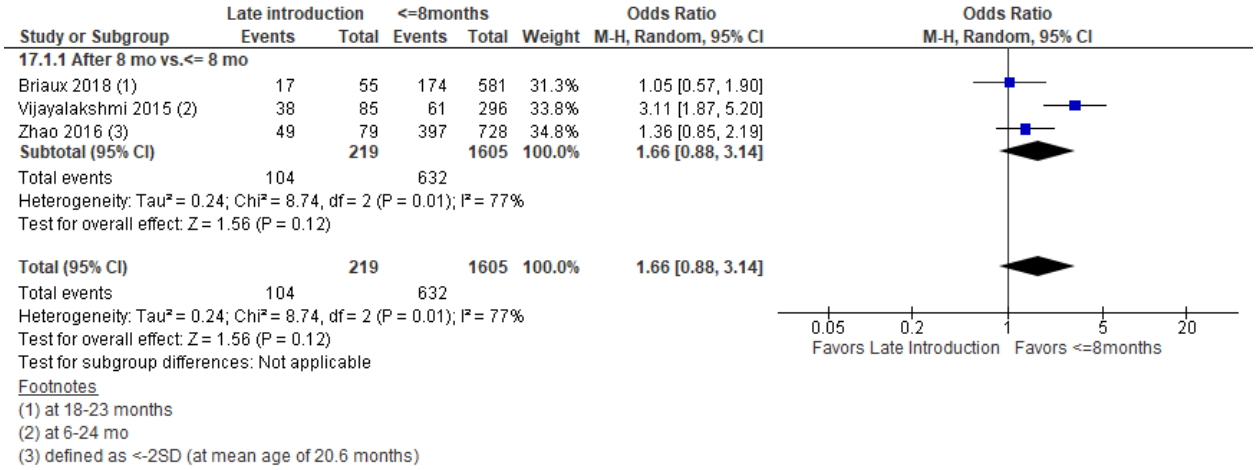


Outcome 5: Head circumference

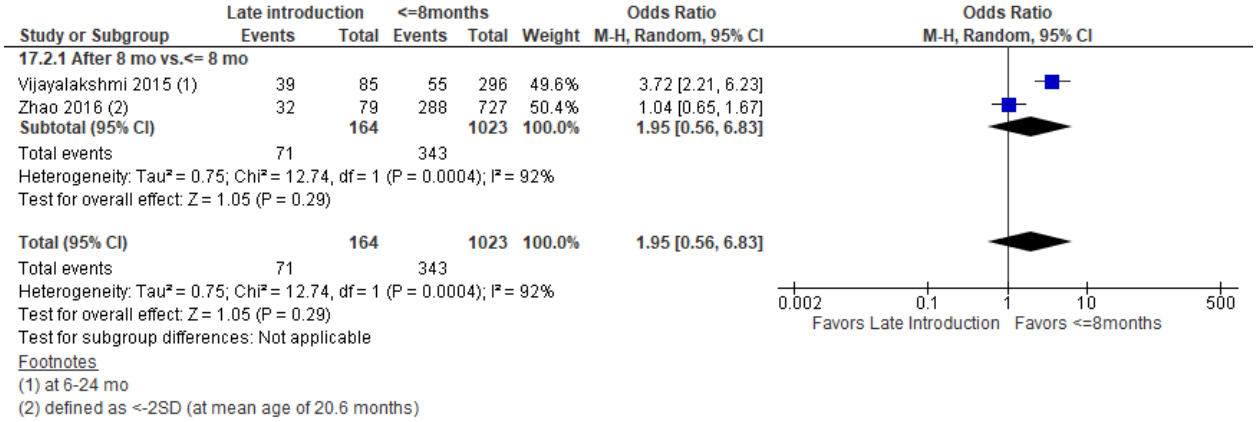


Comparison. Late introduction of CF (> eight months) compared to ≤ eight months of age among normal term infants (Observational studies)

Outcome 1: Stunting



Outcome 2: Underweight

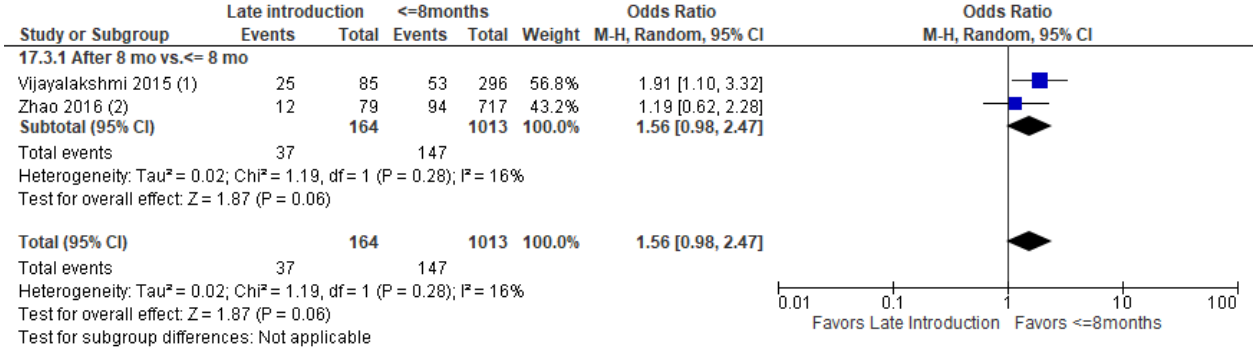


Footnotes

(1) at 6-24 mo

(2) defined as <-2SD (at mean age of 20.6 months)

Outcome 3: Wasting

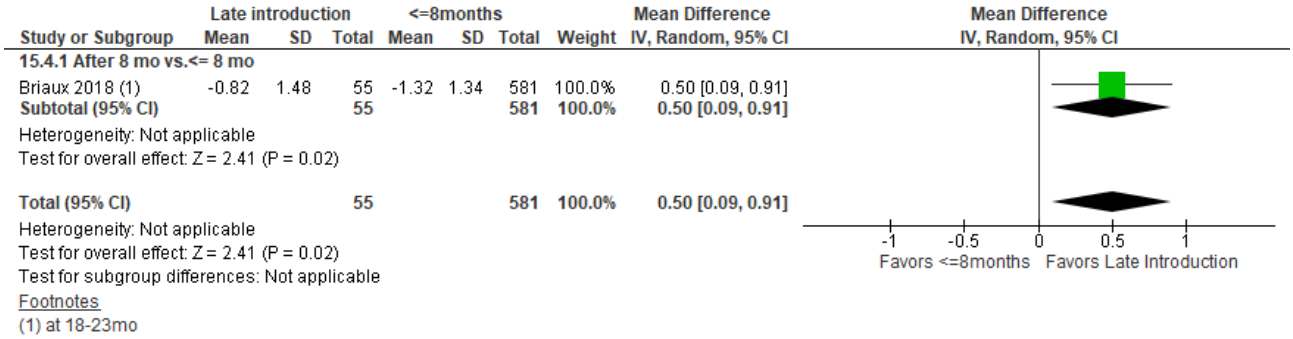


Footnotes

(1) at 6-24 mo

(2) defined as <-2SD (at mean age of 20.6 months)

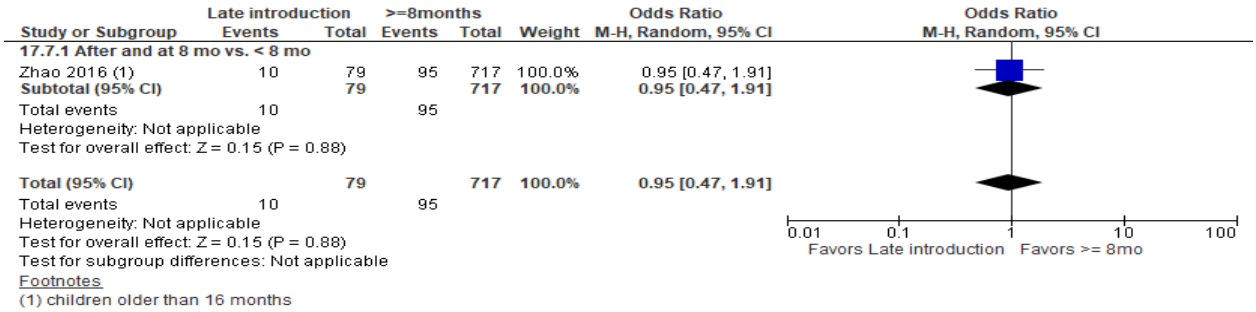
Outcome 4: Height for age Z-score



Footnotes

(1) at 18-23mo

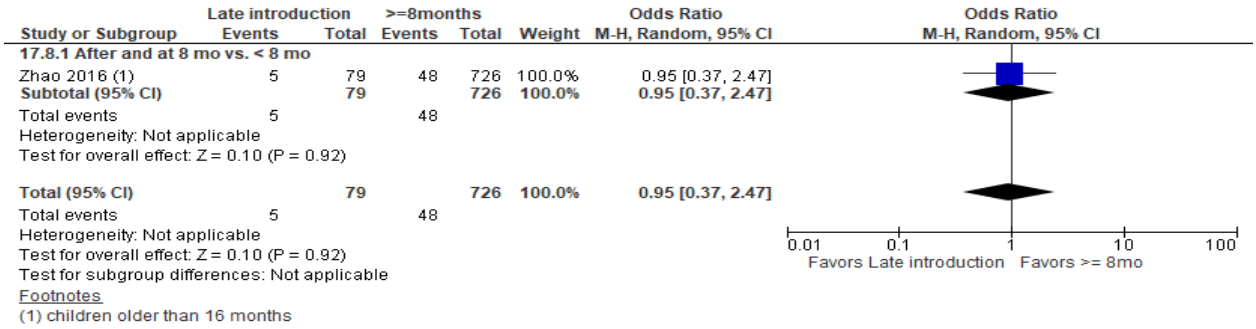
Outcome 5: Head circumference <-2 Z-score



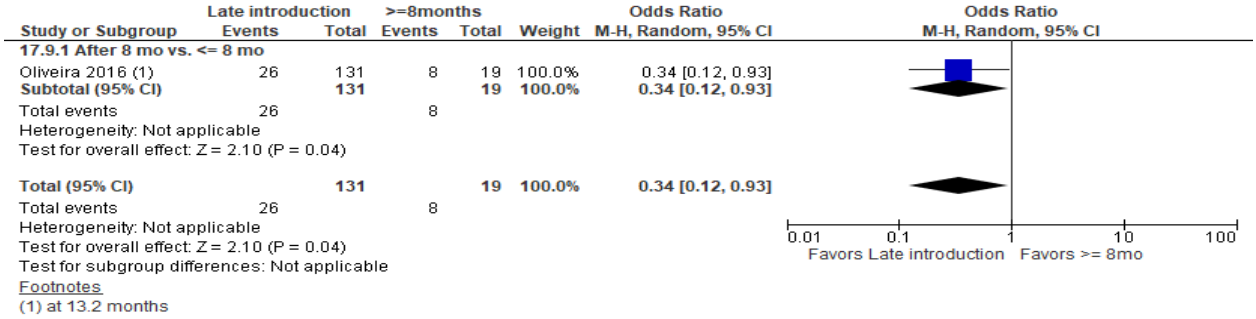
Footnotes

(1) children older than 16 months

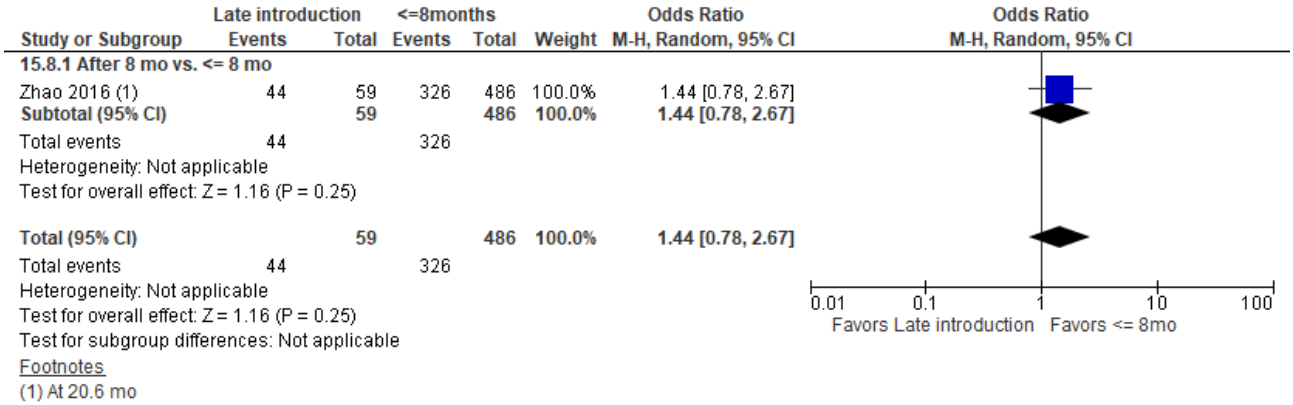
Outcome 6: MUAC <-2 Z-score



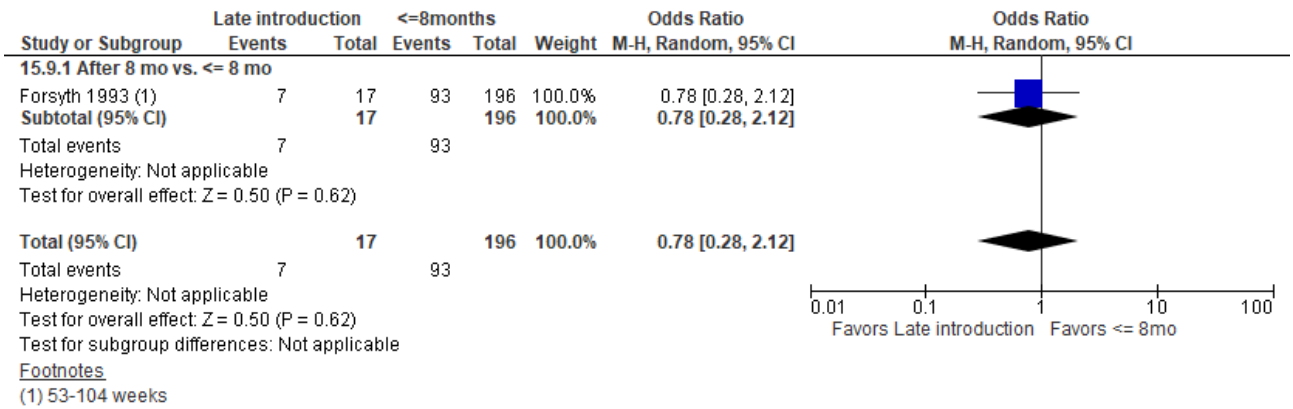
Outcome 9: Anemia



Outcome 10: Diarrhea

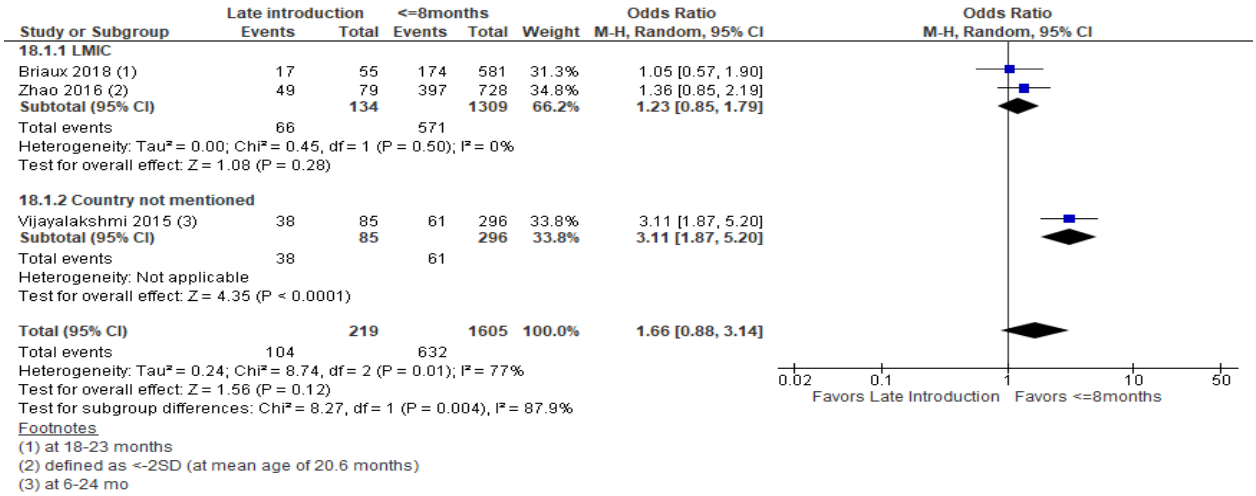


Outcome 10: Gastrointestinal illness



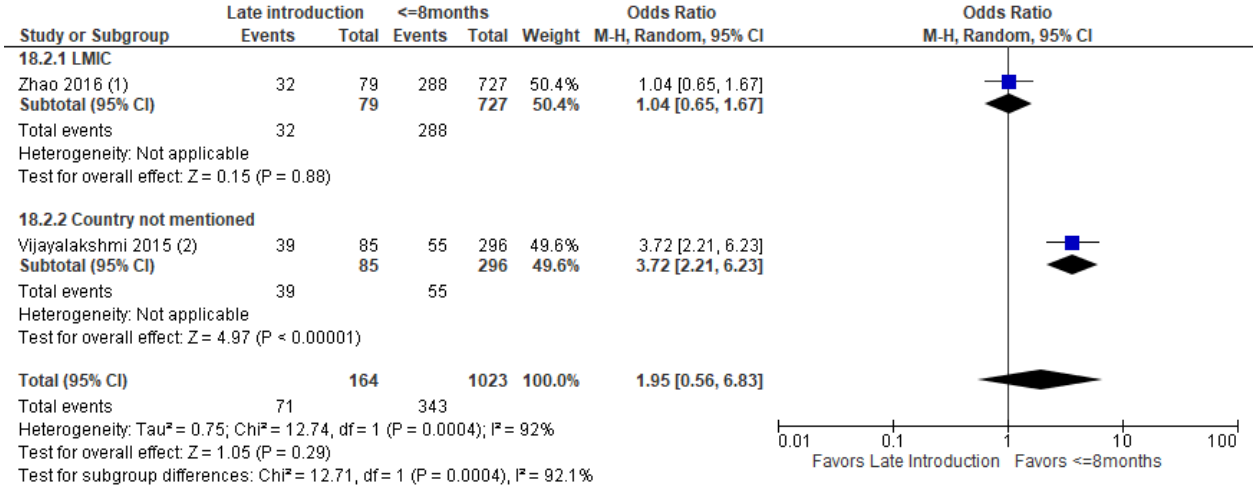
Comparison. Late introduction of CF (> eight months) compared to ≤ eight months of age among normal term infants (Observational studies) – subgroup by setting

Outcome 1: Stunting



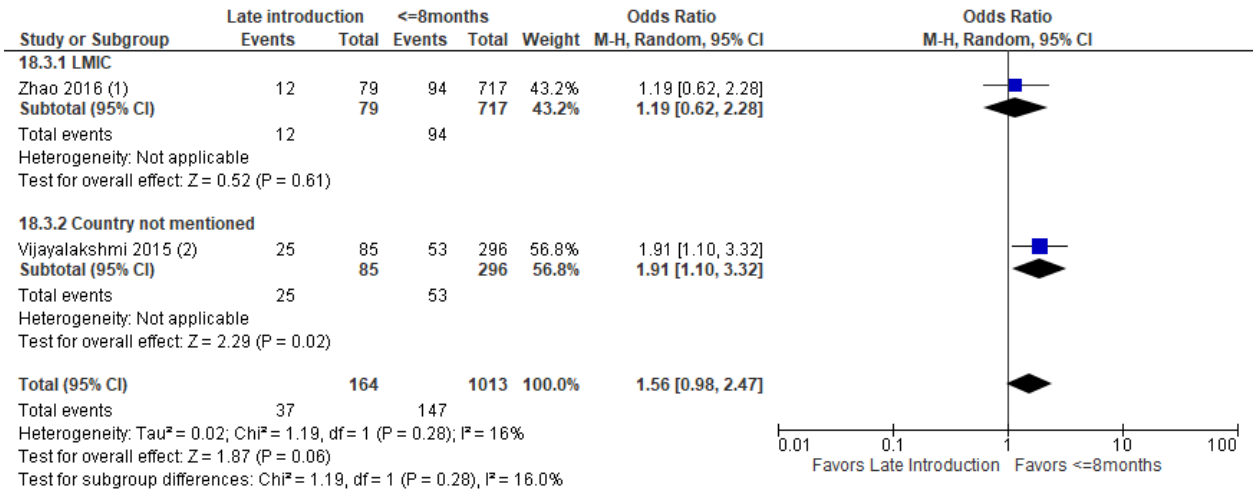
Footnotes
(1) at 18-23 months
(2) defined as <-2SD (at mean age of 20.6 months)
(3) at 6-24 mo

Outcome 2: Underweight



Footnotes
(1) defined as <-2SD (at mean age of 20.6 months)
(2) at 6-24 mo

Outcome 3: Wasting



Footnotes
(1) defined as <-2SD (at mean age of 20.6 months)
(2) at 6-24 mo

CF introduction at 3 months compared to at 4 months (all preterm/LBW and SGA infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With at 4 months (all preterm/LBW and SGA infants)	With CF introduction at 3 months	Relative effect (95% CI)	Risk with at 4 months (all preterm/LBW and SGA infants)	Risk difference with CF introduction at 3 months
Length											
64 (1 RCT)	not serious	not serious	not serious	very serious[a]	none	⨁⨁◯◯ Low	28	36	-	The mean length was **0**	MD **0.2 higher** (0.04 lower to 0.44 higher)
Weight											
64 (1 RCT)	not serious	not serious	not serious	very serious[a]	none	⨁⨁◯◯ Low	28	36	-	The mean weight was **0**	MD **1.4 higher** (8.21 lower to 11.01 higher)
Head circumference											
64 (1 RCT)	not serious	not serious	not serious	very serious[a,b]	none	⨁⨁◯◯ Low	28	36	-	The mean head circumference was **0**	MD **0** (0.13 lower to 0.13 higher)

CI: confidence interval; **MD:** mean difference

Explanations

a. Number of participants <100 (Sample size isvery small)

b. 95% CI <0.75

Early introduction of CF (< 3 months of age) compared to >=3 months of age compared to placebo for complmentaery feeding

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Early introduction of CF (< 3 months of age) compared to >=3 months of age	Relative effect (95% CI)	Risk with placebo	Risk difference with Early introduction of CF (< 3 months of age) compared to >=3 months of age
Weight for Age Z-Score											
317 (1 observational study)	very serious[a]	not serious	not serious	not serious	none	⨁⨁◯◯ Low	196	121	-	The mean weight for Age Z-Score was **0**	MD **0.2 lower** (0.52 lower to 0.12 higher)
Weight											
412 (1 observational study)	serious[b]	not serious	not serious	serious[c]	none	⨁⨁◯◯ Low	107	305	-	-	SMD **0.04 SD higher** (0.07 lower to 0.14 higher)
BMI											
412 (1 observational study)	serious[b]	not serious	not serious	serious[c]	none	⨁⨁◯◯ Low	107	305	-	The mean BMI was **0**	MD **0.09 higher** (0.05 higher to 0.13 higher)
LRTI											

Early introduction of CF (< 3 months of age) compared to >=3 months of age compared to placebo for complmentaery feeding

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
106132 (1 observational study)	serious[d]	not serious	not serious	serious[c]	none	⨁⨁◯◯ Low	416/98420 (0.4%)	49/7712 (0.6%)	**OR 1.51** (1.12 to 2.03)	4 per 1,000	**2 more per 1,000** (from 1 more to 4 more)

Chest Infection

97 (1 observational study)	serious[e]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	11/73 (15.1%)	4/24 (16.7%)	**OR 1.13** (0.32 to 3.94)	151 per 1,000	**16 more per 1,000** (from 97 fewer to 261 more)

Eczema

178 (1 observational study)	serious[e]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	39/138 (28.3%)	13/40 (32.5%)	**OR 1.22** (0.57 to 2.61)	283 per 1,000	**42 more per 1,000** (from 99 fewer to 224 more)

Ear Infection

34 (1 observational study)	serious[e]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	1/27 (3.7%)	0/7 (0.0%)	**OR 1.18** (0.04 to 31.99)	37 per 1,000	**6 more per 1,000** (from 36 fewer to 515 more)

Systolic BP

40 (1 observational study)	serious[b]	not serious	not serious	very serious[g]	none	⨁◯◯◯ Very low	14	26	-	The mean systolic BP was **0**	MD **0.21 lower** (10.4 lower to 9.98 higher)

Early introduction of CF (< 3 months of age) compared to >=3 months of age compared to placebo for complmentaery feeding

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Dystolic BP											
40 (1 observational study)	serious[b]	not serious	not serious	very serious[g]	none	⨁◯◯◯ Very low	14	26	-	-	SMD **0.86 SD higher** (0.53 lower to 2.25 higher)
Gastrointestinal illness											
233 (1 observational study)	serious[h]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	37/175 (21.1%)	14/58 (24.1%)	**OR 1.19** (0.59 to 2.40)	211 per 1,000	**30 more per 1,000** (from 75 fewer to 180 more)
Respiratory illness											
233 (1 observational study)	serious[h]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	40/175 (22.9%)	18/58 (31.0%)	**OR 1.52** (0.79 to 2.93)	229 per 1,000	**82 more per 1,000** (from 39 fewer to 236 more)
Rickets											
233 (1 observational study)	serious[h]	not serious	not serious	very serious[c,f]	none	⨁◯◯◯ Very low	9/175 (5.1%)	4/58 (6.9%)	**OR 1.37** (0.40 to 4.61)	51 per 1,000	**18 more per 1,000** (from 30 fewer to 149 more)
Diarrhea											

Early introduction of CF (< 3 months of age) compared to >=3 months of age compared to placebo for complmentaery feeding

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
212258 (2 observational studies)	serious[i]	not serious	not serious	serious[c]	none	⨁◯◯◯ Very low	220/144790 (0.2%)	122/67468 (0.2%)	**OR 1.91** (0.95 to 1.49)	2 per 1,000	**1 more per 1,000** (from 0 fewer to 1 more)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **SMD:** standardised mean difference

Explanations

a. The study had an overall serious risk of bias, thus we downgrade by 2 levels

b. The exposure was not assessed more than once overtime and the study had an unclear risk of bias for attrition and blinding. Thus, we downgrade by one level

c. Number of participants vary between the groups

d. The study has unclear risk of bias for attrition bias and for blinding of outcome assessors

e. Overall, the study has moderate risk of bias, thus we downgrade by 1 level

f. Total number of events are <100, thus we downgrade by 2 levels

g. Sample size is very small i.e. <100. Thus we downgrade by 2 levels

h. The study was not controlled for potential confounding

i. Downgrade by one level: out of two studies, one study did not provide justification for power calculation while the other study had an overall moderate risk of bias

Early introduction of CF (< 4 months of age) compared to >=4 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With	With Early introduction of CF (< 4 months of age) compared to >=4 months of age	Relative effect (95% CI)	Risk with	Risk difference with Early introduction of CF (< 4 months of age) compared to >=4 months of age
Stunting											
807 (1 observational study)	serious[a]	not serious	not serious	serious[b,c]	none	⨁⨁◯◯ Low	355/662 (53.6%)	91/145 (62.8%)	**OR 1.46** (1.01 to 2.11)	536 per 1,000	**92 more per 1,000** (from 2 more to 173 more)
Underweight											
6643 (3 observational studies)	serious[d]	very serious[e]	not serious	serious[b,c]	none	⨁◯◯◯ Very low	1029/4715 (21.8%)	279/1928 (14.5%)	**OR 0.98** (0.60 to 1.61)	218 per 1,000	**3 fewer per 1,000** (from 75 fewer to 92 more)
Wasting											
796 (1 observational study)	serious[a]	not serious	not serious	serious[b,f]	none	⨁⨁◯◯ Low	88/653 (13.5%)	18/143 (12.6%)	**OR 0.92** (0.54 to 1.59)	135 per 1,000	**9 fewer per 1,000** (from 57 fewer to 64 more)
Height for age Z-score											

Early introduction of CF (< 4 months of age) compared to >=4 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
892 (2 observational studies)	very serious[g]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	746	146	-	The mean height for age Z-score was **0**	MD **0.15 higher** (0.03 lower to 0.32 higher)

Weight for Age Z-Scoe

892 (3 observational studies)	very serious[h]	serious[i]	not serious	serious[b]	none	⨁◯◯◯ Very low	746	146	-	The mean weight for Age Z-Scoe was **0**	MD **0.16 higher** (0.23 lower to 0.55 higher)

Weight for Height Z-Score

45 (1 observational study)	very serious[j]	not serious	not serious	serious[k]	none	⨁◯◯◯ Very low	33	12	-	The mean weight for Height Z-Score was **0**	MD **7.4 lower** (12.65 lower to 2.15 lower)

Height

3764 (4 observational studies)	serious[l]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	3376	388	-	-	SMD **0.18 SD higher** (0.06 higher to 0.3 higher)

Weight

1127 (3 observational studies)	serious[l]	serious[e]	not serious	serious[b]	none	⨁◯◯◯ Very low	911	216	-	-	SMD **0.04 SD higher** (0.26 lower to 0.35 higher)

BMI

Early introduction of CF (< 4 months of age) compared to >=4 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
26221 (5 observational studies)	serious[l]	very serious[e]	not serious	serious[b]	none	⨁◯◯◯ Very low	24204	2017	-	The mean BMI was **0**	MD **2.53 higher** (0.16 lower to 5.23 higher)

BMI Z Score

3294 (2 observational studies)	serious[l]	serious[i]	not serious	serious[b]	none	⨁◯◯◯ Very low	2732	562	-	The mean BMI Z Score was **0**	MD **0.14 higher** (0.12 lower to 0.39 higher)

Head circumference <-2 z-score

796 (1 observational study)	serious[a]	not serious	not serious	serious[b,c,f]	none	⨁⨁◯◯ Low	88/652 (13.5%)	17/144 (11.8%)	**OR 0.86** (0.49 to 1.49)	135 per 1,000	**17 fewer per 1,000** (from 64 fewer to 54 more)

Overweight

9865 (5 observational studies)	serious[m]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	744/6434 (11.6%)	539/3431 (15.7%)	**OR 0.97** (0.83 to 1.13)	116 per 1,000	**3 fewer per 1,000** (from 18 fewer to 13 more)

Obesity

9389 (6 observational studies)	serious[n]	very serious[e]	not serious	serious[b,c]	none	⨁◯◯◯ Very low	1283/5931 (21.6%)	390/3458 (11.3%)	**OR 0.86** (0.30 to 2.45)	216 per 1,000	**24 fewer per 1,000** (from 140 fewer to 187 more)

Overweight and Obesity

Early introduction of CF (< 4 months of age) compared to >=4 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
29178 (5 observational studies)	very serious[o]	very serious[e]	not serious	serious[b,c]	none	⨁◯◯◯ Very low	7708/19331 (39.9%)	3115/9847 (31.6%)	**OR 1.22** (0.55 to 2.71)	399 per 1,000	**48 more per 1,000** (from 131 fewer to 244 more)
Atopic Dermatitis											
22332 (5 observational studies)	very serious[p]	very serious[e]	not serious	serious[b]	none	⨁◯◯◯ Very low	1365/20539 (6.6%)	469/1793 (26.2%)	**OR 1.38** (0.53 to 3.54)	66 per 1,000	**23 more per 1,000** (from 30 fewer to 135 more)
Diarrhea											
106677 (2 observational studies)	serious[q]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	395/72832 (0.5%)	146/33845 (0.4%)	**OR 1.36** (0.97 to 1.91)	5 per 1,000	**2 more per 1,000** (from 0 fewer to 5 more)
Asthma											
2595 (2 observational studies)	very serious[r]	not serious	not serious	very serious[b,s]	none	⨁◯◯◯ Very low	74/2191 (3.4%)	22/404 (5.4%)	**OR 1.22** (0.72 to 2.09)	34 per 1,000	**7 more per 1,000** (from 9 fewer to 34 more)
Wheeze											
1894 (1 observational study)	very serious[t]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	242/1741 (13.9%)	17/153 (11.1%)	**OR 0.77** (0.46 to 1.31)	139 per 1,000	**28 fewer per 1,000** (from 70 fewer to 36 more)
LRTI											

Early introduction of CF (< 4 months of age) compared to >=4 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
106132 (1 observational study)	serious[u]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	279/72398 (0.4%)	186/33734 (0.6%)	**OR 1.43** (1.19 to 1.73)	4 per 1,000	**2 more per 1,000** (from 1 more to 3 more)
Eczema											
16959 (2 observational studies)	serious[v]	serious[i]	not serious	serious[b]	none	⨁◯◯◯ Very low	3901/11668 (33.4%)	1928/5291 (36.4%)	**OR 0.98** (0.69 to 1.39)	334 per 1,000	**4 fewer per 1,000** (from 77 fewer to 77 more)
Food Allergy											
1239 (1 observational study)	serious[a]	not serious	not serious	very serious[s]	none	⨁◯◯◯ Very low	50/778 (6.4%)	34/461 (7.4%)	**OR 1.16** (0.74 to 1.82)	64 per 1,000	**10 more per 1,000** (from 16 fewer to 47 more)
Systolic BP											
2203 (1 observational study)	serious[l]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	2086	117	-	The mean systolic BP was **0**	MD **1.5 higher** (0.11 higher to 2.89 higher)
Dystolic BP											
2203 (1 observational study)	serious[l]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	2086	117	-	The mean dystolic BP was **0**	MD **1.3 higher** (0.27 higher to 2.33 higher)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **SMD:** standardised mean difference

Explanations

a. The study had an unclear risk of bias for blinding, attrition and time of assessment of exposure. Thus, we downgrade by one level

b. Downgrade by one level: Number of participants vary between the groups.

c. 95% CI <0.75 and/or >1.25

d. Two studies had an unclear risk of bias for blinding, attrition and time of assessment of exposure. One study had an overall moderate risk of bias

e. Downgrade by two levels due to high heterogenity

f. Downgrade by one level: Number of events <300.

g. One study had an overall moderate risk of bias and another study had an overall critical risk of bias

h. Two studies had an overall moderate risk of bias and one study had an overall critical risk of bias

i. Downgrade by one level: heterogeneity exists

j. The study had an overall critical risk of bias. Thus, we downgrade by 2 levels

k. Sample size is very small. Thus, we downgrade by 2 levels

l. Studies/study have a moderate overall risk of bias. Thus we downgrade by one level

m. Four studies had an overall moderate risk of bias and one study had an unclear risk of bias for blinding, attrition and time of assessment of exposure

n. Four studies had an overall moderate risk of bias and two studies had an unclear risk of bias for blinding, attrition and time of assessment of exposure

o. Three studies had an overall moderate risk of bias and two studies had an unclear risk of bias for blinding, attrition and time of assessment of exposure

p. Three studies have an overall serious risk of bias and one study has a moderate risk of bias. One study is at high risk for blinding of outcome assessors. Thus we downgrade by 2 levels.

q. Two studies had an unclear risk of bias for attrition and blinding and one study had an unclear risk of bias for time of assessment of exposure. Thus we downgrade by one level

r. One study had an overall serioud risk of bias and one study had an unclear risk of bias for attrition and time of assessment of exposure and high risk of bias for blinding of outcome assessors. Thus we downgrade by 2 levels

s. Downgrade by two levels- Number of events are <100

t. The study had an overall serious risk of bias. Thus, we downgrade by 2 levels

u. The study had an unclear risk of bias for attrition and blinding of outcome assessors. Thus, we downgrade by one level

v. One study had an overall serious risk of bias and one study had an unclear risk of bias for blinding, attrition and time of assessment of exposure

Early introduction of CF <=4 months compared to 6 months (Healthy infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 6 months (Healthy infants)	With Early introduction of CF <=4 months	Relative effect (95% CI)	Risk with 6 months (Healthy infants)	Risk difference with Early introduction of CF <=4 months
Length											
429 (4 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	194	235	-	-	SMD **0.05 higher** (0.16 lower to 0.27 higher)
Weight											
429 (4 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	194	235	-	-	SMD **0.06 lower** (0.26 lower to 0.13 higher)
Head circumference/occipital frontal circumference (OFC)											
288 (3 RCTs)	serious[c]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	144	144	-	-	SMD **0.03 higher** (0.2 lower to 0.26 higher)
BMI											
100 (1 RCT)	not serious	not serious	not serious	very serious[e]	none	⨁⨁◯◯ Low	50	50	-	The mean BMI was **0**	MD **0.02 higher** (0.41 lower to 0.45 higher)

Early introduction of CF <=4 months compared to 6 months (Healthy infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
BMI for age											
100 (1 RCT)	not serious	not serious	not serious	very serious[e]	none	⨁⨁◯◯ Low	50	50	-	The mean BMI for age was **0**	MD **0.15 lower** (0.48 lower to 0.18 higher)
Overweight											
77 (1 RCT)	not serious	not serious	not serious	very serious[f,g]	none	⨁⨁◯◯ Low	1/37 (2.7%)	4/40 (10.0%)	**RR 3.70** (0.43 to 31.61)	27 per 1,000	**73 more per 1,000** (from 15 fewer to 827 more)
Anemia											
216 (2 RCTs)	serious[h]	not serious	not serious	very serious[b,g,i]	none	⨁◯◯◯ Very low	35/85 (41.2%)	50/131 (38.2%)	**RR 0.83** (0.63 to 1.08)	412 per 1,000	**70 fewer per 1,000** (from 152 fewer to 33 more)
Severe anemia											
139 (1 RCT)	serious[j]	not serious	not serious	very serious[b,f,g]	none	⨁◯◯◯ Very low	16/50 (32.0%)	22/89 (24.7%)	**RR 0.77** (0.45 to 1.33)	320 per 1,000	**74 fewer per 1,000** (from 176 fewer to 106 more)
Food acceptance score											
125 (1 RCT)	serious[j]	not serious	not serious	very serious[b,e]	none	⨁◯◯◯ Very low	45	80	-	The mean food acceptance score was **0**	MD **0** (0.18 lower to 0.18 higher)

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations

a. Out of 4 studies, one study is at high risk for sequence generation, another study is at high risk for blindling of participants and personnel and the third study is at high risl for attrition bias

b. Number of participants vary between the groups

c. Out of 3 studies, one study has an unclear risk of bias for sequence generation, one study is at risk for blinding of participants and personnel and one study is at high risk for attrition bias

d. Number of paricipants <300

e. Number of paricipants <100

f. 95% CI <0.75 and >1.25

g. Number of events <100

h. Out of 2 studies one study is at high risk for sequence generation and both the studies are at unclear risk of bias for allocation concealment. The other study is also at unclear risk of bias for sequence generation and at high risk for attrition bias

i. 95% CI is <0.75

j. The study was at high risk for sequence generation

Early introduction of CF at 4 months compared to 6 months (LBW/preterm infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 6 months (LBW/preterm infants)	With Early introduction of CF at 4 months	Relative effect (95% CI)	Risk with 6 months (LBW/preterm infants)	Risk difference with Early introduction of CF at 4 months
Weight for age z-score											
373 (1 RCT)	very serious[a]	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	189	184	-	The mean weight for age z-score was **0**	MD **0** (0.25 lower to 0.25 higher)
Length											
147 (2 RCTs)	very serious[c]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	67	80	-	The mean length was **0**	MD **0.23 lower** (0.57 lower to 0.12 higher)
Weight											
147 (2 RCTs)	very serious[c]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	67	80	-	The mean weight was **0**	MD **7.91 lower** (121.91 lower to 106.09 higher)
Severe anemia (% Hb <100g/L)											

Early introduction of CF at 4 months compared to 6 months (LBW/preterm infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
116 (1 RCT)	very serious[f]	not serious	not serious	very serious[b,g]	none	⨁◯◯◯ Very low	12/57 (21.1%)	4/59 (6.8%)	**RR 0.32** (0.11 to 0.94)	211 per 1,000	**143 fewer per 1,000** (from 187 fewer to 13 fewer)

Acceptable minimum dietary diversity

372 (1 RCT)	very serious[a]	not serious	not serious	serious[h,i]	none	⨁◯◯◯ Very low	104/189 (55.0%)	110/183 (60.1%)	**RR 1.09** (0.92 to 1.30)	550 per 1,000	**50 more per 1,000** (from 44 fewer to 165 more)

Minimum acceptable diet

373 (1 RCT)	very serious[a]	not serious	not serious	serious[h,i]	none	⨁◯◯◯ Very low	103/189 (54.5%)	108/184 (58.7%)	**RR 1.08** (0.90 to 1.29)	545 per 1,000	**44 more per 1,000** (from 54 fewer to 158 more)

Infant Mortality

400 (1 RCT)	very serious[a]	not serious	not serious	very serious[g,h]	none	⨁◯◯◯ Very low	2/197 (1.0%)	4/203 (2.0%)	**RR 1.94** (0.36 to 10.48)	10 per 1,000	**10 more per 1,000** (from 6 fewer to 96 more)

Systolic Blood Pressure

141 (1 RCT)	very serious[a]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	74	67	-	The mean systolic Blood Pressure was **0**	MD **0** (2.12 lower to 2.12 higher)

Early introduction of CF at 4 months compared to 6 months (LBW/preterm infants) for health problem or population

Bibliography: Padhani ZAZA. Timing of Introduction of Complementary Feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Dystolic Blood Pressure											
143 (1 RCT)	very serious[a]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	75	68	-	The mean dystolic Blood Pressure was **0**	MD **0.3 lower** (2.13 lower to 1.53 higher)
Diarrhea											
373 (1 RCT)	very serious[a]	not serious	not serious	very serious[g]	none	⨁◯◯◯ Very low	6/189 (3.2%)	11/184 (6.0%)	**RR 1.88** (0.71 to 4.99)	32 per 1,000	**28 more per 1,000** (from 9 fewer to 127 more)
LRTI											
373 (1 RCT)	very serious[a]	not serious	not serious	very serious[g]	none	⨁◯◯◯ Very low	11/189 (5.8%)	16/184 (8.7%)	**RR 1.49** (0.71 to 3.13)	58 per 1,000	**29 more per 1,000** (from 17 fewer to 124 more)
Sepsis											
373 (1 RCT)	very serious[a]	not serious	not serious	very serious[g]	none	⨁◯◯◯ Very low	1/189 (0.5%)	3/184 (1.6%)	**RR 3.08** (0.32 to 29.36)	5 per 1,000	**11 more per 1,000** (from 4 fewer to 150 more)

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. The study is at high risk for blinding of participants and personnel, for attrition bias and for selective reporting. Thus, we downgrade by 2 levels

b. 95% CI is <0.75

c. Both the studies are at high risk for sequence generation

d. Number of participants <300. Thus, we downgrade by one level.

e. Number of participants vary between the groups

f. The study is at high risk for sequence generation

g. Number of events are <100. Thus, we downgrade by 2 levels

h. 95% CI >1.25

i. Number of events <300. Thus, we downgrade by one level

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With	With Early introduction of CF (< 6 months of age) compared to >=6 months of age	Relative effect (95% CI)	Risk with	Risk difference with Early introduction of CF (< 6 months of age) compared to >=6 months of age
Stunting											
12816 (10 observational studies)	very serious[a]	very serious[b]	not serious	serious[c]	none	⨁◯◯◯ Very low	3774/6539 (57.7%)	3399/6277 (54.2%)	**OR 1.16** (0.77 to 1.75)	577 per 1,000	**36 more per 1,000** (from 65 fewer to 128 more)
Underweight											
5939 (6 observational studies)	very serious[a]	not serious	not serious	serious[c,d]	none	⨁◯◯◯ Very low	342/3481 (9.8%)	316/2458 (12.9%)	**OR 1.29** (1.08 to 1.53)	98 per 1,000	**25 more per 1,000** (from 7 more to 45 more)
Wasting											
1840 (6 observational studies)	very serious[a]	very serious[b]	not serious	serious[c,e]	none	⨁◯◯◯ Very low	193/1281 (15.1%)	125/559 (22.4%)	**OR 1.55** (0.91 to 2.62)	151 per 1,000	**65 more per 1,000** (from 12 fewer to 167 more)
Thinness											

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
139 (1 observational study)	very serious[a]	not serious	not serious	very serious[f]	none	⨁◯◯◯ Very low	3/84 (3.6%)	5/55 (9.1%)	**OR 2.70** (0.62 to 11.79)	36 per 1,000	**55 more per 1,000** (from 13 fewer to 268 more)
Height for Age Z-Score											
1349 (2 observational studies)	serious[g]	not serious	not serious	serious[h]	none	⨁⨁◯◯ Low	676	673	-	The mean height for Age Z-Score was **0**	MD **0.03 higher** (0.13 lower to 0.19 higher)
Weight for Age Z-Scores											
713 (1 observational study)	serious[g]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	123	590	-	The mean weight for Age Z-Scores was **0**	MD **0.08 higher** (0.12 lower to 0.27 higher)
Weight for Height Z-Score											
1995 (1 observational study)	serious[g]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	771	1224	-	The mean weight for Height Z-Score was **0**	MD **0** (0.01 lower to 0)
Height/Length											
2559 (6 observational studies)	serious[i]	very serious[b]	not serious	serious[d]	none	⨁◯◯◯ Very low	732	1827	-	The mean height/Length was **0**	MD **0.12 lower** (0.54 lower to 0.3 higher)
Weight											

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
2077 (6 observational studies)	serious[g]	serious[j]	not serious	serious[d]	none	⨁◯◯◯ Very low	654	1423	-	-	SMD **0.13 SD higher** (0.02 lower to 0.29 higher)

BMI

3532 (3 observational studies)	serious[k]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	1461	2071	-	-	SMD **0.13 SD higher** (0.05 higher to 0.21 higher)

BMI Z score

2447 (1 observational study)	serious[g]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	644	1803	-	-	SMD **0.19 SD higher** (0.09 higher to 0.29 higher)

Head Circumference

41 (1 observational study)	serious[g]	not serious	not serious	very serious[l]	none	⨁◯◯◯ Very low	20	21	-	The mean head Circumference was **0**	MD **0.2 higher** (0.34 lower to 0.74 higher)

Overweight

8423 (4 observational studies)	serious[g]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	432/3799 (11.4%)	501/4624 (10.8%)	**OR 1.17** (0.89 to 1.54)	114 per 1,000	**17 more per 1,000** (from 11 fewer to 51 more)

Obesity

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
13818 (4 observational studies)	serious[g]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	626/5434 (11.5%)	1169/8384 (13.9%)	**OR 1.06** (0.95 to 1.19)	115 per 1,000	**6 more per 1,000** (from 5 fewer to 19 more)
Overweight and Obese											
9078 (4 observational studies)	serious[g]	not serious	not serious	serious[c,d]	none	⨁⨁◯◯ Low	123/1963 (6.3%)	801/7115 (11.3%)	**OR 1.34** (1.09 to 1.65)	63 per 1,000	**20 more per 1,000** (from 5 more to 37 more)
Anemia											
18923 (2 observational studies)	serious[m]	very serious[b]	not serious	serious[c,d]	none	⨁◯◯◯ Very low	2328/16286 (14.3%)	551/2637 (20.9%)	**OR 1.72** (0.90 to 3.27)	143 per 1,000	**80 more per 1,000** (from 12 fewer to 210 more)
Iron deficiency anemia											
870 (1 observational study)	serious[a]	not serious	not serious	very serious[d,f]	none	⨁◯◯◯ Very low	24/273 (8.8%)	19/597 (3.2%)	**OR 0.34** (0.18 to 0.63)	88 per 1,000	**56 fewer per 1,000** (from 71 fewer to 31 fewer)
Diarrhea											
107407 (2 observational studies)	serious[m]	serious[j]	not serious	serious[d]	none	⨁◯◯◯ Very low	242/4712 (5.1%)	208/102695 (0.2%)	**OR 0.64** (0.21 to 1.97)	51 per 1,000	**18 fewer per 1,000** (from 40 fewer to 45 more)
Atopic dermatitis											

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
1425 (1 observational study)	serious[n]	not serious	not serious	serious[d,e]	none	⨁⨁◯◯ Low	107/1034 (10.3%)	42/391 (10.7%)	**OR 1.04** (0.71 to 1.52)	103 per 1,000	**4 more per 1,000** (from 28 fewer to 46 more)
Asthma											
4938 (3 observational studies)	very serious[o]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	66/1876 (3.5%)	135/3062 (4.4%)	**OR 0.99** (0.71 to 1.38)	35 per 1,000	**0 fewer per 1,000** (from 10 fewer to 13 more)
LRTI											
110035 (3 observational studies)	serious[p]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	118/4810 (2.5%)	773/105225 (0.7%)	**OR 1.11** (0.90 to 1.38)	25 per 1,000	**3 more per 1,000** (from 2 fewer to 9 more)
Wheeze											
2320 (1 observational study)	very serious[q]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	70/637 (11.0%)	173/1683 (10.3%)	**OR 0.93** (0.69 to 1.25)	110 per 1,000	**7 fewer per 1,000** (from 31 fewer to 24 more)
Eczema											
2290 (1 observational study)	very serious[q]	not serious	not serious	serious[d]	none	⨁◯◯◯ Very low	113/629 (18.0%)	328/1661 (19.7%)	**OR 1.12** (0.89 to 1.42)	180 per 1,000	**17 more per 1,000** (from 17 fewer to 58 more)
Food Allergy											

Early introduction of CF (< 6 months of age) compared to >=6 months of age compared to for manuscript

Bibliography: . Early initiation versus late iniiation for complmentaery feeding. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
2396 (2 observational studies)	serious[m]	not serious	not serious	serious[d,e]	none	⨁◯◯◯ Very low	61/1039 (5.9%)	84/1357 (6.2%)	**OR 0.90** (0.60 to 1.35)	59 per 1,000	**6 fewer per 1,000** (from 23 fewer to 19 more)
Gastrointestinal illness											
233 (1 observational study)	serious[a]	not serious	not serious	very serious[d,f]	none	⨁◯◯◯ Very low	10/47 (21.3%)	41/186 (22.0%)	**OR 1.05** (0.48 to 2.28)	213 per 1,000	**8 more per 1,000** (from 98 fewer to 169 more)
Respiratory illness											
233 (1 observational study)	serious[a]	not serious	not serious	very serious[d,f]	none	⨁◯◯◯ Very low	9/47 (19.1%)	49/186 (26.3%)	**OR 1.51** (0.68 to 3.35)	191 per 1,000	**72 more per 1,000** (from 53 fewer to 251 more)
Rickets											
233 (1 observational study)	serious[a]	not serious	not serious	very serious[d,f]	none	⨁◯◯◯ Very low	1/47 (2.1%)	12/186 (6.5%)	**OR 3.17** (0.40 to 25.03)	21 per 1,000	**43 more per 1,000** (from 13 fewer to 331 more)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **SMD:** standardised mean difference

Explanations

a. Most of the studies were not adjusted for confounding/ the study was not adjusted for confounding

b. Downgrade by two levels; high heterogeneity

c. 95% CI <0.75 and/or >1.25

d. Number of paricipants vary between the groups

e. Downgrade by one level: Number of events <300

f. Downgrade by two levels: Number of events <100

g. Study/studies had an overall moderate risk of bias

h. We downgrade by one level due to broad confidence intervals

i. Out of 7 studies, 6 have moderate risk of bias, 1 study have overall serious risk of bias

j. Heterogeneity exists; we downgrade by one level

k. Three studies have an overall moderate risk of bias and one study have a low risk of bias

l. Sample size very small

m. Studies have an unclear risk of bias for blinding, attrition bias and blinding of outcome assessors

n. The outcome assessors were not blinded to the exposure status of the participants

o. Two studies had an overall serious risk of bias and one study did not blind the assessors to the exposure status of the participants. Thus, we downgrade by two levels

p. One study has an overall serious risk of bias, second study has unclear risk of bias for blinidng, attrition. and time of exposure assessment, while the third study was at unclear risk of bias for attrition. and blinding of outcome assessors. Thus, we downgrade by one level

q. Overall, the study has an serious risk of bias. Thus, we downgrade by 2 levels

References

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