Breastfeeding and Reduced Risk of Sudden Infant Death Syndrome: A Meta-analysis

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KEY WORDS

SIDS, sudden infant death syndrome, risk factors, breastfeeding

ABBREVIATIONS

SIDS—sudden infant death syndrome
OR—odds ratio
SOR—summary odds ratio
CI—confidence interval

The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The results, conclusions, and recommendations presented in this article are endorsed by the Epidemiology Working Group of the International Society of the Prevention of Infant Deaths.

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abstract

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CONTEXT: Benefits of breastfeeding include lower risk of postneonatal mortality. However, it is unclear whether breastfeeding specifically lowers sudden infant death syndrome (SIDS) risk, because study results have been conflicting.

OBJECTIVE: To perform a meta-analysis to measure the association between breastfeeding and SIDS.

METHODS: We identified 288 studies with data on breastfeeding and SIDS through a Medline search (1966–2009), review articles, and meta-analyses. Twenty-four original case-control studies were identified that provided data on the relationship between breastfeeding and SIDS risk. Two teams of 2 reviewers evaluated study quality according to preset criteria; 6 studies were excluded, which resulted in 18 studies for analysis. Univariable and multivariable odds ratios were extracted. A summary odds ratio (SOR) was calculated for the odds ratios by using the fixed-effect and random-effect inverse-variance methods of meta-analysis. The Breslow-Day test for heterogeneity was performed.

RESULTS: For infants who received any amount of breast milk for any duration, the univariable SOR was 0.40 (95% confidence interval [CI]: 0.35–0.44), and the multivariable SOR was 0.55 (95% CI: 0.44–0.69). For any breastfeeding at 2 months of age or older, the univariable SOR was 0.38 (95% CI: 0.27–0.54). The univariable SOR for exclusive breastfeeding of any duration was 0.27 (95% CI: 0.24–0.31).

CONCLUSIONS: Breastfeeding is protective against SIDS, and this effect is stronger when breastfeeding is exclusive. The recommendation to breastfeed infants should be included with other SIDS risk-reduction messages to both reduce the risk of SIDS and promote breastfeeding for its many other infant and maternal health benefits. *Pediatrics* 2011; 128:103–110

There are many physical and emotional benefits to breastfeeding,[1] including a reduced risk of postneonatal mortality.[2] However, it is unclear whether breastfeeding specifically lowers the risk of sudden infant death syndrome (SIDS). Physiologic sleep studies have shown that breastfed infants have lower arousal thresholds than formula-fed infants,[3,4] which may provide a mechanism for protection against SIDS. However, epidemiologic studies have been inconsistent in showing a protective effect of breastfeeding on the risk of SIDS; some study results have supported a protective effect,[5–11] and others have not.[2,5,8,12–19] The authors of a meta-analysis and qualitative literature review published in 2000 concluded that there was a statistically significant increase in SIDS risk for bottle-fed infants.[20] These authors, however, defined SIDS loosely (as any sudden and unexplained death in an infant or young child) and included studies in which the definitions of breastfeeding exposure differed, and there were other methodologic flaws. A more recent meta-analysis conducted by the Agency for Healthcare Research and Quality analyzed 6 studies and found a statistically significant decrease in SIDS in infants who were ever breastfed compared with infants who were never breastfed (adjusted summary odds ratio [SOR]: 0.64 [95% confidence interval (CI): 0.51–0.81]).[21] We performed our meta-analysis to quantify and evaluate the protective effect of breastfeeding against SIDS, including the influence of exclusive breastfeeding and longer breastfeeding duration, and to make a recommendation on the potential utility of breastfeeding as a strategy for reducing the risk of SIDS. Our hypotheses were that (1) breastfeeding is associated with a decreased risk of SIDS and (2) exclusive breastfeeding and breastfeeding for longer duration are associated with the greatest reduction in risk. This report of our methods and findings follows the guidelines for reporting meta-analyses of observational studies proposed by Stroup et al[22] and the PRISMA Group.[23]

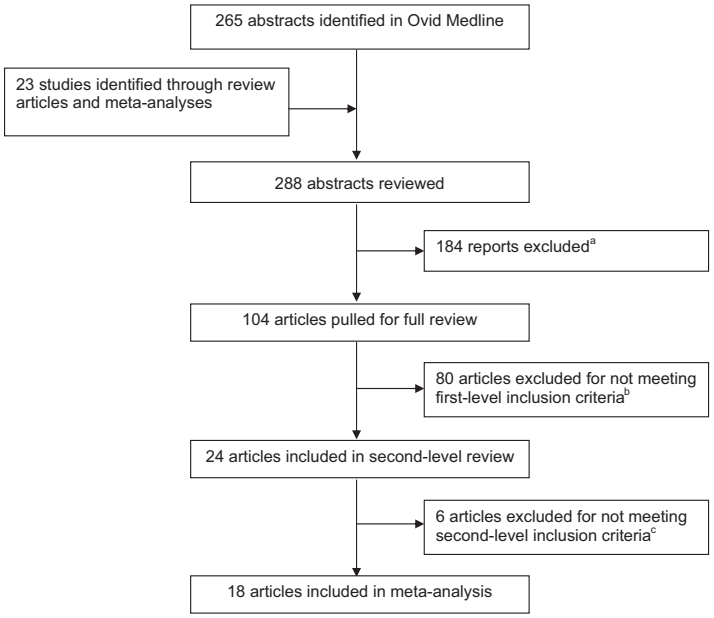

FIGURE 1
Study inclusion and exclusion flow diagram. [a] Exclusion criteria: duplication, no apparent relevance. [b] First-level inclusion criteria: articles that reported an association between breastfeeding and SIDS. [c] Second-level inclusion criteria: see criteria listed in Table 1; an additional study was excluded for not providing ORs that could be used in calculating an SOR.

METHODS

Data Sources and Study Selection

We searched the Ovid Medline database (January 1966 through December 2009) to collect data on breastfeeding and its association with SIDS. The search strategy included published articles limited to humans with the Medical Subject Headings terms "sudden infant death" and "breast feeding" with key words "sudden infant death syndrome," "SIDS," "cot death," and "breastfeeding." Combining searches resulted in 265 abstracts (Fig 1). An additional 23 studies were identified through review articles and meta-analyses, for a total of 288 studies. These studies were reviewed by teams of 2 independent reviewers who evaluated each abstract for relevance on the basis of title and abstract. One hundred eighty-four reports were excluded on the basis of the abstracts alone, and 104 articles were pulled for further review. Two reviewers (Dr Hauck and Ms Tanabe) reviewed all pulled articles for inclusion and for overlapping data. Twenty-four original case-control studies that provided data on the relationship between breastfeeding and SIDS risk[2,5–11,14–19,24–33] were identified. Two teams of 2 reviewers independently evaluated 12 studies each according to preset criteria; in cases of disagreement, a third reviewer evaluated the study, and a consensus opinion was reached.

Because the search was not limited to articles written in English, 12 of the articles were in other languages (3 German, 3 Italian, 1 Japanese, 1 Spanish, 1 Polish, and 3 Norwegian). After reviewing the articles and abstracts, either in the original language or the English translation, none of these studies was deemed relevant except 1 Norwegian study, for which an article published in

English with the same content replaced the one published in Norwegian.

Data Extraction

The teams evaluated the eligible studies on the basis of the 6 criteria developed by the American Academy of Pediatrics Task Force on Positioning and SIDS for its literature review on the relationship between sleeping position and SIDS. These criteria are (1) an appropriate definition for SIDS, (2) autopsies performed in >98% of cases, (3) an adequate description of SIDS ascertainment in the study population, (4) matched control subjects, (5) an adequate description of the process of control selection, and (6) inclusion of sufficient data to calculate ORs and 95% CIs or inclusion of the actual ORs and CIs. In our review, 19 of 24 studies satisfied all 6 criteria; the failed criteria of 5 studies are listed in Table 1.[2,9,16,19,32] Another study could not be included because the ORs were presented in a way that was not compatible with our analyses,[33] which resulted in a total of 18 studies for the meta-analysis.

Statistical Analysis

Several different definitions for breastfeeding were examined: (1) breastfeeding of any amount (partial or exclusive) or duration, including breastfeeding at discharge from hospital ("any breastfeeding"); (2) breastfeeding of any amount at the age of 2 months or older ("breastfeeding ≥ 2 months"); and (3) exclusive breastfeeding (ie, no formula supplementation) for any duration ("exclusive breastfeeding").

The univariable and multivariable ORs were extracted from each study for the different associations between breastfeeding and SIDS. A separate SOR was calculated for the univariable and multivariable ORs by using the fixed-effect and random-effect inverse-variance methods of meta-analysis. The Breslow-Day test for heterogeneity was performed. A P value of <.05 was considered to indicate that heterogeneity was present. Analyses were conducted independently by 2 authors (Drs Thompson and Vennemann), one by using RevMan 5.0 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark) and one by using Comprehensive Meta Analysis 2.2.048 (Biostat, Englewood, NJ). Any discrepancies were investigated and resolved.

RESULTS

Eighteen case-control studies were included in the meta-analysis (Table 1), and data for any breastfeeding were provided for all of them.* The forest plot for the univariable ORs with the random-effect model is shown in Fig 2; the SOR was 0.40 (95% CI: 0.35–0.44; I^2 = 71%). Multivariable ORs were reported for only 7 of the 23 studies[5,7,8,10,17,18,34]; a univariable pooled analysis of the results from these 7 studies resulted in an OR of 0.36 (95% CI: 0.31–0.42), which is consistent with the results when all 18 studies were included. The multivariable pooled estimate revealed a movement of the OR toward the null; however, it remained statistically significant at 0.55 (95% CI: 0.44–0.69) (Fig 3). There was no heterogeneity (I^2 = 40%).

Three studies provided information about any breastfeeding at 2 months of age or older.[5,11,15] The summary univariable estimate for the 3 studies was 0.38 (95% CI: 0.27–0.54; I^2 = 78%). Because only 2 of the studies provided multivariable ORs,[5,11] meta-analysis to obtain a summary multivariable estimate was not performed.

Eight studies provided information on exclusive breastfeeding of any duration.[5–7,14,15,26,29,34] The univariable SOR was 0.27 (95% CI: 0.24–0.31; I^2 = 87%) (Fig 4). None of these studies provided multivariable ORs for exclusive breastfeeding.

As noted previously, 5 studies failed to meet 1 or more quality criteria.[2,9,16,19,32] A sensitivity analysis was conducted to determine the SORs for any breastfeeding with these 5 studies included. The resulting univariable SOR was 0.49 (95% CI: 0.45–0.53). The multivariable SOR was 0.68 (95% CI: 0.58–0.80). These results are slightly higher than the SORs that excluded the respective studies.

DISCUSSION AND RECOMMENDATIONS

Our meta-analysis of 18 studies reveals that breastfeeding to any extent and of any duration is protective against SIDS. The protective effect is stronger for exclusive breastfeeding. The summary multivariable OR suggests that breastfeeding itself is protective and not merely a marker of other potentially protective factors such as the absence of smoke exposure or sociodemographic factors. Therefore, we recommend that mothers breastfeed their infants as a potential way to reduce their risk of SIDS. Ideally, breastfeeding should be exclusive (ie, formula should not be given) for at least 4 to 6 months and should be continued until the infant is at least 1 year of age. Exceptions to this recommendation include conditions under which breastfeeding is contraindicated, such as for infants whose mothers use illegal drugs.[35] This recommendation is consistent with the American Academy of Pediatrics policy statement on breastfeeding and the use of human milk, which endorses exclusive breastfeeding to 6 months and continuation for at least the first year of life.[35]

Some breastfeeding advocates have expressed concern that promotion of other factors shown in epidemiologic studies to be protective against SIDS, such as pacifier use and room-sharing

*Refs 5–8, 10, 11, 14, 15, 17, 18, 24–30, and 34.

TABLE 1 Studies Included in the Meta-analysis

Study (Year)	Country	Years of Study	Total Cases, *N*	Total Controls, *N*	Breastfeeding Cases, *n* (%)	Breastfeeding Controls, *n* (%)	Crude OR (95% CI)	Covariates[a]	Time to Interview[b]	Failed Criteria
Any breastfeeding										
Bartholomew and MacArthur[24] (1988)	Scotland	Unknown	79	79	15 (19)	25 (32)	0.51 (0.23–1.13)	—	2 wk after death	None
Naeye et al[25] (1976)	United States	1952–1966	125	375	16 (13)	60 (16)	0.77 (0.41–1.44)	—	No interview	None
Biering-Sørensen et al[15] (1978)	Denmark	1956–1971	123	520	98 (75)	480 (92)	0.33 (0.18–0.59)	—	No interview	None
Steele and Langworth[26] (1966)	Canada	1960–1961	80	157	21 (26)	75 (48)	0.39 (0.21–0.73)	—	NA[c]	None
Protestos et al[27] (1973)	United Kingdom	1960–1972	94	135	22 (23)	71 (53)	0.28 (0.15–0.52)	—	No interview	None
Murphy et al[28] (1982)	United Kingdom	1965–1973, 1975–1977	99	47 223	16 (16)	14 223 (30)	0.54 (0.29–1.01)	—	NA	None
Grice and McGlashan[29] (1981)	Tasmania	1970–1976	121	153	53 (44)	101 (66)	0.40 (0.24–0.67)	—	No interview	None
McGlashan[30] (1989)	Tasmania	1980–1986	167	334	115 (69)	252 (75)	0.72 (0.47–1.11)	—	Up to 5 wk after death	None
Ford et al[6] (1993)	New Zealand	1987–1990	356	1529	275 (77)	1371 (90)	0.39 (0.29–0.53)	—	Within 1 mo of death	None
Gilbert et al[14] (1995)	United Kingdom	1987–1989, 1990–1991	98	196	56 (57)	144 (73)	0.48 (0.27–0.84)	—	2 interviews; immediately and at 2–3 mo	None
Ponsonby et al[18] (1995)	Tasmania	1988–1991	58	120	22 (38)	63 (53)	0.50 (0.26–0.98)	1, 4	6 wk after death	None
Klonoff-Cohen and Edelstein[31] (1995)	United States	1989–1992	200	200	114 (57)	151 (76)	0.43 (0.27–0.68)	3, 4, 6, 13, 17	NA	None
Mitchell et al[5] (1997)	New Zealand	1991–1993	120	918	98 (82)	809 (88)	0.60 (0.35–1.03)	1–6, 7, 9, 11, 12, 19	NA	None
Wennergren et al[10] (1997)	Denmark, Norway, Sweden	1992–1995	244	863	184 (75)	729 (84)	0.59 (0.41–0.85)	4, 6, 9	NA	None
Schellscheidt et al[11] (1997)	Germany	1993–1994	58	156	29 (50)	129 (83)	0.21 (0.10–0.44)	4, 6, 15, 16, 19	Within 2 wk	None
Fleming et al[17] (1996)	United Kingdom	1993–1995	195	780	88 (45)	470 (60)	0.50 (0.35–0.71)	1–7, 9, 10, 14, 16, 18, 19	2 interviews; within 5 d and 2 wk of death	None
Hauck et al[8] (2003)	United States	1993–1996	260	260	55 (21)	130 (50)	0.20 (0.12–0.35)	1, 5, 11, 13	2 wk after death	None
Vennemann et al[7] (2009)	Germany	1998–2001	333	998	165 (50)	827 (83)	0.19 (0.14–0.25)	1–7, 15, 16, 18	1 mo after death	None
Breastfeeding ≥2 mo										
Biering-Sørensen et al[15] (1978)	Denmark	1956–1971	97	503	22 (23)	278 (55)	0.24 (0.14–0.41)		No interview	None
Mitchell et al[5] (1997)	New Zealand	1991–1993	64	778	46 (72)	600 (77)	0.76 (0.41–1.39)	1–6, 7, 9, 11, 12, 19	NA	None
Schellscheidt et al[11] (1997)	Germany	1993–1994	58	156	7 (12)	50 (32)	0.29 (0.11–0.74)	4, 6, 15, 16, 19	Within 2 wk of death	None
Studies excluded for not meeting eligibility criteria										
Fedrick[31] (1974)	United Kingdom	1966–1970	154	409	63 (37)	157 (31)	1.11 (0.75–1.65)		No interview	1–3
Watson et al[16] (1981)	United Kingdom	1975–1979	308	236	164 (53)	161 (68)	0.53 (0.37–0.76)		2 interviews; immediately and 3 wk later	1–3
Chen and Rogan[2] (2004)	United States	1988	591	7740	187 (32)	3073 (40)	0.70 (0.59–0.84)	1, 3, 4, 5, 9, 12, 19	NA	1–4
Stray-Pedersen et al[19] (2005)	Norway	1989–2003	23	72	16 (73)	65 (90)	0.29 (0.09–0.97)	4, 7	1 mo after death	4, 5
Jonville-Béra et al[9] (2001)	France	1995–1997	111	341	37 (33)	160 (47)	0.57 (0.35–0.92)	3, 4, 6, 9, 14, 17, 19	2 interviews; day of death and 3 mo after death	2
Alm et al[33] (2002)	Denmark, Norway, Sweden	1992–1995	239	841	109 (46)	626 (74)	0.29 (0.21–0.39)	4–6, 8	NA	None[c]

Studies were scored on the following criteria: (1) an appropriate definition for SIDS; (2) autopsies performed in >98% of cases; (3) an adequate description of SIDS ascertainment in the study population; (4) matched control subjects; (5) an adequate description of the process of control selection; and (6) inclusion of sufficient data to calculate ORs and 95% CIs or the actual ORs and CIs were provided. NA indicates not available, not provided.

[a] Covariates: 1, maternal age; 2, parity; 3, birth weight; 4, infant exposure to tobacco smoke (before or after delivery); 5, factors related to socioeconomic status; 6, infant sleep position; 7, bed-sharing; 8, infant age; 9, infant gender; 10, gestation; 11, marital status; 12, race/ethnicity; 13, factors related to prenatal care; 14, factors relating to surface on which infant was placed; 15, pillow/cushion use; 16, factors related to overheating; 17, postneonatal infant health problems; 18, pacifier use; 19, other.

[b] Time to interview was defined as time from infant's death or identification of controls to interview with parents.

[c] ORs in the article were provided for intervals of breastfeeding duration; thus, we could not identify an OR to use in calculating the SOR for this meta-analysis.

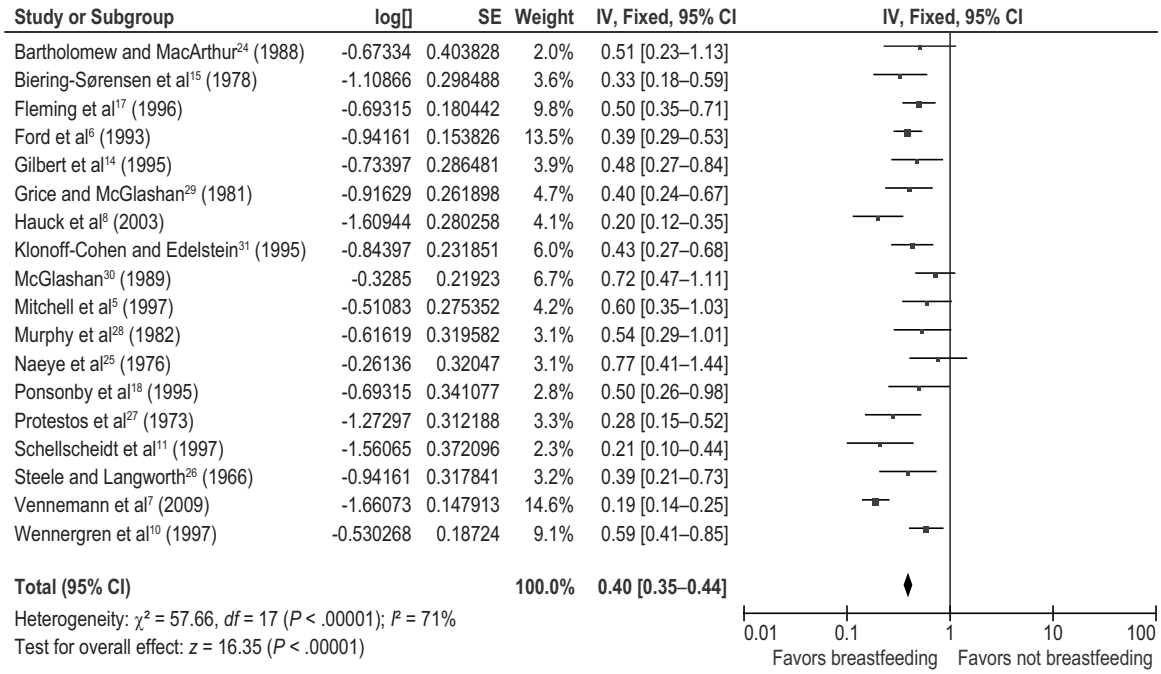

FIGURE 2
Univariable analysis of any breastfeeding versus no breastfeeding.

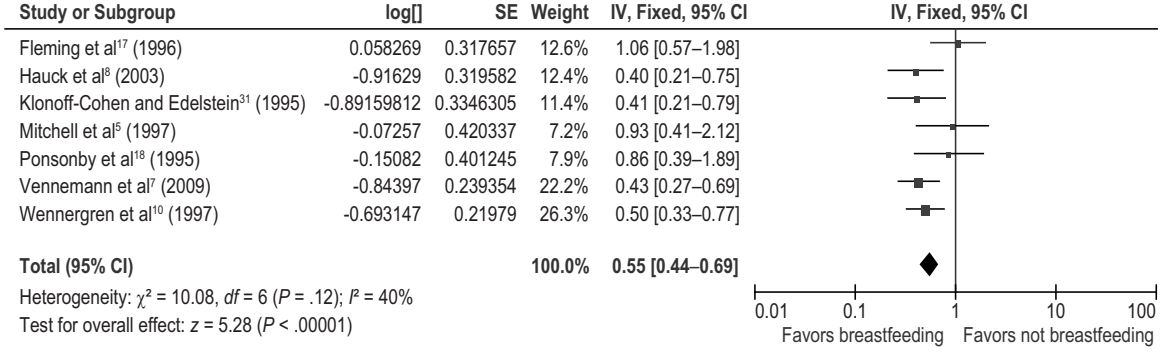

FIGURE 3
Multivariable analysis of any breastfeeding versus no breastfeeding.

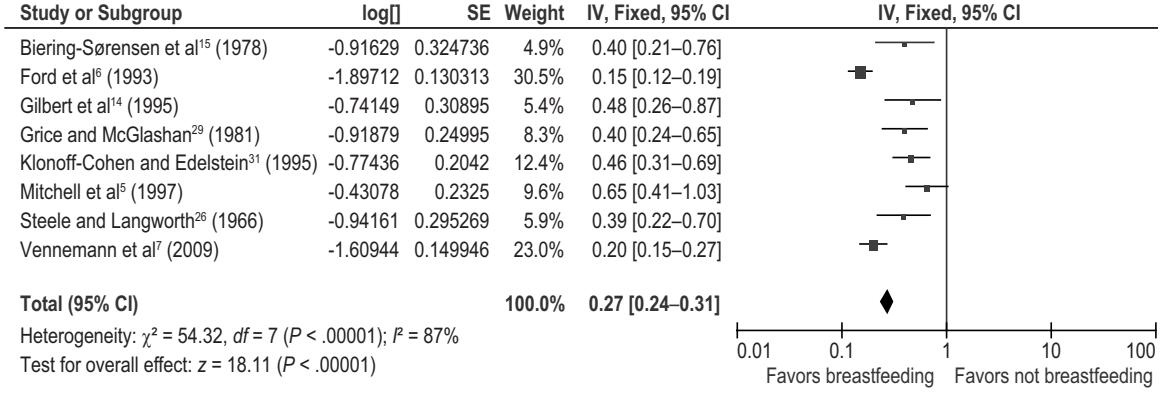

FIGURE 4
Univariable analysis of exclusive breastfeeding of any duration.

without bed-sharing, is inconsistent with promotion of breastfeeding. Although some observational studies have revealed an association between pacifier use and decreased breastfeeding duration,[36–38] this association was not borne out by several randomized clinical trials[39–41] and 1 systematic review.[42] The American Academy of Pediatrics policy statements on breastfeeding and the use of human milk[35] and SIDS[43] both indicate that pacifiers can be used by breastfed infants once breastfeeding has been well established. Mother-infant bed-sharing (or sleeping in the same bed) is often promoted as a way to increase breastfeeding rates[44–46]; however, although bed-sharing is associated with increased breastfeeding duration, it is unclear whether the practice of bed-sharing increases the practice of breastfeeding or if parents who choose to breastfeed subsequently decide to bed-share.[47] Room-sharing without bed-sharing (sleeping in the same room with the infant's crib or bassinet close to the parents' bed) is recommended for all infants as a way to reduce the risk of SIDS and accidental suffocation while facilitating feeding and monitoring of the infant.[43] One study from the Netherlands revealed that the benefits of breastfeeding do not outweigh the increased risk of SIDS associated with bed-sharing.[48] Additional studies to analyze the contribution of multiple simultaneous factors (such as bed-sharing and breastfeeding or pacifier use and breastfeeding) to SIDS risk are needed.

Although causation cannot be proven in case-control studies, on which these results are based, the factors that have been proposed to support causality in observational studies are found in this meta-analysis: (1) consistent findings; (2) strong association; (3) dose-response effect; (4) causal factor preceding the outcome; and (5) biological plausibility.[49] Although the studies were from many different countries, and heterogeneous populations were represented, the individual ORs for breastfeeding in relation to SIDS were similar. The association between breastfeeding and SIDS risk reduction is strong, there is a dose response, and the causal factor (ie, breastfeeding) precedes the outcome. The protective effect of breastfeeding against SIDS also has biological plausibility. Breastfed infants are more easily aroused from active sleep than formula-fed infants at 2 to 3 months of age, which is within the 2- to 4-month peak age during which SIDS occurs.[4] Breastfeeding also confers immunologic advantages over formula feeding by providing immunoglobulins and cytokines that may protect infants during the vulnerable period for SIDS, when their own production of immunoglobulin G is low and their maternally acquired levels are decreasing. Infants who die from SIDS often have had a minor infection in the days preceding death that was not sufficient alone to have caused death. These infections may induce proinflammatory cytokines that may cause respiratory or cardiac dysfunction, fever, shock, hypoglycemia, and arousal deficits.[7,50] Although the possibility of reverse causality cannot be ruled out entirely (ie, certain infants may be difficult to breastfeed because of underlying health conditions that may make them more susceptible to SIDS), most SIDS deaths occur in previously healthy infants; therefore, it would not likely account for many of the SIDS deaths. Another potential concern is that inadequate recall of breastfeeding duration may bias results. However, the time to interview after the infant death in the included studies was generally short.

The 2005 American Academy of Pediatrics policy statement on SIDS did not endorse breastfeeding as a means to reduce the risk of SIDS because of the insufficient strength of evidence available at that time.[43] Although there were several studies that had found a protective effect of breastfeeding, after controlling for possible confounding factors, the protective effect had been eliminated for some, so clear conclusions could not be drawn. Studies published since that statement, which are included in our current meta-analysis, notably the more detailed analysis of Vennemann et al,[7] showed a strongly protective effect of breastfeeding even after controlling for confounders. The meta-analysis by Ip et al[21] consisted of many but not all of the studies included in our current analysis, and our findings were similar to theirs. In the Ip et al analysis, ever breastfeeding was associated with crude and adjusted SORs of 0.41 (95% CI: 0.28–0.58) and 0.64 (95% CI: 0.51–0.81), respectively. The authors did not report results for exclusive breastfeeding or specific durations.

A potential limitation of our meta-analysis is that studies from which significant associations are reported may be preferentially published, which could result in an overestimate of the true effect and could bias the results.[22] It is unlikely that this was the case for several reasons. The breastfeeding results were all part of larger studies that examined potential risk and protective factors for SIDS; thus, results were published along with other findings. There was some heterogeneity of results, which indicates that results were not selectively reported. Studies published in languages other than English were included. Finally, we attend international SIDS meetings regularly, participate in SIDS organizations and Listservs, and have frequent contact with SIDS researchers around the world; we are not aware of other unpublished studies that would contradict these findings. A limitation identi-

fied by this meta-analysis was the small number of studies that presented data on breastfeeding duration, and when presented, there were different ways in which duration was defined, which made it difficult to pool the results. This is an area that needs further investigation.

CONCLUSIONS

There are many known benefits to breastfeeding, and breastfeeding should be recommended for all newborn infants to enhance maternal and infant well-being. The best time to begin the dialogue with mothers about breastfeeding plans is the prenatal period, and it should be included with other SIDS risk-reduction messages and materials that are traditionally given to expectant mothers during pregnancy. The same benefits of breastfeeding in protecting against SIDS are found for black infants as for those in other groups.[8] However, breastfeeding initiation and continuation occur less frequently among black mothers and those of other racial/ethnic minorities and among socially disadvantaged mothers.[51] In addition, these same groups have a higher incidence of SIDS.[52] Thus, it is essential that breastfeeding interventions target these higher-risk populations,[53,54] and future research should focus on developing and evaluating innovative intervention methods. All health professionals should speak in 1 voice about the importance of breastfeeding, which now adds SIDS risk reduction to its long list of maternal and infant health benefits.

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