REGULAR ARTICLE

Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis

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ABSTRACT

Aim: To synthesise the evidence on the association between duration and exclusivity of breastfeeding and the risk of acute otitis media (AOM).
Methods: Systematic review and meta-analysis following searching of PubMed, CINAHL and EMBASE electronic databases.
Results: Twenty-four studies, all from the USA or Europe, met the inclusion criteria. In the pooled analyses, any form of breastfeeding was found to be protective for AOM in the first 2 years of life. Exclusive breastfeeding for the first 6 months was associated with the greatest protection (OR 0.57 95% CI 0.44, 0.75), followed by 'more vs less' breastfeeding (OR 0.67; 0.59, 0.76) and 'ever vs never' breastfeeding (OR 0.67; 0.56, 0.80).
Conclusion: This systematic review and meta-analysis provides evidence that breastfeeding protects against AOM until 2 years of age, but protection is greater for exclusive breastfeeding and breastfeeding of longer duration. Exclusive breastfeeding during the first 6 months was associated with around a 43% reduction in ever having AOM in the first 2 years of life. After 2 years of age, there is no evidence that breastfeeding protects against AOM; however, there were few studies and the evidence quality was low.

INTRODUCTION

Acute otitis media (AOM) is an infection of the middle ear usually caused by a complication of viral infection in the upper respiratory tract (1). The interaction of virus and bacteria plays an important role in the development of AOM and in the latter case can be treated with antibiotics (1,2). Due to limited space in the middle ear and relatively poor drainage through the Eustachian tube, especially in young children, AOM is often accompanied by significant pain and other characteristics including fever, acute loss of hearing and general lethargy. The sequelae of AOM include persistent middle ear effusion with short-term hearing impairment, perforation of the ear drum with chronic discharge (chronic suppurative otitis media) and persistent hearing impairment. Less common complications include mastoiditis, brain abscess and meningitis.

Globally, the incidence of acute otitis media (AOM) is estimated to be 11% per year, representing 709 million cases annually (3). The peak incidence rate is in the 1- to 4-year age group (61%) with a wide variation in overall incidence from 4% in Central Europe to 43% in sub-Saharan Africa (3). AOM is responsible for a huge burden of disease in both emerging and established economies and

Abbreviations

AAAAI, American Academy of Allergy, Asthma and Immunology; AHRQ, Agency for Healthcare Research and Quality; AOM, Acute Otitis Media; ASCIA, Australasian Society of Clinical Immunology and Allergy; CINAHL, Cumulative Index of Nursing and Allied Health Literature; EMBASE, Excerpta Medica database; ESPGHAN, The European Society for Paediatric Gastroenterology Hepatology and Nutrition; GRADE, Grading of Recommendations Assessment, Development and Evaluation; NHMRC, National Health and Medical Research Council; NOS, Newcastle–Ottawa scale; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PUBMED, Search Engine for Published Medical Literature; WHO, Word Health Organization.

Key notes

- Systematic review and meta-analysis found that breast-feeding was associated with a reduced risk of AOM during the first 2 years of life.
- Infants exclusively breastfed for the first 6 months derived the most benefit with around 43% reduction in ever AOM during the first 2 years.
- There was no clear evidence of continued benefits of breastfeeding on AOM incidence after the age of 2 years.

leads to a high use of healthcare resources including local doctor visits, antibiotics and adenoidectomy or tympanostomy (4–6). It is the most common reason for prescription antibiotics in developed countries where AOM is estimated to affect more than 60% of children under one year and more than 80% of children under three years (7–9). There is also a considerable health burden from the sequelae of AOM both in children and adults (10). It is estimated that there are globally around 31 million cases of chronic suppurative otitis media, and the prevalence rate for AOM induced permanent hearing impairment is 31 per 10 000 (3).

Given the high healthcare burden, a number of risk factors for AOM have been investigated. The factors currently identified as associated with a reduced risk of AOM include breastfeeding, avoidance of *in utero* and childhood passive tobacco smoke exposure, and avoidance of indoor air pollution (3,11–13). Evidence from the literature supports a reduction in AOM risk from breastfeeding; however, there has been no recent comprehensive systematic review, particularly addressing issues related to the effect of duration and exclusivity of breastfeeding on the risk of AOM. Therefore, we aimed to systematically review published studies on the effects of exclusive breastfeeding and partial breastfeeding on childhood AOM during the first 2 years of life and beyond.

METHODS
Search strategy
We performed a systematic search of electronic databases in PubMed, CINAHL and EMBASE without any restrictions from their inception to the present. The search strategy included terms related to breastfeeding and otitis media outcomes. The comprehensive search strategy is reported in the supplementary materials (Table S1). In addition to the electronic search, we manually searched reference lists of primary studies and review articles for additional references. Titles and abstracts of all the located articles were screened by two authors (GB and RT) independently. Full texts of the selected articles were reviewed by the two authors to assess for inclusion. A third author (CL) was consulted in any cases of disagreement between the two authors.

Eligibility criteria
We included only observational studies (no experimental studies resulted from electronic search) with full texts published in the English language. We sought studies assessing the association between breastfeeding and acute otitis media. We did not restrict our review to studies of general populations and included high-risk groups (e.g. low socio-economic communities and children at high risk of allergies). Studies on participants who were born prematurely or infants with co-morbidities (e.g. cleft palate) were excluded. We did not include studies where the only outcome was OM with effusion (a common consequence of AOM). Furthermore, we only included studies that

reported effect estimates (odds ratio (OR)/risk ratio (RR)) and their 95% confidence intervals (CIs).

All studies looked at the effect of breastfeeding, and no restrictions were made in the selection of studies based on breastfeeding exposure. The studies had to have reported our outcome of interest, that is development of AOM defined as: physician/doctor diagnosed AOM, parent or self-reported AOM, or AOM recorded on health-related databases. We included studies reporting either current or past disease (doctor diagnosis of AOM by symptoms and otoscopic examination (distinct redness and outward bulging or reduced mobility of the eardrum)) or recorded healthcare utilisation for AOM. Physician/doctor diagnosed AOM and recorded healthcare utilisation for AOM provide an accurate diagnosis of AOM. Parent reported AOM episodes can be less accurate (14); however, high correlation was observed for doctor diagnosed AOM and parent reported AOM when recall duration was shorter (15–17).

### Quality assessment/risk of bias in included studies
Two authors (GB & RT) independently assessed the study quality using the Newcastle–Ottawa scale (NOS) for individual studies (18). NOS study quality was graded by giving a score. Cohort studies: very good = 9–10; good = 7–8; satisfactory = 5–6; unsatisfactory = 0–4. Cross-sectional: very good = 6–7; good = 5; satisfactory = 4; unsatisfactory = 0–3. Risk of bias was then assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) guidelines for quality of evidence of observational studies (19). Any disagreements between two authors were resolved by consulting a third author (CL).

Data extraction
Data extraction was carried out by one author (GB) and checked by a second author (CL). Data extracted included study design; country of the study; age of children; sample size; definition of exposure and outcome; effect estimates and 95% CIs; confounders included in analysis; subgroup analyses; and interactions.

Suitability for inclusion in pooled analysis
Studies which provided an effect estimate and 95% CIs for the association of breastfeeding and AOM were considered suitable to include in the meta-analysis. Inverse effect measures and 95% CIs were calculated when studies considered the exposed group (breastfeeding) as the reference group. Four breastfeeding categories were identified as important groups to be meta-analysed: exclusively breastfed vs not exclusively or not breastfed during the first 6 months; ever vs never breastfed (children who were breastfed for any duration compared with children who were never breastfed); any breastfeeding ≥3–4 months (exclusive or partial) vs ≤3–4 months (exclusive or partial); and more or less breastfeeding (this group included infants who were breastfed more compared to infants who were breastfed less within each study regardless of the duration or type of
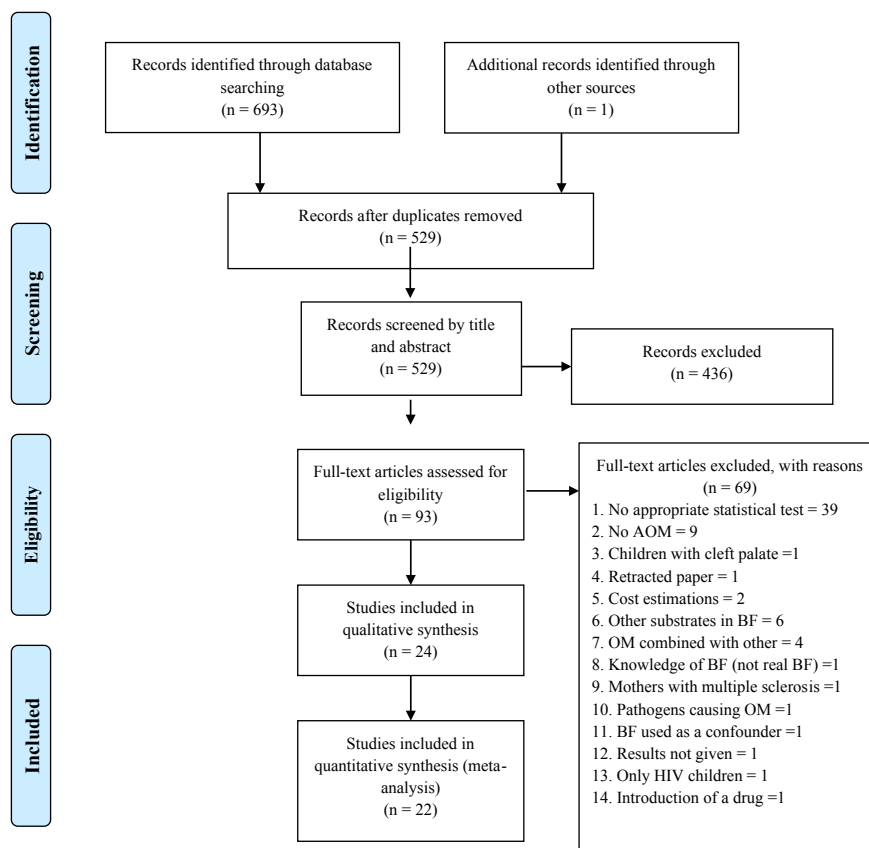
Figure 1 PRISMA flow diagram breastfeeding and AOM.

breastfeeding). When studies reported effect estimates for multiple breastfeeding groups, then priority was given to exclusive breastfeeding. Secondly, the estimate comparing the longest duration of breastfeeding with the shortest was chosen. Meta-analyses were carried out in both fixed- and random-effects models. To assess the heterogeneity among the studies I^2 statistics were carried out, if the I^2 was 25–75%, then random effect pooled effect estimates were presented, and if the I^2 was <25%, then fixed effect pooled effect estimates were presented. Funnel plots were assessed for publication bias, and heterogeneity was tested by excluding studies with high standard errors. Small study effects were tested using Egger's test when the included studies were 10 or more.

RESULTS

The electronic search strategy located 693 articles (search performed 14th October 2014), and one further article was found through a manual search of reviews. Following removal of duplicates, 529 articles were selected for screening. Titles and abstract screening determined 93 articles for full-text review. Finally, 24 articles were selected for inclusion (Fig. 1) and 69 were excluded (Table S2).

Study characteristics

All included studies reported effect estimates as ORs or RRs. Among the 24 included articles, 18 were from cohort studies and 6 were from cross-sectional studies. Three articles were from the same cohort demonstrating differing analytical approaches (14,20,21). All the articles were from studies based in Europe or North America.

The cohort studies followed subjects from birth to a mean of 6 to 24 months; however, two studies reported outcomes at 5 and 6 years. The cross-sectional studies reported outcomes from 12 months up to 8 years. Sample sizes of the 24 studies ranged from 281 to 11 349 (Table S3). NOS quality of the cohort studies ranged from 5 to 10 of 10 (satisfactory to very good) and in the cross-sectional studies from 3 to 5 of 7 (unsatisfactory to good) (Table S4&S5).

Definitions of the exposed group and comparison groups were highly variable concerning duration and methods of feeding practices (exclusive, partial, formula, solid or combinations coupled with duration of feeding). AOM definitions in the studies were also diverse. Several studies defined AOM as parent-reported ear infections (12,22–34) and others used physician-diagnosed AOM symptoms (7,35) or both symptoms combined with otoscopic findings (14,20,21,36). GRADE quality assessment for the outcome of AOM was low to very low quality of

Table 1 GRADE evidence profile: breastfeeding and childhood AOM

	No of studies	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Sample size	OR (95% CI)	Quality
AOM 1st 2 years									
Exclusive BF 1st 6 months	5	Serious limitations	No serious Inconsistency*	No serious indirectness	No serious imprecision	Unlikely	17 735	0.57 (0.44,0.75)	++
Any BF >3–4 months	3	Serious limitations	Serious Inconsistency†	No serious indirectness	No serious imprecision	Unlikely	6793	0.85 (0.78, 0.92)	+
Ever vs never BF	5	Serious limitations	No serious inconsistency*	No serious indirectness	No serious imprecision	Unlikely	19 650	0.67 (0.56, 0.80)	++
More vs less BF	12	Serious limitations	No serious Inconsistency‡	No serious indirectness	No serious imprecision	Unlikely	39 380	0.65 (0.59, 0.72)	++
More vs less BF (cross-sectional)	5	Serious limitations	Serious Inconsistency†	No serious indirectness	No serious imprecision	Unlikely	4127	1.21 (0.60, 2.45)	+
AOM beyond 2nd year of life									
More vs less BF (Cohort+ cross-sec)	7	Serious limitations	Serious Inconsistency†	No serious indirectness	No serious imprecision	Unlikely	3943	1.03 (0.59, 1.79)	+
More vs less BF (Cohort)	3	Serious limitations	Serious Inconsistency†	No serious indirectness	No serious imprecision	Unlikely	2317	0.67 (0.28, 1.63)	+
More vs less BF (Cross-sectional)	4	Serious limitations	Serious Inconsistency†	No serious indirectness	No serious imprecision	Unlikely	1626	1.49 (0.57, 3.92)	+

*heterogeneity can be explained by excluding two ORs in Raisler 1999 study;
‡high heterogeneity resolves with exclusion of Labout 2011.
†Meta-analyses with high heterogeneity.

the overall meta-analysed results. Meta-analyses including only cohort studies showed comparatively higher quality than studies including only cross-sectional studies (Table 1).

Overview of study results

Fourteen cohort studies reported a reduced risk of AOM in childhood in at least one breastfeeding category, and four reported no beneficial effects of breastfeeding on the risk of AOM. However, none of the cohort studies reported an increased risk of AOM associated with breastfeeding. Five cross-sectional studies found a reduced risk of childhood AOM, one showed no association, and two found an increased risk of AOM associated with breastfeeding. Twenty-one studies used breastfeeding as a categorical exposure in the statistical analysis, of which two studies investigated a continuous exposure and categorical exposure, while one investigated breastfeeding as only a continuous exposure. Effect modification by ethnicity and siblings for the association of breastfeeding and AOM was investigated in two studies (Table S3).

One study found that children without siblings gained a greater beneficial effect from breastfeeding compared to children with siblings (37). Another study that stratified by ethnicity found that Caucasian, but not Black, Asian or Hispanic children who were breastfed had significantly reduced AOM during the first 6 months of life when compared with those not breastfed (12).
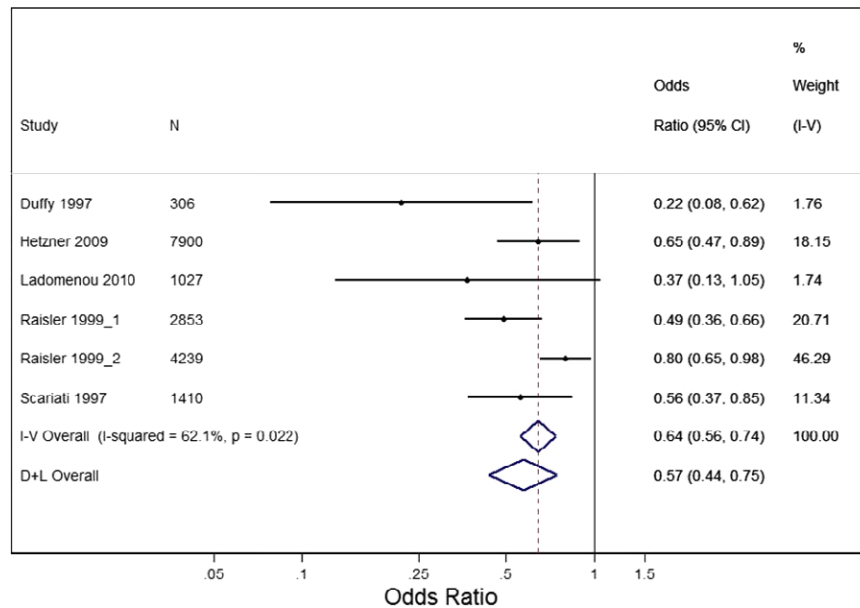
Meta-analysis results

Exclusive breastfeeding for the first 6 months vs nonexclusive breastfeeding for the first 6 months and AOM up to 2 years of age

Exclusive breastfeeding for 6 months and AOM was meta-analysed for five cohort studies (27,30,33,36,37). All except one (27) were adjusted for important confounders (day care attendance, presence of siblings, socio-economic status, second-hand smoke exposure and ethnicity). The quality of studies ranged from 6 to 8: four were 'good' quality, and one was 'satisfactory' quality (Table S4). Infants who were exclusively breastfed for the first 6 months of life showed 43% less AOM risk by 24 months compared to infants who were not exclusively breastfed (OR 0.57 95%CI 0.44, 0. 75 I^2 = 62.1%) (Fig. 2). Excluding two studies with higher standard errors did not result in a substantial difference in the pooled OR compared to meta-analysis including all five studies (Fig. S1).

Any breastfeeding more than 3–4 months vs any breastfeeding <3–4 months and AOM up to 2 years of age

Any breastfeeding for <3–4 months vs more than 3–4 months and childhood AOM was reported by only three cohort studies and two cross-sectional studies (21,26,29,34,38). Among the three cohort studies, two were 'satisfactory' quality, and one was 'very good' quality (Table S4). Only one of the cohort studies adjusted for potential confounders (38). In the pooled analysis for cohort studies, infants who were breastfed for more than
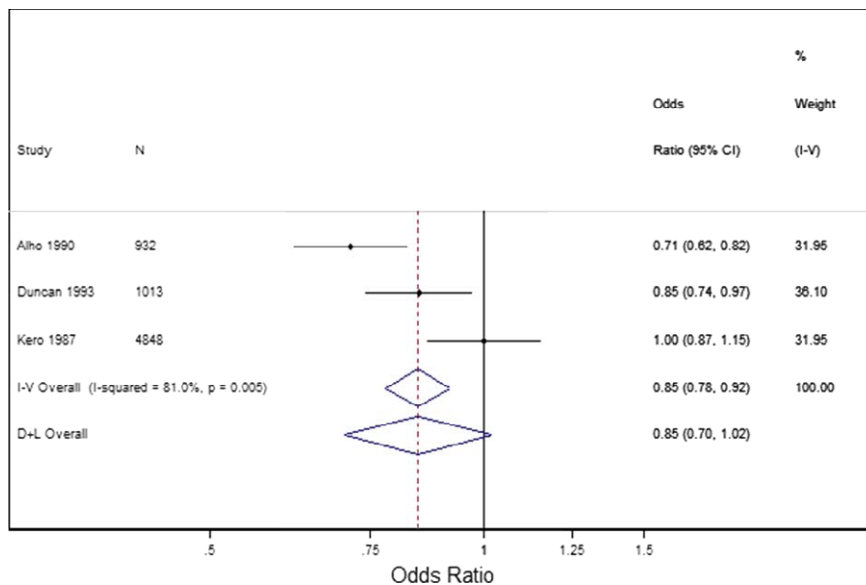
Figure 2 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for exclusive breastfeeding for the first 6 months vs not exclusive breastfeeding for the first 6 months and AOM during first 2 years of life in cohort studies. N – Number of subjects in each study.

3–4 months had less risk of AOM within the first 24 months compared to infants who were breastfed for <3–4 months (OR 0.85 95%CI 0.70, 1.02) (Fig. 3). However, study heterogeneity was high in the pooled analysis ($I^2 = 81\%$). The two cross-sectional studies were of 'good' and 'unsatisfactory' quality (Table S5). Only one study was adjusted for potential confounders (26). One study reported outcomes up to 18 months from retrospectively collected data (34), and the other reported AOM in the preceding

12 months in 1- to 3-year-olds (26). Pooled results of cross-sectional studies also showed a protective effect of AOM for breastfeeding more than 3–4 months compared to breastfeeding <3–4 months (OR 0.71 95%CI 0.42, 1.20 $I^2 = 37.8\%$) (Fig. 4).

Ever vs never breastfeeding and AOM up to 2 years of age
Ever vs never breastfeeding and outcome of AOM during the first 24 months was reported by five cohort studies

Figure 3 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for any breastfeeding more than 3–4 months vs any breastfeeding <3–4 months and AOM during first 2 years of life in cohort studies. N – Number of subjects in each study.
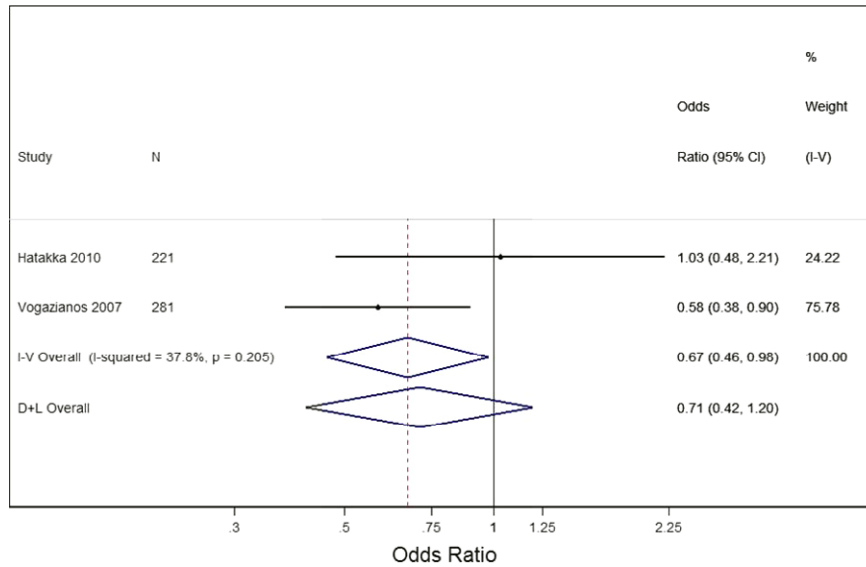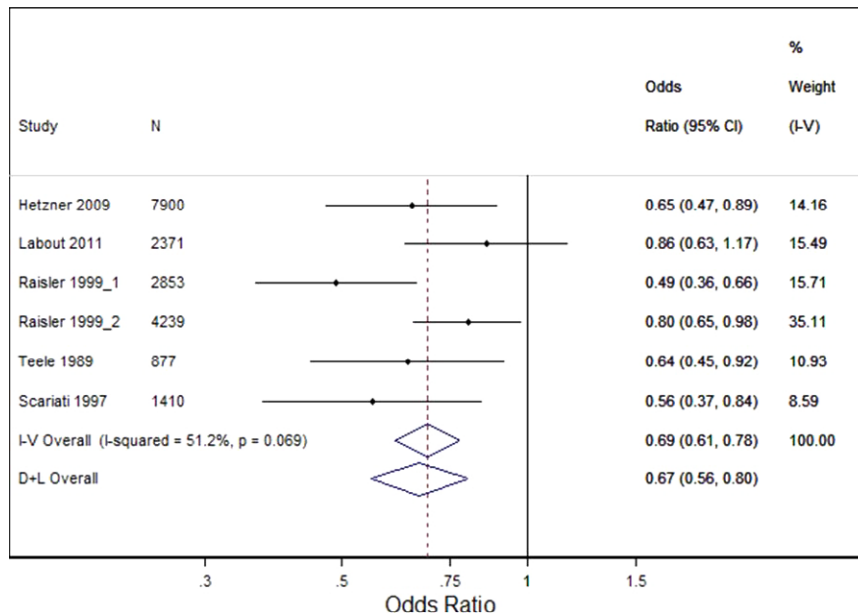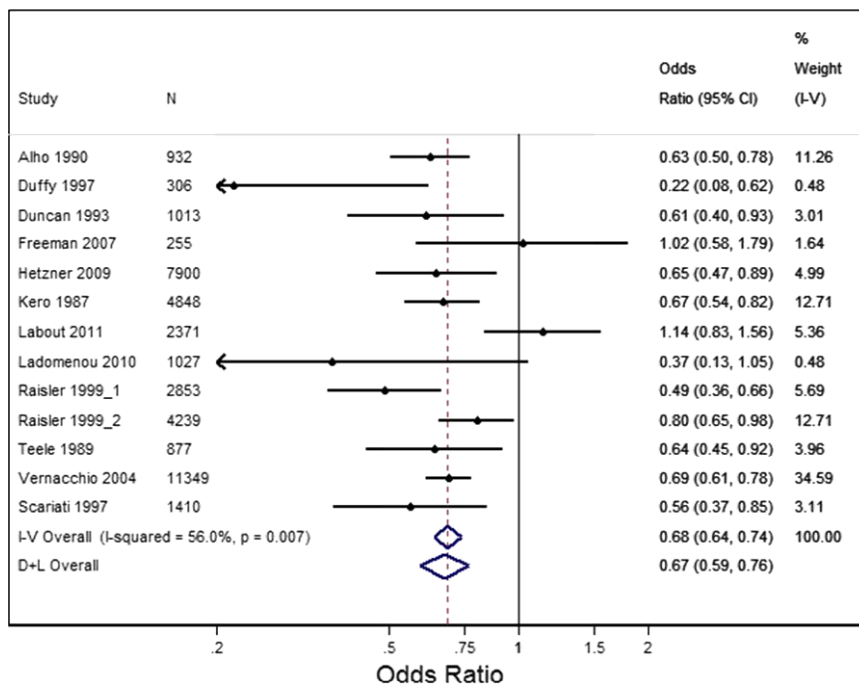
Figure 4 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for any breastfeeding more than 3–4 months vs any breastfeeding <3–4 months and AOM during first 2 years of life in cross-sectional studies. N – Number of subjects in each study.

(7,27,33,37,39). Four included studies' quality ranged from 'satisfactory' to 'good' (Table S4). Infants who were ever breastfed were protected against AOM during the first 24 months of the life compared to infants who never breastfed (OR 0.67 95%CI 0.56, 0.80 I^2 = 51.2%) (Fig. 5). Only one cross-sectional study (24) reported ever vs never breastfeeding (full breastfeeding ≥6 months) and AOM during the first year of life and the study found no significant association (OR 1.57 95%CI 0.91, 2.71) (Table S3).

More vs less breastfeeding and AOM up to 2 years of age
Altogether, 12 cohort studies were included in the more vs less breastfeeding and AOM during the first 2 years of life meta-analysis (7,12,21,27,29,30,33,36–40). Study quality ranged from 'satisfactory' to 'very good' (Table S4). In the pooled analysis, infants who were breastfed longer had greater protection from AOM in the first 24 months when compared with infants who were breastfed for shorter time periods (OR 0.67 95%CI 0.59, 0.76 I^2 = 56.0%) (Fig. 6).
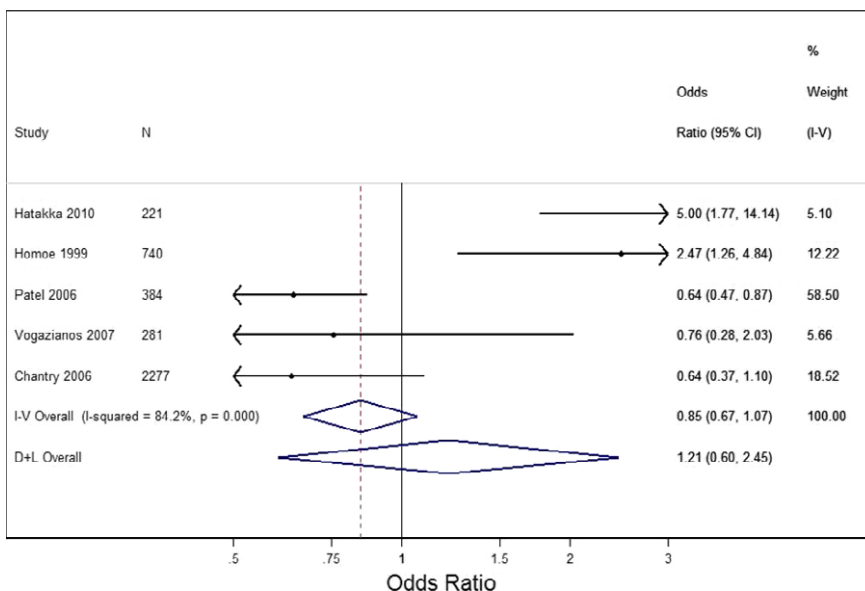

Figure 5 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for ever vs never breastfeeding and AOM during first 2 years of life in cohort studies. N – Number of subjects in each study.

Figure 6 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for more vs less breastfeeding and AOM during first 2 years of life in cohort studies. N – Number of subjects in each study.

Egger's test for small study effects showed weak evidence for publication bias (p = 0.360). There were no substantial differences in effect estimates after removing two studies with higher standard errors (OR 0.69 95%CI 0.61, 0.78) (Fig. S2). Pooled results for more vs less breastfeeding in cross-sectional studies (24,26,28,32,34) did not show a similar protective effect (OR 1.21 95%CI 0.60, 2.45 I^2 = 84.2%) (Fig. 7).

More vs less breastfeeding and risk of AOM after 2 years of age
The association between breastfeeding and the risk of AOM after 2 years of age was reported by 7 studies (three cohorts and four cross-sectional) (7,23,26,28,31,32,34). Studies included in this meta-analysis reported AOM up to 8 years of age. Pooled analysis of cohort and cross-sectional studies showed no beneficial effect of longer breastfeeding duration against AOM beyond 2 years compared to infants who had

Figure 7 Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for more vs less breastfeeding and AOM in cross-sectional studies. N – Number of subjects in each study.

a shorter breastfeeding duration (OR 1.03 95%CI 0.59, 1.79 I^2 = 84.7%) (Fig. S3).

DISCUSSION

There is good evidence from this systematic review and meta-analysis for a protective effect of breastfeeding on the risk of AOM in the first 2 years of life. Exclusive breastfeeding for 6 months was associated with the greatest protective effect in the pooled analyses. Longer duration of breastfeeding and ever breastfeeding were also associated with significant reductions in the risk of AOM in the first 2 years of life. The evidence derived from pooled analysis of cohort studies was stronger than for cross-sectional studies indicating that recall bias may be an issue. There was no significant effect found for breastfeeding during infancy and the risk of AOM after 2 years; however, only a few studies looked at the association of breastfeeding and AOM after 2 years old. None of the studies reported exclusive breastfeeding and AOM after 2 years old.

A systematic review of the relationship between breastfeeding and AOM published in 1996 (41) found that breastfeeding for at least 3 months reduced the risk of AOM. However, this review did not consider the included study quality and did not account for confounders. Also, neither clinical nor statistical heterogeneity of the studies were considered (41). To address these issues, the U.S. Agency for Healthcare Research and Quality (AHRQ) published an updated meta-analysis in 2007 (42), finding that ever breastfeeding and exclusive breastfeeding were associated with reduced risk of AOM. However, they included only six studies in the meta-analysis, two in 'ever vs never' and three in '3 or 6 months exclusive breastfeeding categories', and provided little information on their search strategy. Further, their exclusive breastfeeding meta-analysis included two overlapping results from one study which may have led to bias in the pooled estimate. Another review by McNiel in 2010 (43) reanalysed the same studies included in the AHRQ. In the most recent review in 2011, Abrahams & Labbok (44), narratively reviewed studies published in 2010 and 2011.

In summary, Previous reviews have not provided a comprehensive account of the existing literature (41–44) or meta-analysed relevant studies published after 2007. Furthermore, these reviews did not consider differences in breastfeeding exposure within their meta-analyses. The current systematic review and meta-analysis is a comprehensive update of the current literature in the field.

We assessed the quality of the studies using a NOS scale, which provides an overall quality estimate for each study by considering selection of the sample, comparability of the nonexposed group, definitions of outcomes and definitions of exposure and adequacy of the follow-ups. Consideration of the quality of included studies can assist in interpretation of the strength of evidence provided by the pooled estimate.

Our analysis showed that longer duration of breastfeeding was protective for AOM during the first 2 years of life.

Longer duration of breastfeeding has also been found to be protective for many childhood diseases (45) including acute childhood infections (46), childhood diabetes (47), respiratory and atopic diseases (45) and obesity (48). Human milk contains unique biologically active substances such as immunomodulatory, anti-inflammatory and antimicrobial agents which provide protection to infants while their immune system matures. These substances protect against bacterial pathogens (49,50), support the growth of commensal bacteria which compete with pathogens (50,51) and inhibit the binding capability of pathogenic bacteria to epithelial cells (49,51).

A human breastmilk microbiome is a novel concept. Human milk contains beneficial bacteria which can enhance protection against pathogens for infants and helps in maturation of the infant's immune system (52). Little is known about the infant oral microbiome; however, ecological niches in the human microbiome are a network of communities interconnected with each other experiencing constant exchange (53). Recent studies have demonstrated that microbiota of the pharynx differs between breastfed and nonbreastfed children (54), and have found that colonisation by *Corynebacterium* and *Dolosigranulum* in the upper respiratory tract is associated with a reduced risk of AOM (54–56). *Corynebacterium* is a known member of the breastmilk microbiome (52). We hypothesise that through ingestion of the microbiota in breastmilk, there is colonisation of the mouth, pharynx and also the middle ear with beneficial microbiota that can reduce the risk of AOM. Breastmilk also contains numerous human milk oligosaccharides (HMOs) which act as prebiotics. These HMOs are nondigestible carbohydrates that selectively promote the growth of commensal bacteria (57,58). Neonatal intestinal bacteria are thought to play an important role in shaping the infants immune response. The combination of microbiota and oligosaccharides in human breastmilk may provide greater protection against AOM in breastfed children.

In addition to the biochemical components in human milk, there are also physiological mechanisms explaining the association between breastfeeding and reduced risk of AOM. Strong negative pressure is generated by breastfeeding, in contrast to bottle-feeding. Suck, swallow and breathing patterns are also different from bottle-feeding infants (59). In bottle-feeding children, pooling of formula is more likely (44). The low beneficial biological components in formula coupled with pooling of milk create an increased risk of pathogen colonisation in the eustachian tube leading to an increased risk of AOM.

The protective effect of breastfeeding against AOM was evident among the infants who had breastfed for a longer duration compared to shorter duration, and in infants who were breastfed ever compared to never. This provides evidence that not only exclusive breastfeeding, but shorter duration of breastfeeding provides some degree of protection against AOM during the first two years of life. The protective effect of breastfeeding for AOM after 2 years of life was not evident. However, this

finding is limited by power as only a few studies reported AOM after 2 years.

Assuming around 80% of nonbreastfed children will get AOM at least once by the age of 2 years (7), the absolute risk reduction in ever having AOM would be 52% for children exclusively breastfed for the first 6 months of life. To demonstrate a benefit of breastfeeding against AOM, only two infants need to be exclusively breastfed for 6 months.

Recommendations for duration of exclusive breastfeeding are different locally and globally. Recent guidelines introduced by WHO (60), Australian NHMRC (2013) (61) and the New Zealand National guidelines (2008) (62) recommend exclusive breastfeeding until around 6 months. Guidelines from the Australasian Society of Clinical Immunology and Allergy (ASCIA) (63), American Academy of Allergy, Asthma and Immunology (AAAAI) (60) (64) and the European guidelines (ESPGHAN Committee on Nutrition) (65) recommend the introduction of solids between 4 and 6 months. In this systematic review, we found, in agreement with all the guidelines, that any breastfeeding was protective for AOM in the first two years of life. Although the greatest risk reduction was observed in those exclusively breastfed for 6 months, the available literature did not allow us to directly compare with those exclusively breastfed for 4–6 months, so we are unable to provide any further evidence to inform this debate.

Limitations

We only included articles in the English language, and this may have caused selection bias. All included studies were from North America and Europe; therefore, interpretation of results should be made with caution. Specifically, we are unable to generalise these results to low-income non-Caucasian countries which bear the largest burden of disease in terms of sequelae and deaths from AOM.

Exclusion of the Raisler 1991 study from the meta-analyses (in: exclusive breastfeeding for the first 6 months vs not exclusive breastfeeding for the first 6 months; and ever vs never breastfeeding) resulted in low heterogeneity (0–33% – results not shown). This study reported the risk of AOM in a stratified analysis by having or not having siblings, but did not report effect estimates without stratification. The inclusion of stratified results from Raisler 1991 introduced high heterogeneity into the overall meta-analyses.

Although some studies of breastfeeding and AOM considered parental history of allergy, number of siblings, day care attendance, maternal smoking, gender, ethnicity and socio-economic status as potential confounders, others failed to adjust for these covariates. Some estimates included in the meta-analyses were not adjusted for any confounders and some adjusted for only a few. Not adjusting may have caused some bias in meta-analysis results. There were too few studies in each stratum to perform analyses stratified by good vs poor adjustment for confounders.

Combining different study designs may be a source of heterogeneity in meta-analysis. In the meta-analysis of AOM outcomes beyond 2 years of age, we pooled both cross-sectional and cohort studies.

CONCLUSION AND RECOMMENDATIONS

This systematic review found good evidence that breastfeeding is associated with a reduced risk of AOM during the first two years of life, with an average reduced risk of 30–40% in all categories of breastfeeding. These risk reductions may be mediated through unique biologically active substances found in breastmilk including microbiota and human milk oligosaccharides. Future studies should address the role of these breastmilk components in the colonisation of the middle ear by AOM pathogens and the response of the infant's immune system. Researchers are also advised to record breastfeeding in a uniform manner using validated questions and definitions, to avoid exposure misclassifications.

CONFLICT OF INTEREST AND FUNDING STATEMENT

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Search strategy.
Table S2. Studies excluded for reasons.
Table S3. Study characteristics of studies reporting the association of breastfeeding and AOM.
Table S4. NOS study quality cohort studies.
Table S5. NOS study quality cross-sectional studies.
Figure S1. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for exclusive breast feeding for the first 6 months vs not exclusive breast feeding for the first 6 months and AOM during first 2 years of life in cohort studies – studies without high standard error.
Figure S2. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analysis for more vs less breast feeding and AOM during first 2 years of life in cohort studies – studies without high standard error.
Figure S3. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of meta-analyses for more vs less breast feeding and AOM beyond 2 years of life 1.
Data S1. Excluded References.