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[Intervention Review]

Optimal duration of exclusive breastfeeding

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ABSTRACT

Background

Although the health benefits of breastfeeding are widely acknowledged, opinions and recommendations are strongly divided on the optimal duration of exclusive breastfeeding. Since 2001, the World Health Organization has recommended exclusive breastfeeding for six months. Much of the recent debate in developed countries has centred on the micronutrient adequacy, as well as the existence and magnitude of health benefits, of this practice.

Objectives

To assess the effects on child health, growth, and development, and on maternal health, of exclusive breastfeeding for six months versus exclusive breastfeeding for three to four months with mixed breastfeeding (introduction of complementary liquid or solid foods with continued breastfeeding) thereafter through six months.

Search methods

We searched *The Cochrane Library* (2011, Issue 6), MEDLINE (1 January 2007 to 14 June 2011), EMBASE (1 January 2007 to 14 June 2011), CINAHL (1 January 2007 to 14 June 2011), BIOSIS (1 January 2007 to 14 June 2011), African Index Medicus (searched 15 June 2011), Index Medicus for the WHO Eastern Mediterranean Region (IMEMR) (searched 15 June 2011), LILACS (Latin American and Caribbean Health Sciences) (searched 15 June 2011). We also contacted experts in the field.

The search for the first version of the review in 2000 yielded a total of 2668 unique citations. Contacts with experts in the field yielded additional published and unpublished studies. The updated literature review in December 2006 yielded 835 additional unique citations.

Selection criteria

We selected all internally-controlled clinical trials and observational studies comparing child or maternal health outcomes with exclusive breastfeeding for six or more months versus exclusive breastfeeding for at least three to four months with continued mixed breastfeeding until at least six months. Studies were stratified according to study design (controlled trials versus observational studies), provenance (developing versus developed countries), and timing of compared feeding groups (three to seven months versus later).

Data collection and analysis

We independently assessed study quality and extracted data.

Main results

We identified 23 independent studies meeting the selection criteria: 11 from developing countries (two of which were controlled trials in Honduras) and 12 from developed countries (all observational studies). Definitions of exclusive breastfeeding varied considerably across

studies. Neither the trials nor the observational studies suggest that infants who continue to be exclusively breastfed for six months show deficits in weight or length gain, although larger sample sizes would be required to rule out modest differences in risk of undernutrition. In developing-country settings where newborn iron stores may be suboptimal, the evidence suggests that exclusive breastfeeding without iron supplementation through six months may compromise hematologic status. Based on the Belarusian study, six months of exclusive breastfeeding confers no benefit (versus three months of exclusive breastfeeding followed by continued partial breastfeeding through six months) on height, weight, body mass index, dental caries, cognitive ability, or behaviour at 6.5 years of age. Based on studies from Belarus, Iran, and Nigeria, however, infants who continue exclusive breastfeeding for six months or more appear to have a significantly reduced risk of gastrointestinal and (in the Iranian and Nigerian studies) respiratory infection. No significant reduction in risk of atopic eczema, asthma, or other atopic outcomes has been demonstrated in studies from Finland, Australia, and Belarus. Data from the two Honduran trials and from observational studies from Bangladesh and Senegal suggest that exclusive breastfeeding through six months is associated with delayed resumption of menses and, in the Honduran trials, more rapid postpartum weight loss in the mother.

Authors' conclusions

Infants who are exclusively breastfed for six months experience less morbidity from gastrointestinal infection than those who are partially breastfed as of three or four months, and no deficits have been demonstrated in growth among infants from either developing or developed countries who are exclusively breastfed for six months or longer. Moreover, the mothers of such infants have more prolonged lactational amenorrhea. Although infants should still be managed individually so that insufficient growth or other adverse outcomes are not ignored and appropriate interventions are provided, the available evidence demonstrates no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first six months of life in both developing and developed-country settings.

PLAIN LANGUAGE SUMMARY

Optimal duration of exclusive breastfeeding

Exclusive breastfeeding for six months (versus three to four months, with continued mixed breastfeeding thereafter) reduces gastrointestinal infection and helps the mother lose weight and prevent pregnancy but has no long-term impact on allergic disease, growth, obesity, cognitive ability, or behaviour.

The results of two controlled trials and 21 other studies suggest that exclusive breastfeeding (no solids or liquids besides human milk, other than vitamins and medications) for six months has several advantages over exclusive breastfeeding for three to four months followed by mixed breastfeeding. These advantages include a lower risk of gastrointestinal infection, more rapid maternal weight loss after birth, and delayed return of menstrual periods. No reduced risks of other infections, allergic diseases, obesity, dental caries, or cognitive or behaviour problems have been demonstrated. A reduced level of iron has been observed in developing-country settings.

BACKGROUND

Although the health benefits of breastfeeding are widely acknowledged, opinions and recommendations are strongly divided on the optimal duration of exclusive breastfeeding (Fewtrell 2011). The epidemiologic evidence is now overwhelming that, even in developed countries, breastfeeding protects against gastrointestinal and (to a lesser extent) respiratory infection, and that the protective effect is enhanced with greater duration and exclusivity of breastfeeding (Ip 2007). ('Greater duration and exclusivity' is used in a general sense here; the references cited do not pertain specifically to the subject of this review, i.e., the optimal duration of exclusive breastfeeding.) Prolonged and exclusive breastfeeding has also been associated with a reduced risk of the sudden infant death syndrome and, in preterm infants, necrotizing enterocolitis (Ip 2007). Breastfeeding is life-saving in developing countries; a meta-analysis (WHO 2001a) reported markedly reduced mortality (especially due to infectious disease) with breastfeeding even into the second year of life.

Although growth faltering is uncommon in developed countries, a pooled analysis of U.S., Canadian, and European data sets undertaken by the WHO Working Group on Infant Growth (Dewey 1995) showed that infants from developed countries who followed then current WHO feeding recommendations (to exclusively breastfeed for four to six months of age and to continue breastfeeding with adequate complementary foods up to two years of age) show a deceleration in both weight and length gain relative to the then existing international WHO/CDC growth reference from around three to 12 months, with partial catch-up in the second year. The Euro-Growth study (Haschke 2000) also reported an association between prolonged and exclusive breastfeeding and slower growth during infancy. In developed-country settings, it is not at all clear that the more rapid growth reported in infants who are formula-fed, or breastfed less exclusively and for a shorter duration, is an advantage. Moreover, a large, cluster-randomized trial from Belarus has reported that breastfed infants born and followed at sites randomized to a breastfeeding promotion intervention (and who were breastfed more exclusively and for a longer duration) actually grew more rapidly in the first six to nine months than those born and followed at control (nonintervention) sites (Kramer 2000a). Based on this evidence, WHO has developed new growth standards for infancy and early childhood (De Onis 2006a; De Onis 2006b).

The evidence bearing on longer-term outcomes is more controversial. For allergic (atopic) diseases, meta-analyses support a protective effect against atopic dermatitis (eczema), at least in infancy (Gdalevich 2001a; Ip 2007). For asthma, one earlier meta-analysis (Gdalevich 2001b) also suggested a protective effect, although a recently updated meta-analysis (Ip 2007) that excludes a suspected fraudulent study by Chandra and Hamed (Chandra 1991) suggests no significant effect. The intention-to-treat analysis of the Belarusian trial of a breastfeeding promotion intervention also reported no reduction of asthma risk (Kramer 2000a). The evidence of long-term effects of breastfeeding on obesity and mean body mass index (Kramer 2000a; Owen 2005a; Owen 2005b) or blood pressure, type 1 or type 2 diabetes, or ischemic heart disease (Ip 2007) is also weak. Meta-analyses (Anderson 1999; Ip 2007) have reached opposite conclusions about breastfeeding effects on neurocognitive ability. The intention-to-treat analysis of the Belarusian breastfeeding promotion trial reported significant effects on verbal IQ and teachers' ratings of writing and reading performance in school (Kramer 2000a). Evidence also suggests that prolonged (more than six months) breastfeeding provides protection against both acute lymphoblastic and myeloblastic leukemia in childhood (Ip 2007). Long-term maternal health benefits have also received considerable attention in developed countries, with Ipp et al concluding protection against breast cancer and ovarian cancer and possible reduction in the risk of type 2 diabetes (Ip 2007). Importantly, most of the evidence bearing on these long-term health outcomes is based on comparisons of any breastfeeding, or of an arbitrary "minimum" duration and/or degree of breastfeeding, with no breastfeeding (i.e., formula feeding).

Most of the scientific evidence on the health effects of breastfeeding has been based on observational studies, with well-recognized sources of potential bias. Some of the biases tend to favour exclusively breastfed infants, while others favour those who receive earlier complementary feeding. Reverse causality is an important potential source of bias. Infants who continue to be exclusively breastfed tend to be those who remain healthy and on an acceptable growth trajectory; significant illness or growth faltering can lead to interruption of breastfeeding or supplementation with infant formula or solid foods (Hill 1977; Sauls 1979). Infants who develop a clinically important infection are likely to become anorectic (loss of appetite) and to reduce their breast milk intake, which can in turn lead to reduction in milk production and even weaning (Bauchner 1986). The temporal sequence of the early signs of infection and weaning may not be adequately appreciated; infection may be blamed on the weaning, rather than the reverse. Advanced neuromotor development may also lead to earlier induction of solid foods, which could then receive 'credit' for accelerating motor development (Heinig 1993). Poorly-growing infants (especially those in developing countries) are likely to receive complementary feedings earlier because of their slower growth. In developed countries, however, rapidly-growing infants may require more energy than can be met by the increasingly spaced feedings typical of such settings. This may result in crying and poor sleeping, supplementation with formula or solid foods, or both, reduced suckling, and a vicious cycle leading to earlier weaning (i.e., discontinuation of breastfeeding) (Kramer 2000a). In addition, unmeasured, poorly measured, or uncontrolled confounding variables are also likely to bias the association between introduction of complementary foods and infant health outcomes.

Finally, the underlying assumption in this field has been that 'one size fits all', i.e., that average population effects can be applied to individual infants and that one international recommendation is therefore adequate for all infants. There has been little discussion of the fact that all infants, regardless of how they are fed, require careful monitoring of growth and illness, with appropriate interventions undertaken whenever clinically indicated.

OBJECTIVES

The primary objective of this review was to assess the effects on child health, growth, and development, and on maternal health, of exclusive breastfeeding for six months versus exclusive breastfeeding for three to four months with mixed breastfeeding (introduction of complementary liquid or solid foods with continued breastfeeding) thereafter through six months.

A secondary objective was to assess the child and maternal health effects of prolonged (more than six months) exclusive breastfeeding versus exclusive breastfeeding through six months and mixed breastfeeding thereafter.

METHODS

Criteria for considering studies for this review

Types of studies

We selected controlled clinical trials and observational studies, published in all languages, examining whether or not exclusive breastfeeding (EBF) until six months of age has an impact on growth, development, morbidity, and survival of healthy, term infants and their mothers. Studies of (or including) low birthweight (less than 2500 g) infants were not excluded, provided that such infants were born at term (at least 37 completed weeks). Only those studies with an internal comparison group were included in the review, i.e., we excluded studies based on external comparisons (with reference data). The comparisons must have been based on one group of infants who received EBF for at least three but less than seven months and mixed breastfeeding (MBF) until six months or later (i.e., infants were introduced to liquid or solid foods between three and six months of age), and another group of infants who were exclusively breastfed for at least six months. This restriction was imposed to provide direct relevance to the clinical and public health decision context: whether infants who are exclusively breastfed for the first three to four months should continue EBF or should receive complementary foods in addition to breast milk (MBF). Thus studies comparing EBF and MBF from birth were excluded, as were those that investigated the effects of age at introduction of nonbreast milk liquid or solid foods but did not ensure EBF at least three months prior to their introduction. We also included studies comparing infants receiving prolonged EBF (more than six months) to those exclusively breastfed for six months and continued MBF after six months.

Types of participants

Lactating mothers and their healthy, term, singleton infants.

Types of interventions

Among infants EBF for at least three months, the interventions/exposures compared were continued EBF versus MBF. The 'complementary' foods used in MBF included juices, formula, other milks, other liquids, or solid foods. Although the World Health Organization (WHO) defines EBF as breastfeeding with no supplemental liquids or solid foods other than medications or vitamins, few studies strictly adhered to the WHO's definition. In some studies, so-called 'EBF' included provision of water, teas, or juices (corresponding to WHO's definition of predominant breastfeeding) (WHO 1991) or even small amounts of infant formula. The definitions of EBF and MBF used in each study are described in the Characteristics of included studies table.

Types of outcome measures

No infant or maternal health outcomes were excluded from consideration. The infant outcomes specifically sought (but not necessarily found) included growth (weight, length, and head circumference and z-scores (based on the WHO/CDC reference) for weight-for-age, length-for-age, and weight-for-length), infections, morbidity, mortality, micronutrient status, neuromotor and cognitive development, asthma, atopic eczema, other allergic diseases, type 1 diabetes, blood pressure, and subsequent adult chronic diseases such as coronary heart disease, hypertension, type 2 diabetes, and inflammatory and autoimmune diseases. Maternal outcomes sought included postpartum weight loss, duration of lactational amenorrhea, and such chronic diseases as breast and ovarian cancer and osteoporosis.

Search methods for identification of studies

Electronic searches

See Appendix 1 for details of searches carried out in previous versions of the review. The 2011 updated literature review included the same electronic databases as the 2007 update except for CAB Abstracts and HealthSTAR.

- *The Cochrane LIbrary* (2011, Issue 6)
- MEDLINE (1 January to 14 June 2011)
- EMBASE (1 January 2011 to 14 June 2011)
- CINAHL (1 January 2007 to 14 June 2011)
- BIOSIS (1 January 2007 to 14 June 2011)
- African Index Medicus (searched 15 June 2011)
- Index Medicus for the WHO Eastern Mediterranean Region (IMEMR) (searched 15 June 2011)
- LILACS (searched 15 June 2011

Searching other resources

In addition to the studies found through these electronic searches, we checked reference lists of identified articles, and contacted experts in the field to identify other potentially relevant published or unpublished studies. We attempted to contact the authors of all studies that qualified for inclusion in the review to obtain methodologic details, clarify inconsistencies, and obtain unpublished data.

For all searches, every effort was made to identify relevant non-English language articles and abstracts. Given their own backgrounds, the review authors themselves were able to determine the eligibility of articles in French, Spanish, and Japanese. For publications in other languages, two options were available. Many articles in languages other than English provided English abstracts. As such, all potentially relevant articles were obtained and checked for availability of English abstracts. If such abstracts were not available, or were available but did not provide enough information to determine their eligibility, then assistance was requested from WHO to determine their eligibility for inclusion. No article or abstract was excluded because of language of publication.

Data collection and analysis

We evaluated studies under consideration for methodological quality and appropriateness for inclusion without consideration of their results. The criteria for quality assessment were developed a priori and are presented below.

We used Cochrane criteria for assessing controlled clinical trials. As shown below, this method rates trials on three elements.

1) Adequacy of randomization and concealment:
A. randomized and concealed appropriately;

B. randomized appropriately but concealment unclear from the description;
C. not (or not reported as) randomized or inadequate concealment, or both.

2) Losses to follow-up and analysis:
A. used intention-to-treat (ITT) analysis, with losses to follow-up symmetrical and less than 15% in each group;
B. symmetrical losses were at least 15%, but analysis was based on ITT;
C. asymmetrical losses to follow-up despite use of ITT, or analysis not based on ITT.

3) Measurement of outcome (outcome-specific):
A. blinding of observers or 'objective' outcomes (e.g., measured weight);
B. nonblinding of observers for measurements that could be affected by bias (including length, head circumference, and self-reported outcomes).

The five-point Jadad (Jadad 1996) scale was also used to examine the quality of randomized controlled trials. Details of the scale are as follows.

1) Was the study described as randomized (this includes the use of words such as randomly, random, and randomization)?
a) not random or not mentioned (0);
b) random, described, and inappropriate (0);
c) random, not described (+1);
d) random, described, and appropriate (+2).

2) Was the study described as double-blind?
a) not double-blind (0);
b) double-blind, described, and not appropriate (0);
c) double-blind, not described (+1);
d) double-blind, described, and appropriate (+2).

3) Was there a description of withdrawals and dropouts?
Withdrawals (number and reasons) must be described by group to get 1 point.

Observational (cohort, case-control, and cross-sectional studies) were assessed for control for confounding, losses to follow-up, and assessment of outcome as follows.

1) For growth and morbidity outcomes, control for confounding by socioeconomic status, water supply, sanitation facilities, parental height and weight, birthweight, and weight and length at three months (or age at which complementary feeding was introduced in the mixed breastfeeding group):
A. control for all (or almost all) pertinent confounders;
B. partial control for some confounders;
C. no control for confounding.

2) Losses to follow-up:
A. losses to follow-up were symmetrical and less than 15% in each group;
B. losses were 15% to 25% and symmetrical;
C. losses were greater than 25%, asymmetrical, or not reported (and all cross-sectional studies).

3) Assessment of outcome (outcome-specific):
A. blinding of observers or 'objective' outcomes (e.g., measured weight);
B. nonblinding of observers or measurements that could be affected by bias (including length, head circumference, and self-reported outcomes).

Quality assessments of all eligible studies were carried out independently by the two review authors. Disagreements were resolved by consensus. Data were extracted independently by both review authors, with disagreements resolved by consensus. Attempts were made to contact authors of included studies to obtain additional data, resolve inconsistencies, and obtain additional methodologic details.

The studies were stratified according to study design (controlled trials versus observational studies), provenance (developing versus developed countries), and timing of feeding comparison (three to seven months versus 'prolonged' (more than six months)). (One study (WHO 1997) based on a pooled analysis of two developed and three developing countries has been included with developed-country studies because of the selection criteria (literate, educated, urban mothers) and the observed high infant growth rates.) This resulted in five separate strata for considering the results of the studies located by the literature search: (1) controlled trials of exclusive versus mixed breastfeeding for four to six months from developing countries; (2) observational studies of exclusive versus mixed breastfeeding for three to seven months from developing countries; (3) observational studies of prolonged (more than six months) exclusive versus mixed breastfeeding from developing countries; (4) observational studies of exclusive versus mixed breastfeeding for three to seven months from developed countries; and (5) observational studies of prolonged (more than six months) exclusive versus mixed breastfeeding from developed countries. In accordance with conventional terminology used in Cochrane reviews, these strata are labelled below as 'comparisons'. Outcomes for each comparison are presented sequentially.

Inter-study heterogeneity was evaluated for all outcomes and all comparisons using the I^2 statistic. Fixed-effect measures of association are reported for all analyses except for those for which the I^2 exceeded 50%; the latter analyses are based on random-effect measures. For observational studies that used multivariable regression models to control for potentially confounding covariates, association measures and their 95% confidence intervals are provided in the text of the review but do not appear in the data tables or graphs.

RESULTS

Description of studies

For details of included and excluded studies, *see* the Characteristics of included studies and Characteristics of excluded studies tables.

Results of the search

The June 2011 search yielded 3425 additional unique citations and from these we included one additional study (Duijts 2010) plus a later follow-up from Kramer 2000a. The selected studies are listed in the Characteristics of included studies table. (For details of search results from previous searches, *see* Appendix 1.)

Risk of bias in included studies

See Characteristics of included studies table.

Effects of interventions

Comparison one: controlled trials of exclusive versus mixed breastfeeding for four to six months, developing countries

Two studies were found in this category, both from the same group of investigators and involving the same study setting (Honduras). The first of these studies, Cohen 1994a, involved term infants unselected for birthweight but included 29 infants (19.9%) weighing less than 2500 g at birth. The second, Dewey 1999a, was restricted to term infants weighing less than 2500 g at birth. The quality ratings of these two trials were not high for several reasons. First, in both trials, allocation was within clusters defined by weeks, rather than to individual women, yet the results were analyzed with individual women and infants as the units of analysis; any similarities in outcome within weeks (intracluster correlation) would tend to reduce the true effective sample size and thereby overestimate the precision (i.e., underestimate the variance) of the results. Second, the first trial allocated the weeks by alternation, rather than by strict randomization, thereby creating a potential for nonconcealment and uncontrolled confounding bias at enrollment (although there is no evidence that such bias actually occurred). Third, the published results were not based on analysis by intention-to-treat. Most of the babies not analyzed in these two trials were truly lost to follow-up; however, rather than excluded for noncompliance, the latter were restricted to four babies (three in the exclusive breastfeeding (EBF) group, one in the mixed breastfeeding (MBF) group) in the first trial and three babies (all three in the exclusive breastfeeding group) in the second trial. Moreover, the investigators have provided (unpublished) data on weight and length gain on five of the nine dropouts in the second Honduran trial (three of the nine moved away before six months), thereby substantially reducing the potential for selection bias in the analysis of that trial.

Most importantly, despite the above-noted methodological problems, these two trials are the only studies uncovered by our search that used an experimental design to specifically address the four to six months versus 'about six months' debate. Thus, at least with respect to bias due to known and unknown confounding variables, these trials are methodologically superior to any of the observational studies included in this review despite their methodological imperfections. Furthermore, the investigators made a considerable effort to ensure compliance with the assigned allocation and to standardize the training of the observers who performed the anthropometric measurements, thereby reducing the random error (improving the precision) of these measurements. Finally, detailed comparisons between trial participants and eligible nonparticipants demonstrated no differences that would detract from the external validity (generalizability) of the trials' findings, at least for the specific type of setting where the study was conducted (an urban, low-income population in Honduras).

For all analyses, the two mixed breastfeeding groups (one of which was intended to maintain frequency of breastfeeding) in the first trial were combined for the purposes of this analysis. Monthly weight gain from four to six months was nonsignificantly slightly higher among infants whose mothers were assigned to continued exclusive breastfeeding (mean difference (MD) +20.78; 95% confidence interval (CI) -21.99 to +63.54 g/mo) (Analysis 1.1). Thus the 95% CI is statistically compatible with a weight gain only 22 g/mo lower in the EBF group, which represents approximately 5% of the mean and 15% of the standard deviation (SD) for the monthly weight gain. Weight gain from six to 12 months was almost identical in the two groups (MD -2.62; 95% CI -25.85 to 20.62 g/mo) (Analysis 1.2).

For length gain from four to six months, the MD was 1.0 mm/mo (95% CI -0.40 to +2.40 mm/mo) (Analysis 1.3); the lower confidence limit represents only 2% of the mean and 8% of the SD for monthly length gain. As with weight gain, length gain from 6 to 12 months was nearly identical in the two groups (MD -0.04; 95% CI -0.10 to 0.02 cm/mo) (Analysis 1.4).

Weight-for-age, length-for-age, and weight-for-length z-scores at six months were all nonsignificantly higher in the EBF group (MD +0.18; 95% CI -0.06 to +0.41 (Analysis 1.5); MD +0.11; 95% CI -0.11 to +0.33 (Analysis 1.6); and MD +0.09; 95% CI -0.13 to +0.31 (Analysis 1.7), respectively).

The impact of the small sample size of the two Honduran trials is evident when examining the risk of undernutrition, as represented by anthropometric z-scores less than -2 at six months. For weight-for-age, the pooled risk ratio (RR) was 2.14 (95% CI 0.74 to 6.24) (Analysis 1.8), which is statistically compatible with a six-fold increase in risk. The results were somewhat more reassuring for length-for-age (RR 1.18; 95% CI 0.56 to 2.50) (Analysis 1.9) but not for weight-for-length (RR 1.38; 95% CI 0.17 to 10.98) (Analysis 1.10).

All hematologic results (Analysis 1.11 to Analysis 1.19) are based on the first Honduras trial (Cohen 1994a), since in the second trial (Dewey 1999a, restricted to low birthweight infants), infants with low hemoglobin concentrations at two and four months were supplemented with iron. A nonsignificantly higher proportion of infants in the exclusively breastfed group received iron supplements from six to nine months (RR 1.20; 95% CI 0.91 to 1.58) (Analysis 1.11). This is consistent with the significantly lower average hemoglobin concentration at six months in the exclusively breastfed group (difference = -5.00 (95% CI -8.46 to -1.54) g/L) (Analysis 1.12). A nonsignificantly higher proportion of exclusively breastfed infants had a hemoglobin concentration below 110 g/L at six months (RR 1.20; 95% CI 0.91 to 1.58) (Analysis 1.13). Similarly, mean plasma ferritin concentration was significantly lower at six months in the exclusively breastfed infants (difference = -18.90 (95% CI -37.31 to -0.49) mcg/L) (Analysis 1.17), with a RR for a low (less than 15 mcg/L) ferritin concentration of 2.93 (95% CI 1.13 to 7.56) (Analysis 1.19).

In the second trial, no significant effect was seen on the proportion of infants with a low zinc concentration (less than 70 mcg/dL) at six months (RR 0.75; 95% CI 0.43 to 1.33) (Analysis 1.20).

In the pooled results from both Honduran trials, no significant difference was seen between the EBF and MBF groups for the percentage of days with fever (Analysis 1.21), cough (Analysis 1.22), or nasal congestion (Analysis 1.23), nasal discharge (Analysis 1.24), hoarseness (Analysis 1.25), or diarrhea (Analysis 1.26) from four to six months, nor for fever (Analysis 1.27), nasal congestion (Analysis 1.28), or diarrhea from six to 12 months (Analysis 1.29).

Again based on pooled results from both trials, mothers in the exclusively breastfed group reported that their infants crawled at an average of -0.80 (95% CI -1.26 to -0.34) months sooner (Analysis 1.30). No difference was seen, however, in the mean age at which the infants were reported to have first sat from a lying position (average MD -0.22 (95% CI -0.91 to 0.46) months), random-effects

(Analysis 1.31). The results from the two Honduras trials (Cohen 1994a; Dewey 1999a) differed with respect to maternal reports of walking by 12 months (Analysis 1.32), with a significantly lower proportion of exclusively breastfed infants reported as not having walked by 12 months in the first trial (RR 0.66; 95% CI 0.45 to 0.98) (Cohen 1994a), but a nonsignificantly higher proportion not having done so in the second trial (RR 1.12; 95% CI 0.90 to 1.38) (Dewey 1999a), with statistically significant (P < .01) heterogeneity between the two trials.

Mothers in the exclusively breastfed group (from the two trials combined) had a statistically significantly larger weight loss from four to six months (MD 0.42; 95% CI 0.02 to 0.82) kg) (Analysis 1.33). Women in the exclusively breastfed group were also nonsignificantly less likely to have resumed menses by six months postpartum (RR 0.58; 95% CI 0.33 to 1.03); the effect was statistically significant in the second Honduras trial when considered alone (RR 0.35; 95% CI 0.14 to 0.91) (Dewey 1999a) (Analysis 1.34).

Comparison two: observational studies of exclusive versus mixed breastfeeding for three to seven months, developing countries

The main concern in using an observational design to compare outcomes with EBF versus MBF is confounding due to differences in socioeconomic status, water and sanitation facilities, parental size (a proxy for genetic potential), and (perhaps most importantly) weight and length at the time complementary foods were first introduced in the mixed breastfeeding group. The latter source of confounding (i.e., by indication) will arise if poorly-growing infants are more likely to receive complementary foods.

Four cohort studies in this category from Peru (Brown 1991a), the Philippines (Adair 1993a), Senegal (Simondon 1997a), and Iran (Khadivzadeh 2004) found no evidence of confounding by indication, Adair 1993a found no confounding by several other potential factors, and (in unpublished data provided by the authors). Simondon 1997a calculated adjusted means for weight and length gain from four to six months. Nonetheless, the inability of observational studies to control for subtle (and unknown) sources of confounding and selection bias suggests the need for cautious interpretation. All four studies reported on monthly weight gain from four to six months (Analysis 2.1). The MD was -10.10 (95% CI -27.68 to +7.48) g/mo, a lower confidence limit compatible with a deficit of only 7% of the mean and less than 15% of the SD for monthly weight gain. The Simondon 1997a study also reported on monthly weight gain from six to nine months (difference = -6.00 (95% CI -54.15 to +42.15) g/mo) (Analysis 2.2). All four studies also reported on monthly length gain from four to six months (Analysis 2.3); the MD was 0.04 (95% CI -0.02 to 0.11) cm/mo, a lower confidence limit statistically compatible with a reduced length gain in the EBF group less than 2% of the mean and 4% of the SD. The Simondon 1997a study also reported on monthly length gain from six to nine months (Analysis 2.4), and again the results excluded all but a small reduction in the exclusively breastfed group (difference = 0.04 (95% CI -0.06 to 0.14) cm/mo).

Onayade 2004 actually reported significantly higher absolute weights at both five and six months in the EBF group but did not analyze weight gains; the absence of control for confounding differences between the EBF and MBF groups, as well as the possibility of reverse causality (i.e., those infants with lower weights may have been more likely to receive complementary feeding) argue for cautious interpretation, however.

The Simondon 1997a study also provided (unpublished) data on anthropometric z-scores and mid-upper arm circumference. EBF was associated with nonsignificantly higher MD z-scores at six to seven and nine to 10 months: +0.13 (95% CI -0.09 to +0.35) (Analysis 2.5) and +0.09 (95% CI -0.15 to +0.33) (Analysis 2.6), respectively, for weight-for-age; +0.04 (95% CI -0.14 to +0.22) (Analysis 2.7) and +0.11 (95% CI -0.09 to +0.31) (Analysis 2.8), respectively, for length-for-age; and +0.11 (95% CI -0.09 to +0.31) (Analysis 2.9) and +0.01 (95% CI -0.21 to +0.23) (Analysis 2.10), respectively, for weight-for-length. The risk ratio for low (less than -2) z-scores at six to seven and nine to 10 months were 0.92 (95% CI 0.54 to 1.58) (Analysis 2.11) and 0.93 (95% CI 0.64 to 1.36) (Analysis 2.12), respectively, for weight-for-age; 1.20 (95% CI 0.57 to 2.53) (Analysis 2.13) and 1.21 (95% CI 0.62 to 2.37) (Analysis 2.14), respectively, for length-for-age; and 0.42 (95% CI 0.12 to 1.50) (Analysis 2.15) and 0.82 (95% CI 0.39 to 1.71) (Analysis 2.16), respectively, for weight-for-length. Mid-upper arm circumference was nonsignificantly higher in the EBF group at both six to seven and nine to 10 months: MD 0.20 (95% CI -0.04 to 0.44) cm (Analysis 2.17) and 0.10 (95% CI 0.16 to 0.36) cm (Analysis 2.18), respectively.

Khadivzadeh 2004 found a lower incidence of both gastrointestinal (11 versus 27%; RR 0.41; 95% CI 0.21 to 0.78) (Analysis 2.19) and respiratory (23 versus 35%; RR 0.68; 95% CI 0.43 to 1.06) Analysis 2.20) infection at four to six months in the EBF group. Onayade 2004 reported corresponding crude ORs of 0.02 (95% CI 0.01 to 0.09) and 0.43 (95% CI 0.17 to 1.00), respectively, but did not provide numerators and denominators and did not control for confounding differences between the EBF and MBF groups.

Huffman 1987 reported a longer median duration of lactational amenorrhea associated with EBF (for at least seven months) versus MBF (16.1 versus 15.3 months, respectively), but means and SDs were not reported. In a multivariate (Cox) regression model adjusting for maternal education, parity, religion, and weight, EBF for at least six months was associated with a significantly longer time to resumption of menses versus EBF for less than one month, but no direct comparison was reported versus MBF. Simondon 1997a reported a lower risk of resumption of menses by six to seven months (Analysis 2.21) in the EBF group: crude RR 0.19 (95% CI 0.05 to 0.79), adjusted odds ratio (OR) 0.19 (95% CI 0.04 to 0.86).

Cross-sectional studies share all of the methodological shortcomings of other observational designs (*see* above) plus one important additional one: selective loss to follow-up. In particular, children who die, are hospitalized, or are referred to a site other than the one under study, may be more likely to experience morbidity or suboptimal growth. If such (unstudied) infants are more heavily represented in one of the feeding groups, the resulting comparison will be biased.

One large cross-sectional study from Chile (Castillo 1996) reported a similar risk of weight-for-age z-score less than -1 and height-for-age z-score less than -1 from three to five and six to eight months in the two feeding groups, but the prevalences, CIs, and standard errors for the reported prevalence ratios are not published, thus precluding any assessment of sampling variation.

Comparison three: observational studies of prolonged (more than six months) exclusive versus mixed breastfeeding, developing countries

One small cross-sectional study from Pune, India (Rao 1992) permitted analysis only of male infants, since a relatively large fraction of female infants in the MBF group received artificial feeding in the first six months of life. The results (Analysis 3.1) showed a nonsignificant reduction of low (less than 75% of the reference mean) weight-for-age at six to 12 months of age in the exclusively breastfed males (RR 0.61; 95% CI 0.26 to 1.43). The strong possibility of confounding by age, even within the range of six to 12 months (the EBF group is likely to have been younger, on average, and therefore less undernourished), further limits the reported result.

A cohort study from Bangladesh (Khan 1984) reported similar weight and length gains in infants who were exclusively breastfed, those who were breastfed with supplements beginning at six to 11 months, and those who were exclusively breastfed for 12 months and supplemented between 12 and 15 months. Unfortunately, the data are presented only graphically and without standard deviations, thus preventing a quantitative assessment or pooling with data from other studies.

Comparison four: observational studies of exclusive versus mixed breastfeeding for three to seven months, developed countries

A pooled sample of breastfed infants from seven studies carried out in six developed countries (WHO 1994a), a pooled analysis from five countries (two developed, three developing, but in which study women were all literate and of middle to high socioeconomic status) (WHO 1997), a large cohort study nested within a randomized trial in Belarus (Kramer 2000a), and a small study from Sweden (Akeson 1996a) reported on weight gain between three and eight months. WHO 1997 and Kramer 2000a controlled for confounding by indication (size or growth in first three to four months) and other potential confounders using multilevel (mixed) regression analyses. Substantial (I^2 = 69%) heterogeneity was observed among the four studies, with considerably larger mean weight gains in both groups from Belarus and a slightly but significantly higher gain in the MBF group (Analysis 4.1). The pooled random-effects MD is -7.95 [-31.84, 15.93] g/mo. Heinig 1993 and Kramer 2000a also reported on weight gain between six and nine months (Analysis 4.2). Again, the results show significant heterogeneity (I^2 = 76%) but are dominated by the larger size of the Belarussian study. The pooled random-effects MD is 21.11 [-44.70, 86.91] g/mo. Akeson 1996a, Heinig 1993, and Kramer 2000a reported on weight gain from eight to 12 months (Analysis 4.3); the MD was -1.82 (95% CI -16.72 to +13.08) g/mo, which excludes a reduced length gain in the EBF group of 5% of the mean and 10% of the SD for the Belarusian study.

For length gain at three to eight months (Analysis 4.4), the studies again show significant (I^2 = 76%) heterogeneity. Kramer 2000a found a slightly but significantly lower length gain in the EBF group at four to eight months (-0.11 [-0.17, 0.05] mm/mo), whereas the pooled analysis yielded a random-effects average MD of -0.03 [-0.11, 0.06] mm/mo. Heinig 1993 and Kramer 2000a also reported on length gain at six to nine months (MD -0.04; 95% CI -0.10 to 0.01) cm/mo) (Analysis 4.5). For the eight to 12 month period, the results show a slightly but significantly higher length gain in the EBF group (MD +0.09; 95% CI 0.03 to +0.14) cm/mo (Analysis 4.6).

Observational analyses from the Belarusian study (Kramer 2000a) also include data on weight-for-age, length-for-age, and weight-for-length z-scores at six, nine, and 12 months. Means in both the EBF and MBF groups were well above (+0.5 to +0.6) the reference values at all three ages. Nonetheless, the weight-for-age z-score was slightly but significantly lower in the EBF group at all three ages: MD -0.09 (95% CI -0.16 to -0.02) (Analysis 4.7) at six months, -0.10 (95% CI -0.18 to -0.02) (Analysis 4.8) at nine months, and -0.09 (95% CI -0.17 to -0.01) (Analysis 4.9) at 12 months. Length-for-age z-scores were very close to the reference (0) at six and nine months and slightly above the reference (0.15) at 12 months. Again, the EBF group had slightly but significantly (except at 12 months) lower values: MD -0.12 (95% CI -0.20 to -0.04) (Analysis 4.10) at six months, -0.14 (95% CI -0.22 to -0.06) (Analysis 4.11) at nine months, and -0.02 (95% CI -0.10 to +0.06) (Analysis 4.12) at 12 months. Mean weight-for-length z-scores were high and rose (from about 0.65 to 0.80) from six to 12 months, with no significant differences between the EBF and MBF groups at any age: MD +0.02 (95% CI -0.07 to +0.11) (Analysis 4.13) at six months, +0.03 (95% CI -0.06 to +0.12) (Analysis 4.14) at nine months, and -0.08 (95% CI -0.17 to +0.01) (Analysis 4.15 at 12 months.

The prevalence of low (less than -2) z-scores did not differ significantly in the two Belarusian feeding groups for any of the three z-scores at any of the three ages, although the small number of infants with low z-scores provided low statistical power to detect such differences. RRs (and 95% CIs) for low weight-for-age were 0.92 (0.04 to 19.04) (Analysis 4.16) at six months, 1.52 (0.16 to 14.62) (Analysis 4.17) at nine months and 1.15 (0.13 to 10.31) (Analysis 4.18) at 12 months. For length-for-age, the corresponding figures were 1.53 (0.84 to 2.78) at six months (Analysis 4.19), 1.46 (0.80 to 2.64) (Analysis 4.20) at nine months, and 0.66 (0.23 to 1.87) (Analysis 4.21) at 12 months. For weight-for-length, the figures were 0.31 (0.02 to 5.34) (Analysis 4.22) at six months, 1.14 (0.24 to 5.37) (Analysis 4.23) at nine months, and 1.15 (0.13 to 10.31) (Analysis 4.24) at 12 months.

The Belarusian study also provided data on head circumference. No significant differences were observed at six months (difference 0.19 (95% CI 0.06 to 0.32) cm) (Analysis 4.25) or nine months (0.07 (95% CI -0.06 to 0.20) cm) (Analysis 4.26), but the EBF group had a slightly but significantly larger circumference at 12 months (Analysis 4.27): difference = 0.19 (95% CI 0.06 to 0.32) cm.

Heinig 1993 reported nearly identical sleeping time (729 versus 728 minutes/day) in the two groups (Analysis 4.28). Akeson 1996a reported similar total amino acid and essential amino acid concentrations at six months of age in the two feeding groups (Analysis 4.29; Analysis 4.30). Both Kramer 2000a and a cohort study from Finland (Kajosaari 1983) reported on atopic eczema at one year (Analysis 4.31). The two studies showed substantial (I^2 = 78%) heterogeneity, with Kajosaari 1983 reporting a significantly reduced risk, but the larger Belarusian study finding a much lower absolute risk in both feeding groups and no risk reduction with EBF; the pooled random-effects average RR was 0.65 (0.27, 1.59) (Analysis 4.31). Although Kajosaari 1983 also reported a reduced risk of a history of food allergy (Analysis 4.32), double food challenges showed no significant risk reduction (RR 0.77; 95% CI 0.25 to 2.41) (Analysis 4.33). Neither Oddy 1999 nor Kramer 2000a

found a significant reduction in risk of recurrent (two or more episodes) wheezing in the EBF group (pooled RR 0.79; 95% CI 0.49 to 1.28) (Analysis 4.34).

A small Italian study of hematologic outcomes at 12 months by Pisacane in 1995 reported a statistically significantly higher hemoglobin concentration (117 versus 109 g/L (95% CI for the difference = +4.03 to +11.97 g/L)) (Analysis 4.35), a nonsignificant reduction in anemia (hemoglobin less than 110 g/L) (RR 0.12; 95% CI 0.01 to 1.80) (Analysis 4.36), a nonsignificantly higher ferritin concentration (MD +4.70; 95% CI -6.30 to +15.70 mcg/L) (Analysis 4.37), and a nonsignificant reduction in the risk of low (less than 10 mcg/L) ferritin concentration (RR 0.42; 95% CI 0.12 to 1.54) (Analysis 4.38) among infants in the EBF group. Of note in this study is that the exclusive and mixed breastfeeding continued in both groups until at least 12 months (a criterion for selection into the Pisacane 1995 study).

In the Belarusian study (Kramer 2000a), the EBF group had a significantly reduced risk of one or more episodes of gastrointestinal infection in the first 12 months of life (RR 0.67; 95% CI 0.46 to 0.97) (Analysis 4.39), which was maintained in a multivariate mixed model controlling for geographic origin, urban versus rural location, maternal education, and number of siblings in the household (adjusted OR 0.61; 95% CI 0.41 to 0.93). Importantly, when a mixed-level, multivariate Poisson model was used to estimate the adjusted incidence density ratio (IDR) by age period. From zero to three months (when both groups were exclusively breastfed), the IDR was 0.97 (95% CI 0.46 to 2.04), while at three to six months (when the feeding differed), the protective effect of EBF was strong (IDR 0.35: 95% CI 0.13 to 0.96). No significant reduction in risk was observed for hospitalization for gastrointestinal infection, however (RR 0.79; 95% CI 0.42 to 1.49) (Analysis 4.40). In the above-mentioned Australian cohort study, Oddy 1999 found no significant reduction of risk for one or more episodes of upper respiratory tract infection (Analysis 4.41) in the EBF group (RR 1.07; 95% CI 0.96 to 1.20). Neither Oddy 1999 nor Kramer 2000a found a significantly reduced risk of two or more such episodes (pooled RR 0.91; 95% CI 0.82 to 1.02) (Analysis 4.42). Nor did Oddy 1999 find a significant reduction in risk of four or more episodes of upper respiratory infection (RR 0.82; 95% CI 0.52 to 1.29) (Analysis 4.43) or of one or more episodes of lower respiratory tract infection (RR 1.07; 95% CI 0.86 to 1.33) (Analysis 4.44). Kramer 2000a found a small and nonsignificant reduction in risk of two or more respiratory tract infections (upper and lower combined) (RR 0.90; 95% CI 0.79 to 1.03) (Analysis 4.45). Duijts 2010 reported substantially lower adjusted odds ratios (versus a never-breastfed group) for both upper and lower respiratory tract infection in their EBF group compared with their MBF group in the first six months of life but not for months seven to 12 (data not shown). The combined crude results of Oddy 1999 and Kramer 2000a show a substantial and statistically significant reduction in risk for hospitalization for respiratory tract infection (pooled RR 0.75; 95% CI 0.60 to 0.94) (Analysis 4.46), but the crude risk reduction in Kramer 2000a was nearly abolished and became statistically nonsignificant in a multivariate mixed model controlling for geographic region, urban versus rural location, maternal education and cigarette smoking, and number of siblings in the household (adjusted OR 0.96; 95% CI 0.71 to 1.30). In a study from Tucson, Arizona, (Duncan 1993) reported no difference in the average number of episodes of acute otitis media in the first 12 months of life (Analysis 4.47) in the exclusive versus MBF groups (1.48 versus 1.52 episodes, respectively) (95% CI for the difference -0.49 to +0.41 episodes). Duncan 1993 and Kramer 2000a both found a slightly elevated risk for one or more episodes of otitis media (pooled RR 1.28; 95% CI 1.04 to 1.57) (Analysis 4.48), but Duncan 1993 found a nonsignificant reduction in risk for frequent otitis media (RR 0.81; 95% CI 0.43 to 1.52) (Analysis 4.49). Kramer 2000a recorded only one and two deaths (Analysis 4.50) among the 621 and 2862 Belarusian infants in the EBF and MBF groups, respectively (RR 2.30; 95% CI 0.21 to 25.37).

Reported outcomes beyond infancy have included dental caries, growth and adiposity measures, blood pressure, allergy, cognitive ability, and behaviour. Kramer 2000a reported no difference in decayed, missing, or filled teeth either in the total dentition (Analysis 4.51) or the incisors (Analysis 4.52) at age six years. At 6.5 years, no significant differences were observed for height (Analysis 4.53), leg length (Analysis 4.54), head circumference Analysis 4.55), or waist circumference (Analysis 4.59) between the EBF and MBF groups. Body mass index (BMI, Analysis 4.56), triceps (Analysis 4.57) and subscapular (Analysis 4.58) skinfold thicknesses, hip circumference (Analysis 4.60), and systolic (Analysis 4.61) and diastolic blood pressure (Analysis 4.62) were actually significantly higher in the EBF group, however, although multivariate mixed models with adjustment for clustering and for potential confounding variables yielded nonsignificant adjusted MDs for subscapular skinfold thickness [+0.2 (95% CI -0.02 to +0.5) mm], systolic blood pressure [0.0 (95% CI -1.0 to +0.9) mm Hg], and diastolic blood pressure [-0.3 (95% CI -1.2 to +0.5) mm Hg]. For allergic outcomes at ages five to seven years (Kajosaari 1983, Oddy 1999, and Kramer 2000a), no reduction in risk was observed for atopic eczema (Analysis 4.63), hay fever (Analysis 4.64), asthma (Analysis 4.65), food allergy (Analysis 4.66), allergy to animal dander (Analysis 4.67), or positive skin-prick tests (Analysis 4.68 to Analysis 4.73). Despite higher IQ scores at age 6.5 years observed in intention-to-treat analyses of the breastfeeding promotion intervention in PROBIT (Kramer 2000a), no significant differences were observed in these outcomes in observational comparisons of EBF versus MBF (Analysis 4.74 to Analysis 4.80), except for block designs (Analysis 4.77). The latter difference favouring the EBF group was no longer significant, however, in multivariate mixed models with adjustment for clustering and for potential confounding variables (adjusted MD -0.7; 95% CI -1.6 to 0.3). Teachers' ratings of the PROBIT children's academic performance at age 6.5 years (Analysis 4.81 to Analysis 4.84) were actually higher for all subjects except for mathematics (Analysis 4.83), but the differences all became statistically nonsignificant in multivariate mixed models with adjustment for clustering and for potential confounding variables. Finally, no significant differences were observed in the latter study for parents' or teachers' rating of the children's behaviour at age 6.5 years (Analysis 4.85 to Analysis 4.96).

Comparison five: observational studies of prolonged (more than six months) exclusive versus mixed breastfeeding, developed countries

A small observational cohort study from the Baltimore-Washington area (U.S.) (Ahn 1980) reported "no differences in the overall rates of gain in weight and length" for the first year of life in infants who were exclusively breastfed beyond six months versus those exclusively breastfed for less than six months and mixed breastfed thereafter. The actual data were not reported, however, and thus cannot be assessed quantitatively in this review.

One small Finnish study (Savilahti 1987a) reported no difference in lipid concentrations at nine months among infants exclusively breastfed for nine months versus those exclusively breastfed for six months and mixed breastfed from six to nine months. Similar concentrations were observed for very low density lipoprotein, low density lipoprotein, high-density lipoprotein-2, high-density lipoprotein-3, apoprotein B, and total triglycerides (Analysis 5.1 to Analysis 5.6).

DISCUSSION

Neither the controlled clinical trials nor the observational studies (predominantly cohort studies) from either developing or developed countries suggest that infants who continue to be exclusively breastfed for six months show deficits in weight or length gain from three to seven months or thereafter. Owing to the large sample sizes required to detect modest effects on the incidence of low (less than -2) anthropometric z-scores, however, the data are insufficient to rule out a modest increase in risk of undernutrition with exclusive breastfeeding for six months and grossly inadequate to reach conclusions about the effects of prolonged (more than six months) exclusive breastfeeding.

Consistent with the results of previous observational studies, none of which met the selection criteria for this review, the large Belarussian study (Kramer 2000a) found a significant reduction in risk of one or more episodes of gastrointestinal infection. Two recent studies from Iran (Khadivzadeh 2004) and Nigeria (Onayade 2004) reported reductions in risk of both gastrointestinal and respiratory infection. Combined data from Finland, Australia, and Belarus do not suggest a protective effect against short- or long-term atopic outcomes.

The data are conflicting with respect to iron status, but the controlled trials from Honduras (Cohen 1994a; Dewey 1999a) suggest that, at least in developing-country settings where maternal iron status (and thus newborn iron stores) may be suboptimal, exclusive breastfeeding without iron supplementation may compromise hematologic status by six months of age. The reasons for the superior hematologic status reported in Italian infants exclusively breastfed for at least seven months are unclear.

Data from the two Honduran trials (Cohen 1994a; Dewey 1999a) and the Bangladeshi cohort study (Huffman 1987) suggest that exclusive breastfeeding through six months is associated with delayed resumption of menses, at least in settings with high breastfeeding frequency. The more prolonged lactational amenorrhea represents an additional advantage of continued exclusive breastfeeding in developing-country settings.

The two Honduran trials (Cohen 1994a; Dewey 1999a) also found prolonged exclusive breastfeeding to be associated with more rapid maternal postpartum weight loss. Such an effect would be an additional benefit if it were generalizable to developed-country settings where gestational weight gains and postpartum weight retention are high, but would be a disadvantage if it applied to undernourished women in developing countries.

In the two Honduran trials (Cohen 1994a; Dewey 1999a), mothers allocated to the prolonged exclusive breastfeeding group reported that their infants crawled at a significantly younger age. No such difference was seen, however, in the age at which the infants first sat from lying position, and the results for walking by 12 months differed in the two trials. The inconsistency of these results, coupled with the potential for biased maternal reporting due to nonblinding, suggest the need for cautious interpretation and further study.

AUTHORS' CONCLUSIONS

Implications for practice

Infants breastfed exclusively for six months have a reduced risk of gastrointestinal infection and no observable deficits in growth. Mothers who exclusively breastfeed for six months are more likely to remain amenorrheic for six months postpartum and to lose weight postpartum at a slightly faster rate. No benefits of introducing complementary foods between four and six months have been demonstrated, with the exception of improved iron status in one developing-country setting (Honduras). Since the latter benefit can be achieved more effectively by medicinal iron supplementation (e.g., vitamin drops), it does not appear to justify incurring the adverse effects of liquid or solid food supplementation on infectious morbidity, and lactational amenorrhea. Exclusive breastfeeding for six months does not seem to confer any long-term (at least to early school age) protection against obesity or allergic disease, nor any benefits in cognitive ability or behaviour, compared with exclusive breastfeeding for three to four months with continued partial breastfeeding to six months. Thus, with the caveat that individual infants must still be managed individually, so that insufficient growth or other adverse outcomes are not ignored and appropriate interventions are provided, the overall evidence demonstrates no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first six months of life in both developing and developed-country settings. In fact, in response to the original version of this review, World Health Organization and the World Health Assembly modified its recommendations for the duration of exclusive breastfeeding (WHO 2001b).

Implications for research

The investigators involved in the two Honduran trials took a step in the right direction when they opted for an experimental design to overcome problems with confounding (particularly confounding by indication) and selection bias inherent in observational designs. The results of observational studies from developing countries are consistent with the results of the two Honduran trials, especially with respect to growth. Nonetheless, the small number of studies and of infants studied, as well as uncertainty about the net direction and magnitude of potential biases, underscore the need for further research, particularly to rule out modest differences in risk of undernutrition.

It would seem prudent, therefore, to undertake larger randomized trials of exclusive breastfeeding for six months to exclude differences in risk of malnutrition in developing countries, and to confirm the finding of reduced infectious morbidity. Because of the strong potential for contamination (similar practices among women who interact with one another), cluster randomization by clinic or even community may well be the preferred research design strategy. Longer-term (beyond early school age) impacts on health and development are also worth pursuing.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adair 1993a

Methods	Design: prospective cohort. Quality assessment Control for confounding: A. Follow-up: A. Blinding: A for weight, B for length.
Participants	1204 Filipino infants.
Interventions	EBF = little or no nutritive foods or fluids other than BF for 6 months (n = 370). MBF = BF with introduction of nutritive foods or liquids at 4 months (n = 834).
Outcomes	Weight and length gain 4-6 months.
Notes	Multivariate analysis did not affect outcome comparison, but data not presented.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Ahn 1980

Methods	Design: retrospective cohort. Quality assessment Control for confounding: B. Follow-up: C. Blinding: A for weight, B for length.
Participants	96 healthy U.S. infants living in Baltimore-Washington area who were EBF for at least 6 months.
Interventions	EBF = BF with no solids or liquids other than human milk for > 6 months (n = 50). MBF = EBF for <= 6 months, then MBF until > 6 months (n = 46).
Outcomes	Weight and length gain in first 12 months.
Notes	1. No quantitative data provided. 2. Data requested on weight and length gain and illnesses in first year.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Akeson 1996a

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A for weight and blood analyses, B for length.
Participants	44 healthy Swedish infants EBF for the first 3 months.
Interventions	EBF = BF + < 125 ml/day of formula for >= 6 months (n = 26). MBF = EBF for >= 3 months, then BF >= 2 times/day + > 125 ml/day of formula for >= 6 months (n = 18).
Outcomes	Weight and length gain 4-8 months, 6-9, and 8-12 months; total and essential amino acid concentrations at 6 months.
Notes	1. N's in tables not provided for weight and length. 2. Identical data for length gain for the 2 groups at 8-12 months: misprint?

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Brown 1991a

Methods	Design: prospective cohort. Quality assessment Control for confounding: B. Follow-up: C. Blinding: A for weight, B for length.
Participants	36 poor, peri-urban Peruvian infants.
Interventions	EBF = little or no nutritive foods or fluids other than BF for 6 months (n = 15). MBF = BF with introduction of nutritive foods and fluids at 4 months (n = 21).
Outcomes	Weight and length gain 4-6 months.
Notes	Multivariate analysis did not affect outcome comparison, but data not presented.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Castillo 1996

Methods	Design: cross-sectional. Quality assessment Control for confounding: C.

Castillo 1996 *(Continued)*

	Follow-up: C. Blinding: A for weight, B for length.
Participants	1122 Chilean children 3.0-5.9 months of age.
Interventions	EBF = BF only (unclear if water, juices, or other liquids permitted) (n = 974). MBF = EBF for >= 2.9 months, then BF + solid food (n = 148).
Outcomes	Low WAZ, LAZ, high WLZ.
Notes	1. Cannot use data quantitatively, because prevalences, confidence intervals, and SEs not provided. 2. Low WAZ and LAZ defined as <- 1, high WLZ as >+ 1.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Cohen 1994a

Methods	Design: controlled trial. Quality assessment Randomization: C. Follow-up: C. Blinding: A for weight and maternal postpartum weight loss, B for length, developmental milestones, and lactational amenorrhea. Jadad scale Randomization: 0/2. Double-blinding: 0/2. Withdrawals: 1/1. Total Jadad scale score: 1/5.
Participants	141 Honduran infants of low-income families with poor sanitation.
Interventions	EBF = BF with no other liquids or solids until 6 months (n = 50). MBF = introduction of complementary solid food at 4 months with either ad libitum nursing (SF) or maintenance of baseline nursing frequency (SF-M) (n = 91).
Outcomes	Weight and length gain 4-6 and 6-12 months; WAZ, LAZ, and WLZ at 6 months; receipt of Fe supplements 6-9 months; hemoglobin and ferritin at 6 months; % of days with fever, cough, nasal congestion, nasal discharge, hoarseness, and diarrhea; age first crawled, age first sat from lying position, walking by 12 months; maternal postpartum weight loss 4-6 months; resumption of menses by 6 months.
Notes	1. Nonrandom allocation. 2. Cluster allocation by week of birth, while analyses done at individual level. 3. Analysis not based on intention to treat. 4. SF-M and SF groups combined as MBF group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	C - Inadequate

Dewey 1999a

Methods	Design: controlled trial. Quality assessment Randomization: B. Follow-up: C. Blinding: A for weight, B for length. Jadad scale Randomization: 1/2. Double-blinding: 0/2. Withdrawals: 1/1. Total Jadad scale score: 2/5.
Participants	119 LBW Honduran term infants.
Interventions	EBF = BF with no other liquids or solids until 6 months (n = 59). MBF = introduction of complementary solid food at 4 months with maintenance of baseline nursing frequency (n = 60).
Outcomes	Weight and length gain 4-6 and 6-12 months; WAZ, LAZ, and WLZ at 6 months; plasma zinc concentration at 6 months; % of days with fever, cough, nasal congestion, nasal discharge, hoarseness, and diarrhea; age first crawled, age first sat from lying position, walking by 12 months; maternal postpartum weight loss 4-6 months; resumption of menses by 6 months.
Notes	1. Cluster-randomized by week of birth, while analyses done at individual level. 2. Analysis not based on intention to treat.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Duijts 2010

Methods	Prospective, population-based pregnancy/birth cohort study (Generation R Study from Rotterdam.)
Participants	1095 healthy Dutch singleton infants.
Interventions	EBF = BF without other milk or solids until 6 months (n = 58). MBF = introduction of milk and/or solids between 4 and 6 months with continuation of partial BF until 6 months (n = 1037).
Outcomes	1 or more episodes of upper respiratory tract, lower respiratory tract, and gastrointestinal tract infection in first 6 months and from 7-12 months.
Notes	1. Outcomes based on mailed questionnaires (maternal report) sent at 6 and 12 months postpartum. 2. Of 7893 total infants enrolled in the cohort, breastfeeding, outcome, and covariate (potential confounder) data were available in only ˜3500 (44%) at 6 months and ˜3000 (38%) at 12 months.

Risk of bias

Duijts 2010 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not done

Duncan 1993

Methods	Design: prospective cohort. Quality assessment Control for confounding: A. Follow-up: B. Blinding: B.
Participants	279 healthy U.S. infants.
Interventions	EBF = EBF for >= 6 months (n = 138). MBF = EBF for 4 months with introduction of formula or solid foods between 4 and 6 months (n = 141).
Outcomes	Number of episodes of OM, 1 or more episodes of OM, and frequent OM in first 12 months.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Heinig 1993

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A for weight, B for length and sleeping time.
Participants	60 healthy U.S. infants living in Davis, CA.
Interventions	EBF = BF ± <= 120 ml/day of other milk or formula for >= 12 months and no solids < 6 months (n = 19). MBF = BF ± <= 120 ml/day of other milk or formula for >= 12 months; solids introduced at 4-6 months (n = 41).
Outcomes	Monthly weight and length gain at 6-9 and 9-12 months; total sleeping time at 9 months.
Notes	1. Data on weight and length gain 4-6 months included in pooled analysis of WHO 1994. 2. No quantitative data presented on morbidity.

Risk of bias

Bias	Authors' judgement	Support for judgement

Heinig 1993 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	D - Not used

Huffman 1987

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: B. Blinding: A.
Participants	1018 Bangladeshi women with live births.
Interventions	EBF = BF with no other liquids or solids for >= 7 months (n = 647). MBF = EBF for 4 months with introduction of liquid or solid supplements before 7 months (n = 371).
Outcomes	Duration of lactational amenorrhea.
Notes	1. Over 95% of study women BF > 16 months, so all MBF women assumed to continue BF >= 6 months. 2. Multivariate (Cox) regression controlled for maternal education, parity, religion, and weight, but reference group EBF < 1 month.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Kajosaari 1983

Methods	Design: prospective cohort. Quality assessment Control for confounding: B. Follow-up: C. Blinding: C.
Participants	135 healthy Finnish infants of atopic parents.
Interventions	EBF = BF without cow milk-based formula; occasional water permitted; solids introduced at about 6 months (n = 70). MBF = BF with introduction of solids at about 3 months (n = 65).
Outcomes	Atopic eczema and food allergy at 1 year; any atopy, atopic eczema, pollen allergy, asthma, food allergy, and allergy to animal dander at 5 years.
Notes	Discrepancy between 1- and 5-year follow-up reports regarding sample sizes per group (inverted from 1 report to the other).

Risk of bias

Bias	Authors' judgement	Support for judgement

Kajosaari 1983 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	D - Not used

Khadivzadeh 2004

Methods	Design: prospective cohort. Quality assessment Control for confounding: A. Follow-up: A. Blinding: A for weight, B for morbidity measures.
Participants	193 healthy, term Iranian infants followed at 1 of 5 randomly urban health centres.
Interventions	EBF = no other liquid or solid before 6 months (n = 98). MBF = EBF for 4 months, then complementary foods.
Outcomes	Weight and length gains; incidence of respiratory and gastrointestinal infection during the period of 4 to 6 months.
Notes	1. EBF and MBF infants 'matched' for sex and for weight and length at 4 months, but matching criteria for weight and length not provided. 2. 2 EBF and 5 MBF infants excluded for "noncompliance" with self-selected group assignment.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	D - Not used

Khan 1984

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A for weight, B for length.
Participants	48 rural Bangladeshi children.
Interventions	EBF = no other liquid or semi-solid food (water permitted) and introduction of supplementation between 12 and 15 months. MBF = BF + introduction of supplements between 6 and 15 months.
Outcomes	Weight and length through 24 months; number of diarrheal episodes; average duration of diarrhea.
Notes	1. Graphical presentation of data only without SDs, thus precluding quantitative reporting. 2. Misprint in legend for Figure 2.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Khan 1984 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	D - Not used

Kramer 2000a

Methods	Design: prospective cohort nested within randomized trial. Quality assessment Control for confounding: A. Follow-up: A. Blinding: A for weight, B for length and head circumference.
Participants	3483 healthy, term Belarussian infants.
Interventions	EBF = no liquids or solids other than breast milk for >= 6 months (n = 621). MBF = EBF for 3 months with introduction of nonbreast milk liquids or solids, or both, by 6 months (n = 2862).
Outcomes	Monthly weight and length gain 3-6, 6-9, and 9-12 months; WAZ, LAZ, WLZ, and head circumference at 6, 9, and 12 months; death; occurrence of and hospitalization for gastrointestinal and respiratory infection; atopic eczema and recurrent wheezing in first 12 months; height, weight, adiposity, allergy symptoms and diagnoses, skin-prick tests, dental caries, IQ, teacher's academic ratings, and parent's and teacher's assessments of behaviour at 6.5 years.
Notes	Outcomes analyzed using multilevel regression accounting for clustering and controlling for geographic region, urban vs rural location, parental education, family atopic history, and maternal smoking during pregnancy.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	D - Not used

Oddy 1999

Methods	Design: prospective cohort within randomized trial. Quality assessment Control for confounding: C. Follow-up: A for 1-year outcomes, B for asthma at 6 years, C for skin-prick tests at 6 years. Blinding: B.
Participants	510 Australian infants.
Interventions	EBF = no nonbreast milk or solids for >= 6 months (n = 246). MBF = EBF for 4 months, with introduction of nonbreast milk or solids, or both, at 4-6 months (n = 264).
Outcomes	Occurrence of and hospitalization for upper and lower respiratory tract infection and recurrent wheezing in first 12 months; asthma and skin-prick tests at 6 years.
Notes	1. Published article includes multivariate control for confounders, but data included here are raw and unpublished.

Oddy 1999 *(Continued)*

	2. Current asthma at 6 years defined as doctor-diagnosed + wheeze in previous year without a cold + receipt of asthma medication.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Onayade 2004

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: A for illness episodes, C for weight. Blinding: A for weight, B for morbidity measures.
Participants	309 healthy, term infants born in Nigerian urban university teaching hospital.
Interventions	EBF = no other liquid or solid for >= 6 months (n = 264). MBF = EBF for 4 to < 6 months, then water, formula, or cereal (n = 45).
Outcomes	Respiratory infection, gastrointestinal infection, weight, and length.
Notes	1. Only 34 of 45 MBF infants had recorded weights an lengths. 2. Error in Table 4: recorded n = 266 (vs 264 total) EBF infants with recorded weight and length. 3. No control for apparent (but small) sociodemographic differences between groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Pisacane 1995

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A.
Participants	30 term, appropriate-for-gestational-age Italian infants recruited at 6 months and BF for first year of life.
Interventions	EBF = BF only without any other fluids or solids for >= 7 months (n = 9). MBF = EBF for 4-6 months with other foods introduced before 7 months (n = 21).
Outcomes	Hemoglobin and serum ferritin concentrations at 12 months.
Notes	

Pisacane 1995 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Rao 1992

Methods	Design: cross-sectional. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A for weight, B for length.
Participants	31 poor East Indian children < 3 years living under poor hygienic conditions.
Interventions	EBF = no supplementation with other milk or traditional solid foods for 6-12 months (n = 11). MBF = EBF for 6 months, then supplementation with other milk or traditional foods from 6-12 months (n = 20).
Outcomes	Weight-for-age < 75% of reference mean.
Notes	1. Study population included all children < 3 years living in 3 villages. 2. Data extracted for males only, because large proportion of females not initially EBF for >= 6 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Savilahti 1987a

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A.
Participants	26 healthy Finnish infants.
Interventions	EBF = BF without supplementary formula or solid foods for 9 months (n = 7). MBF = BF with introduction of solids at 6 months (n = 19).
Outcomes	VLDL, LDL, HDL2, HDL3, apoprotein B, and total triglyceride concentration at 9 months.
Notes	Atopic outcomes not compared in EBF vs MBF groups as defined here.

Risk of bias

Bias	Authors' judgement	Support for judgement

Savilahti 1987a *(Continued)*

Allocation concealment (selection bias)	Unclear risk	D - Not used

Simondon 1997a

Methods	Design: prospective cohort. Quality assessment Control for confounding: A for monthly weight and length gain 4-6 months, C for other outcomes. Follow-up: B. Blinding: A for weight and length.
Participants	370 Senegalese infants recruited at 2-3 months.
Interventions	EBF = breast milk and water only until at least 6-7 months (n = 154). MBF = breast milk, water, and introduction of complementary food between 4 and 7 months of age (n = 216).
Outcomes	Monthly weight and length gain 4-6 and 6-9 months; WAZ, LAZ, WLZ, and mid-upper arm circumference at 4-5, 6-7, and 9-10 months; duration of lactational amenorrhea.
Notes	1. EBF = 'very late' group, MBF = 'early' and 'late' groups combined. 2. Monthly weight and length gains 4-6 months based on multivariate control for maternal size and education and z-score at 2-3 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

WHO 1994a

Methods	Design: prospective cohort. Quality assessment Control for confounding: C. Follow-up: C. Blinding: A for weight, B for length.
Participants	Pooled sample of healthy developed-country infants (n = 358).
Interventions	EBF = BF ± other liquids for >= 6 months (n = 200). MBF = BF ± other liquids for >= 4 months with other milk ± solids introduced between 4 and 6 months (n = 158).
Outcomes	Monthly weight and length gain 4-6 months.
Notes	Multivariate control for initial weight and length, but data not presented.

Risk of bias

Bias	Authors' judgement	Support for judgement

WHO 1994a *(Continued)*

Allocation concealment (selection bias)	Unclear risk	D - Not used

WHO 1997

Methods	Design: prospective cohort. Quality assessment Control for confounding: A. Follow-up: C. Blinding: A for weight, B for length.
Participants	Pooled sample of mid-to high-SES infants from 2 developed and 3 developing countries (n = 556).
Interventions	EBF = BF ± noncaloric liquids for >= 6 months (n = 179). MBF = BF ± caloric liquids or solids introduced at 4-6 months (n = 377).
Outcomes	Monthly weight and length gain 4-8 months.
Notes	1. Multilevel regression used to control for maternal size and education and infant size and growth < 4 months. 2. Large losses to follow-up; retained sample 'similar' to full sample, but details not provided.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

BF: breastfeeding
EBF: exclusive breastfeeding
HDL2: high-density lipoprotein-2
HDL3: high-density lipoprotein-3
LAZ: length-for-age z-score
LBW: low birthweight
LDL: low density lipoprotein
MBF: mixed breastfeeding
OM: otitis media
SD: standard deviation
SE: standard error
SES: socioeconomic status
VLDL: very low density lipoprotein
vs: versus
WAZ: weight-for-age z-score
WLZ: weight-for-length z-score

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chantry 2006	The group with full breastfeeding from 4 to < 6 months did not necessarily continue mixed (partial) breastfeeding to at least 6 months.

Study	Reason for exclusion
Chantry 2007	The group with full breastfeeding from 4 to < 6 months did not necessarily continue mixed (partial) breastfeeding to at least 6 months.
Evelein 2011	The group with exclusive breastfeeding from 3-6 months did not necessarily continue mixed (partial) breastfeeding to at least 6 months.
Ly 2006	Both intervention and control groups were free to consume locally available complementary foods prior to 4 months and during the intervention period from 4 to 7 months.
Meinzen-Derr 2006	The group with exclusive breastfeeding from 4-6 months did not necessarily continue mixed (partial) breastfeeding to at least 6 months.
Rebhan 2009	The group with full/exclusive breastfeeding from 4-6 months did not necessarily continue mixed (partial) breastfeeding to at least 6 months.
Wang 2005	Those infants in the control group (mixed breastfeeding at ages 4-6 months) were not necessarily exclusively breastfed until 4 months.
Weyermann 2006	Comparing the 533 total (207+326) infants who were breastfed to any extent for at least 6 months with the 599 (277+322) who were exclusively breastfed for at least 3 months, it appears as if 66 (599-533) of the 277 infants listed as exclusively breastfed for 3-< 6 months discontinued breastfeeding before 6 months (*see* Table 1),

DATA AND ANALYSES

Comparison 1. Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Monthly weight gain from 4-6 months (g/mo)	2	265	Mean Difference (IV, Fixed, 95% CI)	20.78 [-21.99, 63.54]
2 Monthly weight gain from 6-12 months (g/mo)	2	233	Mean Difference (IV, Fixed, 95% CI)	-2.62 [-25.85, 20.62]
3 Monthly length gain 4-6 months (cm/mo)	2	265	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.04, 0.24]
4 Monthly length gain 6-12 months (cm/mo)	2	233	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.10, 0.02]
5 Weight-for-age z-score at 6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	0.18 [-0.06, 0.41]
6 Length-for-age z-score at 6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.11, 0.33]
7 Weight-for-length z-score at 6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.13, 0.31]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8 Weight-for-age z-score < -2 at 6 months	2	260	Risk Ratio (M-H, Fixed, 95% CI)	2.14 [0.74, 6.24]
9 Length-for-age z-score < -2 at 6 months	2	260	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.56, 2.50]
10 Weight-for-length z-score < -2 at 6 months	2	260	Risk Ratio (M-H, Fixed, 95% CI)	1.38 [0.17, 10.98]
11 Receipt of Fe supplements 6-9 months	1	139	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.91, 1.58]
12 Hemoglobin concentration (g/L) at 6 months	1	139	Mean Difference (IV, Fixed, 95% CI)	-5.0 [-8.46, -1.54]
13 Hemoglobin concentration < 110 g/L at 6 months	1	139	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.91, 1.58]
14 Hemoglobin concentration < 103 g/L at 6 months	1	139	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.75, 2.23]
15 Hematocrit (%) at 6 months	1	139	Mean Difference (IV, Fixed, 95% CI)	-1.20 [-2.15, -0.25]
16 Hematocrit < 33% at 6 months	1	139	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.85, 2.64]
17 Plasma ferritin concentration (mcg/L) at 6 months	1	135	Mean Difference (IV, Fixed, 95% CI)	-18.9 [-37.31, -0.49]
18 Plasma ferritin concentration < 12 mcg/L at 6 months	1	135	Risk Ratio (M-H, Fixed, 95% CI)	2.34 [0.86, 6.35]
19 Plasma ferritin concentration < 15 mcg/L at 6 months	1	135	Risk Ratio (M-H, Fixed, 95% CI)	2.93 [1.13, 7.56]
20 Plasma zinc concentration < 70 mcg/dL at 6 months	1	101	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.43, 1.33]
21 % of days with fever 4-6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	0.26 [-1.29, 1.81]
22 % of days with cough 4-6 months	2	260	Mean Difference (IV, Random, 95% CI)	2.33 [-6.00, 12.65]
23 % of days with nasal congestion 4-6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	0.11 [-4.41, 4.63]
24 % of days with nasal discharge 4-6 months	2	260	Mean Difference (IV, Random, 95% CI)	-0.72 [-6.81, 5.38]
25 % of days with hoarseness 4-6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-1.17, 0.79]

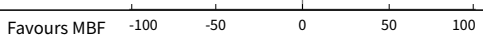
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26 % of days with diarrhea 4-6 months	2	260	Mean Difference (IV, Fixed, 95% CI)	1.15 [-0.35, 2.65]
27 % of days with fever 6-12 months	2	258	Mean Difference (IV, Fixed, 95% CI)	-0.39 [-2.80, 2.02]
28 % of days with nasal congestion 6-12 months	2	258	Mean Difference (IV, Fixed, 95% CI)	3.11 [-0.12, 6.35]
29 % of days with diarrhea 6-12 months	2	258	Mean Difference (IV, Fixed, 95% CI)	-0.74 [-2.34, 0.86]
30 Age first crawled (mo)	2	240	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-1.26, -0.34]
31 Age first sat from lying position (mo)	2	238	Mean Difference (IV, Random, 95% CI)	-0.22 [-0.91, 0.46]
32 Did not walk by 12 months	2	233	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.50, 1.55]
33 Maternal postpartum weight loss 4-6 months (kg)	2	260	Mean Difference (IV, Fixed, 95% CI)	0.42 [0.02, 0.82]
34 Maternal resumption of menses 6 months postpartum	2	189	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.33, 1.03]

Analysis 1.1. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 1 Monthly weight gain from 4-6 months (g/mo).

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Cohen 1994a	50	546 (178)	91	514 (154)		53.24%	32[-26.61,90.61]
Dewey 1999a	63	511.5 (173)	61	503.5 (182)		46.76%	8[-54.54,70.54]
Total ***	**113**		**152**			**100%**	**20.78[-21.99,63.54]**

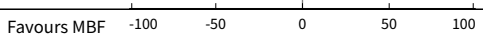
Heterogeneity: $Tau^2=0$; $Chi^2=0.3$, df=1(P=0.58); $I^2=0\%$

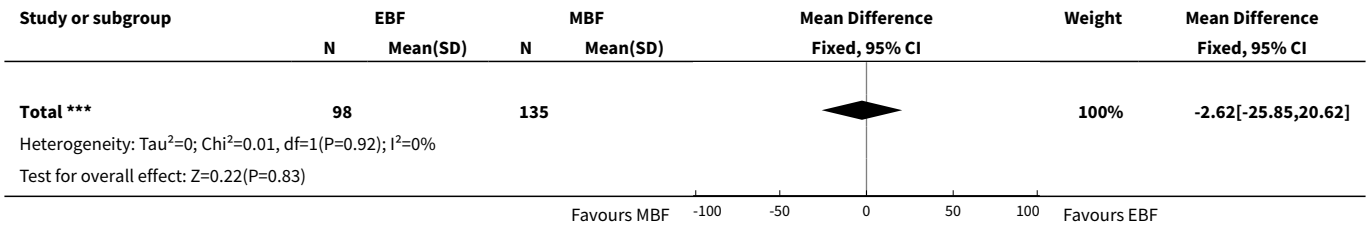
Test for overall effect: Z=0.95(P=0.34)



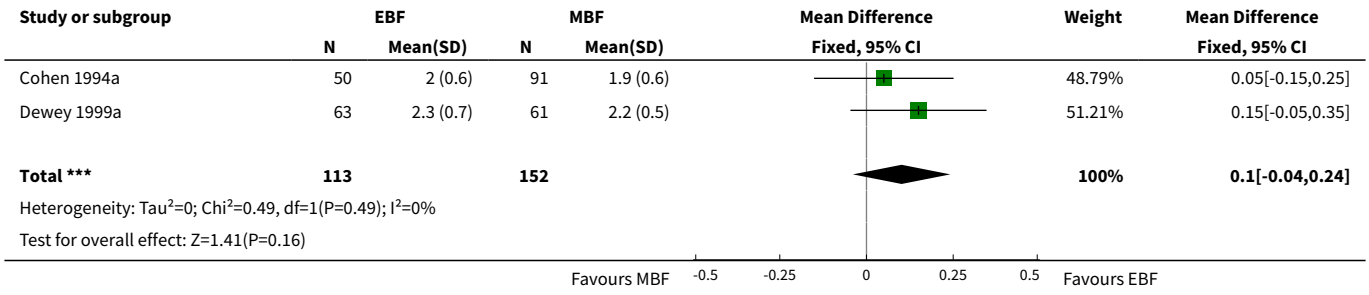
Analysis 1.2. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 2 Monthly weight gain from 6-12 months (g/mo).

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Cohen 1994a	47	212.8 (91.9)	87	216.6 (84.5)		53.73%	-3.74[-35.44,27.96]
Dewey 1999a	51	221.5 (87.2)	48	222.8 (86.2)		46.27%	-1.31[-35.47,32.85]

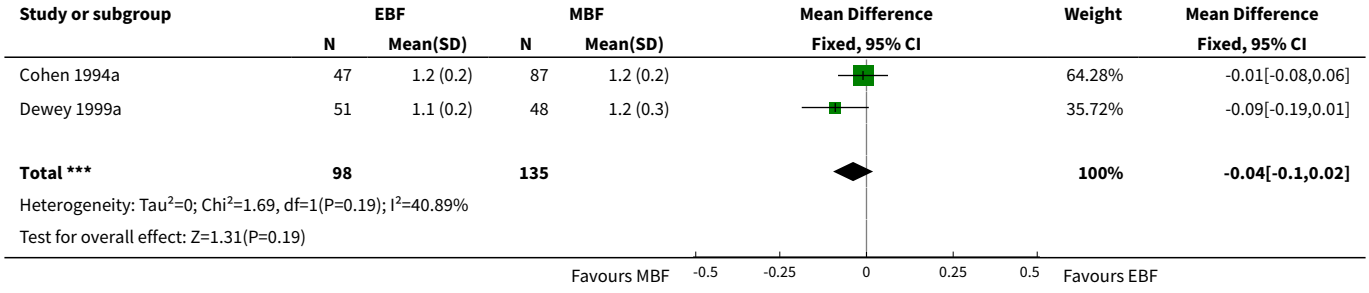




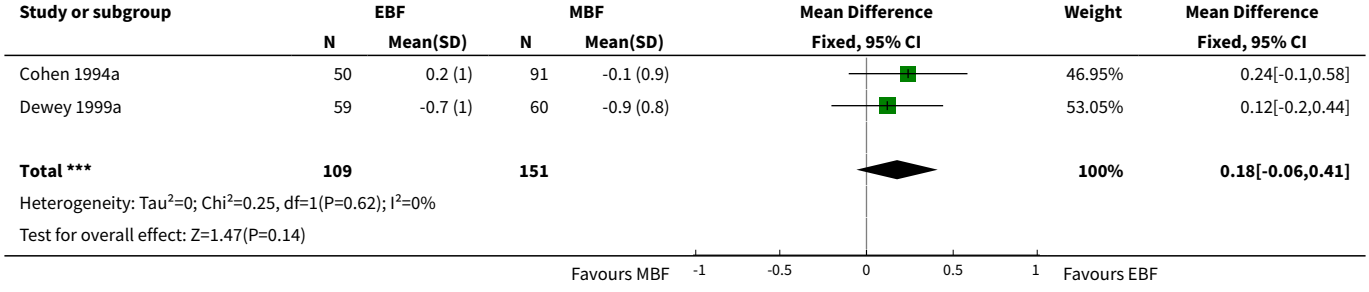
Analysis 1.3. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 3 Monthly length gain 4-6 months (cm/mo).



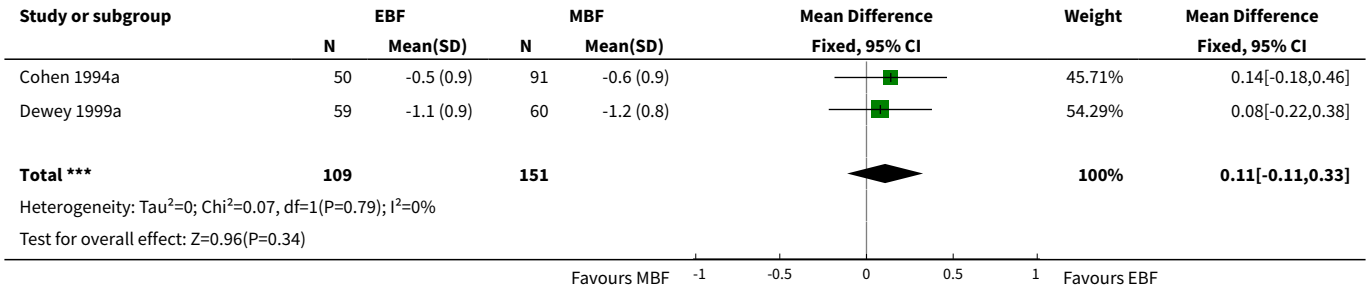
Analysis 1.4. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 4 Monthly length gain 6-12 months (cm/mo).



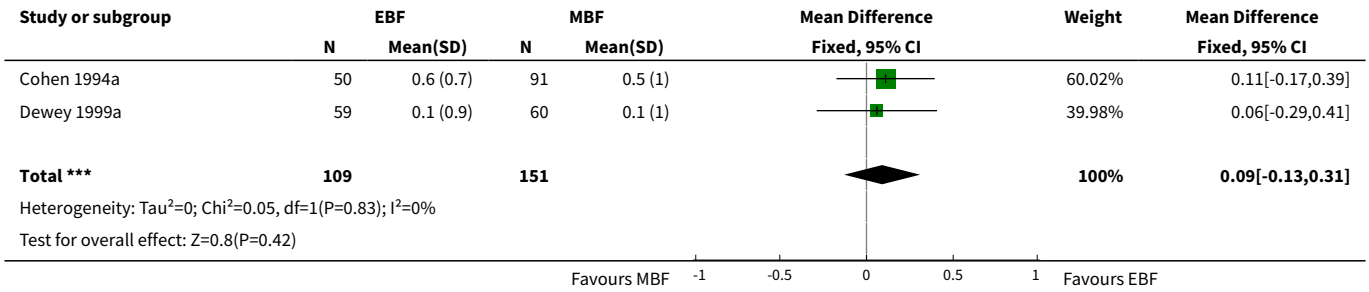
Analysis 1.5. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 5 Weight-for-age z-score at 6 months.



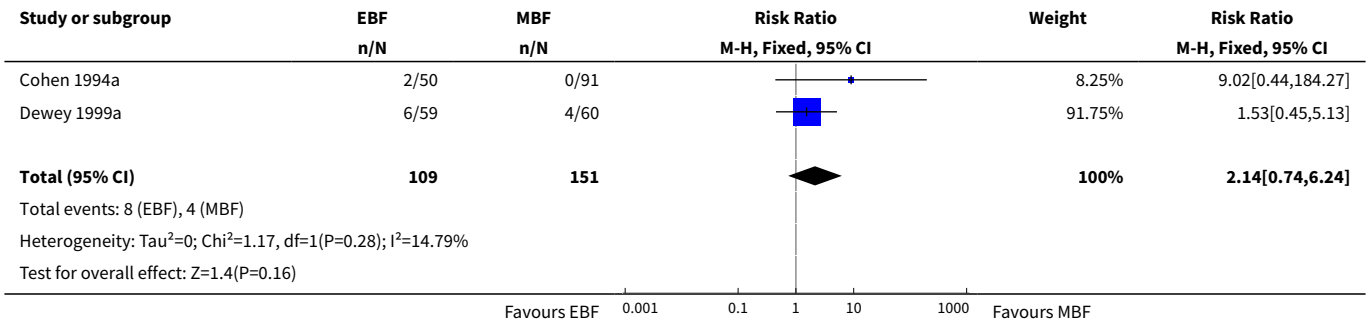
Analysis 1.6. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 6 Length-for-age z-score at 6 months.



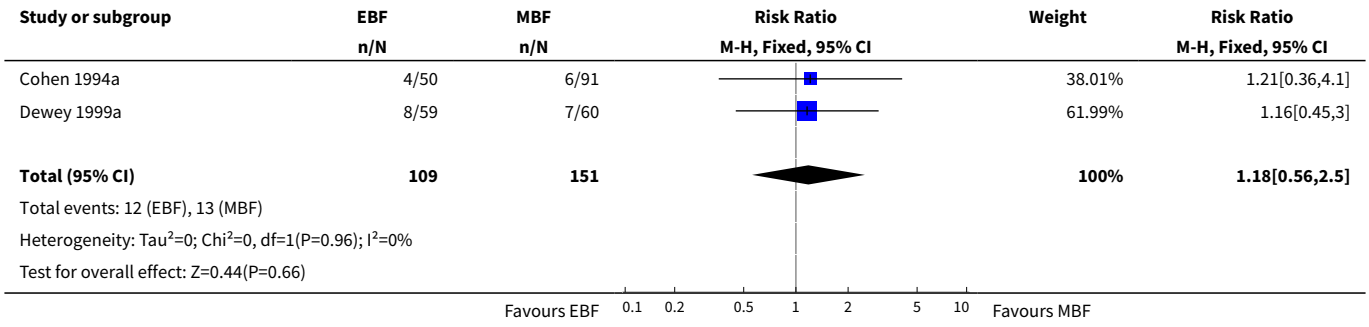
Analysis 1.7. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 7 Weight-for-length z-score at 6 months.



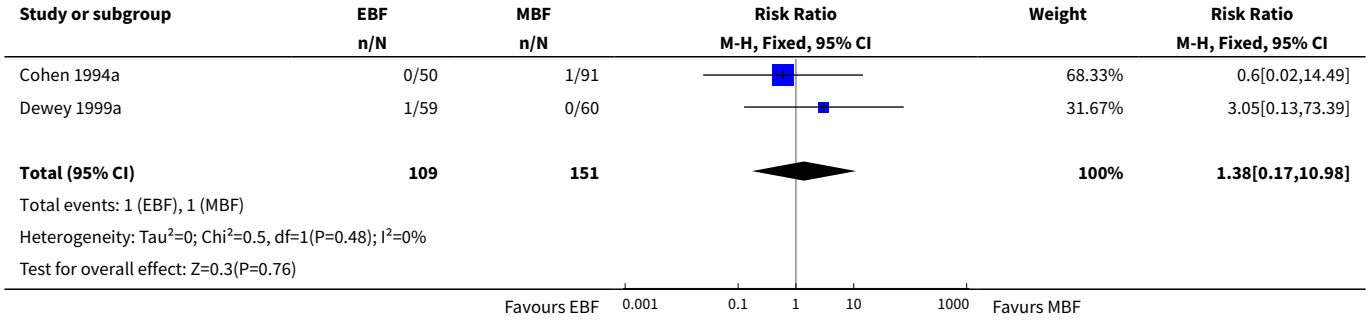
Analysis 1.8. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 8 Weight-for-age z-score < -2 at 6 months.



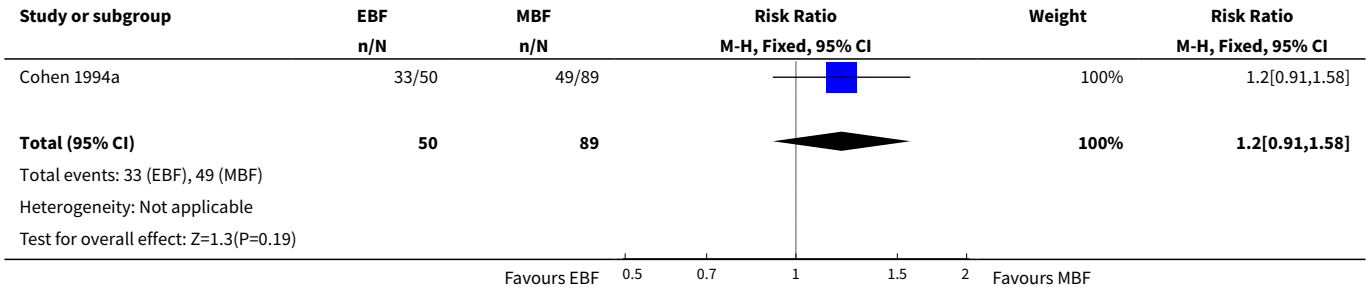
Analysis 1.9. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 9 Length-for-age z-score < -2 at 6 months.



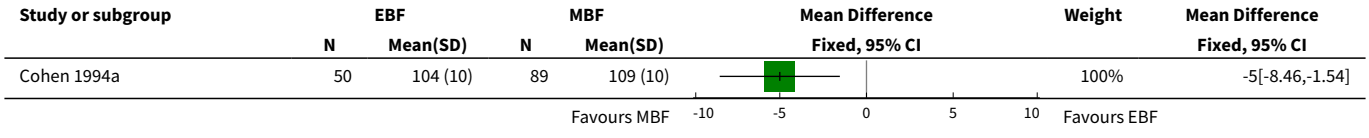
Analysis 1.10. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 10 Weight-for-length z-score < -2 at 6 months.

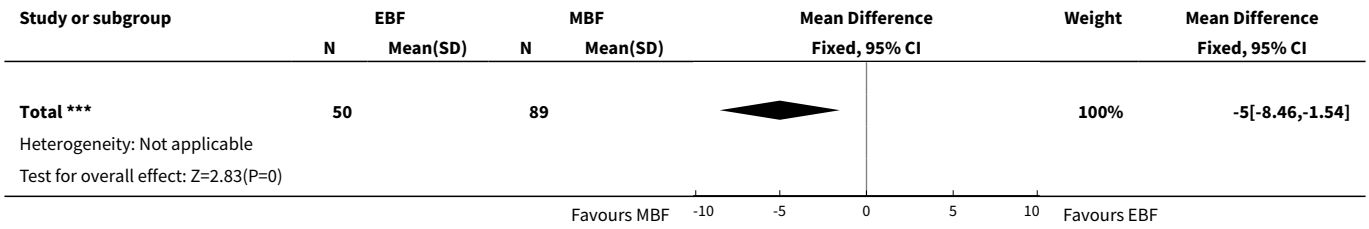


Analysis 1.11. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 11 Receipt of Fe supplements 6-9 months.

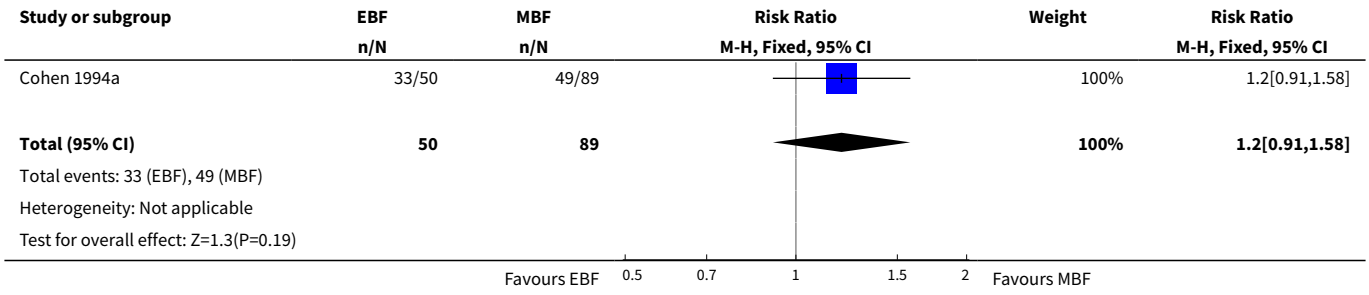


Analysis 1.12. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 12 Hemoglobin concentration (g/L) at 6 months.

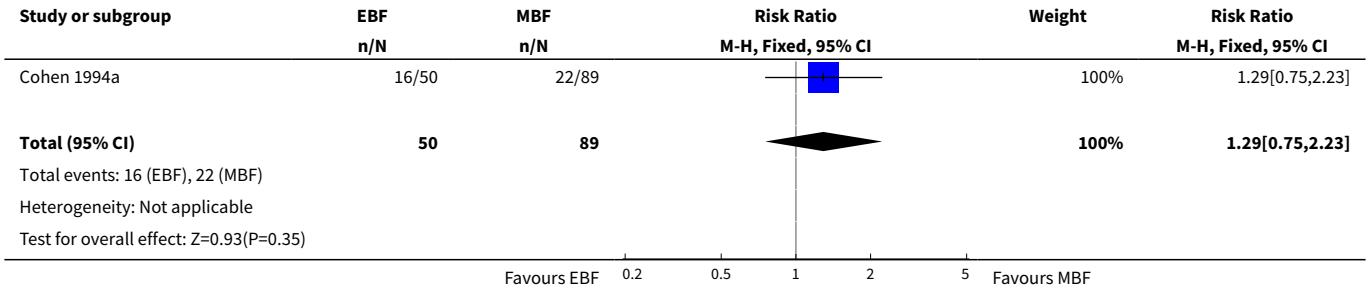




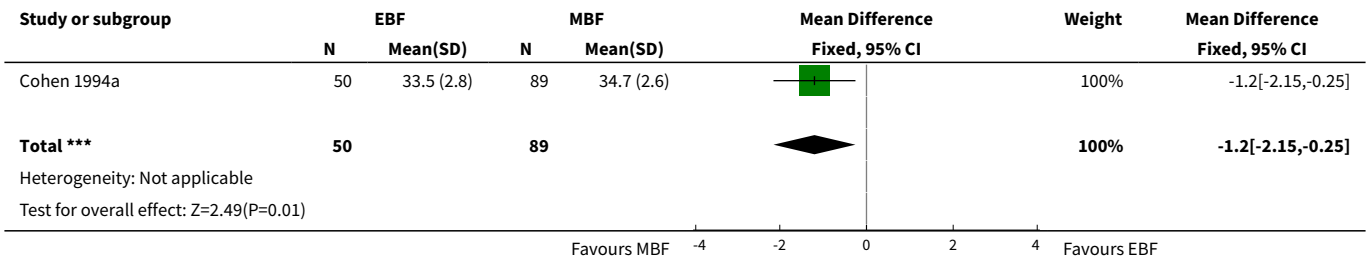
Analysis 1.13. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 13 Hemoglobin concentration < 110 g/L at 6 months.



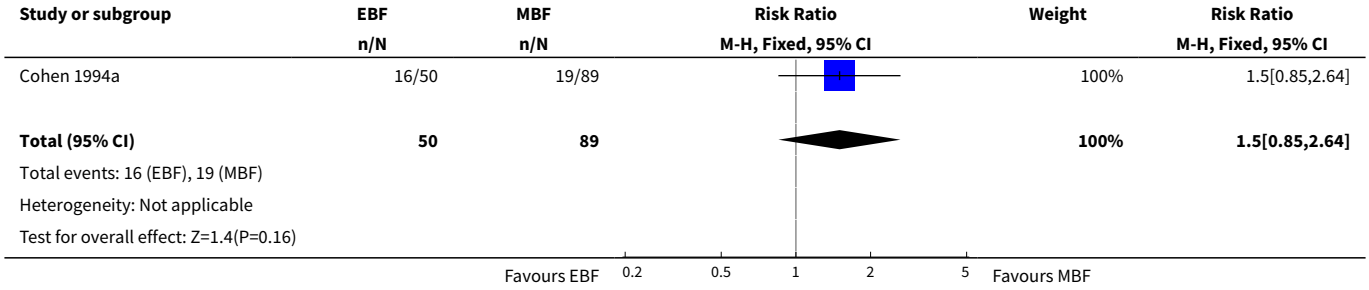
Analysis 1.14. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 14 Hemoglobin concentration < 103 g/L at 6 months.



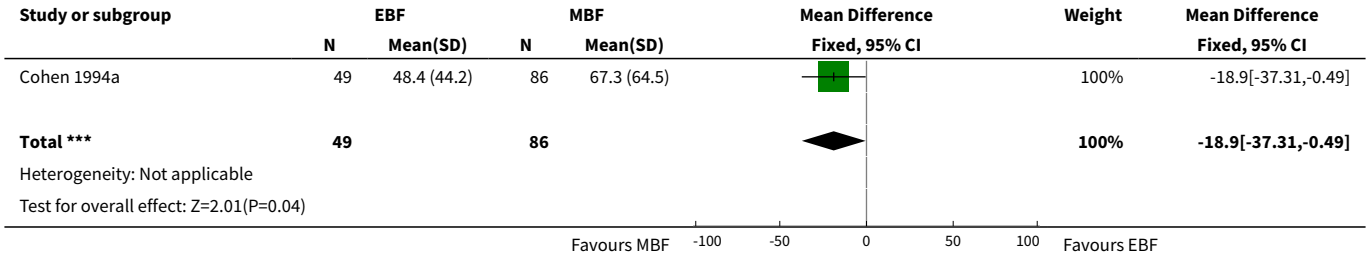
Analysis 1.15. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 15 Hematocrit (%) at 6 months.



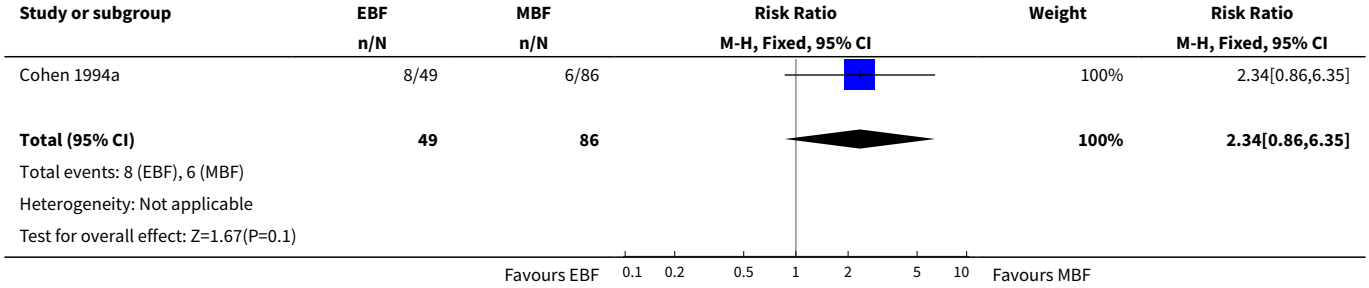
Analysis 1.16. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 16 Hematocrit < 33% at 6 months.



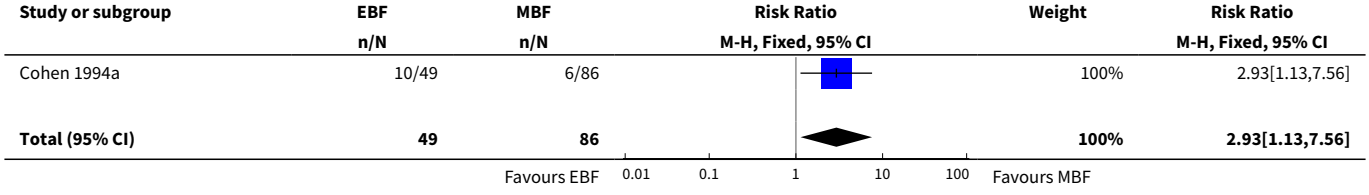
Analysis 1.17. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 17 Plasma ferritin concentration (mcg/L) at 6 months.

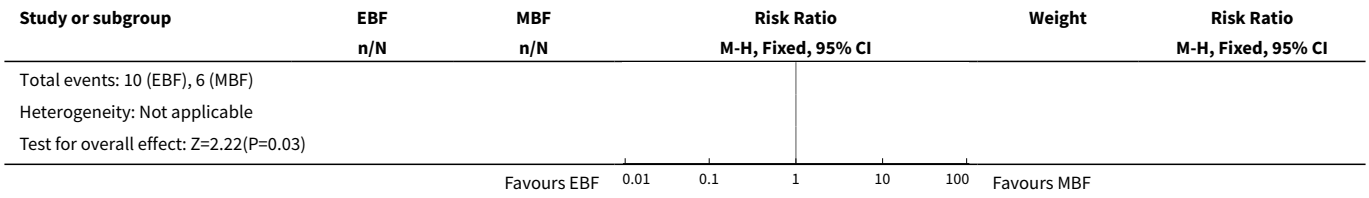


Analysis 1.18. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 18 Plasma ferritin concentration < 12 mcg/L at 6 months.

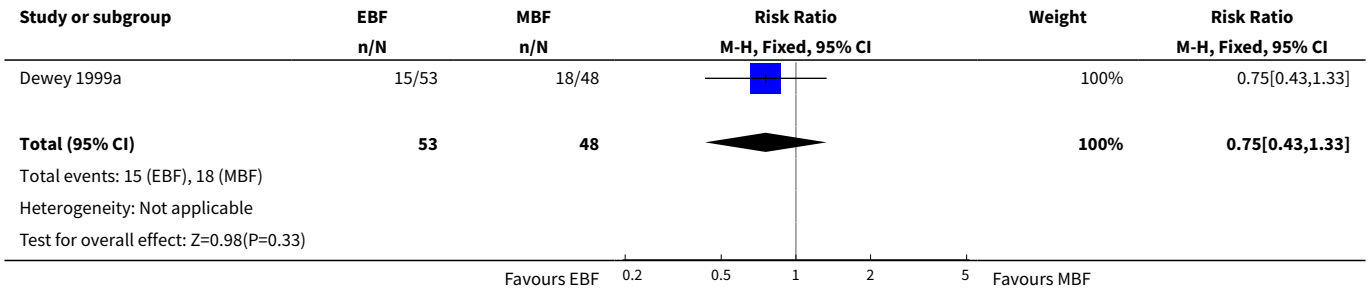


Analysis 1.19. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 19 Plasma ferritin concentration < 15 mcg/L at 6 months.

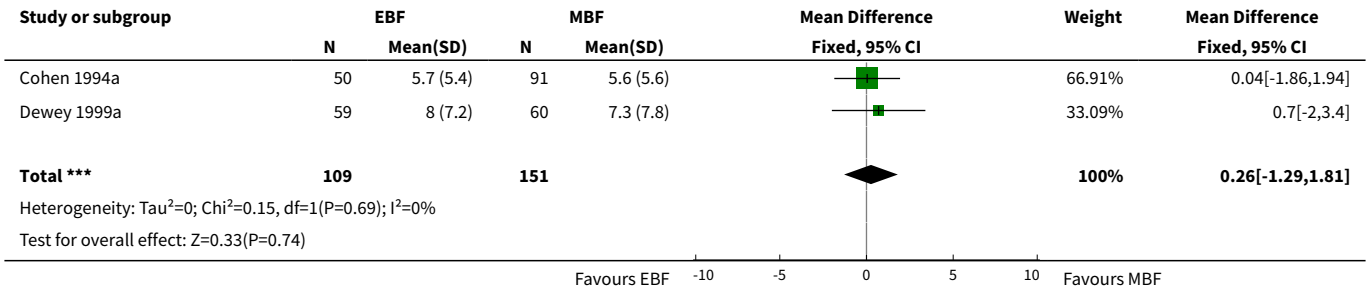




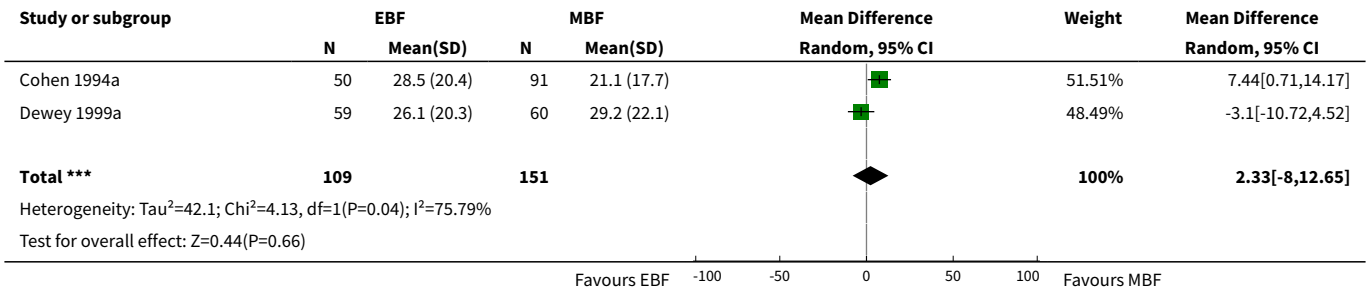
Analysis 1.20. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 20 Plasma zinc concentration < 70 mcg/dL at 6 months.



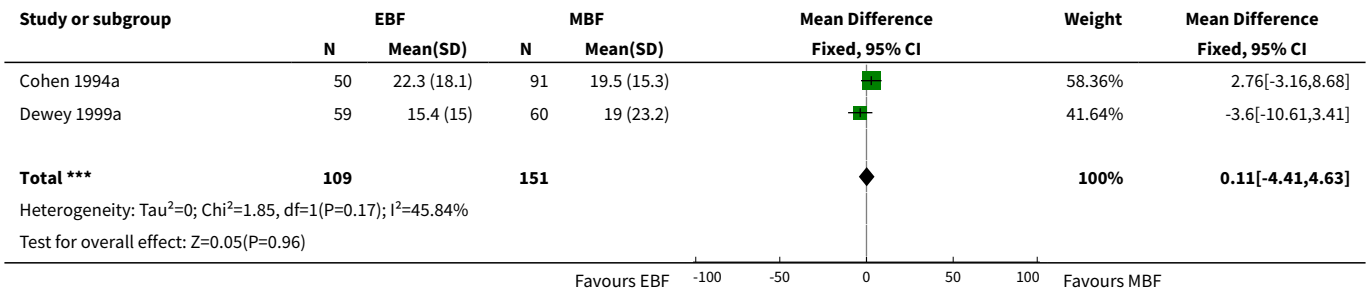
Analysis 1.21. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 21 % of days with fever 4-6 months.



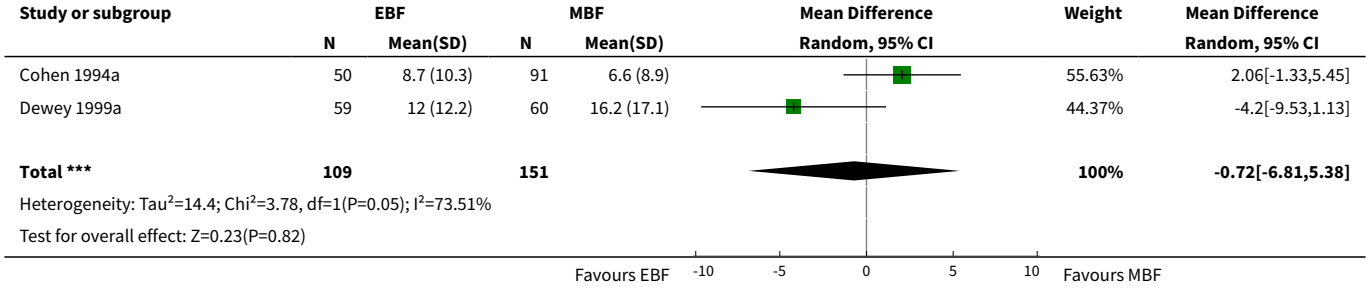
Analysis 1.22. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 22 % of days with cough 4-6 months.



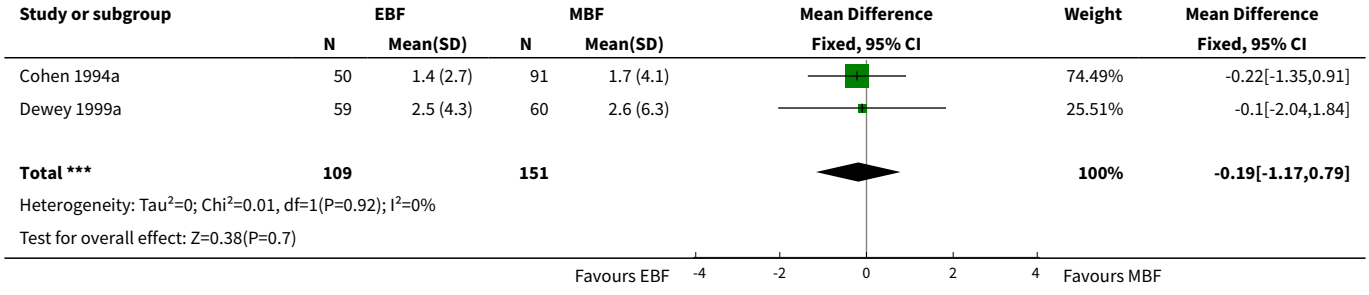
Analysis 1.23. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 23 % of days with nasal congestion 4-6 months.



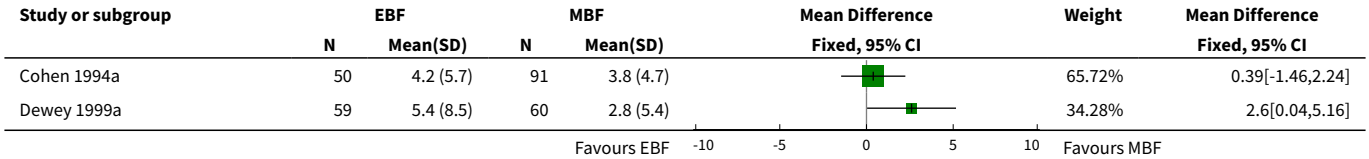
Analysis 1.24. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 24 % of days with nasal discharge 4-6 months.

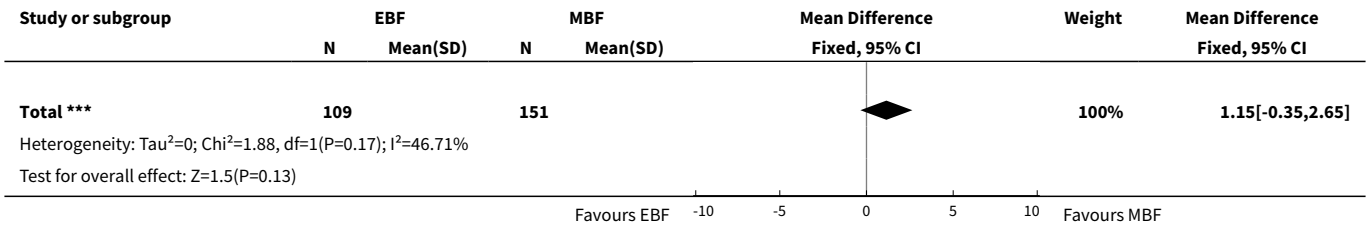


Analysis 1.25. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 25 % of days with hoarseness 4-6 months.

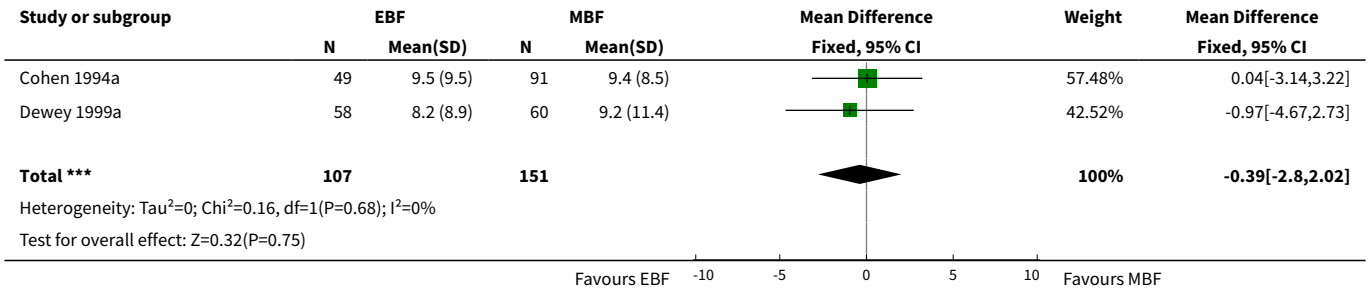


Analysis 1.26. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 26 % of days with diarrhea 4-6 months.

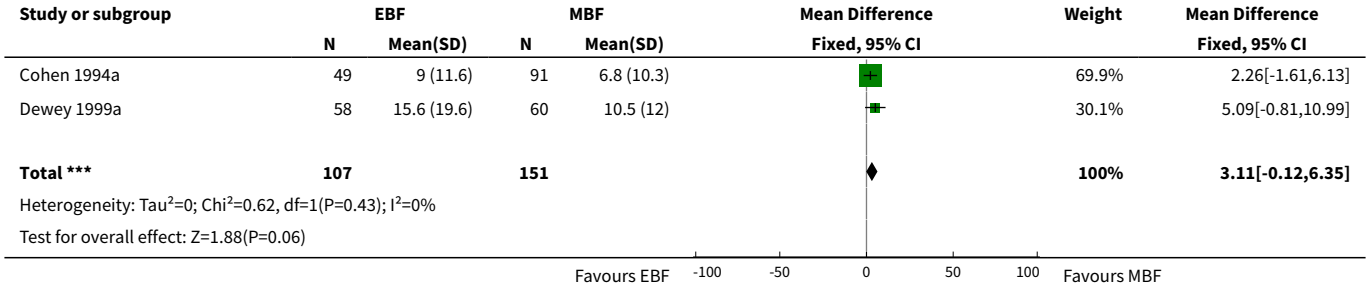




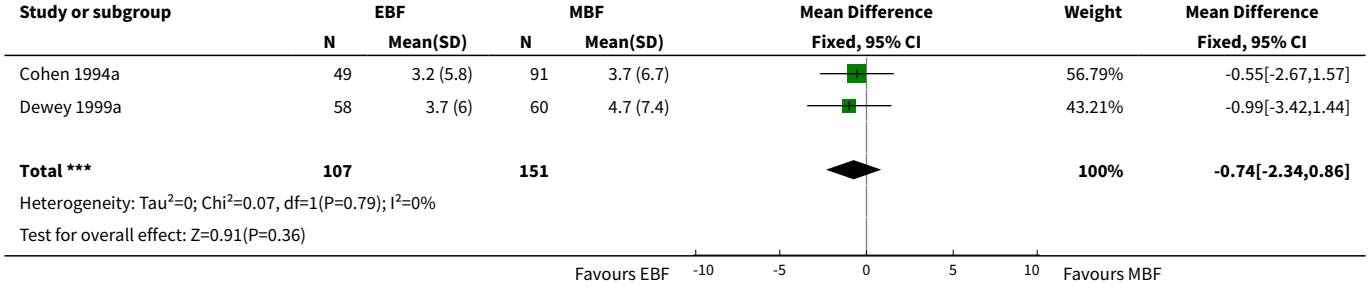
Analysis 1.27. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 27 % of days with fever 6-12 months.



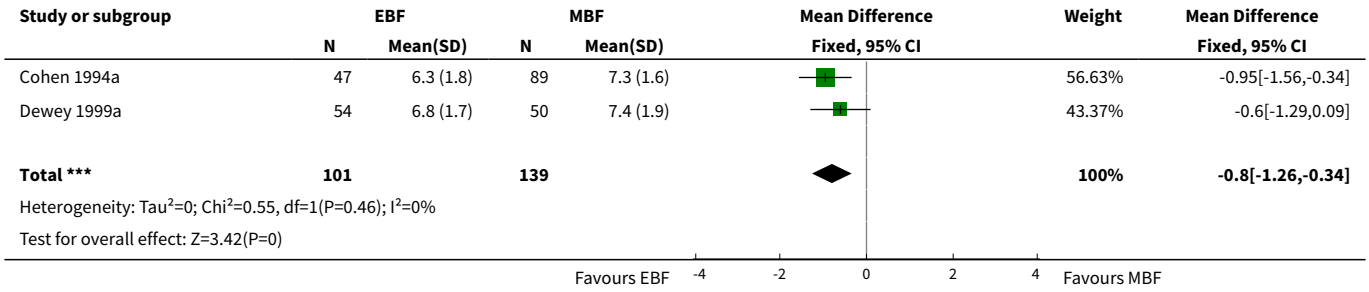
Analysis 1.28. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 28 % of days with nasal congestion 6-12 months.



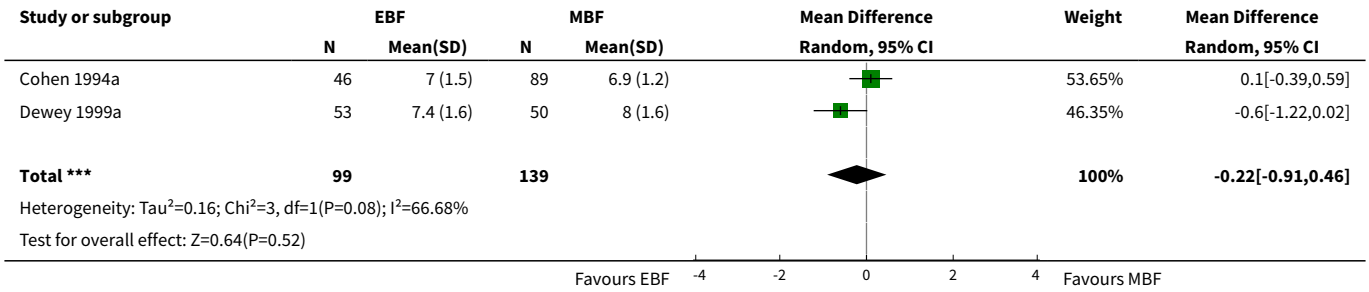
Analysis 1.29. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 29 % of days with diarrhea 6-12 months.



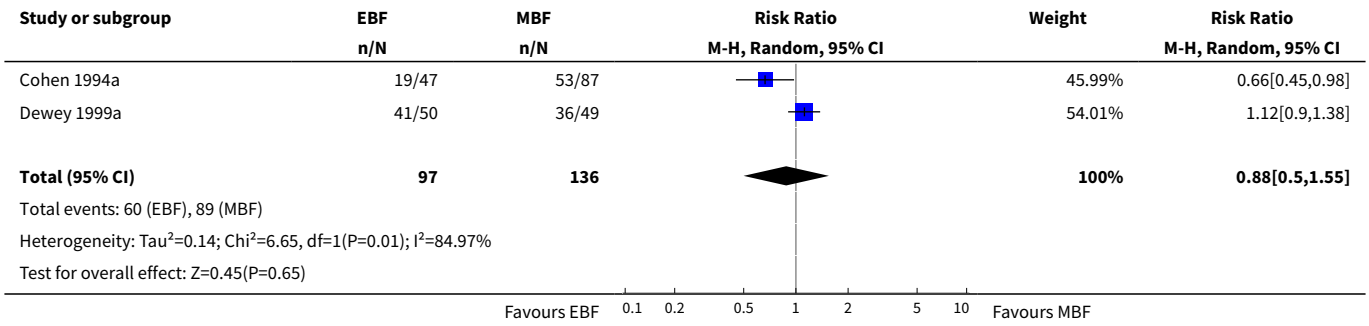
Analysis 1.30. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 30 Age first crawled (mo).



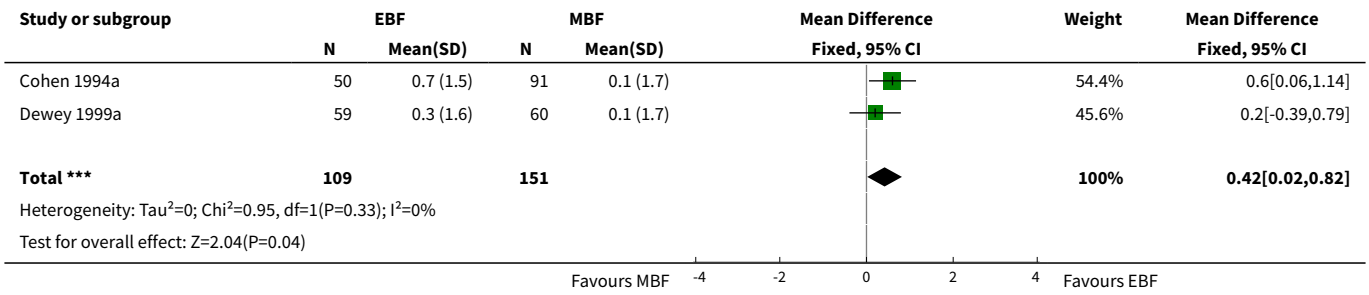
Analysis 1.31. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 31 Age first sat from lying position (mo).



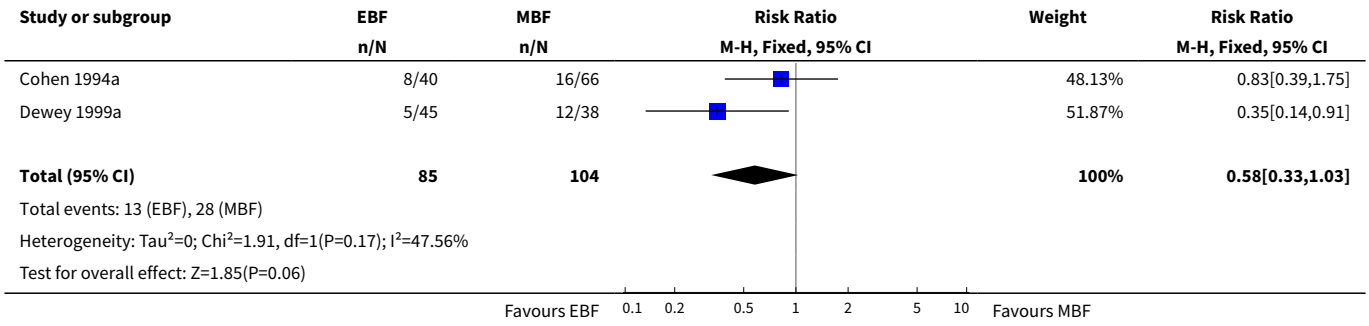
Analysis 1.32. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 32 Did not walk by 12 months.



Analysis 1.33. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 33 Maternal postpartum weight loss 4-6 months (kg).



Analysis 1.34. Comparison 1 Exclusive breastfeeding for 6 versus 4 months, developing countries, controlled trials, Outcome 34 Maternal resumption of menses 6 months postpartum.



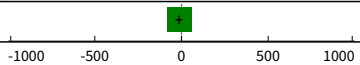
Comparison 2. Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies

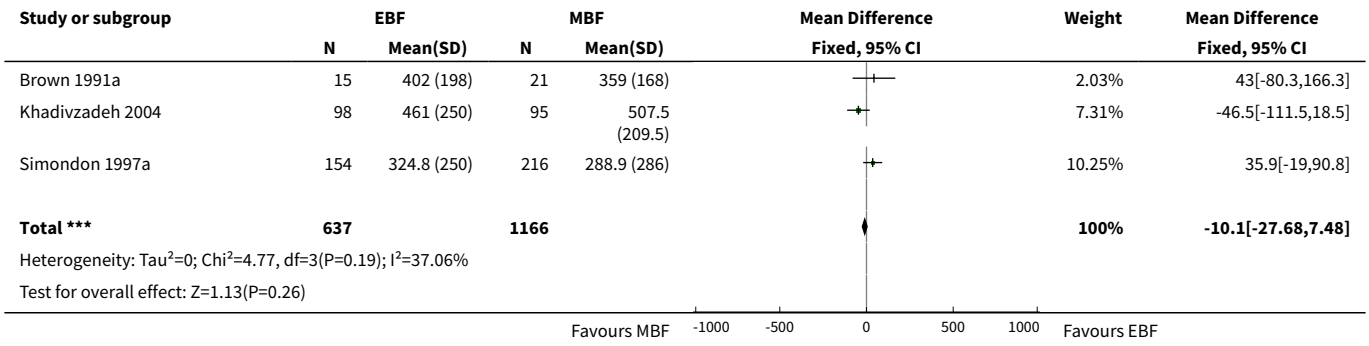
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Monthly weight gain 4-6 months (g/mo)	4	1803	Mean Difference (IV, Fixed, 95% CI)	-10.10 [-27.68, 7.48]
2 Monthly weight gain 6-9 months (g/mo)	1	319	Mean Difference (IV, Fixed, 95% CI)	-6.0 [-54.15, 42.15]
3 Monthly length gain 4-6 months (cm/mo)	4	1803	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.02, 0.11]
4 Monthly length gain 6-9 months (cm/mo)	1	319	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.06, 0.14]
5 Weight-for-age z-score at 6-7 months	1	370	Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.09, 0.35]
6 Weight-for-age z-score at 9-10 months	1	319	Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.15, 0.33]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Length-for-age z-score at 6-7 months	1	370	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.14, 0.22]
8 Length-for-age z-score at 9-10 months	1	319	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.09, 0.31]
9 Weight-for-length z-score at 6-7 months	1	370	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.09, 0.31]
10 Weight-for-length z-score at 9-10 months	1	319	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.21, 0.23]
11 Weight-for-age z-score < -2 at 6-7 months	1	370	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.54, 1.58]
12 Weight-for-age z-score < -2 at 9-10 months	1	319	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.64, 1.36]
13 Length-for-age z-score < -2 at 6-7 months	1	370	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.57, 2.53]
14 Length-for-age z-score < -2 at 9-10 months	1	319	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.62, 2.37]
15 Weight-for-length z-score < -2 at 6-7 months	1	370	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.12, 1.50]
16 Weight-for-length z-score < -2 at 9-10 months	1	319	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.39, 1.71]
17 Mid-upper arm circumference at 6-7 months (cm)	1	370	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.04, 0.44]
18 Mid-upper arm circumference at 9-10 months (cm)	1	319	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.16, 0.36]
19 One or more episodes of gastrointestinal infection at 4-6 months	1	193	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.21, 0.78]
20 One or more episodes of respiratory infection at 4-6 months	1	193	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.43, 1.06]
21 Resumption of menses by 6-7 months postpartum	1	686	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.05, 0.79]

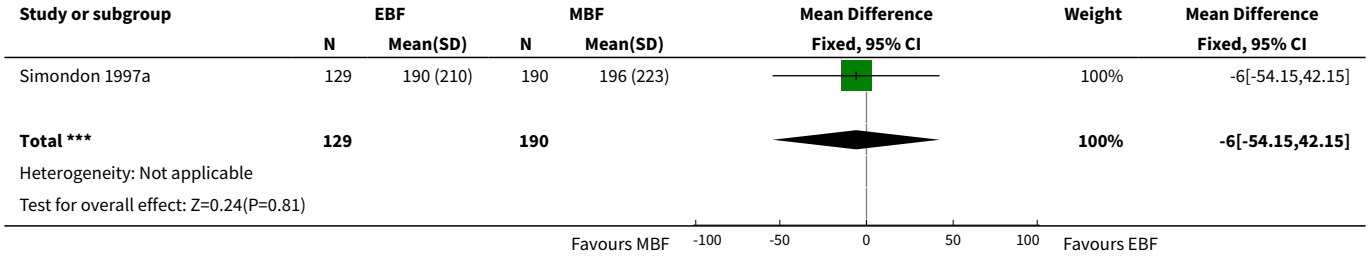
Analysis 2.1. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 1 Monthly weight gain 4-6 months (g/mo).

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Adair 1993a	370	336 (157)	834	350 (167)		80.4%	-14[-33.61,5.61]

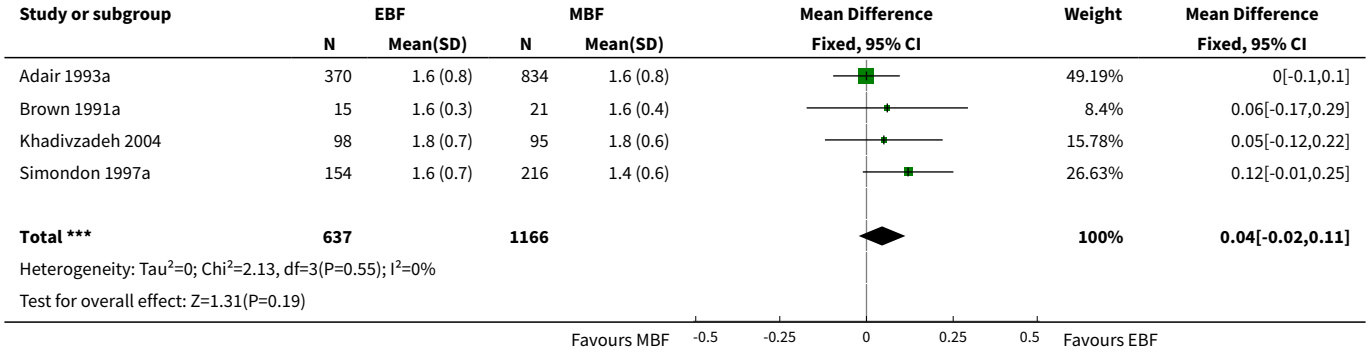




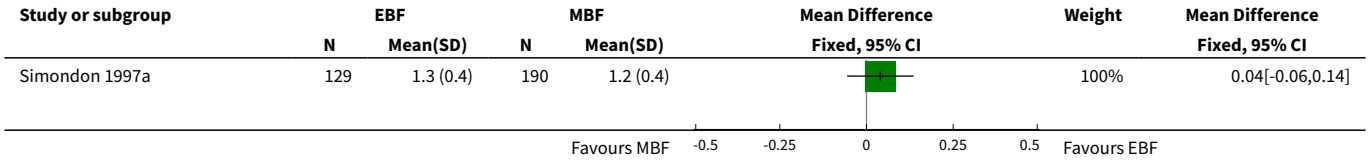
Analysis 2.2. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 2 Monthly weight gain 6-9 months (g/mo).

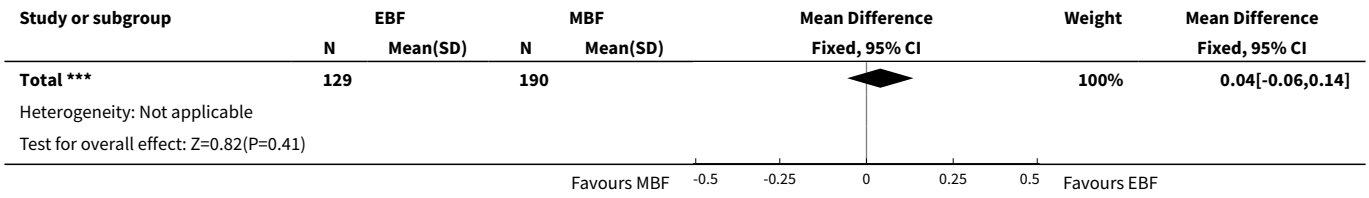


Analysis 2.3. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 3 Monthly length gain 4-6 months (cm/mo).

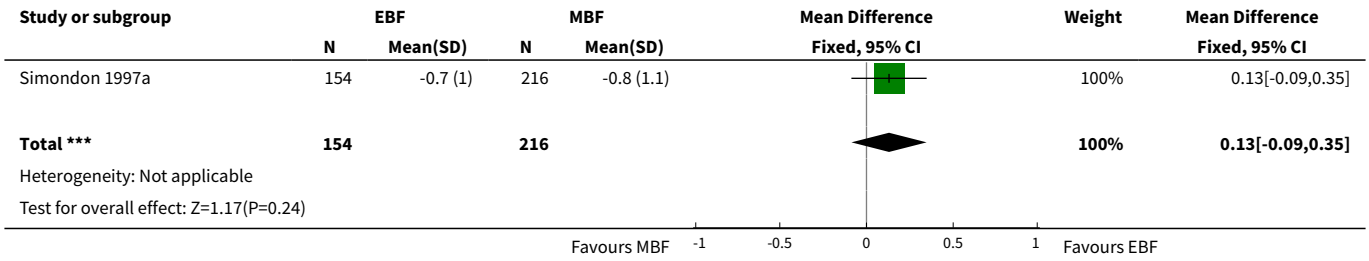


Analysis 2.4. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 4 Monthly length gain 6-9 months (cm/mo).

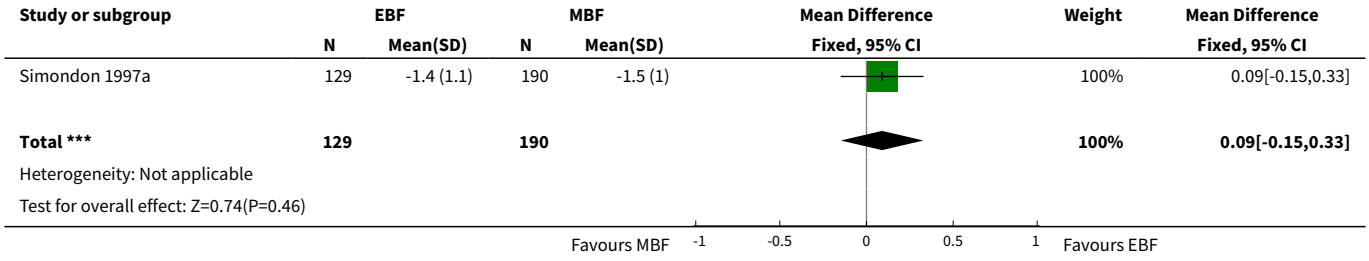




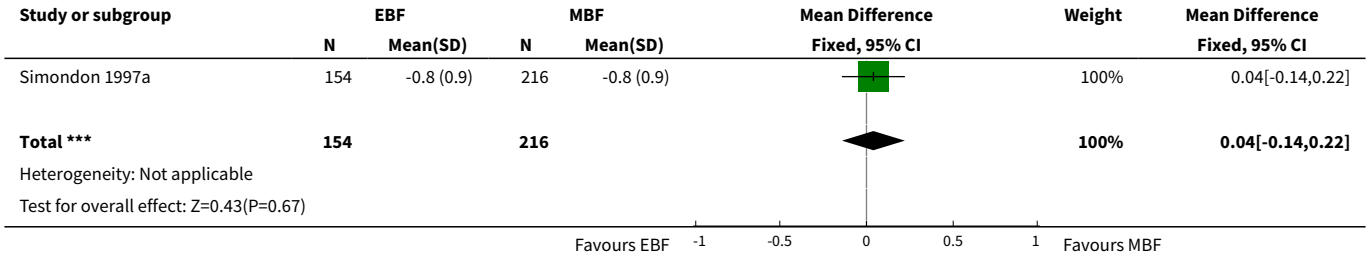
Analysis 2.5. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 5 Weight-for-age z-score at 6-7 months.



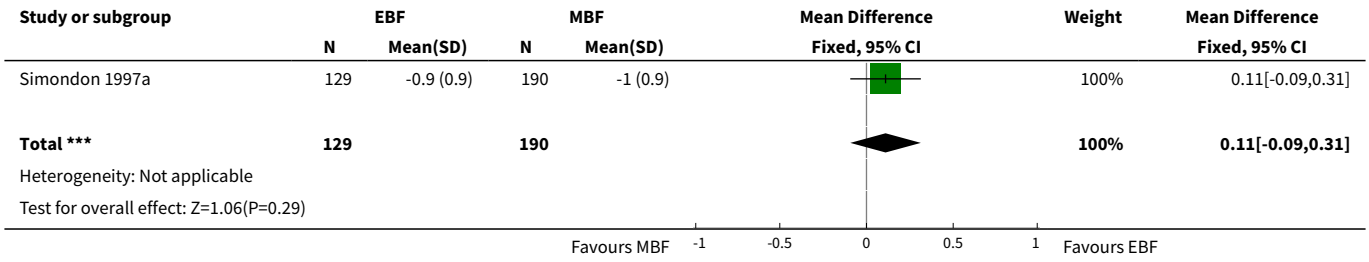
Analysis 2.6. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 6 Weight-for-age z-score at 9-10 months.



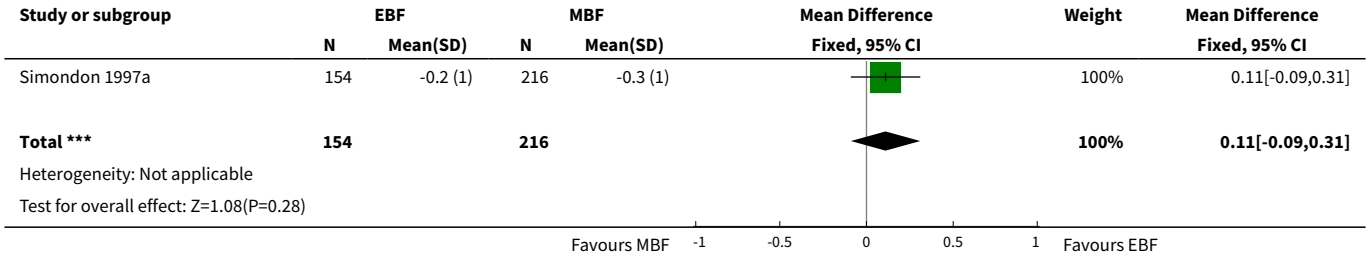
Analysis 2.7. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 7 Length-for-age z-score at 6-7 months.



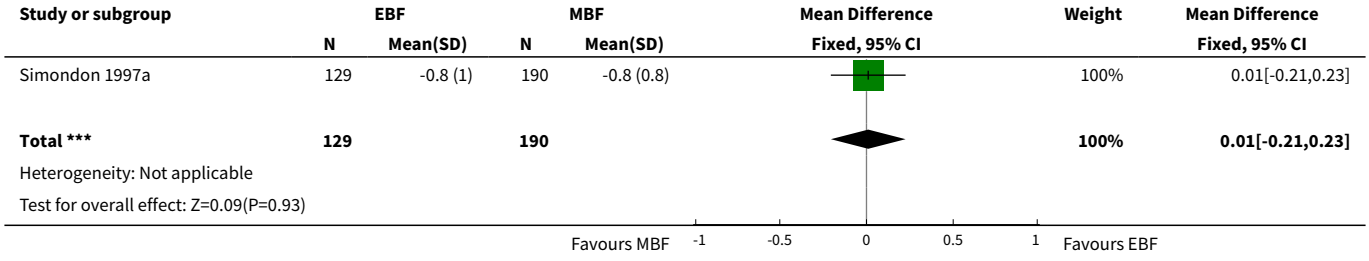
Analysis 2.8. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 8 Length-for-age z-score at 9-10 months.



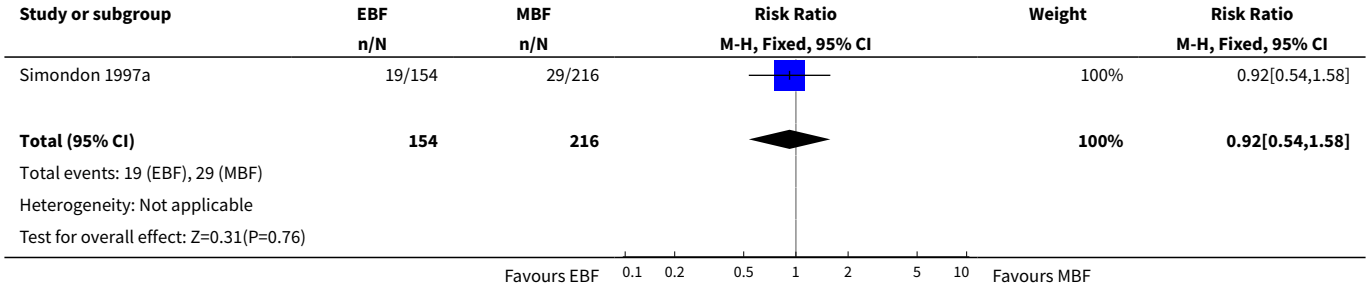
Analysis 2.9. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 9 Weight-for-length z-score at 6-7 months.



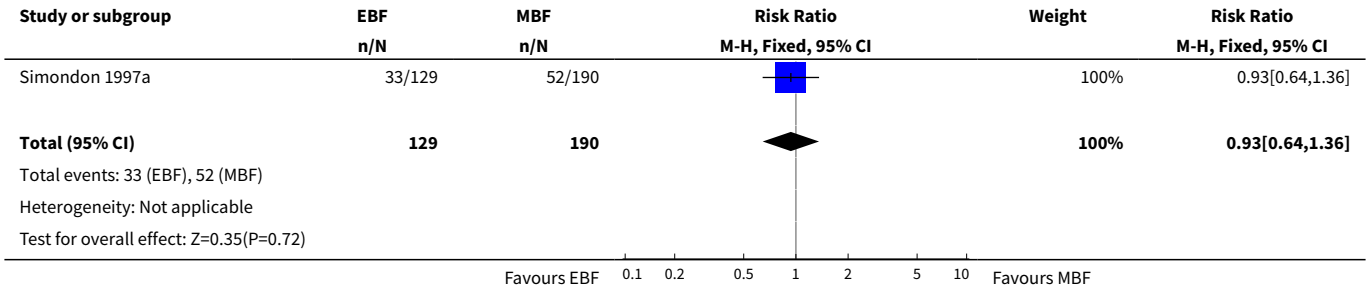
Analysis 2.10. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 10 Weight-for-length z-score at 9-10 months.



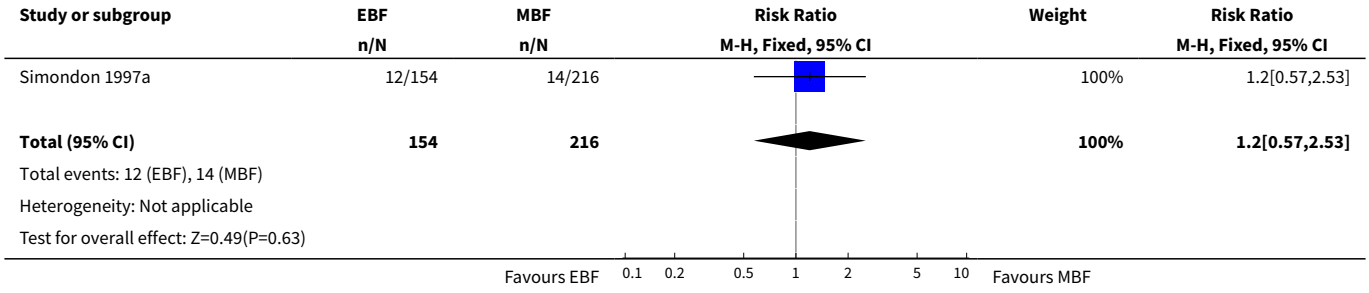
Analysis 2.11. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 11 Weight-for-age z-score < -2 at 6-7 months.



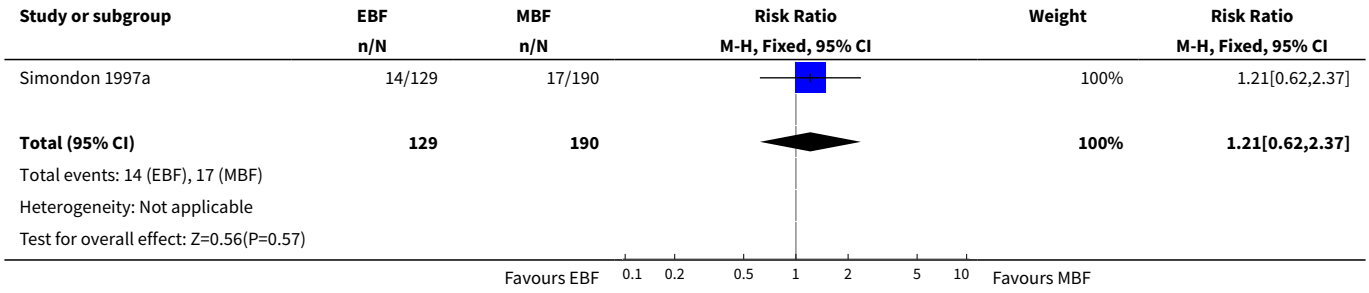
Analysis 2.12. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 12 Weight-for-age z-score < -2 at 9-10 months.



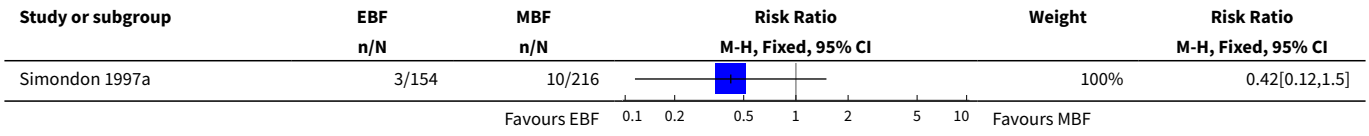
Analysis 2.13. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 13 Length-for-age z-score < -2 at 6-7 months.

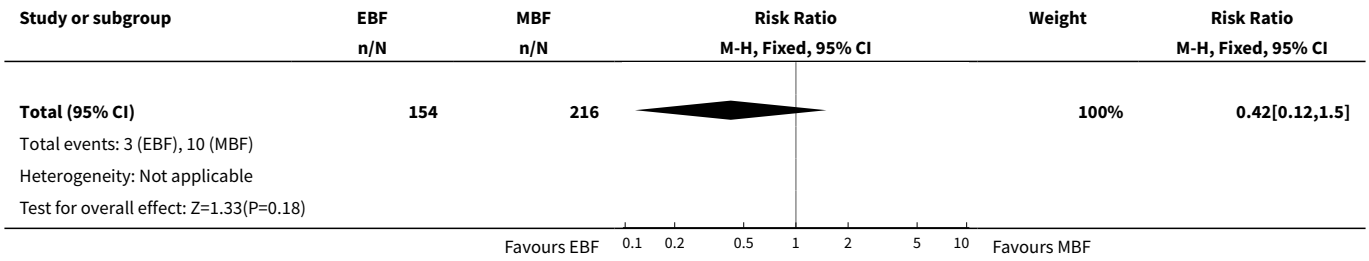


Analysis 2.14. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 14 Length-for-age z-score < -2 at 9-10 months.

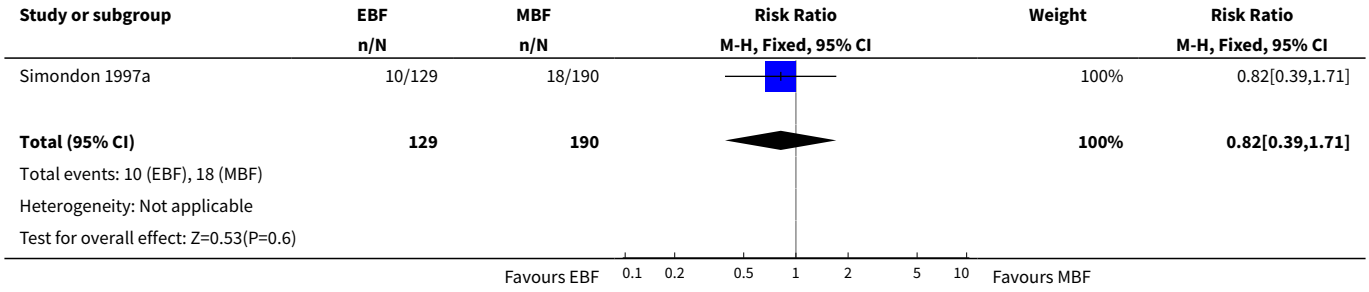


Analysis 2.15. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 15 Weight-for-length z-score < -2 at 6-7 months.

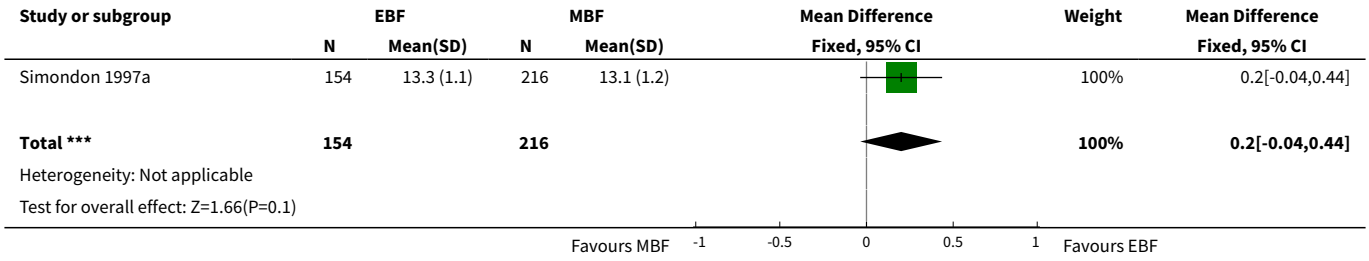




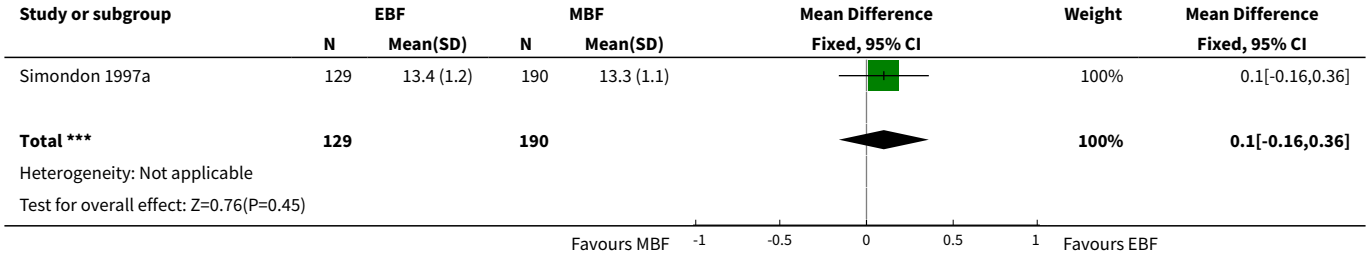
Analysis 2.16. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 16 Weight-for-length z-score < -2 at 9-10 months.



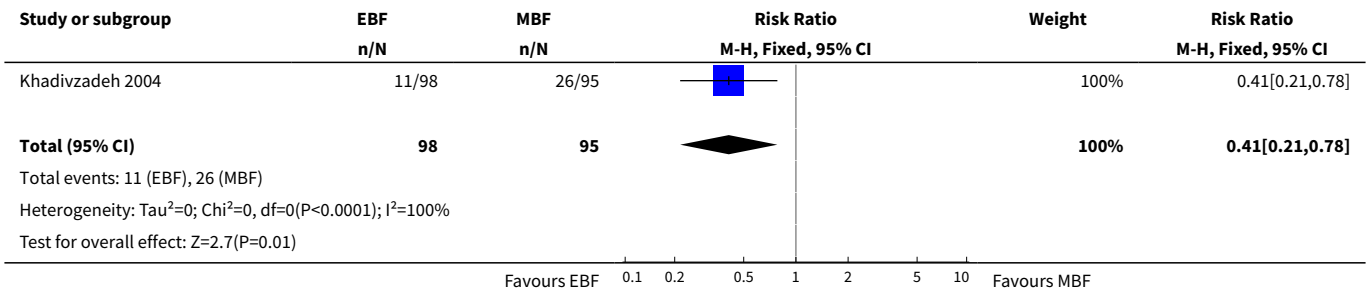
Analysis 2.17. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 17 Mid-upper arm circumference at 6-7 months (cm).



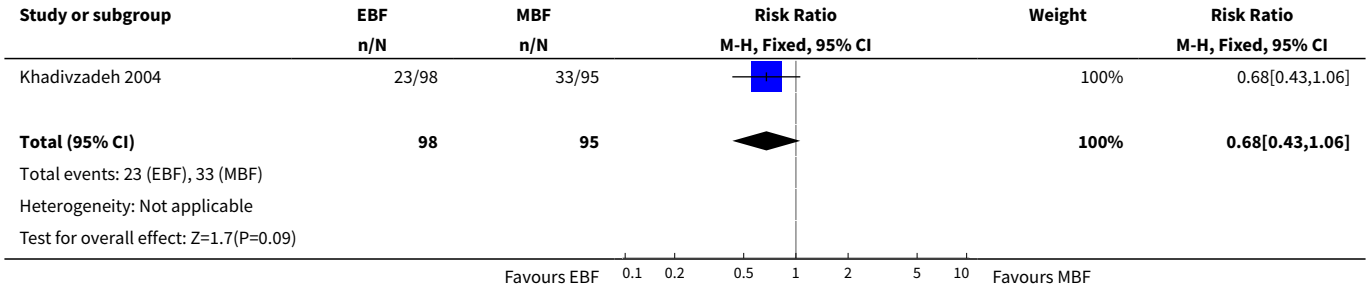
Analysis 2.18. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 18 Mid-upper arm circumference at 9-10 months (cm).



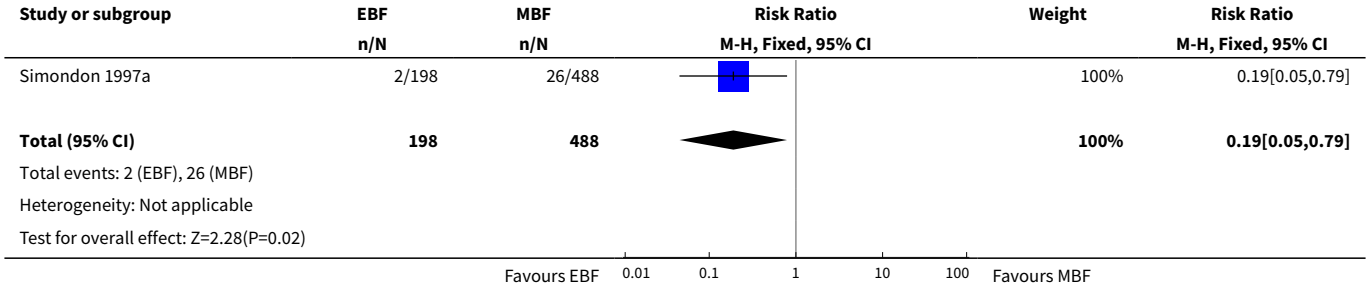
Analysis 2.19. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 19 One or more episodes of gastrointestinal infection at 4-6 months.



Analysis 2.20. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 20 One or more episodes of respiratory infection at 4-6 months.



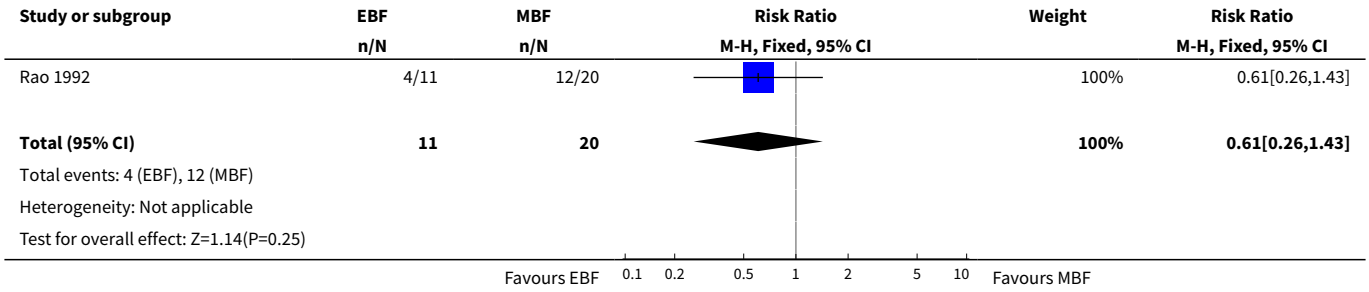
Analysis 2.21. Comparison 2 Exclusive breastfeeding for 6-7 versus 3-4 months, developing countries, observational studies, Outcome 21 Resumption of menses by 6-7 months postpartum.



Comparison 3. Exclusive breastfeeding for > 6 months versus 6 months, developing countries, observational studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight-for-age < 75% of reference mean	1	31	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.26, 1.43]

Analysis 3.1. Comparison 3 Exclusive breastfeeding for > 6 months versus 6 months, developing countries, observational studies, Outcome 1 Weight-for-age < 75% of reference mean.



Comparison 4. Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Monthly weight gain 3-8 months (g/mo)	4	4388	Mean Difference (IV, Random, 95% CI)	-7.95 [-31.84, 15.93]
2 Monthly weight gain 6-9 months (g/mo)	2	3432	Mean Difference (IV, Random, 95% CI)	21.11 [-44.70, 86.91]
3 Monthly weight gain 8-12 months (g/mo)	3	3450	Mean Difference (IV, Fixed, 95% CI)	-1.82 [-16.72, 13.08]
4 Monthly length gain 3-8 months (cm/mo)	4	4385	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.11, 0.06]
5 Monthly length gain 6-9 months (cm/mo)	2	3430	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.10, 0.01]
6 Monthly length gain 8-12 months (cm/mo)	3	3448	Mean Difference (IV, Fixed, 95% CI)	0.09 [0.03, 0.14]
7 Weight-for-age z-score at 6 months	1	3455	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.16, -0.02]
8 Weight-for-age z-score at 9 months	1	3400	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.18, -0.02]
9 Weight-for-age z-score at 12 months	1	3458	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.17, -0.01]
10 Length-for-age z-score at 6 months	1	3454	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.20, -0.04]
11 Length-for-age z-score at 9 months	1	3398	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.22, -0.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12 Length-for-age z-score at 12 months	1	3458	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.10, 0.06]
13 Weight-for-length z-score at 6 months	1	3454	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.07, 0.11]
14 Weight-for-length z-score at 9 months	1	3398	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.06, 0.12]
15 Weight-for-length z-score at 12 months	1	3458	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.17, 0.01]
16 Weight-for-age z-score < -2 at 6 months	1	3461	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.04, 19.04]
17 Weight-for-age z-score < -2 at 9 months	1	3408	Risk Ratio (M-H, Fixed, 95% CI)	1.52 [0.16, 14.62]
18 Weight-for-age z-score < -2 at 12 months	1	3466	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.13, 10.31]
19 Length-for-age z-score < -2 at 6 months	1	3460	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [0.84, 2.78]
20 Length-for-age z-score < -2 at 9 months	1	3406	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [0.80, 2.64]
21 Length-for-age z-score < -2 at 12 months	1	3466	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.23, 1.87]
22 Weight-for-length z-score < -2 at 6 months	1	3460	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.02, 5.34]
23 Weight-for-length z-score < -2 at 9 months	1	3406	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.24, 5.37]
24 Weight-for-length z-score < -2 at 12 months	1	3466	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.13, 10.31]
25 Head circumference at 6 months (cm)	1	3440	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.23, 0.03]
26 Head circumference at 9 months (cm)	1	3389	Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.06, 0.20]
27 Head circumference at 12 months (cm)	1	3450	Mean Difference (IV, Fixed, 95% CI)	0.19 [0.06, 0.32]
28 Sleeping time at 9 months (min/day)	1	50	Mean Difference (IV, Fixed, 95% CI)	1.0 [-36.65, 38.65]
29 Total essential amino acid concentration (umol/L) at 6 months	1	44	Mean Difference (IV, Fixed, 95% CI)	22.0 [-59.60, 103.60]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
30 Total amino acid concentration (umol/L) at 6 months	1	44	Mean Difference (IV, Fixed, 95% CI)	73.0 [-118.22, 264.22]
31 Atopic eczema in first 12 months	2	3618	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.27, 1.59]
32 Food allergy at 1 year (by history)	1	135	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.08, 0.48]
33 Food allergy at 1 year (by double challenge)	1	135	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.25, 2.41]
34 Two or more episodes of wheezing in first 12 months	2	3993	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.49, 1.28]
35 Hemoglobin concentration (g/L) at 12 months	1	30	Mean Difference (IV, Fixed, 95% CI)	8.0 [4.03, 11.97]
36 Hemoglobin concentration < 110 g/L at 12 months	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.01, 1.80]
37 Serum ferritin concentration (mcg/L) at 12 months	1	30	Mean Difference (IV, Fixed, 95% CI)	4.70 [-6.30, 15.70]
38 Serum ferritin concentration < 10 mcg/L at 12 months	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.12, 1.54]
39 One or more episodes of gastrointestinal infection in first 12 months	1	3483	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.46, 0.97]
40 Hospitalization for gastrointestinal infection in first 12 months	1	3483	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.42, 1.49]
41 One or more episodes of upper respiratory tract infection in first 12 months	1	510	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.96, 1.20]
42 Two or more episodes of upper respiratory tract infection in first 12 months	2	3993	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.82, 1.02]
43 Four or more episodes of upper respiratory tract infection in first 12 months	1	510	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.52, 1.29]
44 One or more episodes of lower respiratory tract infection in first 12 months	1	510	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.86, 1.33]
45 Two or more episodes of respiratory tract infection (upper or lower) in first 12 months	1	3483	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.79, 1.03]
46 Hospitalization for respiratory tract infection in first 12 months	2	3993	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.94]

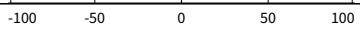
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
47 Number of episodes of otitis media in first 12 months	1	279	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.49, 0.41]
48 One or more episodes of otitis media in first 12 months	2	3762	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [1.04, 1.57]
49 Frequent otitis media in first 12 months	1	279	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.43, 1.52]
50 Death in first 12 months	1	3483	Risk Ratio (M-H, Fixed, 95% CI)	2.30 [0.21, 25.37]
51 Any dental caries (decayed, missing, or filled teeth) at 6 years	1	2948	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.94, 1.03]
52 Any incisor caries (decayed, missing, or filled teeth) at 6 years	1	2948	Odds Ratio (M-H, Fixed, 95% CI)	0.91 [0.72, 1.16]
53 Height at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.40, 0.60]
54 Leg length at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.14, 0.54]
55 Head circumference at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.04, 0.24]
56 BMI at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.20 [0.02, 0.38]
57 Triceps skinfold thickness at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.90 [0.51, 1.29]
58 Subscapular skinfold thickness	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.5 [0.25, 0.75]
59 Waist circumference at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.42, 0.42]
60 Hip circumference at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	0.5 [0.05, 0.95]
61 Systolic blood pressure at 6.5 years	1	2951	Mean Difference (IV, Fixed, 95% CI)	1.30 [0.39, 2.21]
62 Diastolic blood pressure at 6.5 years (mm Hg)	1	2951	Mean Difference (IV, Fixed, 95% CI)	1.0 [0.29, 1.71]
63 Atopic eczema at 5-7 years	2	3584	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.47, 1.58]
64 Hay fever at 5-7 years	2	3584	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.39, 1.65]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
65 Asthma at 5-7 years	3	4023	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.72, 1.44]
66 Food allergy at 5 years	1	113	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.12, 3.19]
67 Allergy to animal dander at 5 years	1	113	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.24, 2.72]
68 Positive skin-prick test to house dust mite at 6.5 years	1	2320	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.62, 1.20]
69 Positive skin-prick test to cat dander at 6.5 years	1	2320	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.60, 1.24]
70 Positive skin-prick test to birch pollen at 6.5 years	1	2320	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.55, 1.18]
71 Positive skin-prick test to mixed northern grasses at 6.5 years	1	2320	Odds Ratio (M-H, Fixed, 95% CI)	0.71 [0.50, 1.01]
72 Positive skin-prick test to Alternaria at 6.5 years	1	2320	Odds Ratio (M-H, Fixed, 95% CI)	0.74 [0.47, 1.17]
73 Any positive skin-prick test at 6-7 years	2	2651	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.81, 1.11]
74 Wechsler cognitive ability test at 6.5 years: vocabulary	1	2944	Mean Difference (IV, Fixed, 95% CI)	0.5 [-0.57, 1.57]
75 Wechsler cognitive ability test at 6.5 years: similarities	1	2944	Mean Difference (IV, Fixed, 95% CI)	0.30 [-0.56, 1.16]
76 Wechsler cognitive ability test at 6.5 years: matrices	1	2944	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.07, 0.67]
77 Wechsler cognitive ability test at 6.5 years: block designs	1	2944	Mean Difference (IV, Fixed, 95% CI)	1.30 [0.40, 2.20]
78 Wechsler cognitive ability test at 6.5 years: verbal IQ	1	2944	Mean Difference (IV, Fixed, 95% CI)	0.5 [-0.95, 1.95]
79 Wechsler cognitive ability test at 6.5 years: performance IQ	1	2944	Mean Difference (IV, Fixed, 95% CI)	0.80 [-0.55, 2.15]
80 Wechsler cognitive ability test at 6.5 years: full-scale IQ	1	2944	Mean Difference (IV, Fixed, 95% CI)	0.80 [-0.58, 2.18]
81 Teacher's academic rating at 6.5 years: reading	1	2196	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.19, -0.01]
82 Teacher's academic rating at 6.5 years: writing	1	2196	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.20, -0.04]

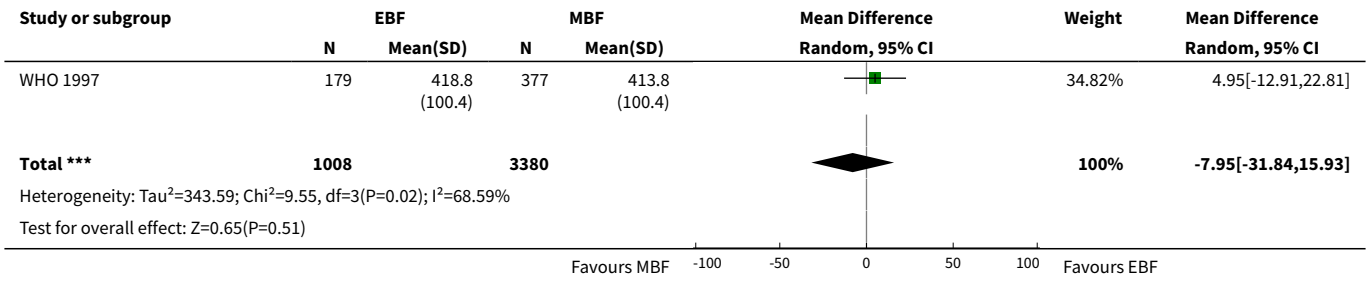
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
83 Teacher's academic rating at 6.5 years: mathematics	1	2196	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.12, 0.04]
84 Teacher's academic rating at 6.5 years: other subjects	1	2196	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.17, -0.03]
85 Parent's behavior rating at 6.5 years: total difficulties	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.30 [-0.16, 0.76]
86 Parent's behavior rating at 6.5 years: emotional symptoms	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.09, 0.29]
87 Parent's behavior rating at 6.5 years: conduct problems	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.13, 0.13]
88 Parent's behavior rating at 6.5 years: hyperactivity/inattention	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.01, 0.41]
89 Parent's behavior rating at 6.5 years: peer problems	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.05, 0.25]
90 Parent's behavior rating at 6.5 years: prosocial behavior	1	2941	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.05, 0.25]
91 Teacher's behavior rating at 6.5 years: total difficulties	1	2525	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.46, 0.66]
92 Teacher's behavior rating at 6.5 years: emotional symptoms	1	2525	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.18, 0.18]
93 Teacher's behavior rating at 6.5 years: conduct problems	1	2525	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.17, 0.17]
94 Teacher's behavior rating at 6.5 years: hyperactivity/inattention	1	2525	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.37, 0.17]
95 Teacher's behavior rating at 6.5 years: peer problems	1	2525	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.08, 0.28]
96 Teacher's behavior rating at 6.5 years: prosocial behavior	1	2525	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.33, 0.13]

Analysis 4.1. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 1 Monthly weight gain 3-8 months (g/mo).

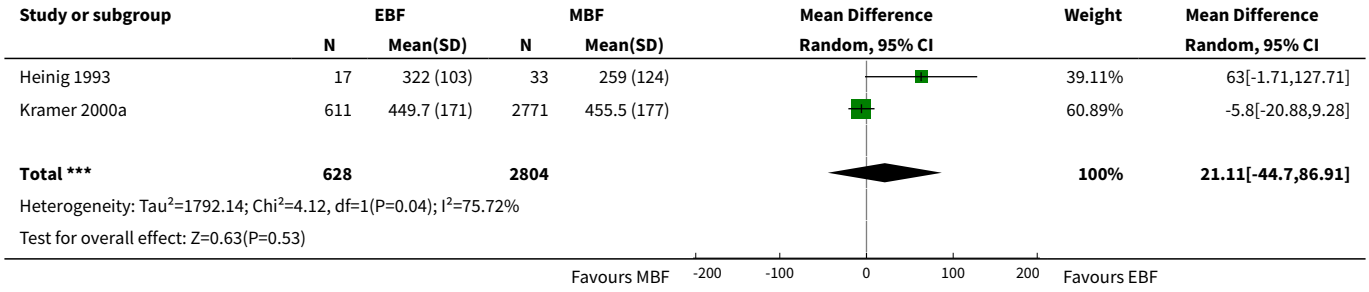
Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Akeson 1996a	10	498 (118)	9	438 (127)		4.21%	60[-50.6,170.6]
Kramer 2000a	619	612.2 (180)	2836	641 (186)		36.4%	-28.8[-44.55,-13.05]
WHO 1994a	200	463 (142)	158	470 (159)		24.58%	-7[-38.65,24.65]



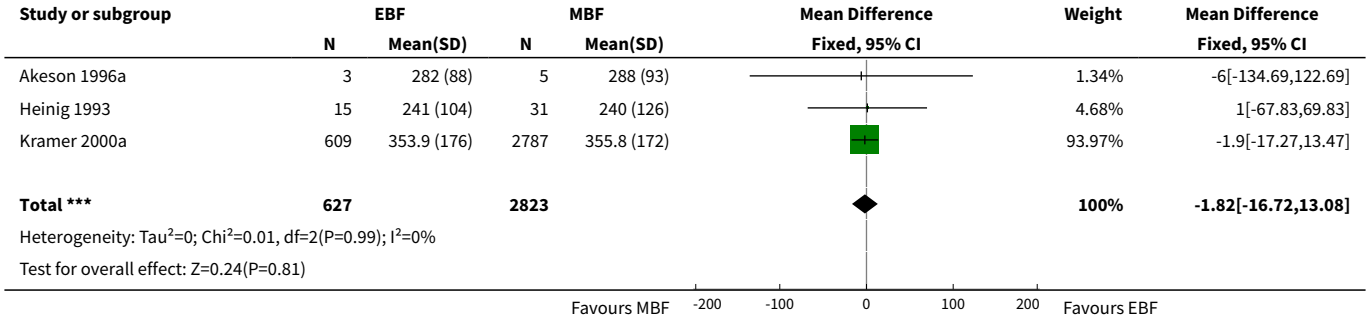
Favours MBF Favours EBF



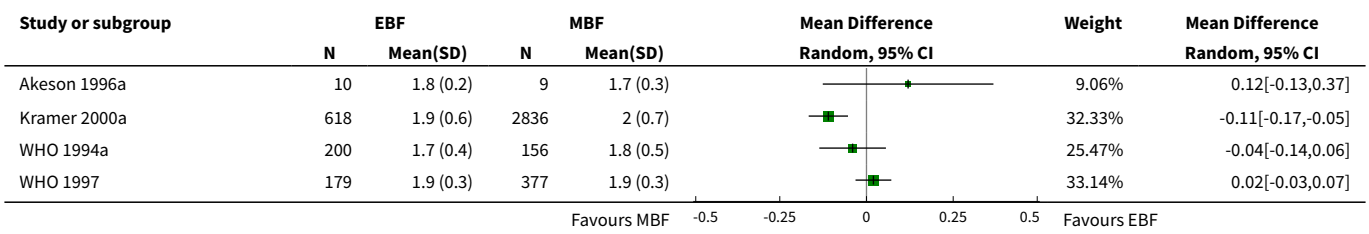
Analysis 4.2. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 2 Monthly weight gain 6-9 months (g/mo).

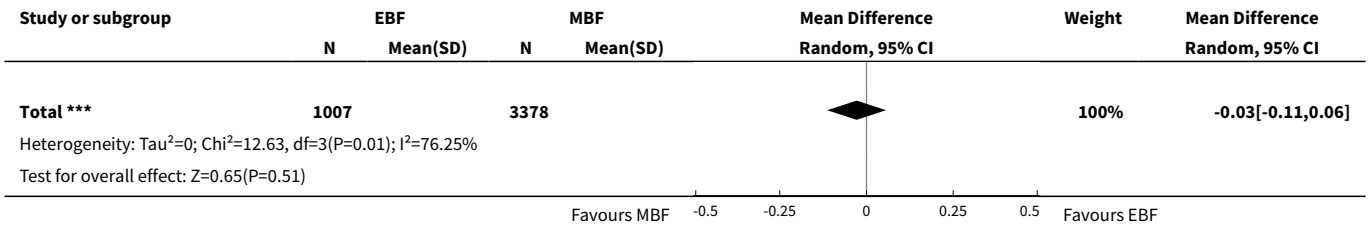


Analysis 4.3. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 3 Monthly weight gain 8-12 months (g/mo).

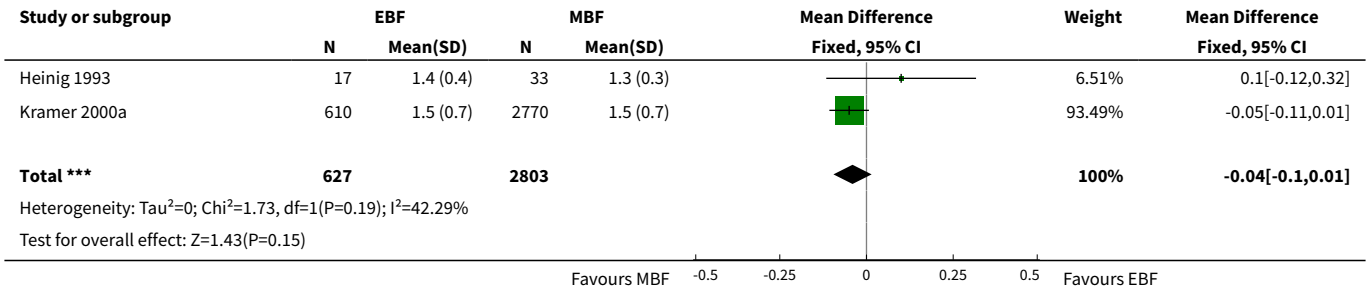


Analysis 4.4. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 4 Monthly length gain 3-8 months (cm/mo).

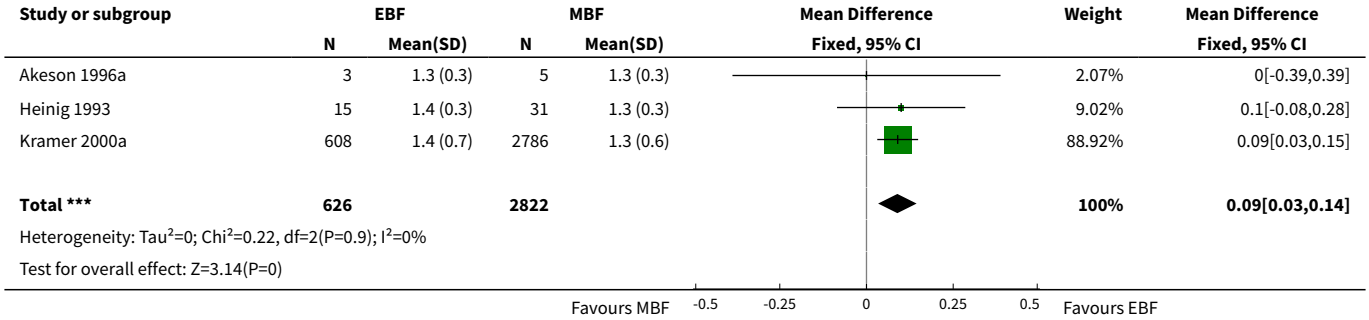




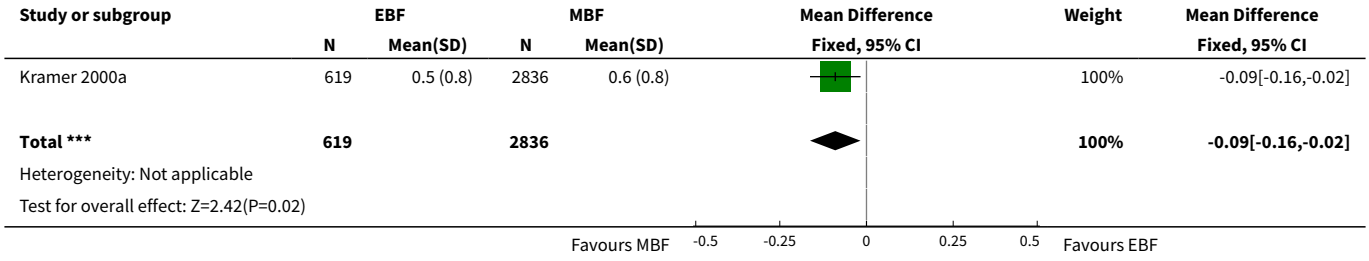
Analysis 4.5. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 5 Monthly length gain 6-9 months (cm/mo).



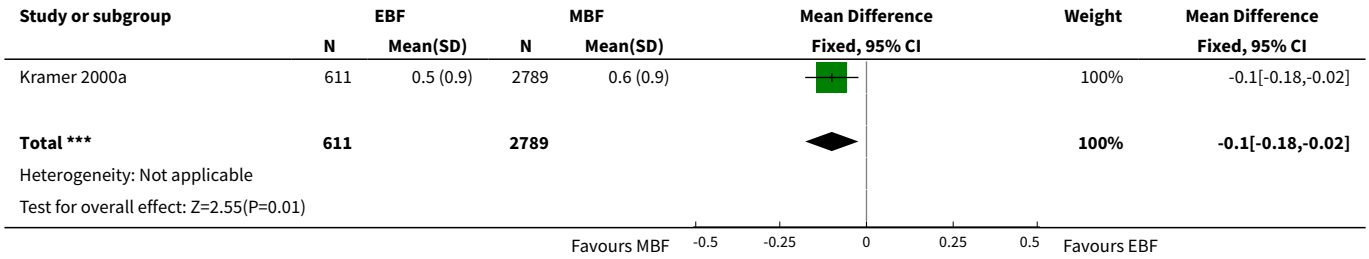
Analysis 4.6. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 6 Monthly length gain 8-12 months (cm/mo).



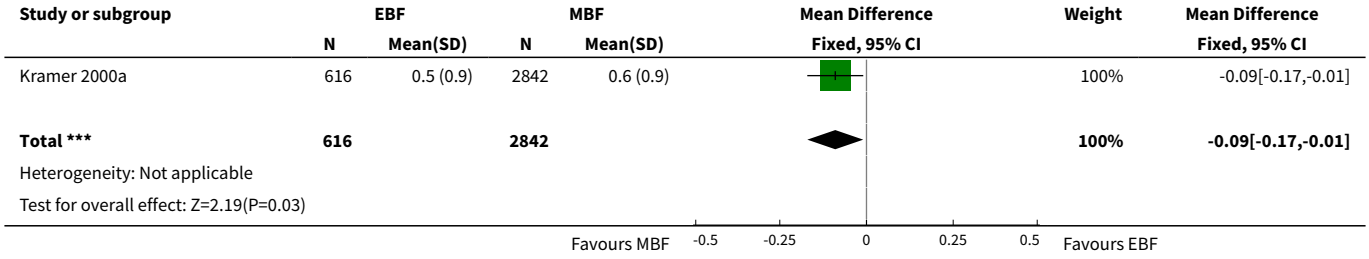
Analysis 4.7. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 7 Weight-for-age z-score at 6 months.



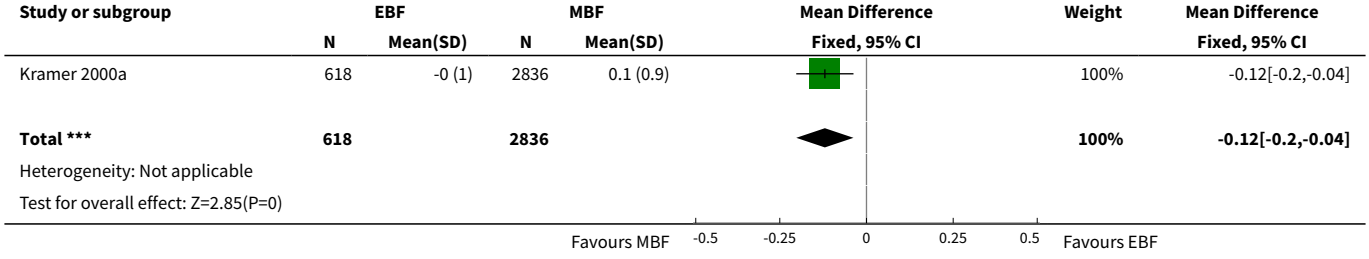
Analysis 4.8. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 8 Weight-for-age z-score at 9 months.



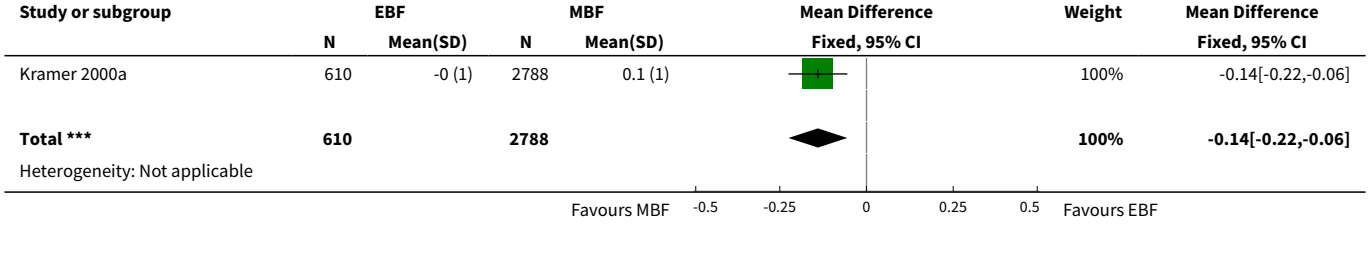
Analysis 4.9. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 9 Weight-for-age z-score at 12 months.

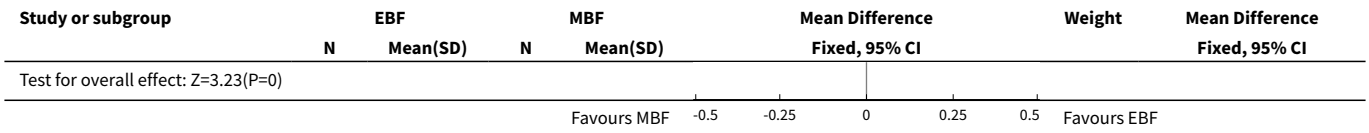


Analysis 4.10. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 10 Length-for-age z-score at 6 months.

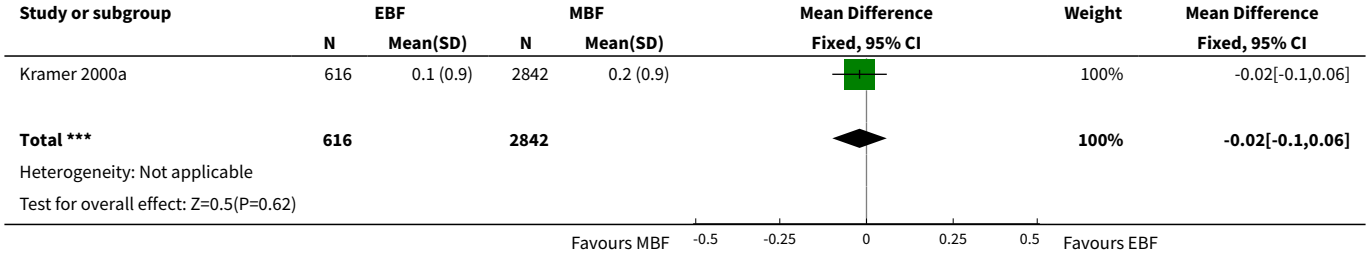


Analysis 4.11. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 11 Length-for-age z-score at 9 months.

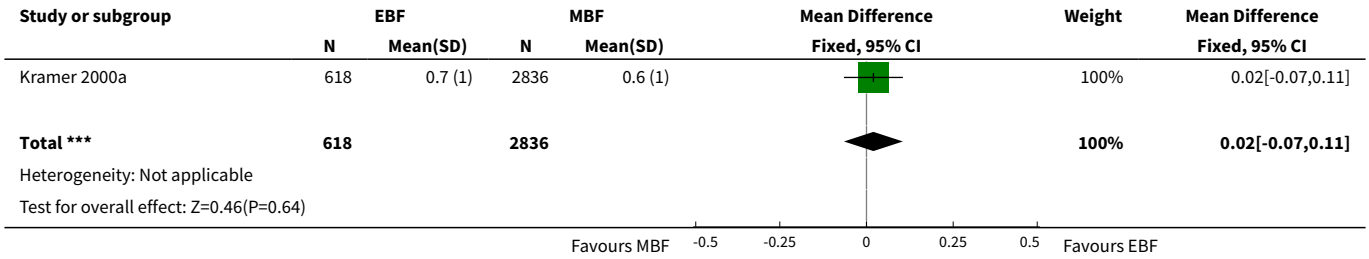




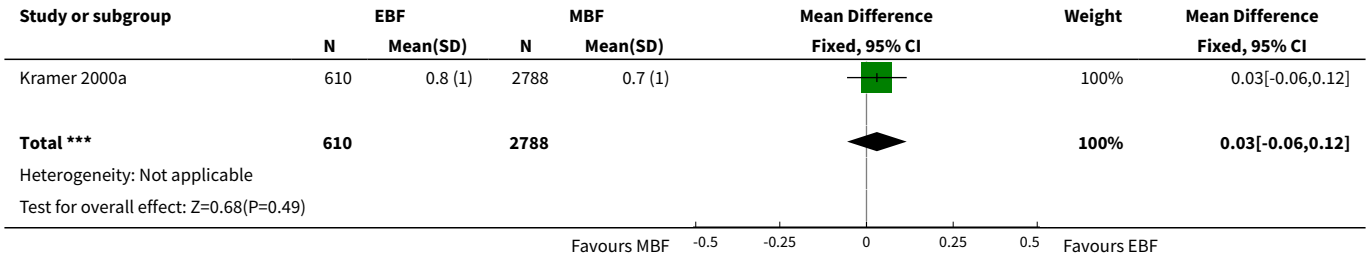
Analysis 4.12. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 12 Length-for-age z-score at 12 months.



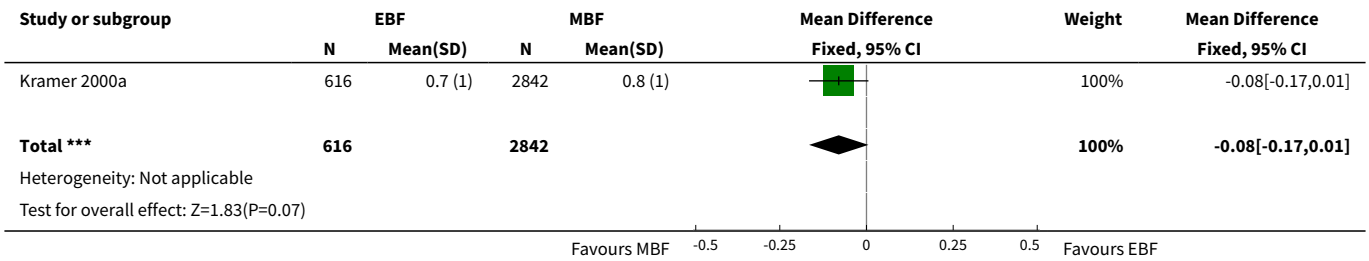
Analysis 4.13. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 13 Weight-for-length z-score at 6 months.



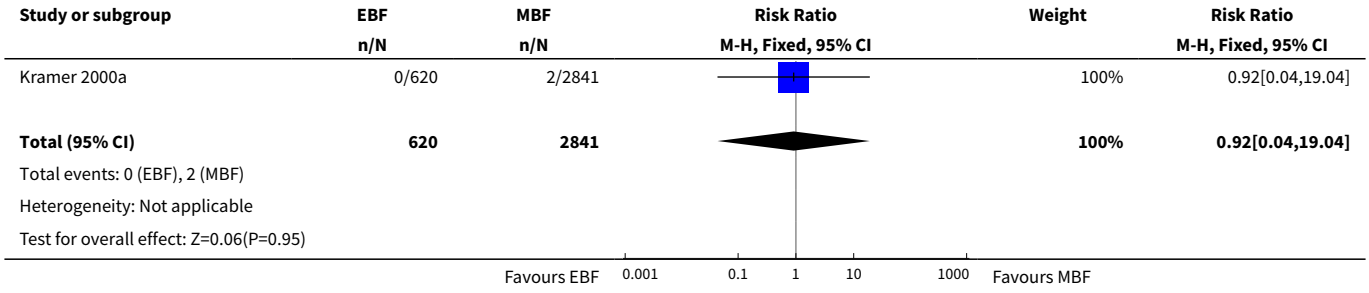
Analysis 4.14. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 14 Weight-for-length z-score at 9 months.



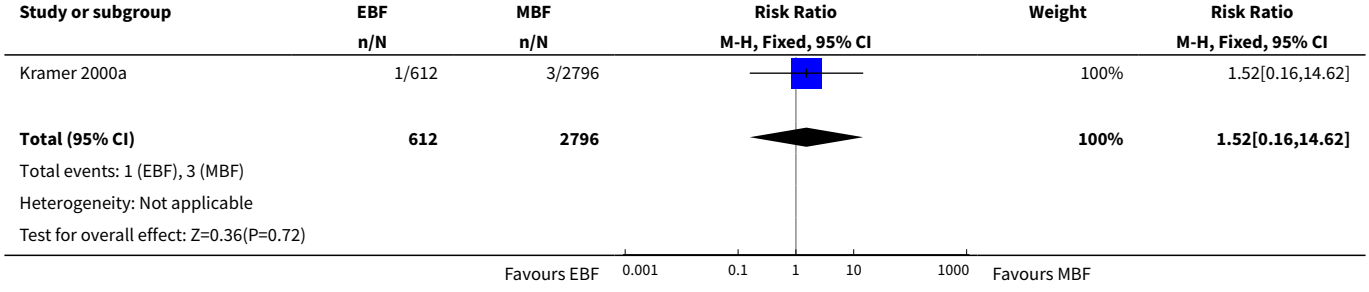
Analysis 4.15. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 15 Weight-for-length z-score at 12 months.



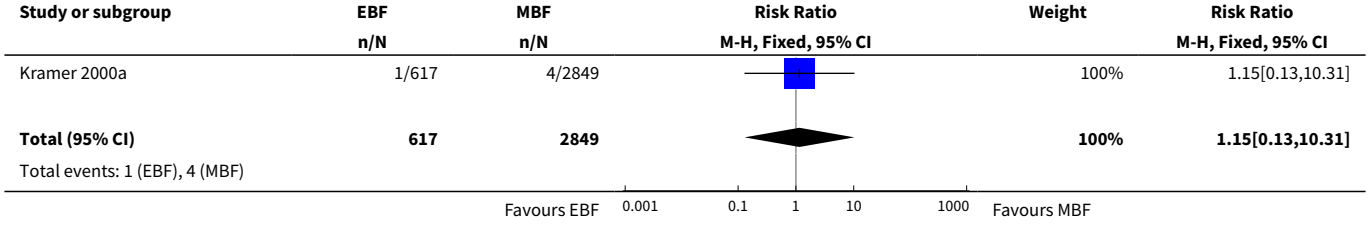
Analysis 4.16. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 16 Weight-for-age z-score < -2 at 6 months.

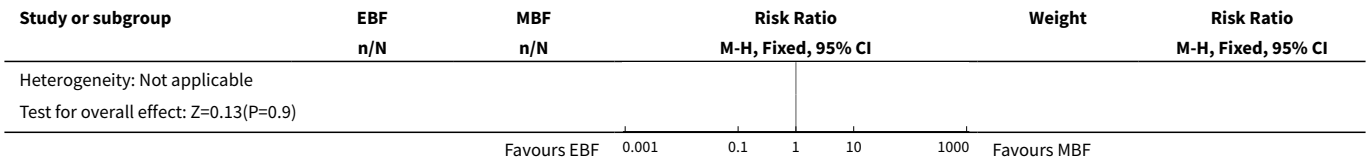


Analysis 4.17. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 17 Weight-for-age z-score < -2 at 9 months.

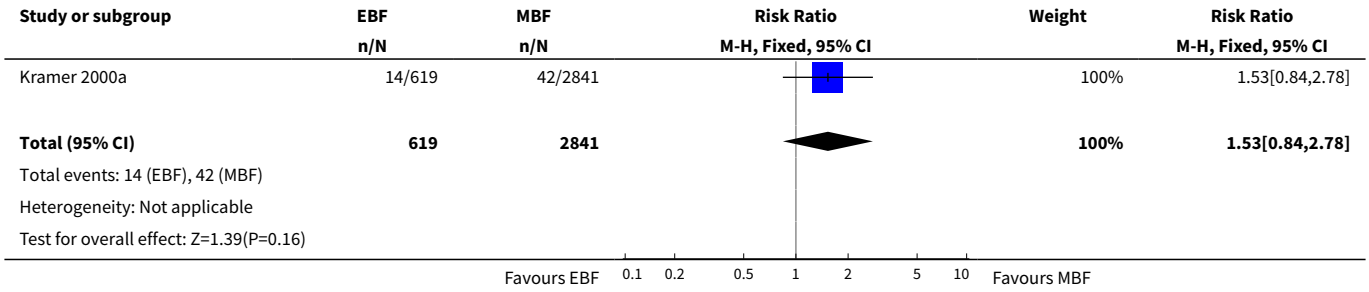


Analysis 4.18. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 18 Weight-for-age z-score < -2 at 12 months.

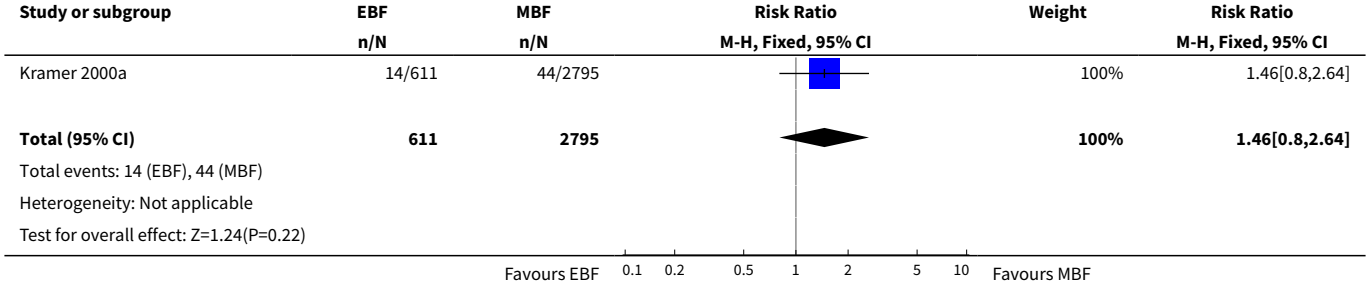




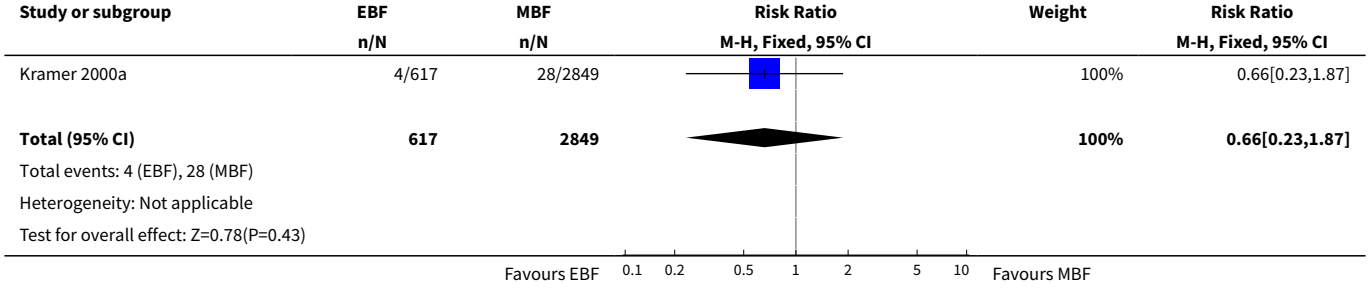
Analysis 4.19. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 19 Length-for-age z-score < -2 at 6 months.



Analysis 4.20. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 20 Length-for-age z-score < -2 at 9 months.

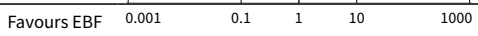


Analysis 4.21. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 21 Length-for-age z-score < -2 at 12 months.



Analysis 4.22. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 22 Weight-for-length z-score < -2 at 6 months.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kramer 2000a	0/619	7/2841		100%	0.31[0.02,5.34]
Total (95% CI)	**619**	**2841**		**100%**	**0.31[0.02,5.34]**
Total events: 0 (EBF), 7 (MBF)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.81(P=0.42)					

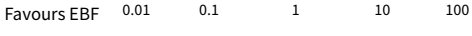


Analysis 4.23. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 23 Weight-for-length z-score < -2 at 9 months.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kramer 2000a	2/611	8/2795		100%	1.14[0.24,5.37]
Total (95% CI)	**611**	**2795**		**100%**	**1.14[0.24,5.37]**
Total events: 2 (EBF), 8 (MBF)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.17(P=0.86)					

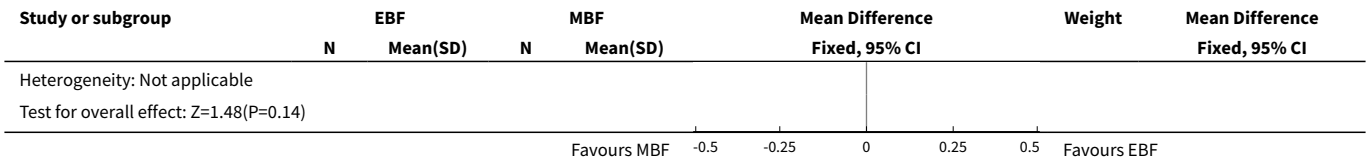
Analysis 4.24. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 24 Weight-for-length z-score < -2 at 12 months.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kramer 2000a	1/617	4/2849		100%	1.15[0.13,10.31]
Total (95% CI)	**617**	**2849**		**100%**	**1.15[0.13,10.31]**
Total events: 1 (EBF), 4 (MBF)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.13(P=0.9)					

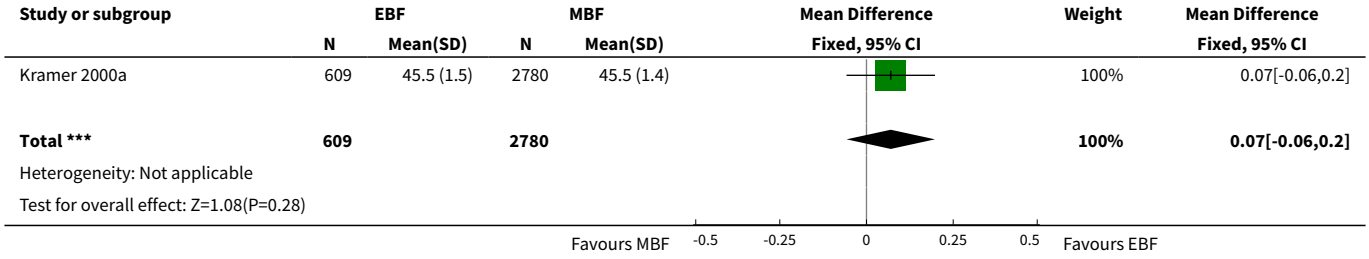


Analysis 4.25. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 25 Head circumference at 6 months (cm).

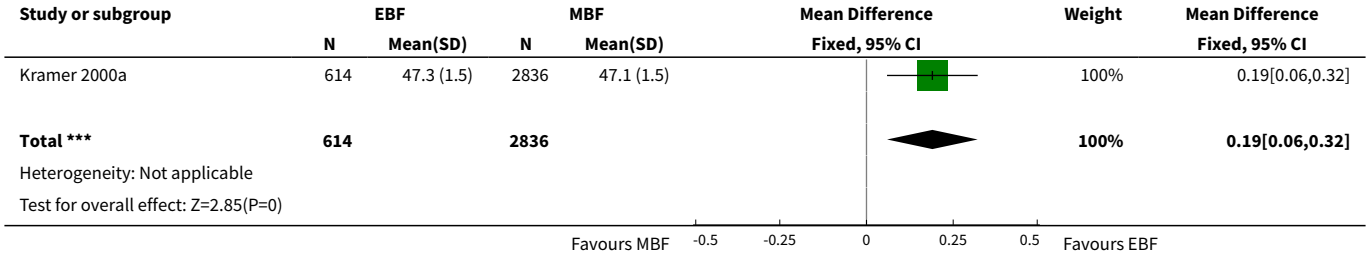
Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	615	43.3 (1.5)	2825	43.4 (1.5)		100%	-0.1[-0.23,0.03]
Total ***	**615**		**2825**			**100%**	**-0.1[-0.23,0.03]**



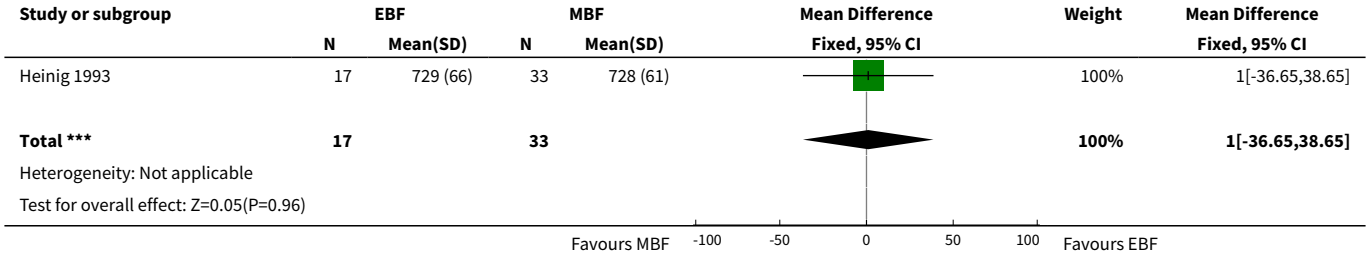
Analysis 4.26. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 26 Head circumference at 9 months (cm).



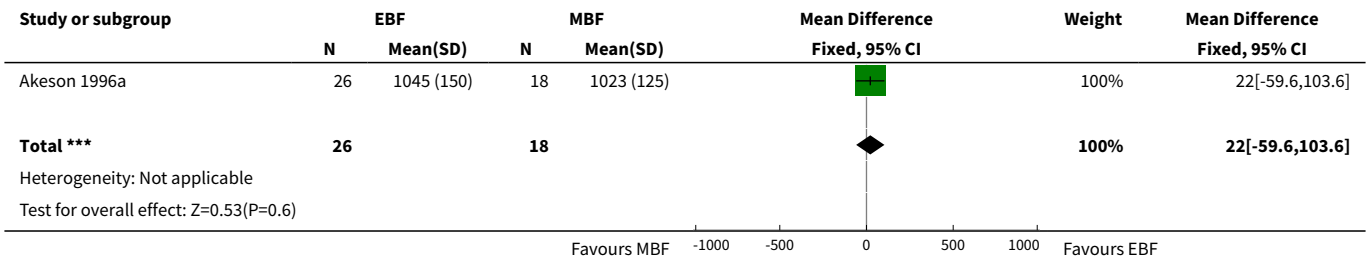
Analysis 4.27. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 27 Head circumference at 12 months (cm).



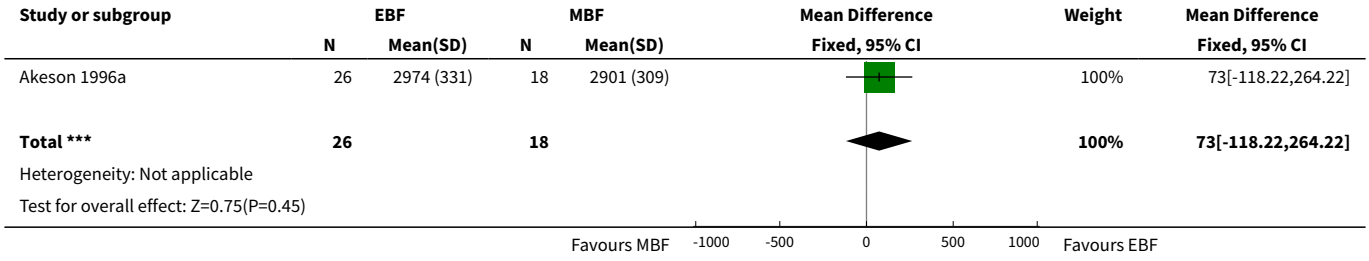
Analysis 4.28. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 28 Sleeping time at 9 months (min/day).



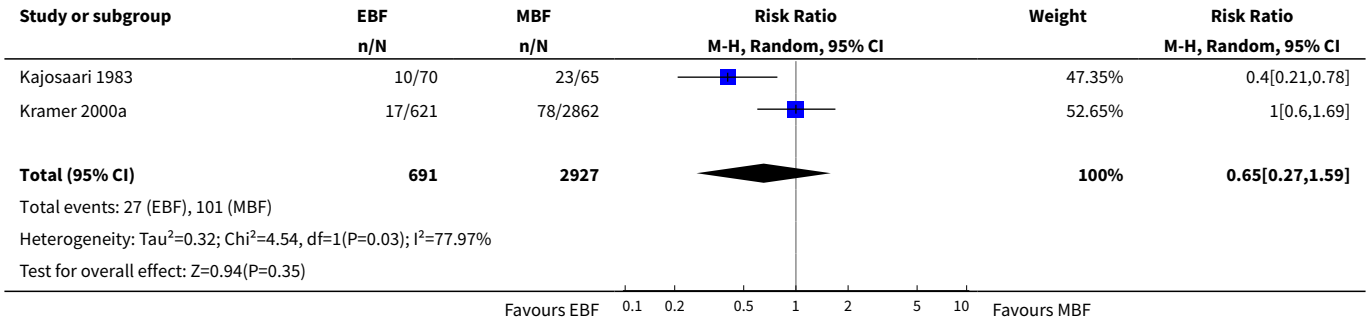
Analysis 4.29. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 29 Total essential amino acid concentration (umol/L) at 6 months.



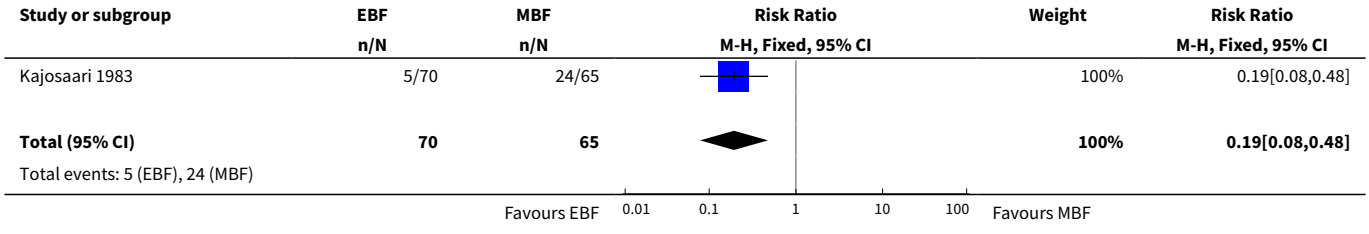
Analysis 4.30. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 30 Total amino acid concentration (umol/L) at 6 months.

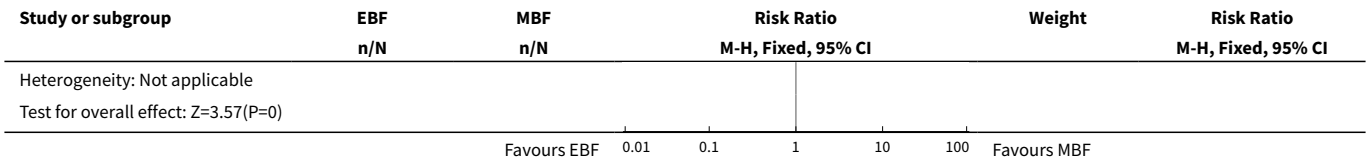


Analysis 4.31. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 31 Atopic eczema in first 12 months.

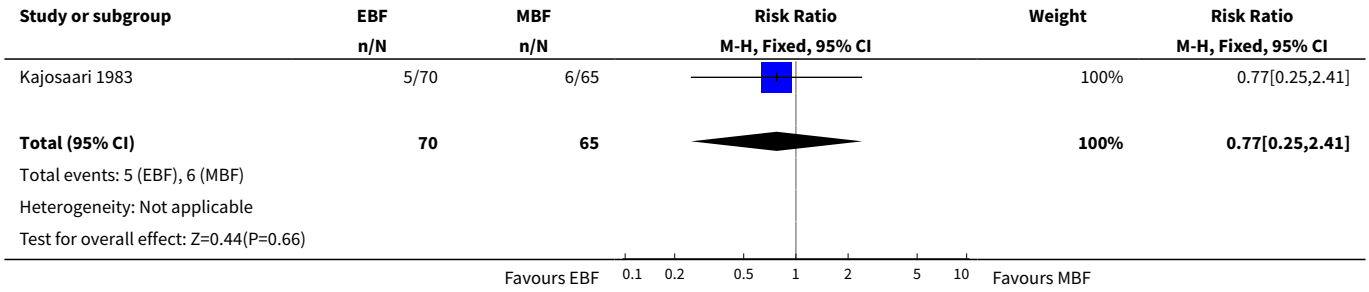


Analysis 4.32. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 32 Food allergy at 1 year (by history).

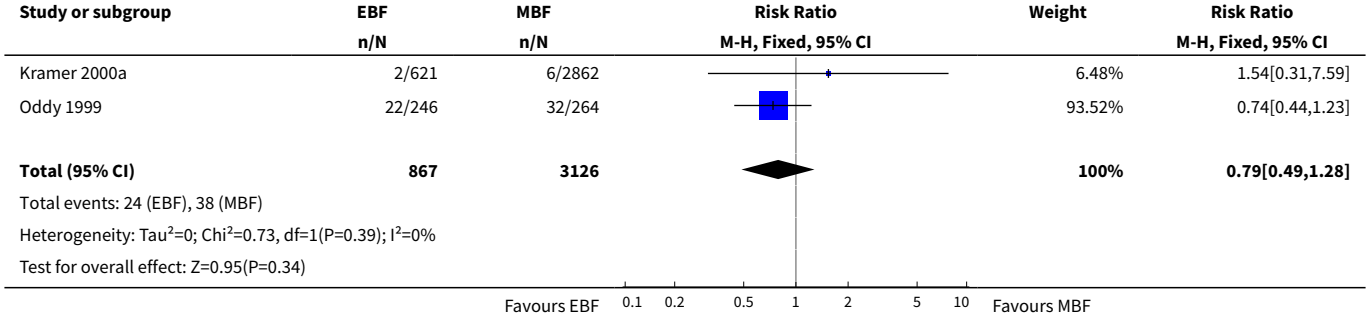




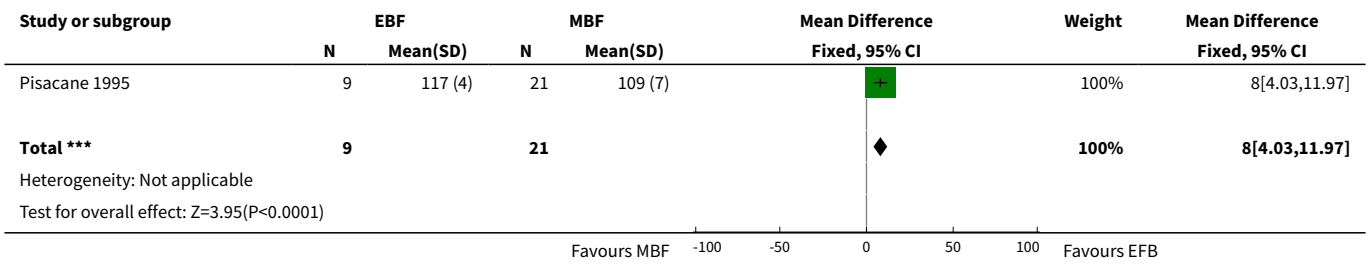
Analysis 4.33. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 33 Food allergy at 1 year (by double challenge).



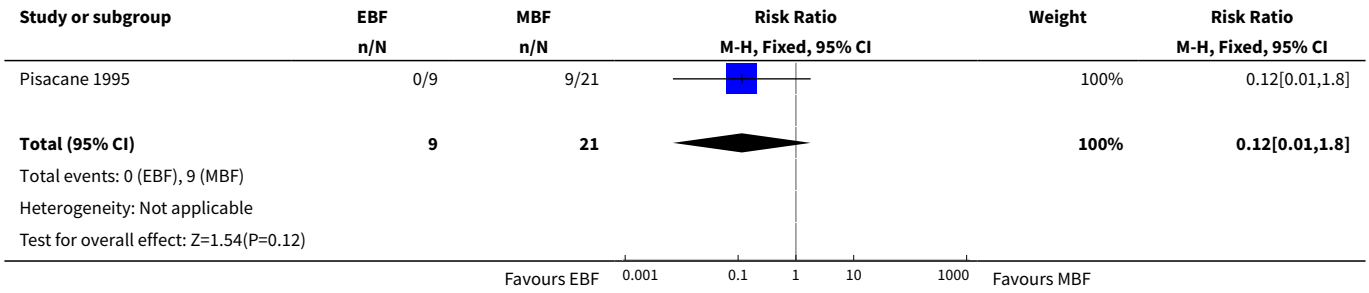
Analysis 4.34. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 34 Two or more episodes of wheezing in first 12 months.



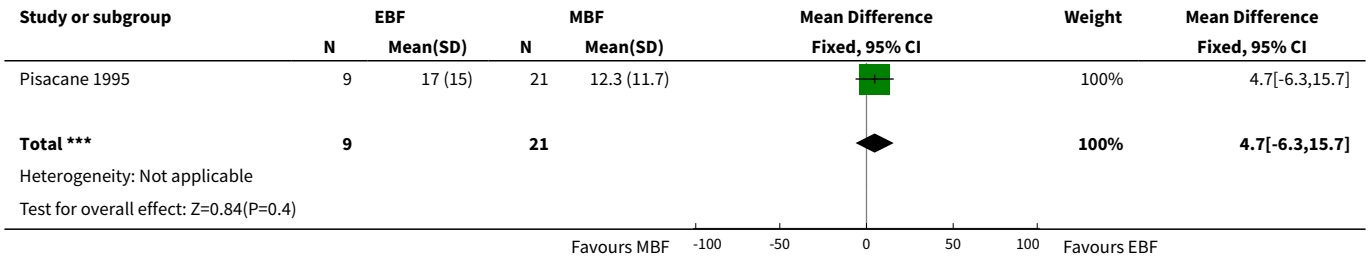
Analysis 4.35. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 35 Hemoglobin concentration (g/L) at 12 months.



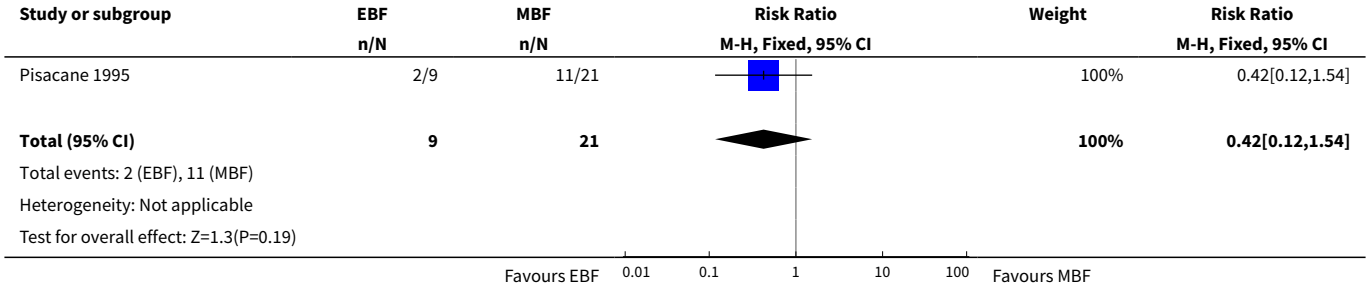
Analysis 4.36. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 36 Hemoglobin concentration < 110 g/L at 12 months.



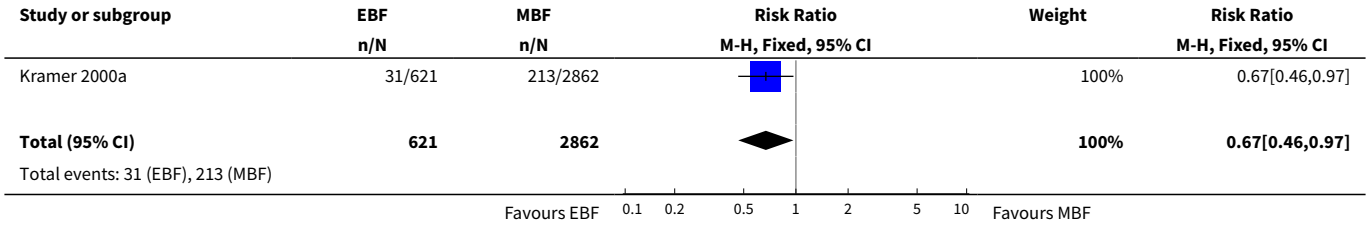
Analysis 4.37. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 37 Serum ferritin concentration (mcg/L) at 12 months.

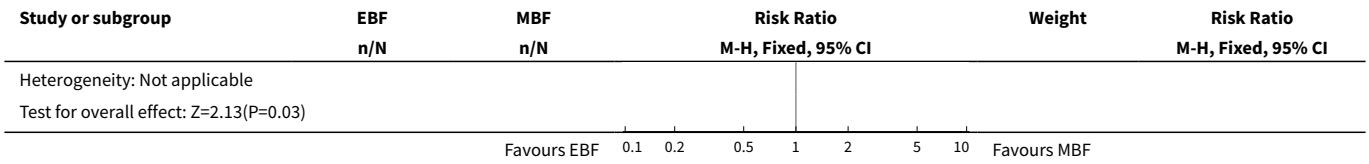


Analysis 4.38. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 38 Serum ferritin concentration < 10 mcg/L at 12 months.

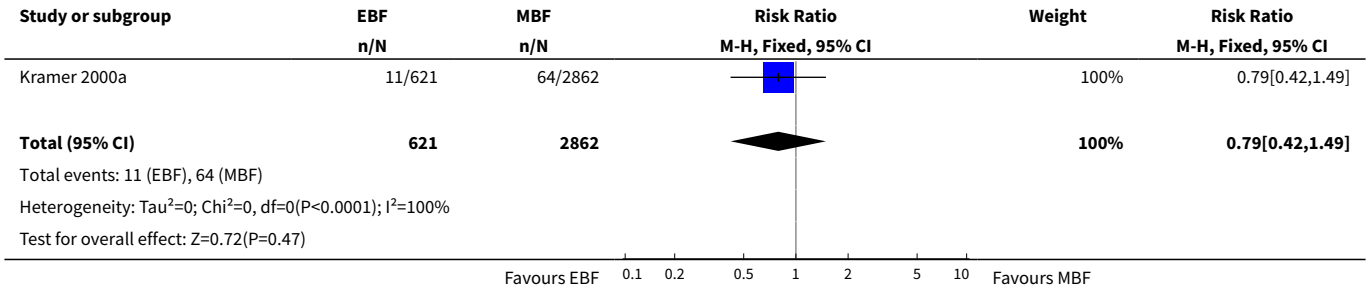


Analysis 4.39. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 39 One or more episodes of gastrointestinal infection in first 12 months.

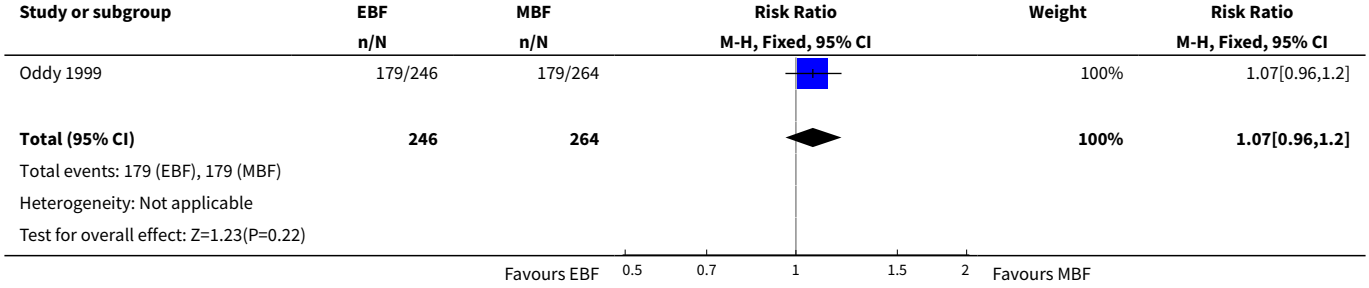




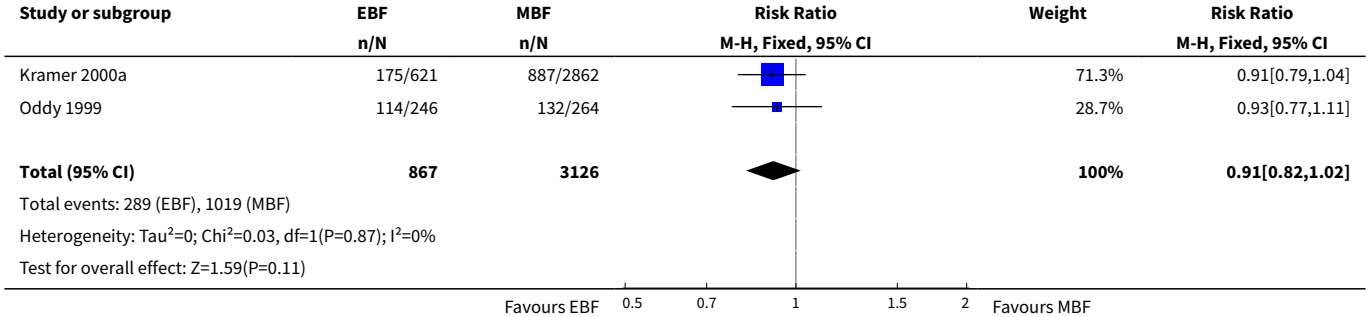
Analysis 4.40. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 40 Hospitalization for gastrointestinal infection in first 12 months.



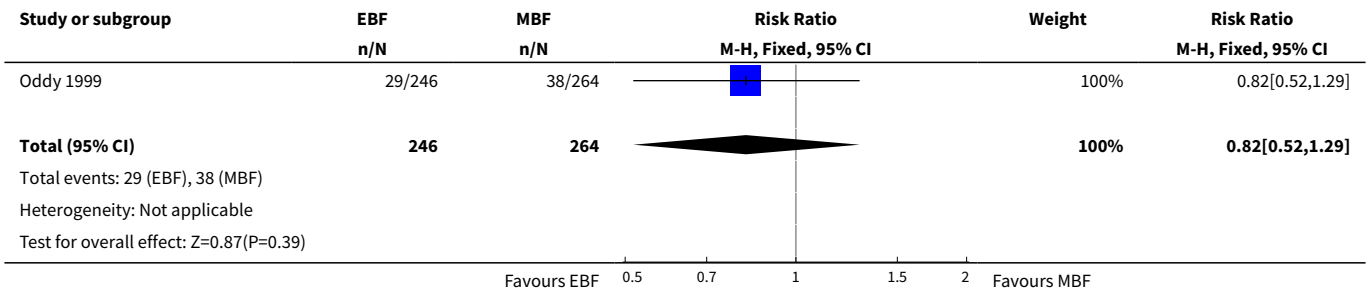
Analysis 4.41. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 41 One or more episodes of upper respiratory tract infection in first 12 months.



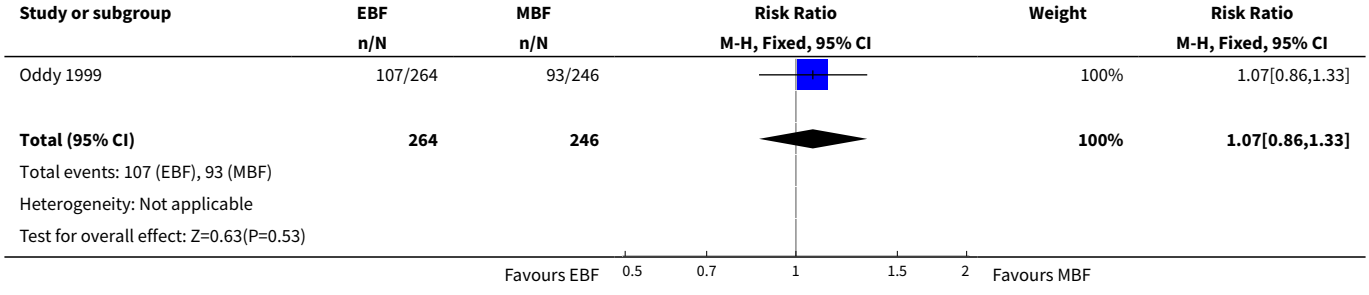
Analysis 4.42. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 42 Two or more episodes of upper respiratory tract infection in first 12 months.



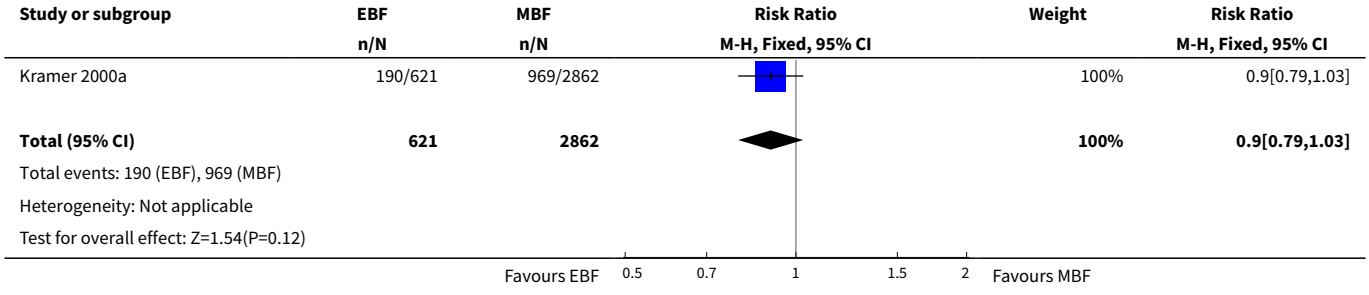
Analysis 4.43. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 43 Four or more episodes of upper respiratory tract infection in first 12 months.



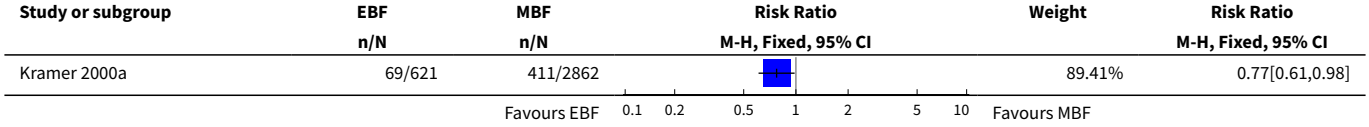
Analysis 4.44. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 44 One or more episodes of lower respiratory tract infection in first 12 months.

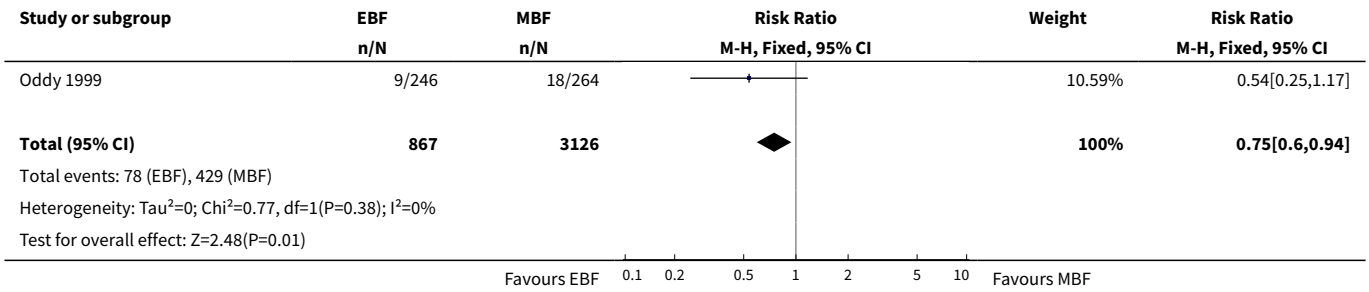


Analysis 4.45. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 45 Two or more episodes of respiratory tract infection (upper or lower) in first 12 months.

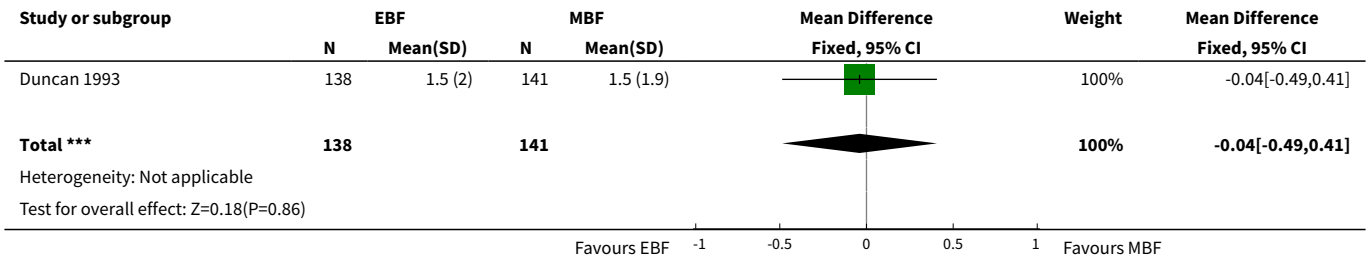


Analysis 4.46. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 46 Hospitalization for respiratory tract infection in first 12 months.

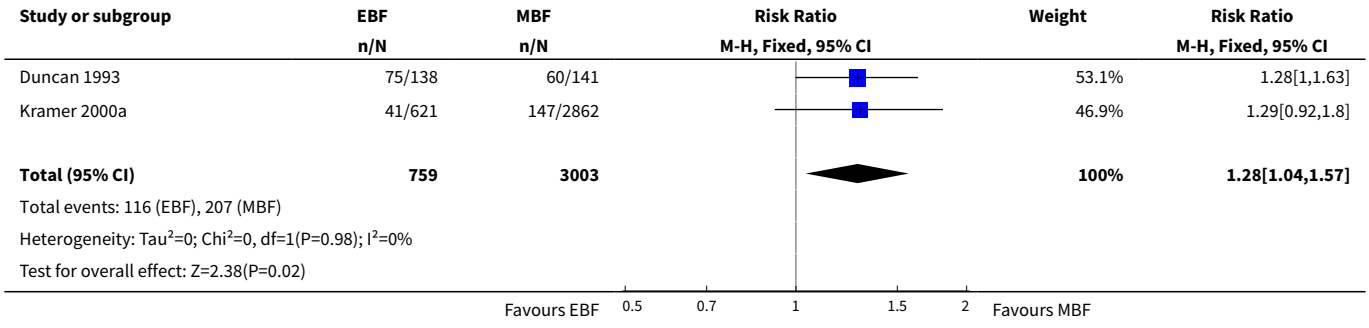




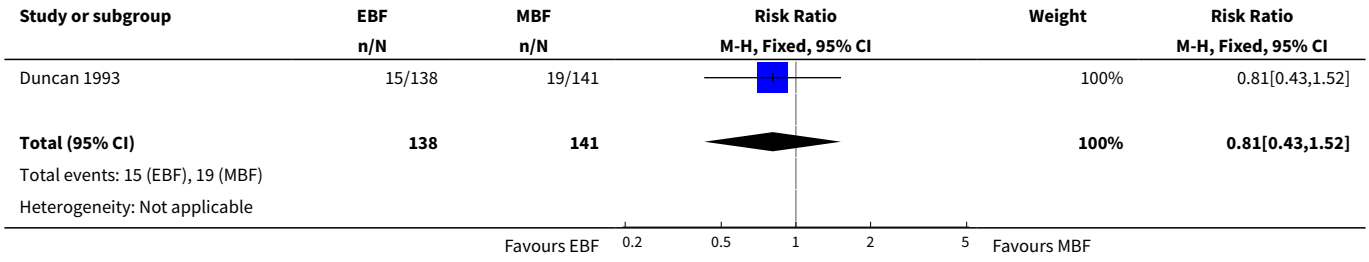
Analysis 4.47. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 47 Number of episodes of otitis media in first 12 months.

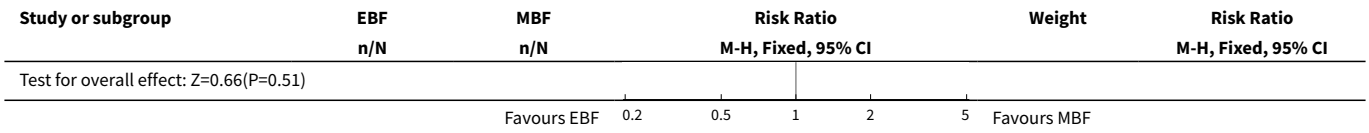


Analysis 4.48. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 48 One or more episodes of otitis media in first 12 months.

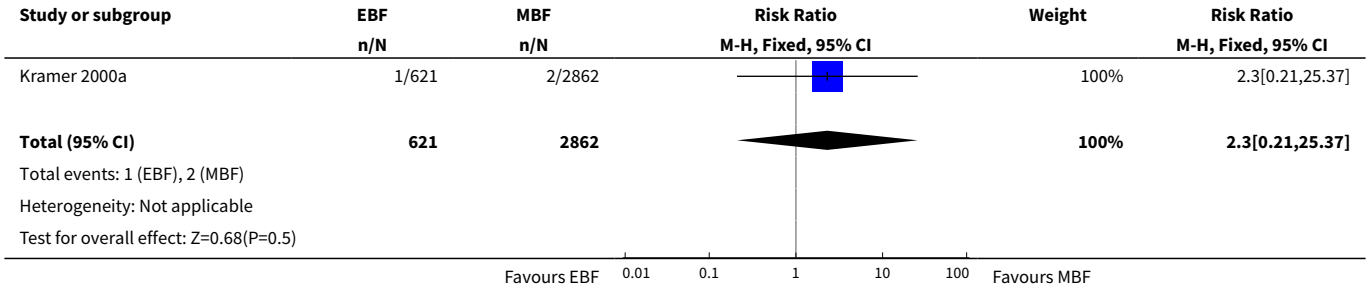


Analysis 4.49. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 49 Frequent otitis media in first 12 months.

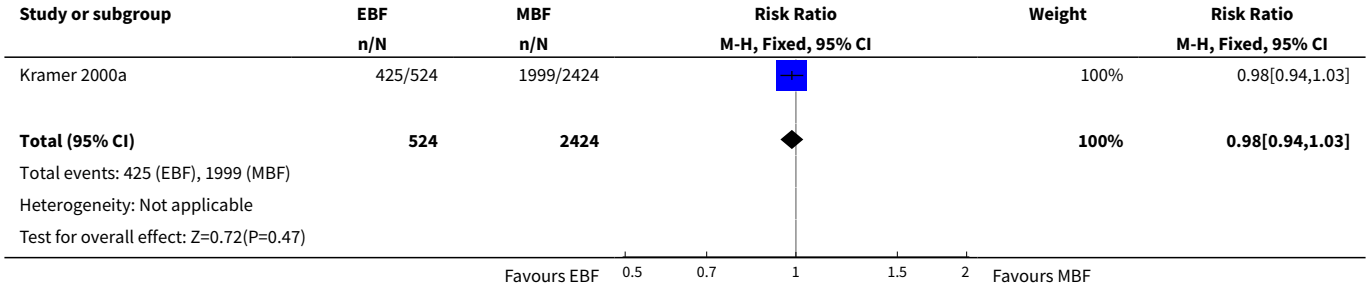




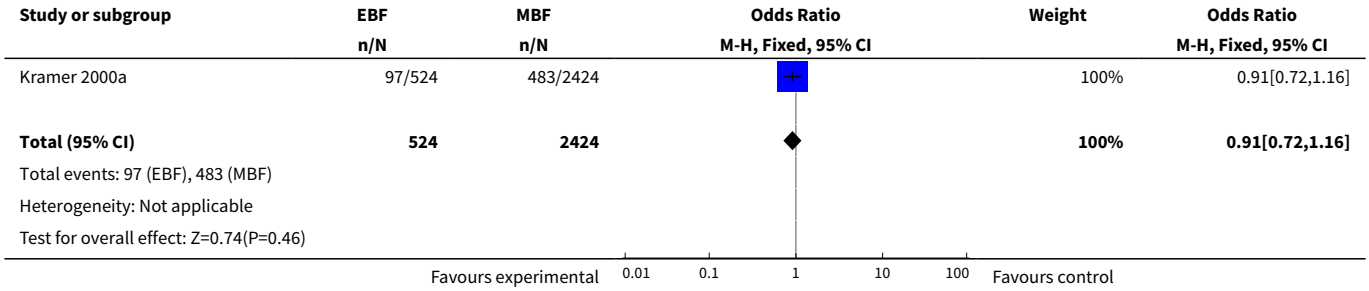
Analysis 4.50. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 50 Death in first 12 months.



Analysis 4.51. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 51 Any dental caries (decayed, missing, or filled teeth) at 6 years.



Analysis 4.52. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 52 Any incisor caries (decayed, missing, or filled teeth) at 6 years.

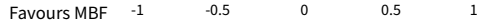


Analysis 4.53. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 53 Height at 6.5 years.

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	524	120.7 (5.3)	2427	120.6 (5)		100%	0.1[-0.4,0.6]
Total ***	**524**		**2427**			**100%**	**0.1[-0.4,0.6]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.4(P=0.69)							

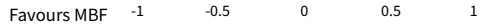
Analysis 4.54. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 54 Leg length at 6.5 years.

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	524	55.1 (3.5)	2427	54.9 (4.1)		100%	0.2[-0.14,0.54]
Total ***	**524**		**2427**			**100%**	**0.2[-0.14,0.54]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.15(P=0.25)							



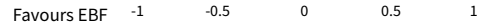
Analysis 4.55. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 55 Head circumference at 6.5 years.

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	524	52 (1.5)	2427	51.9 (1.5)		100%	0.1[-0.04,0.24]
Total ***	**524**		**2427**			**100%**	**0.1[-0.04,0.24]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=1.38(P=0.17)							

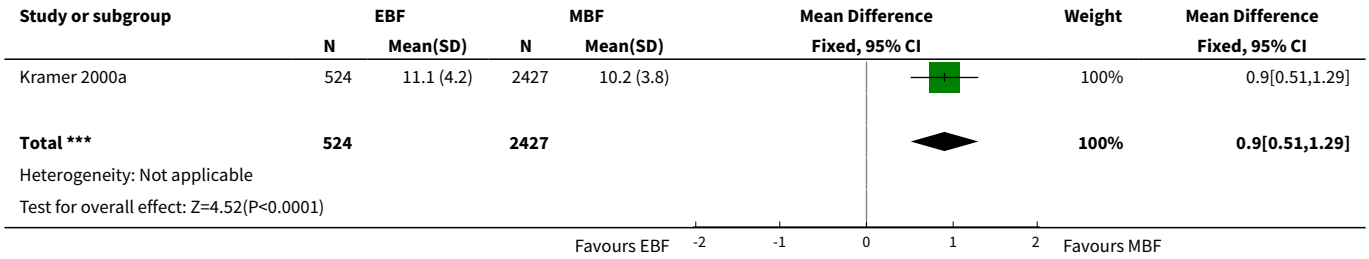


Analysis 4.56. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 56 BMI at 6.5 years.

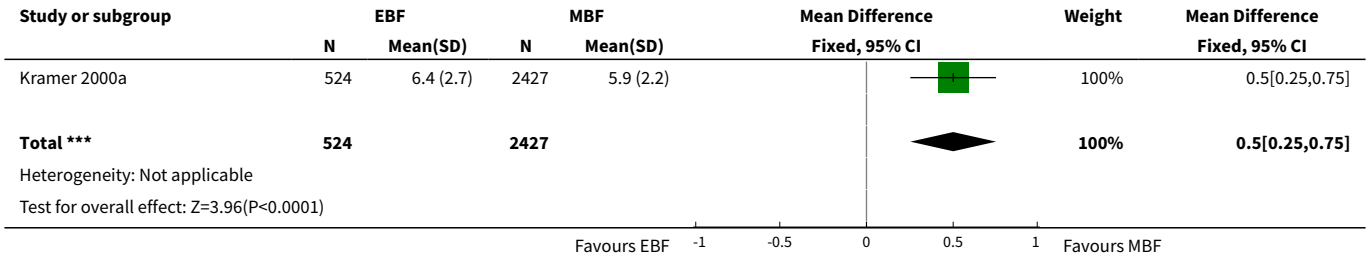
Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	524	15.8 (1.9)	2427	15.6 (1.7)		100%	0.2[0.02,0.38]
Total ***	**524**		**2427**			**100%**	**0.2[0.02,0.38]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.22(P=0.03)							



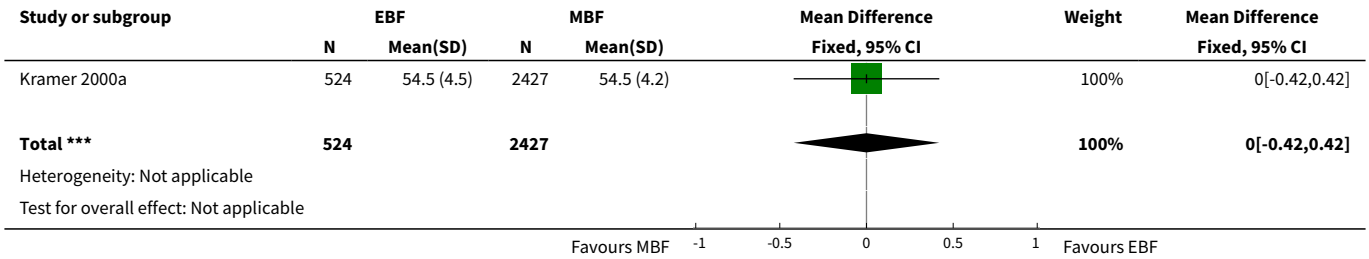
Analysis 4.57. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 57 Triceps skinfold thickness at 6.5 years.



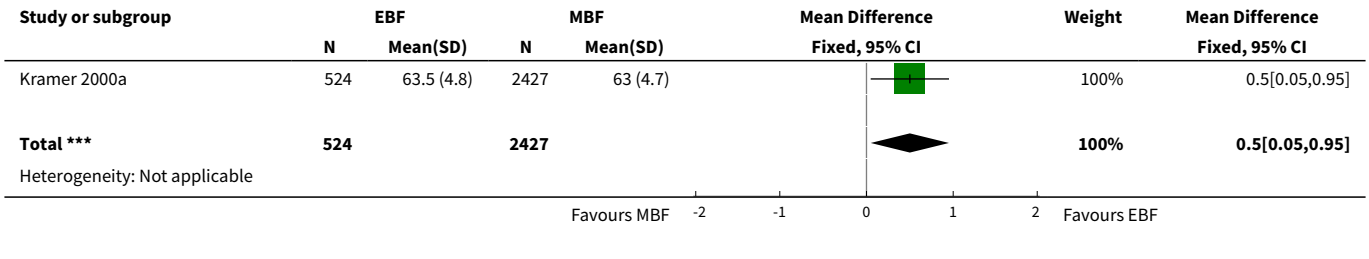
Analysis 4.58. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 58 Subscapular skinfold thickness.

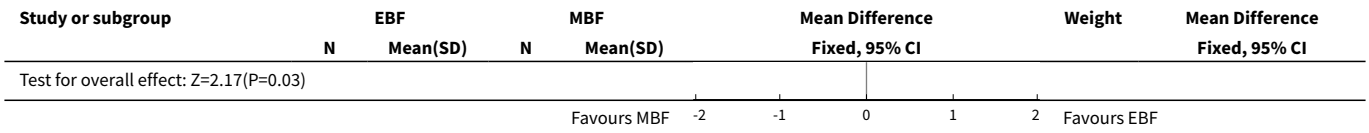


Analysis 4.59. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 59 Waist circumference at 6.5 years.

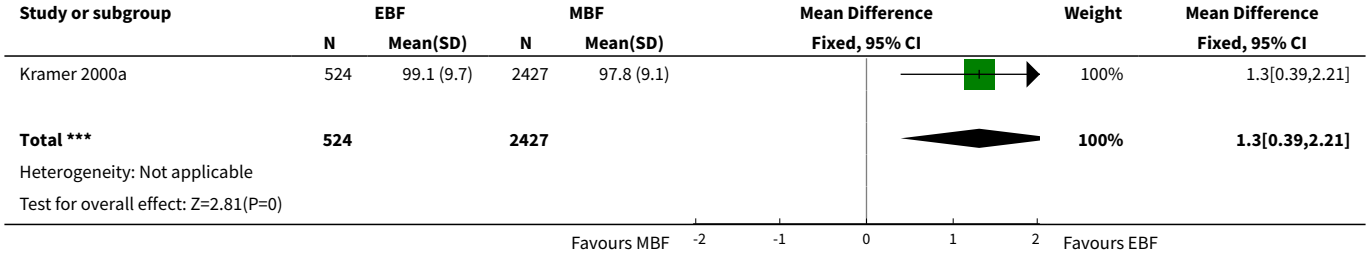


Analysis 4.60. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 60 Hip circumference at 6.5 years.

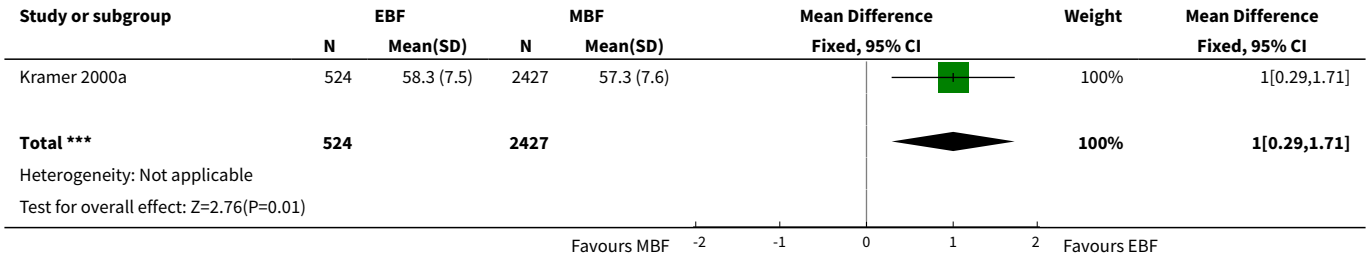




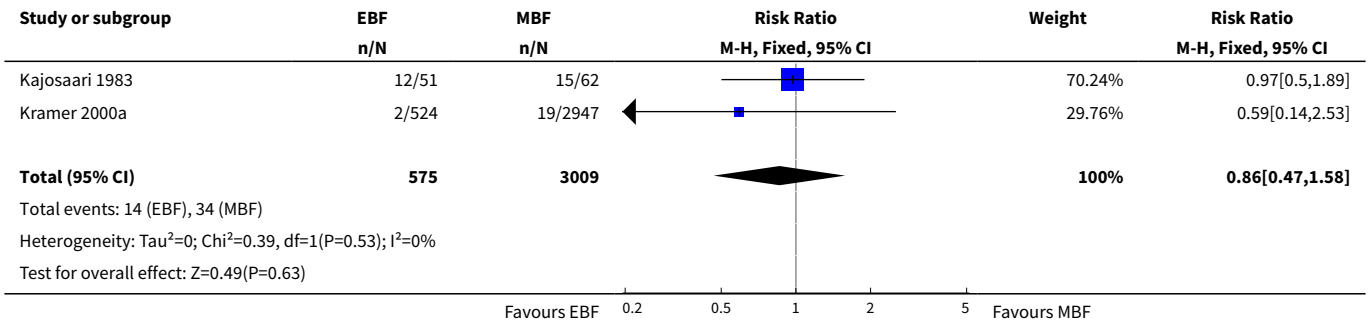
Analysis 4.61. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 61 Systolic blood pressure at 6.5 years.



Analysis 4.62. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 62 Diastolic blood pressure at 6.5 years (mm Hg).

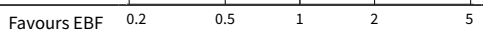


Analysis 4.63. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 63 Atopic eczema at 5-7 years.



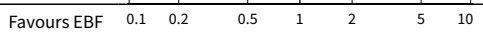
Analysis 4.64. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 64 Hay fever at 5-7 years.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Kajosaari 1983	10/51	23/62		44.82%	0.53[0.28,1.01]
Kramer 2000a	23/524	116/2947		55.18%	1.12[0.72,1.73]
Total (95% CI)	**575**	**3009**		**100%**	**0.8[0.39,1.65]**
Total events: 33 (EBF), 139 (MBF)					
Heterogeneity: Tau^2=0.2; Chi^2=3.55, df=1(P=0.06); I^2=71.8%					
Test for overall effect: Z=0.61(P=0.54)					



Analysis 4.65. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 65 Asthma at 5-7 years.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kajosaari 1983	4/51	9/62		15.16%	0.54[0.18,1.65]
Kramer 2000a	9/524	35/2947		19.72%	1.45[0.7,2.99]
Oddy 1999	33/207	37/232		65.12%	1[0.65,1.54]
Total (95% CI)	**782**	**3241**		**100%**	**1.02[0.72,1.44]**
Total events: 46 (EBF), 81 (MBF)					
Heterogeneity: Tau^2=0; Chi^2=2.14, df=2(P=0.34); I^2=6.41%					
Test for overall effect: Z=0.1(P=0.92)					



Analysis 4.66. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 66 Food allergy at 5 years.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kajosaari 1983	2/51	4/62		100%	0.61[0.12,3.19]
Total (95% CI)	**51**	**62**		**100%**	**0.61[0.12,3.19]**
Total events: 2 (EBF), 4 (MBF)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.59(P=0.56)					

Analysis 4.67. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 67 Allergy to animal dander at 5 years.

Study or subgroup	EBF n/N	MBF n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kajosaari 1983	4/51	6/62		100%	0.81[0.24,2.72]
Total (95% CI)	**51**	**62**		**100%**	**0.81[0.24,2.72]**
Total events: 4 (EBF), 6 (MBF)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.34(P=0.73)					

Analysis 4.68. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 68 Positive skin-prick test to house dust mite at 6.5 years.

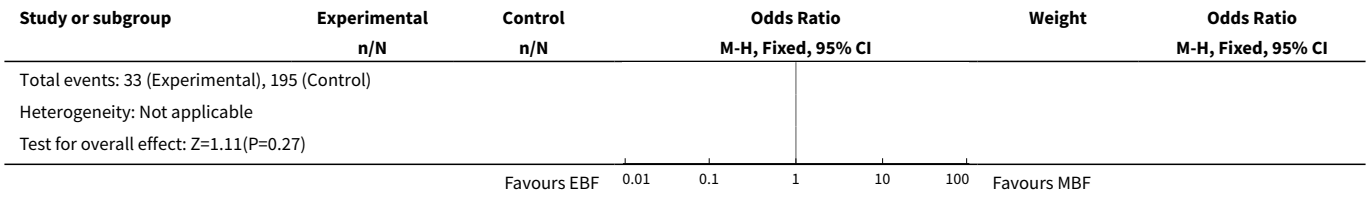
Study or subgroup	Experimental n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Kramer 2000a	47/397	259/1923		100%	0.86[0.62,1.2]
Total (95% CI)	**397**	**1923**		**100%**	**0.86[0.62,1.2]**
Total events: 47 (Experimental), 259 (Control)					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=0(P<0.0001); $I^2=100\%$					
Test for overall effect: Z=0.87(P=0.38)					

Analysis 4.69. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 69 Positive skin-prick test to cat dander at 6.5 years.

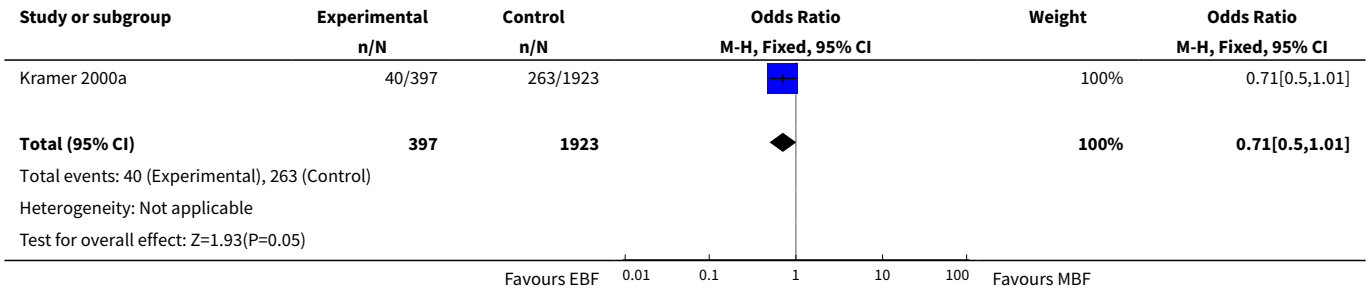
Study or subgroup	Experimental n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Kramer 2000a	38/397	210/1923		100%	0.86[0.6,1.24]
Total (95% CI)	**397**	**1923**		**100%**	**0.86[0.6,1.24]**
Total events: 38 (Experimental), 210 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.79(P=0.43)					

Analysis 4.70. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 70 Positive skin-prick test to birch pollen at 6.5 years.

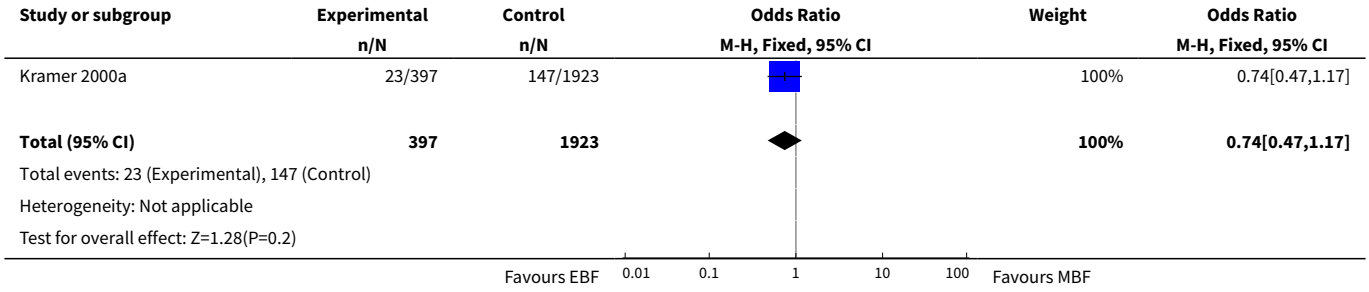
Study or subgroup	Experimental n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Kramer 2000a	33/397	195/1923		100%	0.8[0.55,1.18]
Total (95% CI)	**397**	**1923**		**100%**	**0.8[0.55,1.18]**



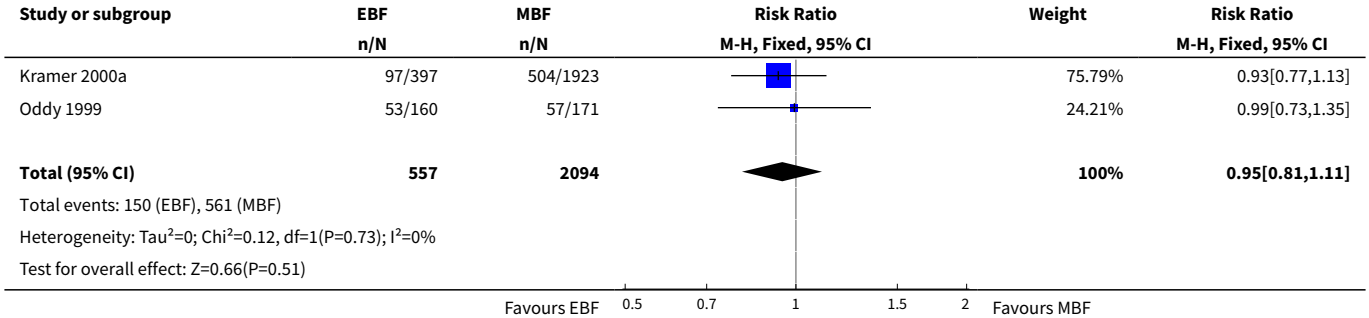
Analysis 4.71. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 71 Positive skin-prick test to mixed northern grasses at 6.5 years.



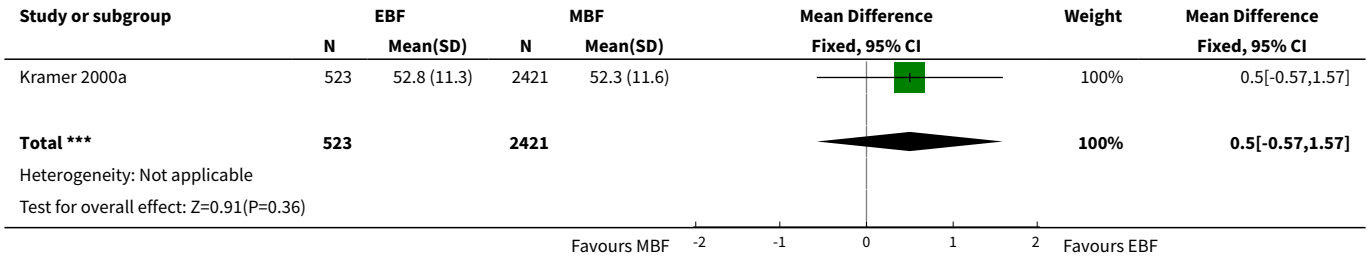
Analysis 4.72. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 72 Positive skin-prick test to Alternaria at 6.5 years.



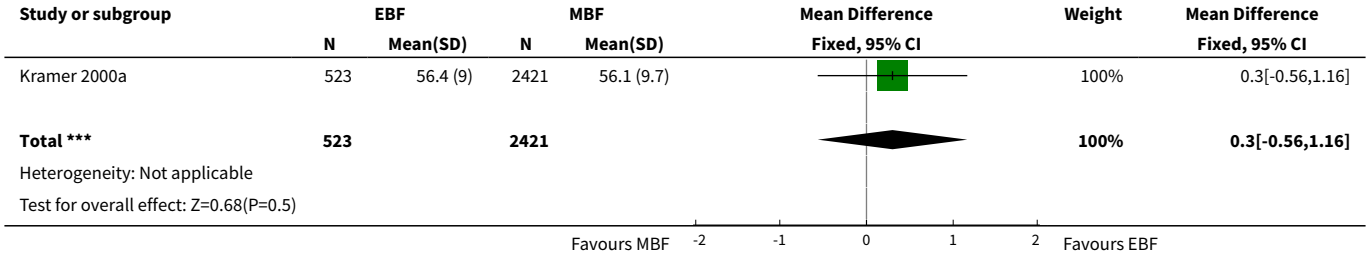
Analysis 4.73. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 73 Any positive skin-prick test at 6-7 years.



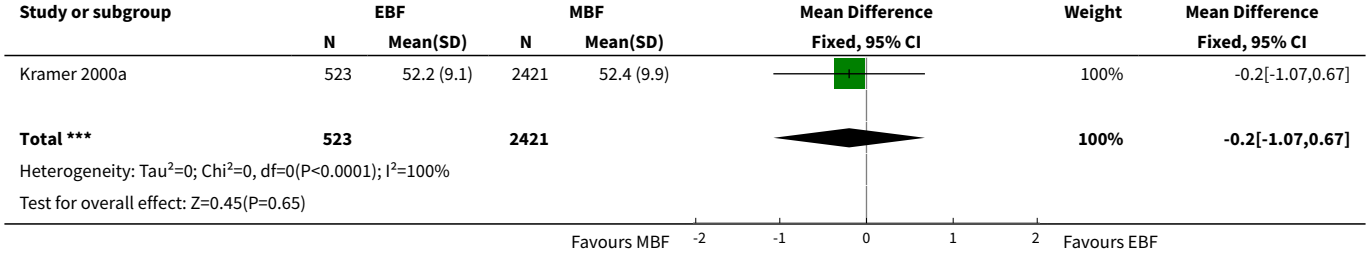
Analysis 4.74. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 74 Wechsler cognitive ability test at 6.5 years: vocabulary.



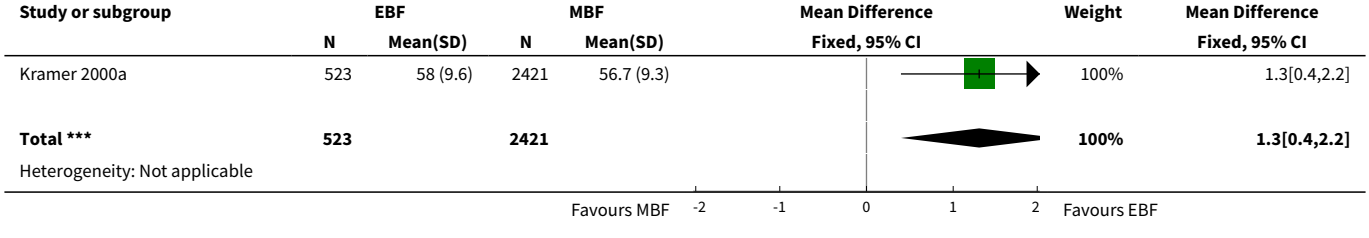
Analysis 4.75. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 75 Wechsler cognitive ability test at 6.5 years: similarities.

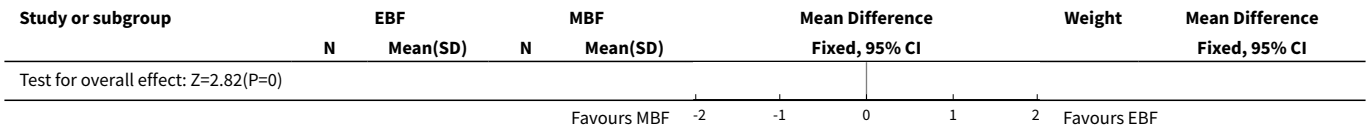


Analysis 4.76. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 76 Wechsler cognitive ability test at 6.5 years: matrices.

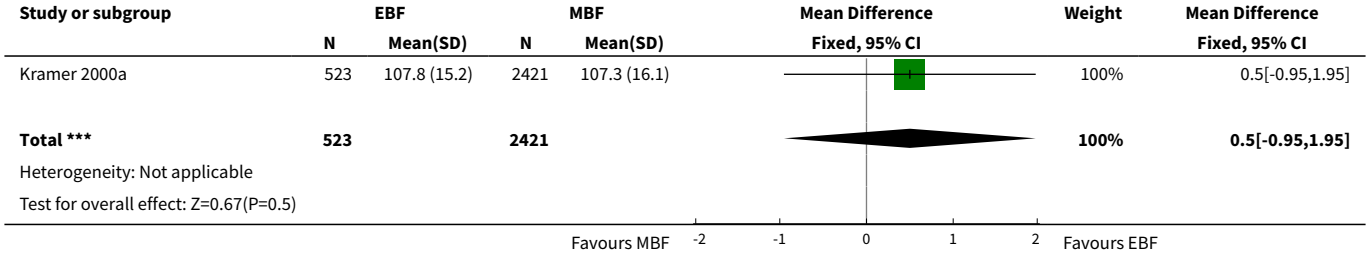


Analysis 4.77. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 77 Wechsler cognitive ability test at 6.5 years: block designs.

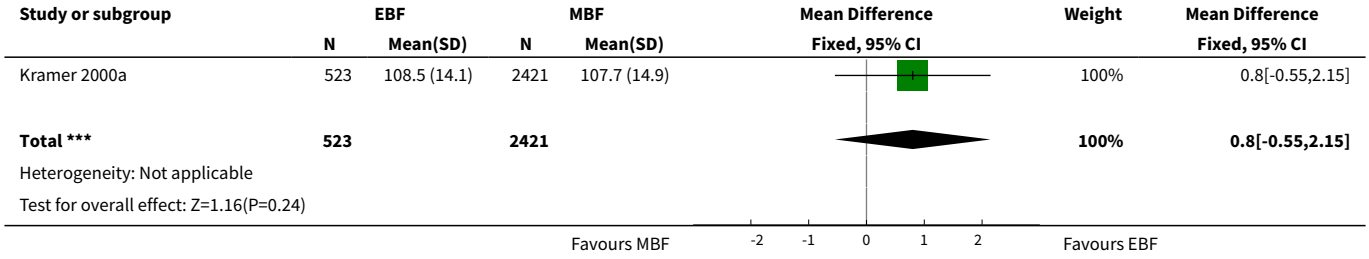




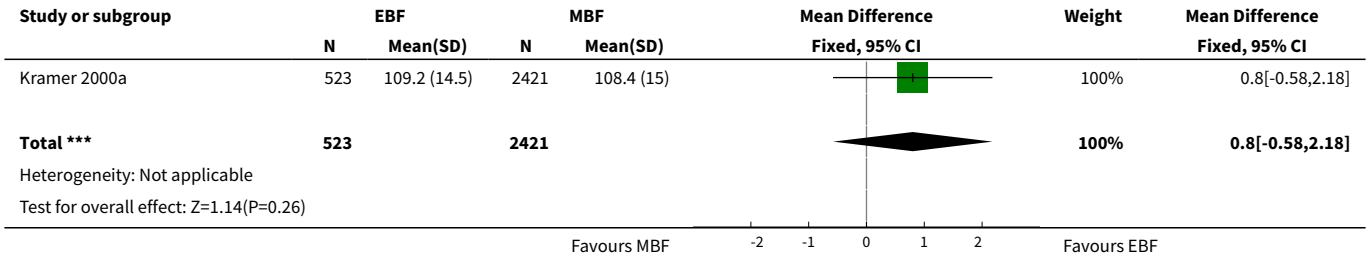
Analysis 4.78. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 78 Wechsler cognitive ability test at 6.5 years: verbal IQ.



Analysis 4.79. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 79 Wechsler cognitive ability test at 6.5 years: performance IQ.

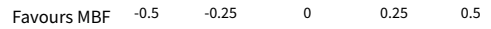


Analysis 4.80. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 80 Wechsler cognitive ability test at 6.5 years: full-scale IQ.



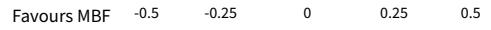
Analysis 4.81. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 81 Teacher's academic rating at 6.5 years: reading.

Study or subgroup	EBF N	EBF Mean(SD)	MBF N	MBF Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	400	3.2 (0.9)	1796	3.3 (0.8)		100%	-0.1[-0.19,-0.01]
Total ***	**400**		**1796**			**100%**	**-0.1[-0.19,-0.01]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.13(P=0.03)							



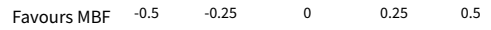
Analysis 4.82. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 82 Teacher's academic rating at 6.5 years: writing.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	400	3.1 (0.8)	1796	3.2 (0.8)		100%	-0.12[-0.2,-0.04]
Total ***	**400**		**1796**			**100%**	**-0.12[-0.2,-0.04]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=2.79(P=0.01)							



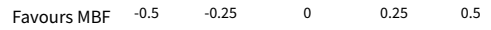
Analysis 4.83. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 83 Teacher's academic rating at 6.5 years: mathematics.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	400	3.2 (0.7)	1796	3.3 (0.8)		100%	-0.04[-0.12,0.04]
Total ***	**400**		**1796**			**100%**	**-0.04[-0.12,0.04]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.97(P=0.33)							

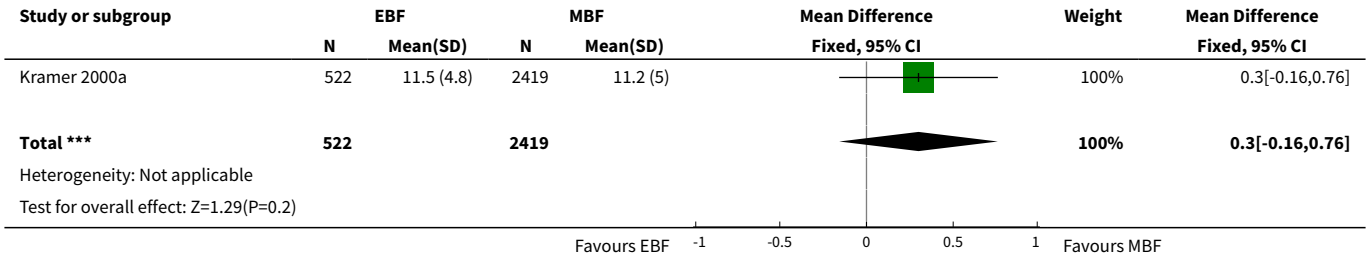


Analysis 4.84. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 84 Teacher's academic rating at 6.5 years: other subjects.

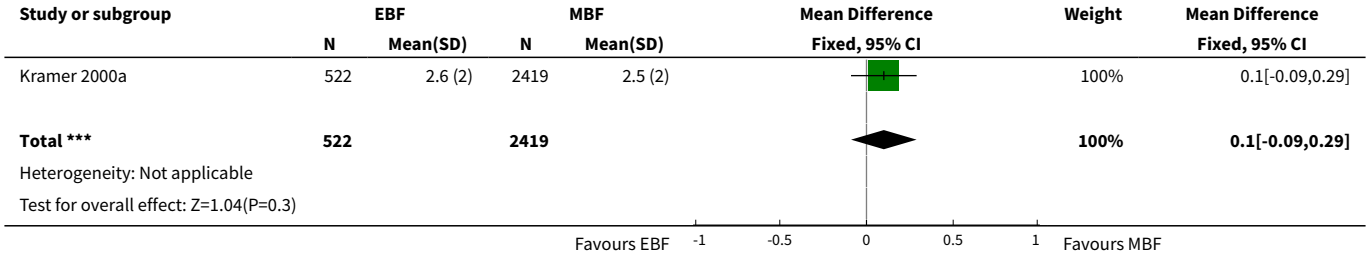
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kramer 2000a	400	3.2 (0.7)	1796	3.3 (0.7)		100%	-0.1[-0.17,-0.03]
Total ***	**400**		**1796**			**100%**	**-0.1[-0.17,-0.03]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.77(P=0.01)							



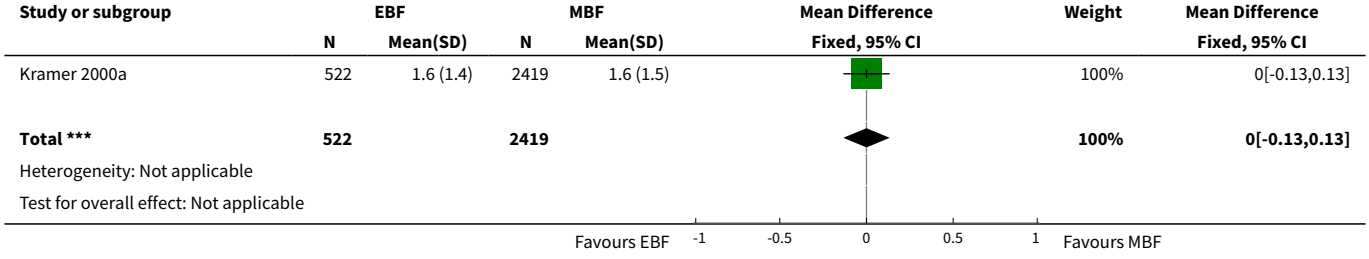
Analysis 4.85. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 85 Parent's behavior rating at 6.5 years: total difficulties.



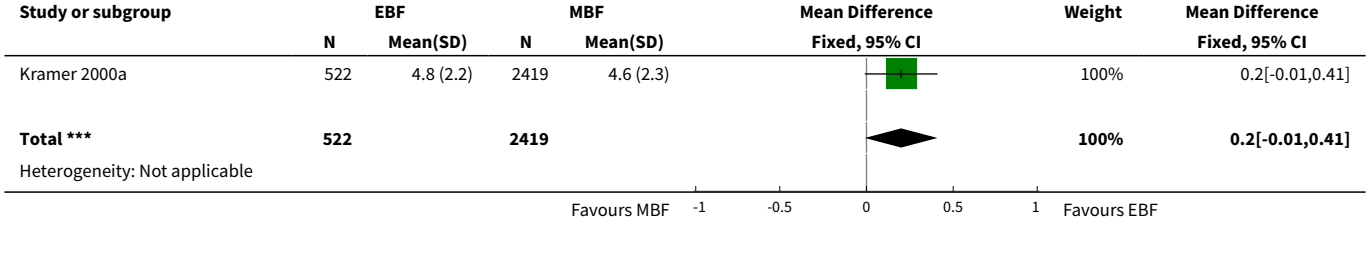
Analysis 4.86. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 86 Parent's behavior rating at 6.5 years: emotional symptoms.

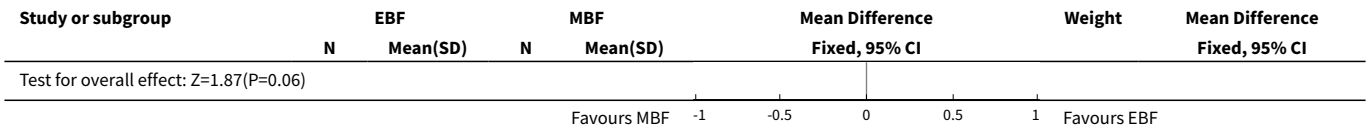


Analysis 4.87. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 87 Parent's behavior rating at 6.5 years: conduct problems.

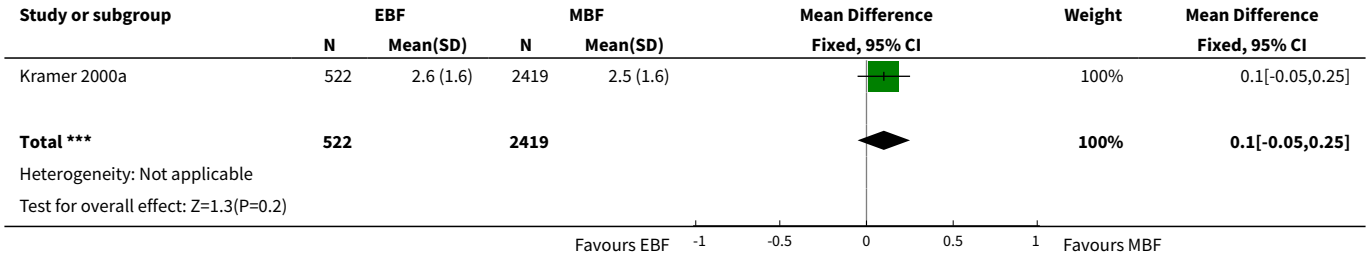


Analysis 4.88. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 88 Parent's behavior rating at 6.5 years: hyperactivity/inattention.

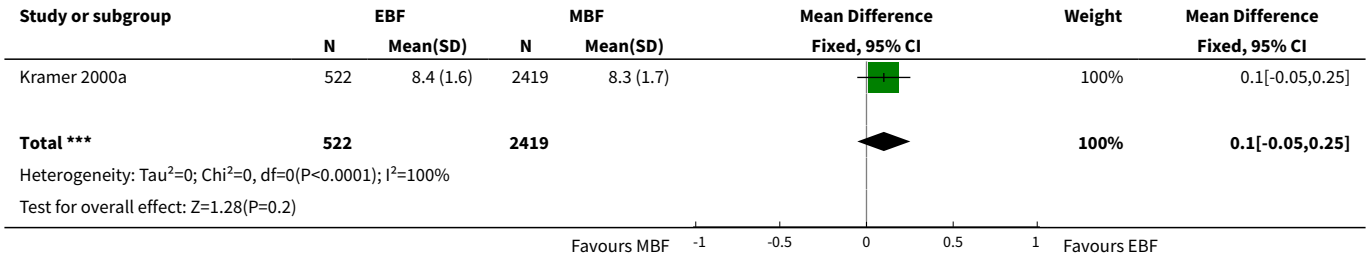




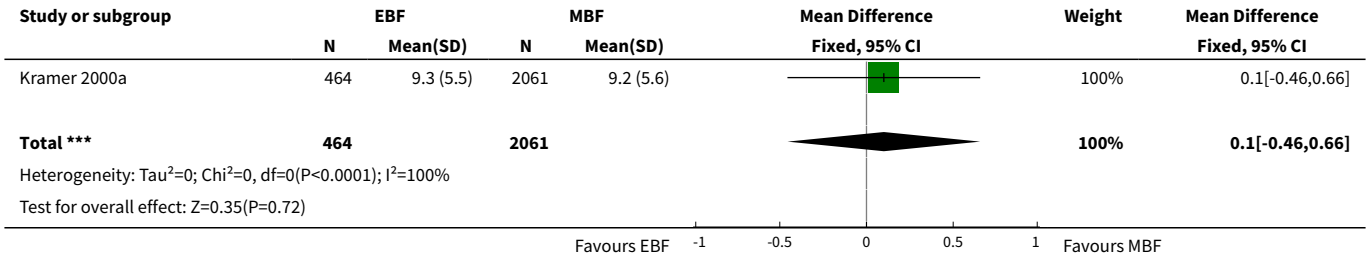
Analysis 4.89. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 89 Parent's behavior rating at 6.5 years: peer problems.



Analysis 4.90. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 90 Parent's behavior rating at 6.5 years: prosocial behavior.



Analysis 4.91. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 91 Teacher's behavior rating at 6.5 years: total difficulties.

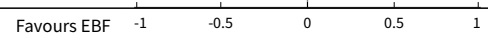


Analysis 4.92. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 92 Teacher's behavior rating at 6.5 years: emotional symptoms.

Study or subgroup	Experimental		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kramer 2000a	464	1.9 (1.8)	2061	1.9 (1.9)		100%	0[-0.18,0.18]
Total ***	**464**		**2061**			**100%**	**0[-0.18,0.18]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

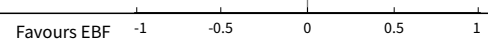
Analysis 4.93. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 93 Teacher's behavior rating at 6.5 years: conduct problems.

Study or subgroup	EBF		MBF		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kramer 2000a	464	1.3 (1.7)	2061	1.3 (1.7)		100%	0[-0.17,0.17]
Total ***	**464**		**2061**			**100%**	**0[-0.17,0.17]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



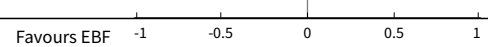
Analysis 4.94. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 94 Teacher's behavior rating at 6.5 years: hyperactivity/inattention.

Study or subgroup	EBF		MBF		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kramer 2000a	464	3.8 (2.7)	2061	3.9 (2.7)		100%	-0.1[-0.37,0.17]
Total ***	**464**		**2061**			**100%**	**-0.1[-0.37,0.17]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.72(P=0.47)							

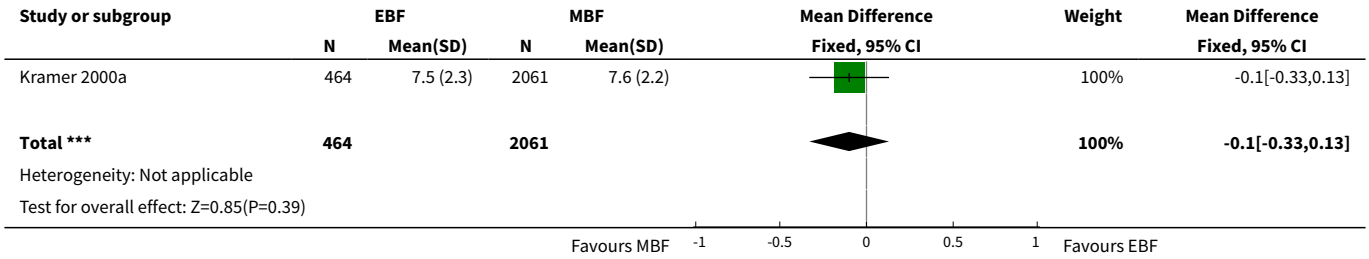


Analysis 4.95. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 95 Teacher's behavior rating at 6.5 years: peer problems.

Study or subgroup	EBF		MBF		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kramer 2000a	464	2.3 (1.8)	2061	2.2 (1.7)		100%	0.1[-0.08,0.28]
Total ***	**464**		**2061**			**100%**	**0.1[-0.08,0.28]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.09(P=0.27)							



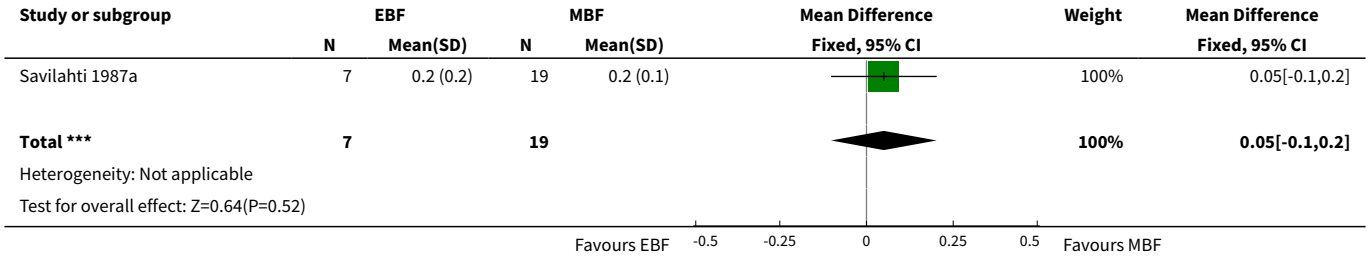
Analysis 4.96. Comparison 4 Exclusive breastfeeding for 6-7 months versus 3-4 months, developed countries, observational studies, Outcome 96 Teacher's behavior rating at 6.5 years: prosocial behavior.



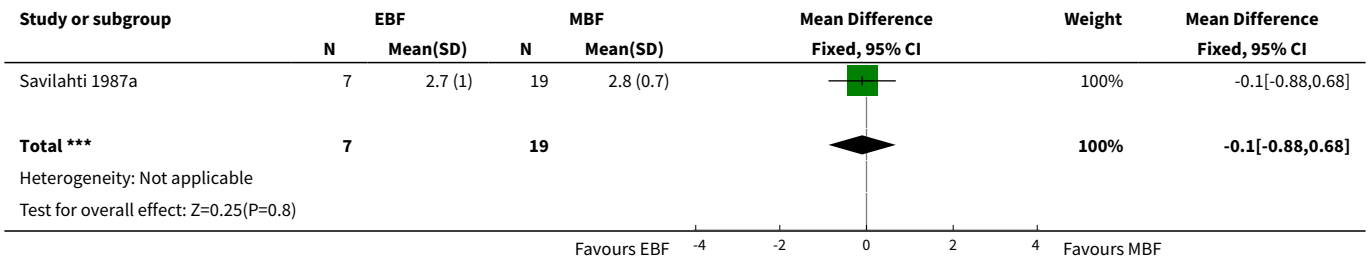
Comparison 5. Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Very low density lipoprotein concentration (mmol/L) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.10, 0.20]
2 Low density lipoproteinconcentration (mmol/L) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.88, 0.68]
3 High-density lipoprotein-2 concentration (mmol/L) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.05, 0.21]
4 High-density lipoprotein-3 concentration (mmol/L) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.07, 0.07]
5 Apoprotein B concentration (mg/dL) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	5.0 [-14.93, 24.93]
6 Total triglyceride concentration (mmol/L) at 9 months	1	26	Mean Difference (IV, Fixed, 95% CI)	0.3 [-0.23, 0.83]

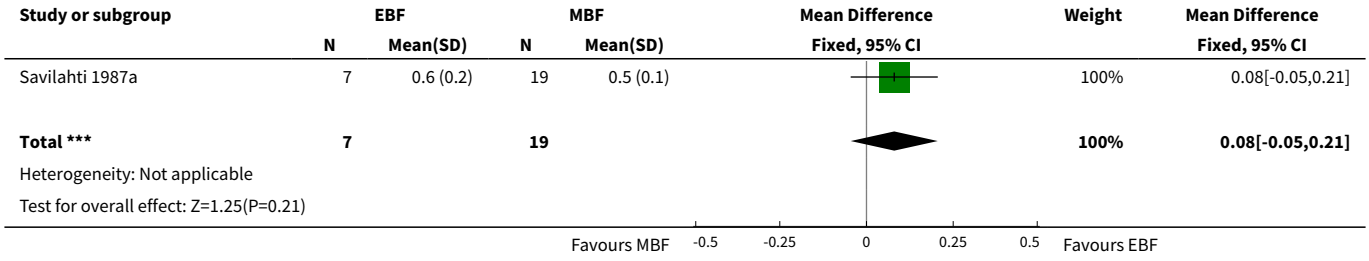
Analysis 5.1. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 1 Very low density lipoprotein concentration (mmol/L) at 9 months.



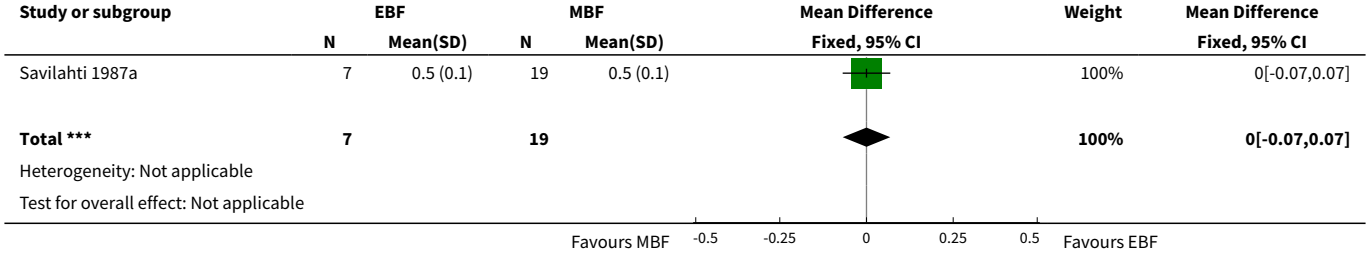
Analysis 5.2. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 2 Low density lipoproteinconcentration (mmol/L) at 9 months.



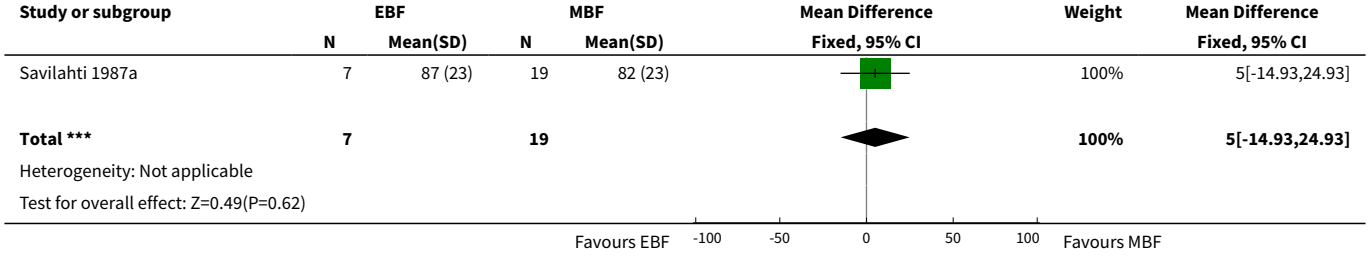
Analysis 5.3. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 3 High-density lipoprotein-2 concentration (mmol/L) at 9 months.



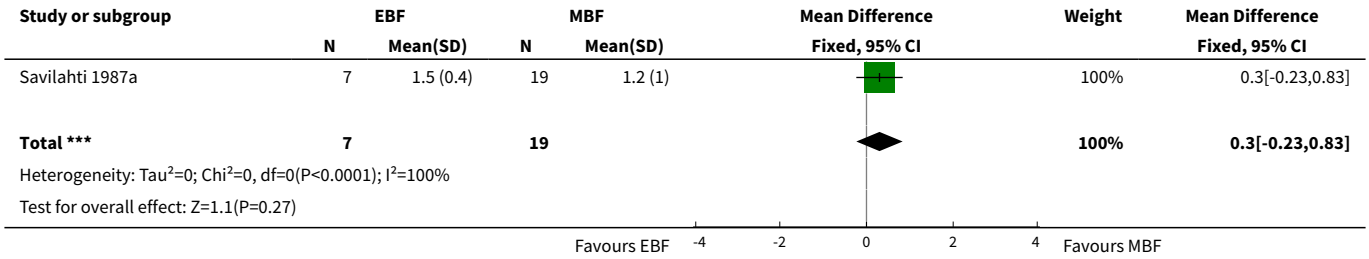
Analysis 5.4. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 4 High-density lipoprotein-3 concentration (mmol/L) at 9 months.



Analysis 5.5. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 5 Apoprotein B concentration (mg/dL) at 9 months.



Analysis 5.6. Comparison 5 Exclusive breastfeeding for > 6 months versus 6 months, developed countries, observational studies, Outcome 6 Total triglyceride concentration (mmol/L) at 9 months.



APPENDICES

Appendix 1. Search methods used in previous versions of the review

In order to capture as many relevant studies as possible, two independent literature searches were conducted for the first version of this review: one by staff at the Nutrition Unit of the World Health Organization (WHO) and one by the authors. The search details are shown below.

The search by WHO was conducted between June and August 2000 in the following databases: MEDLINE (1966 to June 2000), OLDMEDLINE (Index Medicus previous to 1966), CINAHL (1982 to June 2000), HealthSTAR (1975 to August 2000), EBM Reviews-Best Evidence (1991 to July/August 2000), SocioFile (1974 to July 2000), Cochrane Database of Systematic Reviews (*The Cochrane Library* 2000, Issue 2), CAB Abstracts (1973 to July 2000), EMBASE-Psychology (1987 to 3rd Quarter, 2000), EconLit (1969 to August 2000), Index Medicus for the WHO Eastern Mediterranean (IMEMR), African Index Medicus (AIM), and LILACS (Latin American and Caribbean Health Sciences). Where applicable, the medical subject heading (MeSH) 'breast feeding,' and otherwise the free language terms 'breast-feeding,' 'breast feeding,' or 'breastfeeding' combined with 'exclusive' or 'exclusively' were used in the search strategy. The search yielded 1423 citations (MEDLINE 686, OLDMEDLINE 15, CINAHL 25, HealthSTAR 1, EBM-Best Evidence 2, SocioFile 2, Cochrane Database of Systematic Reviews 8, CAB Abstracts 680, EMBASE-Psychology 4, other databases 0). Once duplicates were removed, 1035 citations remained; these were then assessed for eligibility.

The authors' search was conducted on August 12, 2000 in the following databases: MEDLINE (1966 to June 2000), CINAHL (1982 to April 2000), HealthSTAR (1975 to August 2000), BIOSIS (1989 to 2000), CAB Abstracts (1973 to June 2000), Cochrane Database of Systematic Reviews (*The Cochrane Library* 2000, Issue 3), Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2000, Issue 3), and EMBASE-Medicine (1980 to 2000). The terms 'breast feeding,' 'infant,' and 'growth,' as MeSH headings and text words, were combined in the search strategy. This search yielded a total of 2496 citations (MEDLINE yielded 1079 citations, CINAHL 75, HealthSTAR 2, BIOSIS 190, CAB 614, Cochrane Database of Systematic Reviews 25, Cochrane Controlled Trials Register 122, and EMBASE 389). Once duplicates among the databases were removed, 1845 citations remained, 1633 of which were different from the 1035 identified by the WHO search. Thus 2668 unique citations were identified by the two searches.

The literature search for the updated (2007) review was conducted in December 2006 on the same electronic databases and search terms and logic as the second search above, with the addition of the LILACS, SocioFile, and EBM Reviews-Best Evidence databases. This updated search yielded 835 additional unique citations.

The 2011 updated literature review included the same electronic databases as the 2007 update except CAB Abstracts and HealthSTAR. That database yielded 3425 additional unique citations.

For all searches, every effort was made to identify relevant non-English language articles and abstracts. Given their own backgrounds, the review authors themselves were able to determine the eligibility of articles in French, Spanish, and Japanese. For publications in other languages, two options were available. Many articles in languages other than English provided English abstracts. As such, all potentially relevant articles were obtained and checked for availability of English abstracts. If such abstracts were not available, or were available but did not provide enough information to determine their eligibility, then assistance was requested from WHO to determine their eligibility for inclusion. No article or abstract was excluded because of language of publication.

In addition to the studies found through these electronic searches, reference lists of identified articles were checked, and contacts with experts in the field were made to identify other potentially relevant published or unpublished studies. Attempts were made to contact the authors of all studies that qualified for inclusion in the review to obtain methodologic details, clarify inconsistencies, and obtain unpublished data.

Many studies were identified that either compared outcomes in infants receiving exclusive breastfeeding (EBF) versus mixed breastfeeding (MBF) or investigated the effects of age at introduction of nonbreast-milk liquid or solid foods. The vast majority of these studies were ineligible for inclusion, however, because they did not ensure EBF at least three months prior to introducing these complementary foods in the MBF group or a comparison group with EBF at least six months, or both.

We identified 41 unique citations (articles or abstracts) that met the selection criteria, comprising 22 separate studies. Of the 22 included studies, 11 were carried out in developing countries and the other 11 in developed countries.

Ten of the 41 total citations were found by both of the two original searches (Ahn 1980; Akeson 1998a; Castillo 1996; Cohen 1994b; Cohen 1995; Dewey 1996; Dewey 1998a; Dewey 1998b; Dewey 1999b; Khan 1984); 11 were identified only by the WHO search (Akeson 1998b; Duncan 1993; Heiskanen 1994; Kajosaari 1983; Kajosaari 1991; Kajosaari 1994; Kallio 1992; Oddy 1999; Pisacane 1995; Rao 1992; Savilahti 1987b); six were found only by the authors' search (Adair 1993b; Akeson 1996b; Dewey 1995; Frongillo 1997a; Heinig 1993; Simondon 1997b). Eleven additional citations were located through contacts with experts and reference lists of relevant articles (Brown 1991b; Brown 1998; Dewey 1997; Dewey 2001; Huffman 1987; Kramer 2000b; Kramer 2000c; Kramer 2001; WHO 1994b; WHO 1995; WHO 2002).

The updated literature search from December 2006 resulted in two additional studies that met the eligibility criteria (Khadivzadeh 2004; Onayade 2004), plus a new citation from one of the original included studies (Simondon 2003).

Appendix 2. Search methods used for the current review

MEDLINE (1 January 2007 to 14 June 2011)

1 exp Breast Feeding/
2 ((breastfe$ or breast-fe$) adj4 (alone or only or exclusive$)).ti,ab.
3 exclusive*.ti,ab.
4 1 and 3
5 2 or 4

EMBASE (1 January 2007 to 14 June 2011)

1. exp BREAST FEEDING/
2. exclusive*.ti,ab
3. ((breastfe* OR breast-fe*) adj4 (exclusive* OR alone OR only)).ti,ab
4. 1 AND 2
5. 3 OR 4

The Cochrane Library (2011, Issue 6)

BIOSIS (1 January 2007 to 14 June 2011)

#9 #8 AND #5

#8 #7 OR #6

#7 TS=exclusive* or TS=only or TS=alone

#6 TI=exclusive* or TI=only or TI=alone

#5 #4 OR #3 OR #2 OR #1

#4 TI="breast fed" or TI="breast feeding" or TI="breast feed"

#3 TI=breast-fe*

#2 TI=breastfe*

#1 Topic=(breastfeeding)

CINAHL (1 January 2006 to 14 June 2011)

1. exp BREAST FEEDING/

2. ((breastfe* OR breast-fe*) AND (exclusive* OR alone OR only)).ti,ab

3. exclusive*.ti,ab

4. 1 AND 3

5. 2 OR 4

African Index Medicus (searched 15 June 2011)

(breastfeeding or breastfed or breastfeed or breast-fed or breast-feeding or breast-feed or "breast feed" or "breast fed" or "breast feeding" [Key Word]) and (exclusive or exclusively or exclusiveness or alone or only [Key Word])

IMEMR (searched 15 June 2011)

(breastfeeding or breastfed or breastfeed or breast-fed or breast-feeding or breast-feed or "breast feed" or "breast fed" or "breast feeding") and (exclusive or exclusively or exclusiveness or alone or only)

LILACS (searched 15 June 2011)

(breastfeeding or breastfed or breastfeed or breastfeeding or breast-fed or breast-feeding or breast-feed or "breast feed" or "breast fed" or "breast feeding" or lactancia) and (exclusive or exclusively or exclusiveness or alone or only or exclusiva or exclusivo)

WHAT'S NEW

Date	Event	Description
14 June 2011	New citation required but conclusions have not changed	New evidence from the Belarusian study (Kramer 2000a) suggests that six months of exclusive breastfeeding confers no benefit (versus three months of exclusive breastfeeding followed by continued partial breastfeeding through six months) on height, weight, body mass index, dental caries, cognitive ability, or behaviour at 6.5 years of age. The overall conclusions have not changed.
14 June 2011	New search has been performed	Search updated. One new study included (Duijts 2010) and an additional report of Kramer 2000a identified. Five new excluded studies (Chantry 2007; Evelein 2011; Meinzen-Derr 2006; Rebhan 2009; Weyermann 2006).

HISTORY

Protocol first published: Issue 1, 2002
Review first published: Issue 1, 2002

Date	Event	Description
20 September 2008	Amended	Converted to new review format.
22 May 2007	New search has been performed	Search updated December 2006. We identified five new trials; two have been included (Khadivzadeh 2004; Onayade 2004) and three have been excluded (Chantry 2006; Ly 2006; Wang 2005). The conclusions of the review have not changed.

CONTRIBUTIONS OF AUTHORS

Ritsuko Kakuma: carried out the initial screening of all citations located in the literature search, independently rated each study for quality, independently extracted the data and entered them into Review Manager, and reviewed the drafts for accuracy.

Mike Kramer: planned the review, made the final selection of included studies, independently rated the study quality and extracted the data into Review Manager, and prepared the text.

DECLARATIONS OF INTEREST

Dr Kramer is the principal investigator of one of the studies (Kramer 2000a) included in this review.

SOURCES OF SUPPORT

Internal sources

- McGill University, Canada.

External sources

- Canadian Institutes of Health Research, Canada.
- Canadian Cochrane Network, Canada.
- Department of Nutrition for Health and Development, WHO, Switzerland.

NOTES

This review has been processed through the Cochrane Pregnancy and Childbirth Group although its subject matter falls outside the scope of the Group. The Group's scope does include the initiation of breastfeeding, but not the timing of its cessation. However, the topic is clearly of global importance and because it did not readily fit within the scope of any Cochrane review group, the Pregnancy and Childbirth Group was happy to assist with publication. This review was based on a systematic review by M Kramer, that was commissioned by the World Health Organization (WHO). The WHO review was very extensively peer reviewed by experts in review methodology and statistics, and in infant nutrition and lactation, including experts that the Review Group would have approached for our own refereeing purposes. We have therefore not sought an initial protocol, nor subjected the Cochrane review to further peer review of this type. The review has, however, been reviewed by the Consumer Panel of the Pregnancy and Childbirth Group.

There are other unusual features of this review:

1. Its title does not fit with the standard Cochrane format but we have been unable to construct a satisfactory title that does, whilst doing justice to the scope of the topic.
2. It includes data from studies in addition to randomized trials.
3. Maintenance and updating will be the sole responsibility of the contact author as the search strategy of our Review Group does not extend to this topic.

Jim Neilson
Co-ordinating Editor
Cochrane Pregnancy and Childbirth Group

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant Nutritional Physiological Phenomena; Age Factors; Breast Feeding [*statistics & numerical data]; Child Development; Developed Countries; Developing Countries; Gastrointestinal Diseases [prevention & control]; Growth; Infections; Maternal Welfare; Time Factors

MeSH check words

Female; Humans; Infant