

Duration of Breastfeeding and Risk of SIDS: An Individual Participant Data Meta-analysis

John M.D. Thompson, PhD,^a Kawai Tanabe, MPH,^b Rachel Y. Moon, MD,^c Edwin A. Mitchell, FRSNZ, FRACP, FRCPC, DSc (Med),^a Cliona McGarvey, PhD,^d David Tappin, MBBS, MD, MSc,^e Peter S. Blair, PhD,^f Fern R. Hauck, MD, MS^b

abstract

CONTEXT: Sudden infant death syndrome (SIDS) is a leading cause of postneonatal infant mortality. Our previous meta-analyses showed that any breastfeeding is protective against SIDS with exclusive breastfeeding conferring a stronger effect. The duration of breastfeeding required to confer a protective effect is unknown.

OBJECTIVE: To assess the associations between breastfeeding duration and SIDS.

DATA SOURCES: Individual-level data from 8 case-control studies.

STUDY SELECTION: Case-control SIDS studies with breastfeeding data.

DATA EXTRACTION: Breastfeeding variables, demographic factors, and other potential confounders were identified. Individual-study and pooled analyses were performed.

RESULTS: A total of 2267 SIDS cases and 6837 control infants were included. In multivariable pooled analysis, breastfeeding for <2 months was not protective (adjusted odds ratio [aOR]: 0.91, 95% confidence interval [CI]: 0.68–1.22). Any breastfeeding \geq 2 months was protective, with greater protection seen with increased duration (2–4 months: aOR: 0.60, 95% CI: 0.44–0.82; 4–6 months: aOR: 0.40, 95% CI: 0.26–0.63; and >6 months: aOR: 0.36, 95% CI: 0.22–0.61). Although exclusive breastfeeding for <2 months was not protective (aOR: 0.82, 95% CI: 0.59–1.14), longer periods were protective (2–4 months: aOR: 0.61, 95% CI: 0.42–0.87; 4–6 months: aOR: 0.46, 95% CI: 0.29–0.74).

LIMITATIONS: The variables collected in each study varied slightly, limiting our ability to include all studies in the analysis and control for all confounders.

CONCLUSIONS: Breastfeeding duration of at least 2 months was associated with half the risk of SIDS. Breastfeeding does not need to be exclusive to confer this protection.



^aDepartment of Paediatrics: Child and Youth Health and Obstetrics and Gynaecology, University of Auckland, Auckland, New Zealand; Departments of ^bFamily Medicine and ^cPediatrics, University of Virginia, Charlottesville, Virginia; ^dNational Paediatric Mortality Register, Temple Street Children's University Hospital, Dublin, Ireland; ^eDepartment of Child Health, School of Medicine, University of Glasgow, Glasgow, United Kingdom; and ^fSchool of Social and Community Medicine, University of Bristol, Bristol, United Kingdom

Dr Thompson conceptualized and designed the study, conducted the analyses, and drafted the initial manuscript; Ms Tanabe and Drs Moon and Hauck conceptualized and designed the study, participated in the interpretation of the data, and critically reviewed and revised the manuscript; Drs Mitchell, McGarvey, Tappin, and Blair provided data for the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

DOI: <https://doi.org/10.1542/peds.2017-1324>

Accepted for publication Aug 7, 2017

Address correspondence to John M.D. Thompson, PhD, Department of Paediatrics: Child and Youth Health, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand. E-mail: j.thompson@auckland.ac.nz

To cite: Thompson J.M.D., Tanabe K, Moon RY, et al. Duration of Breastfeeding and Risk of SIDS: An Individual Participant Data Meta-analysis. *Pediatrics*. 2017;140(5):e20171324

Breastfeeding has been shown in several studies to be associated with a decreased risk of sudden infant death syndrome (SIDS).¹⁻³ In a previous meta-analysis, we have shown that breastfeeding is protective against SIDS (adjusted odds ratio [aOR]: 0.55, 95% confidence interval [CI]: 0.44–0.69 for any breastfeeding) and that this protective effect is stronger with exclusive breastfeeding (odds ratio [OR]: 0.27, 95% CI: 0.24–0.31).³

However, it has been difficult to determine what duration of breastfeeding is required to confer a protective effect against SIDS. This may partly be because the incidence of breastfeeding across countries and different cultures varies and because the authors of different studies investigating the association with SIDS use different definitions for any breastfeeding, exclusive breastfeeding, and the duration of either practice. Meta-analyses of breastfeeding duration at the study level are difficult to undertake, and, so far, the effect size and the duration of breastfeeding required to confer this protective effect have not been quantified.

We therefore aimed to use individual-level data from international studies and, with cooperation of the individual authors, to assess the associations between duration of any breastfeeding versus exclusive breastfeeding and SIDS.

METHODS

We used the same review protocol as that in our previously reported meta-analysis.³ 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” and with the key words “sudden

infant death syndrome,” “SIDS,” “cot death,” and “breastfeeding.” Of the 18 studies included in the meta-analysis, individual level data were provided from 8 large case-control studies of SIDS deaths, which comprise all of the published case-control studies with individual-level data about breastfeeding status. In all studies, there were strict definitions and protocols for determining SIDS cases. The cause of death had to be ascertained by local medical examiners or pediatric or forensic pathologists. No studies without individual-level data were included. All data were obtained via direct contact with the original investigators for each case-control study. Data were checked by the original investigators for completeness and consistency before being released for this analysis. The studies included are detailed below.

The New Zealand Cot Death Study

The New Zealand Cot Death Study (NZCDS) was a national case-control study of all SIDS deaths that took place from November 1987 through October 1990. The authors of the study successfully recruited and obtained data from 393 case patients and 1592 controls, who were randomly selected from all birth cohorts, but with an age distribution to match the age of patients from cases from 1979 to 1984.⁴ Data were obtained by an interviewer-administered questionnaire and from hospital obstetric records, which included data about the type of feeding at the time of hospital discharge. Parents were asked whether the infant received any breast milk at any stage of life, in the first 4 weeks, and in the last 2 days. In addition, parents of infants who received any breast milk were asked at what stage breastfeeding stopped (age in weeks). Coding was available for never started and still breastfeeding.

The Chicago Infant Mortality Study

The authors of the Chicago Infant Mortality Study (CIMS) studied all SIDS deaths in Chicago, Illinois, between November 1993 and April 1996, and they included 260 case patients and 260 controls, who were matched by maternal ethnicity, age at death, and birth weight.⁵ Data on breastfeeding were collected by a standardized interviewer-administered questionnaire. Parents were asked if the child had ever been breastfed, if the child was still being breastfed, and how old the child was when breastfeeding stopped. In addition, data on other methods of feeding and when they were started were collected so that duration of exclusive breastfeeding could be calculated.

The German SIDS Study

The German SIDS Study (GeSID) was conducted in 11 of 18 states in the former Federal Republic of Germany between November 1998 and October 2001. The study included 333 SIDS case patients and 998 controls, who were matched by geographic region, age, sex, and reference sleep (ie, time of sleep was matched to the time of death for the respective case).⁶ Data on breastfeeding were collected by a standardized, interviewer-administered questionnaire. Questions were asked about breastfeeding at 2 weeks of age and at each month of age through 12 months (when applicable) and about whether this breastfeeding was exclusive.

The Scottish Cot Death Trust Study

The Scottish Cot Death Trust study took place between January 1996 and May 2000. Data were collected on 131 SIDS case patients and 278 control infants, who were matched by age, season, and obstetric unit.⁷ Data on breastfeeding were collected by a standardized, interviewer-administered questionnaire.

Questions were asked about which types of feeding the infant had and, if not breastfed currently, whether they had ever breastfed and when they stopped.

European Concerted Action on SIDS

The European Concerted Action on SIDS (ECAS) comprised case-control studies in 20 regions in Europe between September 1992 and April 1996.⁸ Data for the current analyses were restricted to those centers for which we had not obtained data from elsewhere (Sweden, Norway, Denmark, Netherlands, Austria, Hungary, Ukraine, Spain, Italy, Russia, Slovenia, France, Belgium, Poland, and the United Kingdom [Cambridge]). Data were collected for 382 SIDS case patients and 1159 controls. Data on breastfeeding exclusivity and duration were collected by interviewer-administered questionnaires. Questions were asked about how the infant was being fed at the time of death or interview.

Irish Study of Infant Death

The Irish study was part of an ongoing case-control study of infant death in the Republic of Ireland that began collecting data in 1994 and continued until 2010.^{9,10} Controls were matched by date of birth and geographical location. The data included in this analysis comprise 363 case patients and 1163 controls for the period from 1994 to 2003. Data on breastfeeding exclusivity and duration were collected during standardized home interviews.

Confidential Inquiry Into Stillbirth and Deaths in Infancy

The Confidential Inquiry Into Stillbirth and Deaths in Infancy (CESDI) included 5 regions of England between 1993 and 1996.¹¹ Data were collected for 325 SIDS case patients and 1300 controls, who were matched by age and health visitor. Data were collected for

duration of breastfeeding; however, no information on the duration of exclusive breastfeeding was collected.

South-West England Infant Sleep Study

The South-West England Infant Sleep Study (SWISS) included 2 regions in the South-West of England between 2003 and 2006.¹² Data were collected for 80 SIDS case patients and 87 controls. Data were collected for the duration of breastfeeding; however, no information on the duration of exclusive breastfeeding was collected.

Definitions of Breastfeeding Variables

Duration of any breastfeeding was defined as the length of time that the infant received any human milk, through breastfeeding or expressed breast milk, either exclusively or in combination with other foods (including infant formula). We defined the duration of any breastfeeding as a continuous variable; we created a categorical variable for the duration of any breastfeeding (0–2, 2–4, 4–6, and >6 months).

Duration of exclusive breastfeeding was defined as the length of time that the infant received only human milk, either through breastfeeding or expressed breast milk.¹³ We defined the duration of exclusive breastfeeding as a continuous variable; we created a categorical variable for the duration of exclusive breastfeeding (0–2, 2–4, and >4 months). A variable for >6 months was not created because of the small numbers in this group in most of the studies.

Statistical Analysis

Analysis was performed for each study individually, and then data were combined for a pooled analysis. A pooled univariable analysis, using all 8 studies, was conducted,

controlling for study. A multivariable model was then fitted by using 3 of the studies (the NZCDS, CIMS, and GeSID) for which all 19 potential confounders were available (model 1). These confounders had initially been assessed as being available and consistent across these 3 studies at the inception of each study and have been identified as risk or protective factors for SIDS: sleep position at last sleep (supine, side, prone), maternal smoking during pregnancy (yes/no), bed-sharing in the last sleep (infant sleeping with another person on the same surface) (yes/no), room-sharing in the last sleep (infant sleeping in the same room as an adult caregiver but on a separate surface) (yes/no), use of a dummy or pacifier in the last sleep (yes/no), maternal age, prenatal care received (yes/no), marital status (married/not married), parity (primiparous/multiparous), maternal education (university graduate or not), socioeconomic status (SES) (low, middle, high), infant age (<13, 13–19, 20–26, and >26 weeks), infant sex, admission to a special care infant unit (yes/no), season at death, birth weight (<2500 g, 2500–2999 g, 3000–3499 g, and ≥3500 g), gestational age at birth (28–33, 34–37, and 38+ weeks), multiple pregnancy (yes/no), and cesarean delivery (yes/no). Additional models were then fitted to include the other 5 studies, at the expense of reducing the number of confounders but increasing the sample size. These sequential models did not include the following confounders: cesarean delivery (the CESDI and SWISS included in model, model 2), SES and season (the Irish and ECAS studies included, model 3), and, finally, antenatal care and maternal education level (the Scottish study included, model 4).

All analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC). ORs were estimated by using the proc logistic procedure, with

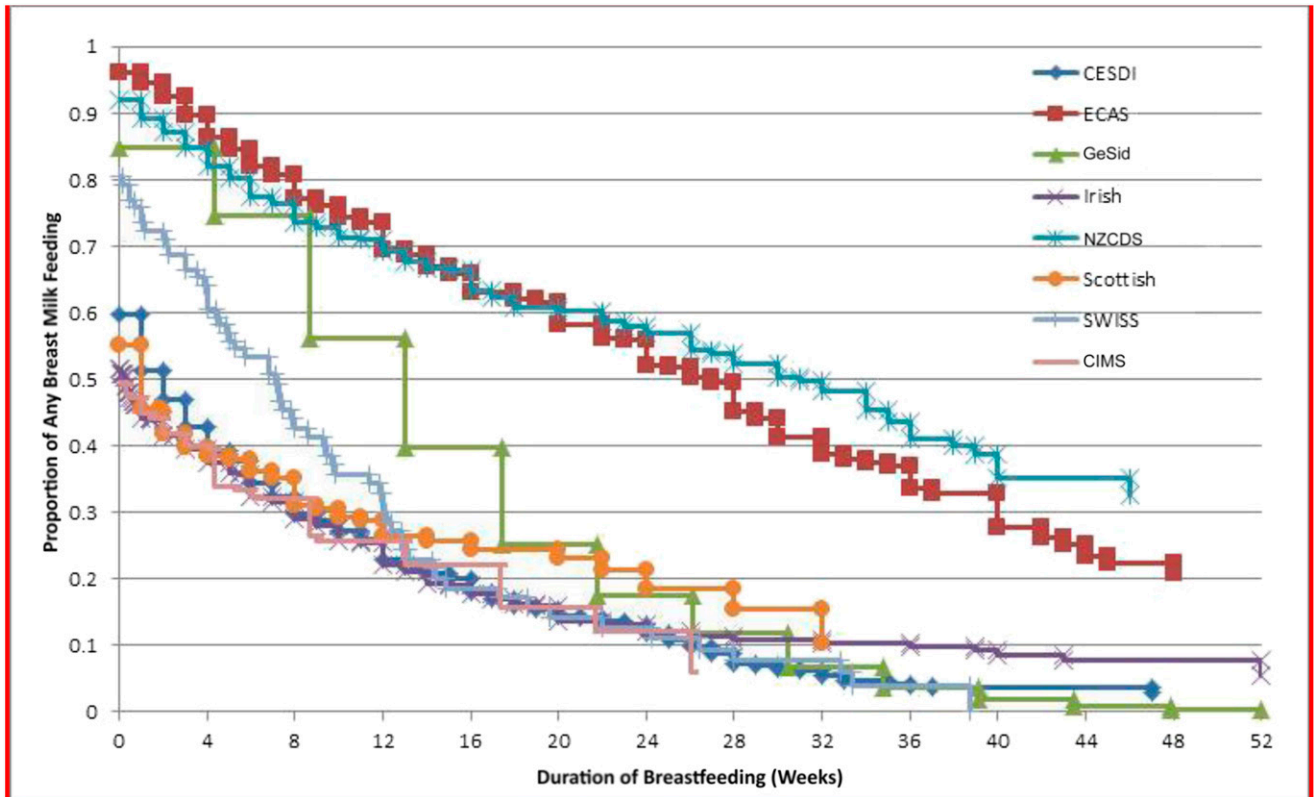


FIGURE 1
Kaplan-Meier survival curves for the proportion of controls still breastfeeding, stratified by study.

a strata statement for study in pooled analyses. Survival curves were produced for duration of any breastfeeding for control groups by using proc lifetest, with data censored if breastfeeding was still taking place. Statistical significance was defined at the 5% level.

This study was approved by the institutional review board at the University of Virginia. In addition, the individual studies were approved by the institutional ethical review boards and/or ethics committees according to the laws and standards of each country.

RESULTS

There are 8 SIDS case-control studies with individual-level data; all were included (see Supplemental Fig 2 flow diagram). A total of 2267 SIDS case patients and 6837 control infants were included in this analysis.

There was great variability in the rates of any breastfeeding and exclusive breastfeeding in the studies (log rank: 1659.6, $P < .0001$). This is illustrated in Fig 1, which shows survival curves for any breastfeeding for controls from each of the studies. Breastfeeding rates were highest in New Zealand and lowest in the United States, with the European countries having intermediate rates. At 6 months, the rate of any breastfeeding ranged from over 50% in the NZCDS and ECAS to <10% in several of the studies.

Any Breastfeeding

The univariable effects of any breastfeeding stratified by study and the pooled analyses are shown in Table 1. The analysis categorizing duration of any breastfeeding showed that those who breastfed for <2 months incurred a protective effect (OR: 0.61, 95% CI: 0.54–0.69)

and that those breastfeeding for 2 to 4 months had a greater protective effect (OR: 0.26, 95% CI: 0.22–0.30). Breastfeeding duration beyond 4 months provided further small increases in protection (4–6 months: OR: 0.18, 95% CI: 0.14–0.23; 6+ months: OR: 0.13, 95% CI: 0.10–0.18). The multivariable pooled analysis for the 3 studies with all 19 confounders controlled for found ongoing protective effects of any breastfeeding beyond 2 months (2–4 months: aOR: 0.60, 95% CI: 0.44–0.82; 4–6 months: aOR: 0.40, 95% CI: 0.26–0.63; and 6+ months: aOR: 0.36, 95% CI: 0.22–0.61) (Table 2). However, breastfeeding for 0 to 2 months did not have a statistically significant protective effect (aOR: 0.91, 95% CI: 0.68–1.21). The removal of cesarean delivery from the model had little effect on the ORs; however, the removal of SES and season in model 3

TABLE 1 Stratified and Pooled Univariable ORs (95% CIs) of SIDS for Duration of Any and Exclusive Breastfeeding

	NZCDS	GeSID	CIMS	Scottish	ECAS	GESDI	SWISS	Irish	Pooled
Any breastfeeding, mo	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Never	0.79 (0.55–1.13)	0.70 (0.48–1.02)	0.43 (0.28–0.65)	0.65 (0.41–1.05)	0.56 (0.36–0.88)	0.61 (0.46–0.81)	0.79 (0.37–1.67)	0.68 (0.51–0.92)	0.61 (0.54–0.69)
>0–2	0.49 (0.33–0.71)	0.18 (0.13–0.25)	0.07 (0.03–0.21)	0.16 (0.06–0.47)	0.21 (0.13–0.33)	0.42 (0.28–0.64)	0.42 (0.16–1.12)	0.16 (0.09–0.29)	0.26 (0.22–0.30)
>2–4	0.32 (0.19–0.53)	0.10 (0.06–0.16)	0.06 (0.01–0.51)	0.20 (0.04–0.90)	0.20 (0.12–0.33)	0.39 (0.20–0.78)	0.15 (0.02–1.40)	0.04 (0.01–0.26)	0.18 (0.14–0.23)
>4–6	0.19 (0.09–0.37)	0.15 (0.10–0.25)	Undefined	Undefined	0.07 (0.03–0.14)	0.25 (0.09–0.70)	0.11 (0.01–0.95)	0.22 (0.07–0.72)	0.13 (0.10–0.18)
Exclusive breastfeeding, mo	1.00	1.00	1.00	1.00	1.00	Not available	Not available	1.00	1.00
Never	0.88 (0.58–1.34)	0.40 (0.28–0.56)	0.46 (0.28–0.76)	0.63 (0.39–1.03)	0.98 (0.73–1.32)	Not available	Not available	0.40 (0.28–0.58)	0.61 (0.53–0.71)
>0–2	0.41 (0.27–0.64)	0.22 (0.15–0.33)	0.18 (0.02–1.51)	0.21 (0.06–0.73)	0.29 (0.21–0.41)	Not available	Not available	0.12 (0.05–0.30)	0.25 (0.20–0.30)
>2–4	0.32 (0.10–1.03)	0.13 (0.09–0.20)	Undefined	Undefined	0.19 (0.12–0.31)	Not available	Not available	0.48 (0.16–1.41)	0.16 (0.12–0.21)

saw the protective effects of any breastfeeding become stronger. The further removal of maternal education and antenatal care in model 4 had little additional influence on the aOR, but this result reached statistical significance (aOR: 0.83, 95% CI: 0.70–0.99).

Exclusive Breastfeeding

The stratified and pooled analysis for the univariable effects of exclusive breastfeeding is shown in Table 1. The analysis categorizing the duration of exclusive breastfeeding showed that those who exclusively breastfed for <2 months incurred a protective effect (OR: 0.61 95% CI: 0.53–0.71) and that those breastfeeding 2 to 4 months had a greater protective effect (OR: 0.25, 95% CI: 0.20–0.30). Exclusive breastfeeding for >4 months provided a further increase in protection (OR: 0.16, 95% CI: 0.12–0.21). As in the multivariable analysis for any breastfeeding, which controlled for all potential confounders, those who breastfed exclusively for <2 months did not see any statistically significant protective effect (aOR: 0.82, 95% CI: 0.59–1.14), but those who breastfed for longer than 2 months incurred a protective effect (aOR: 0.61, 95% CI: 0.42–0.97) for 2 to 4 months, with increasing protection with longer duration (aOR: 0.46, 95% CI: 0.29–0.74) for those exclusively breastfeeding >4 months. Similarly, the removal of SES and season from the model made the effect sizes slightly stronger (Table 3).

DISCUSSION

We conducted a pooled analysis of individual-level data from 8 major international case-control studies with 2259 case patients and 6894 controls to assess the association between duration of

any breastfeeding versus exclusive breastfeeding and SIDS. Although there was some protection seen with breastfeeding for <2 months in univariable analysis, after controlling for potential confounders, we found no statistically significant protection against SIDS until infants had breastfed for at least 2 months. After 2 months, the aOR for any breastfeeding was 0.60 (95% CI: 0.44–0.82), whereas the aOR for exclusive breastfeeding was 0.61 (95% CI: 0.42–0.87). It is thus important that public health messages about SIDS risk reduction emphasize that breastfeeding, if it is to be protective, must continue for at least 2 months. This analysis does not reveal any advantage to exclusive breastfeeding over partial breastfeeding, which may be reassuring to some parents who cannot or do not wish to exclusively breastfeed their infant.

It is yet unclear why breastfeeding offers protective effects against SIDS. The authors of physiologic, neuropathologic, and genetic studies point to dysfunctional arousal responses as a mechanism that creates an intrinsic vulnerability in the infant, which predisposes the infant to SIDS,¹⁴ and breastfed infants are more easily aroused from sleep than are formula-fed infants.^{15,16} There are also differences in maternal responses to an infant's behavioral cues, depending on feeding mode, which may impact infant sleep and arousal patterns.^{17,18} Additionally, breastfeeding provides immune benefits and is associated with a lower incidence of viral infections, which are associated with an increased risk of SIDS.^{19–21} Breast milk contains substances that may contribute to myelin development; Kinney and co-authors found that infants who died of SIDS had delayed myelination of the brain compared with control infants.²² Breast milk also contains higher levels than formula of docosahexaenoic acid,

TABLE 2 Stratified and Pooled Multivariable ORs (95% CIs) of SIDS for Duration of Any Breastfeeding

Duration, mo	NZCDS	GeSID	CIMS	Scottish	ECAS	CESDI	SWISS	Irish	Pooled Model 1 ^a (n = 3386)	Pooled Model 2 ^b (n = 5008)	Pooled Model 3 ^c (n = 6121)	Pooled Model 4 ^d (n = 7842)
Never	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
>0-2	0.86 (0.53-1.40)	0.89 (0.49-1.63)	0.69 (0.36-1.31)	0.69 (0.31-1.52)	0.79 (0.25-2.51)	0.96 (0.65-1.40)	0.12 (0.01-2.18)	1.13 (0.59-2.17)	0.91 (0.68-1.21)	0.90 (0.72-1.12)	0.83 (0.69-1.01)	0.83 (0.70-0.99)
>2-4	0.67 (0.40-1.11)	0.51 (0.29-0.88)	0.16 (0.04-0.71)	0.38 (0.09-1.54)	0.82 (0.25-2.75)	0.78 (0.45-1.34)	0.02 (<0.001-0.93)	0.19 (0.07-0.51)	0.60 (0.44-0.82)	0.62 (0.48-0.80)	0.52 (0.41-0.65)	0.46 (0.37-0.56)
>4-6	0.39 (0.19-0.80)	0.37 (0.18-0.74)	0.16 (0.01-1.72)	0.20 (0.03-1.57)	0.94 (0.23-3.94)	0.64 (0.24-1.75)	<0.001 (<0.001-3.50)	0.08 (0.01-0.86)	0.40 (0.26-0.63)	0.42 (0.29-0.61)	0.38 (0.27-0.54)	0.40 (0.30-0.53)
>6	0.44 (0.17-1.13)	0.30 (0.15-0.63)	Undefined	Undefined	0.06 (0.00-0.94)	0.26 (0.05-1.25)	0.001 (<0.001-1.71)	0.45 (0.06-3.09)	0.36 (0.22-0.61)	0.34 (0.22-0.54)	0.33 (0.21-0.50)	0.25 (0.17-0.37)

^a Model 1 controlled for sleep position at last sleep, maternal smoking during pregnancy, bed-sharing in the last sleep (infant sleeping with another person on the same surface), room-sharing in the last sleep (infant sleeping in the same room as an adult caregiver but on a separate surface), dummy or pacifier in the last sleep, maternal age, prenatal care, marital status, parity, maternal education, SES, infant age, infant sex, admission to a special care infant unit, season at death, birth weight, gestational age, multiple pregnancy, and cesarean delivery.

^b Model 2 controlled for variables in model 1, except for cesarean delivery, to include the CESDI and SWISS studies.

^c Model 3 controlled for variables in model 2, except season and SES, to include the ECAS and Irish studies.

^d Model 4 controlled for variables in model 3, except for antenatal care and maternal education, to include the Scottish study.

TABLE 3 Stratified and Pooled Multivariable ORs (95% CIs) of SIDS for Duration of Exclusive Breastfeeding

Duration, mo	NZCDS	GeSID	SIMS	Scottish	ECAS	CESDI	SWISS	Irish	Pooled Model 1 ^a (n = 3397)	Pooled Model 2 ^b	Pooled Model 3 ^c (n = 4319)	Pooled Model 4 ^d (n = 6006)
Never	1.00	1.00	1.00	1.00	1.00	Not available	Not available	1.00	1.00	—	1.00	1.00
>0-2	1.02 (0.56-1.84)	0.70 (0.41-1.19)	0.81 (0.39-1.69)	0.61 (0.26-1.44)	1.27 (0.46-3.48)	Not available	Not available	0.68 (0.33-1.42)	0.82 (0.59-1.14)	—	0.75 (0.58-0.98)	0.82 (0.67-1.01)
>2-4	0.47 (0.27-0.83)	0.51 (0.29-0.90)	0.61 (0.04-8.85)	0.63 (0.12-3.23)	0.48 (0.15-1.53)	0.61 (0.42-0.87)	0.09 (0.02-0.53)	0.09 (0.02-0.53)	0.61 (0.42-0.87)	—	0.44 (0.32-0.60)	0.40 (0.31-0.51)
4-6	0.56 (0.15-2.07)	0.31 (0.17-0.58)	Undefined	Undefined	0.60 (0.14-2.54)	0.64 (0.24-1.75)	3.14 (0.56-17.55)	3.14 (0.56-17.55)	0.46 (0.29-0.74)	—	0.47 (0.31-0.71)	0.37 (0.26-0.52)

—, Data were not available because these 2 studies had no data on exclusive breastfeeding.

^a Model 1 controlled for sleep position at last sleep, maternal smoking during pregnancy, bed-sharing in the last sleep (infant sleeping with another person on the same surface), room-sharing in the last sleep (infant sleeping in the same room as an adult caregiver but on a separate surface), dummy or pacifier in the last sleep, maternal age, prenatal care, marital status, parity, maternal education, SES, infant age, infant sex, admission to a special care infant unit, season at death, birth weight, gestational age, multiple pregnancy, and cesarean delivery.

^b Model 2 could not be run because the CESDI and SWISS studies had no data on exclusive breastfeeding.

^c Model 3 controlled for variables in model 2, except for season and SES, to include the ECAS and Irish studies.

^d Model 4 controlled for variables in model 3, except for antenatal care and maternal education, to include the Scottish study.

which is an important structural and functional component of the developing infant brain. One study of autopsied brains of SIDS infants found that the frontal lobes of the breastfed infants had higher levels of docosahexaenoic acid than those of formula-fed infants; it is unknown if this difference exists in non-SIDS infants.²³ Finally, it is possible that breastfeeding is a distal marker of or proxy for complex protective infant care practices that have not yet been measured, although we would expect that such a marker would be related to sociodemographic variables that have been controlled for in these analyses.

It is unclear why exclusive breastfeeding did not offer any additional protection against SIDS than any, that is, partial, breastfeeding. This is a common challenge in studies in which the differential effects of exclusive and partial breastfeeding have been examined, because of the differing definitions of breastfeeding and confounding factors.^{1,24} The analysis accounted for as many demographic and risk factor variables as were possible, but we acknowledge that the effects reported could be caused by residual confounding, although this would be unlikely. It was notable that the inclusion of studies that did not have data on SES increased the protective effect further from the null, thus seemingly showing the importance of SES as a confounder in relation to breastfeeding. Given that lower SES is a risk factor for SIDS, it is possible that the protective effect of SES may in part be explained by increased breastfeeding rates. However, model 3, which did not have data on SES, also did not have data on season. Although SES is associated with breastfeeding, it is unlikely that there is a relationship between season and breastfeeding; thus, we believe that these changes in estimates are likely to be associated with SES.

Other limitations of this study are related to issues with combining data in the individual case-control studies. These case-control studies were all conducted in a rigorous manner and are the basis for most of the current infant safe sleep guidelines in developed countries.^{25–27} However, as noted above, the variables collected in the course of each study varied slightly, limiting our ability to include all studies in the analysis and control for all confounders. However, the results of the univariable analysis using only the 3 countries included in the completely controlled multivariable model (model 1) did not differ greatly from the univariable analysis with all 8 studies, so it is unlikely that including the additional studies would have changed the results of the analysis in any meaningful way.

Given these findings, there should be ongoing concerted efforts to increase the rates of breastfeeding initiation and maintenance. Among the control infants in 5 of the 8 countries in this analysis, the proportion of infants who were breastfeeding was <50% at 2 months of age and <30% at 4 months of age. In more recent years, national breastfeeding rates have increased; 2007 Organisation for Economic Co-operation and Development data show that the proportions of infants who were ever breastfed in the countries included in our study were 42% in Ireland, 75% in the United States, 77% in the United Kingdom, 85% in New Zealand, and 89% in the European Union.²⁸ The World Health Organization's 2025 targets for breastfeeding are to have >50% of infants exclusively breastfeeding for at least 6 months.¹³ Further increases in breastfeeding rates will result in lower infant mortality as a whole^{24,29} and in decreases in SIDS rates,³ specifically.

CONCLUSIONS

Breastfeeding duration of a minimum of 2 months appears to be necessary to confer a significant protective effect against SIDS, with an almost halving of the risk. The protective benefits of breastfeeding increase as the duration increases. However, exclusive breastfeeding does not confer additional benefits over partial breastfeeding with regards to SIDS risk reduction. Therefore, mothers should be encouraged to breastfeed for at least 2 months (and preferably longer). Even if mothers are unable to exclusively breastfeed, they can feel reassured that any breastfeeding provides protection against SIDS for their infants. Further study is still needed to better understand the mechanisms by which breastfeeding offers protection.

ACKNOWLEDGMENTS

We acknowledge Drs Robert Carpenter (deceased) and Mechtild Vennemann for their work in data collection and data analysis for this study.

ABBREVIATIONS

aOR: adjusted odds ratio
CESDI: Confidential Inquiry into Stillbirth and Deaths in Infancy
CI: confidence interval
CIMS: Chicago Infant Mortality Study
ECAS: European Concerted Action on SIDS
GeSID: German SIDS Study
NZCDS: New Zealand Cot Death Study
OR: odds ratio
SES: socioeconomic status
SIDS: sudden infant death syndrome
SWISS: South-West England Infant Sleep Study

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funding for the New Zealand Cot Death Study was provided by the Health Research Council of New Zealand and the Hawkes Bay Medical Research Foundation. Funding for the Chicago Infant Mortality Study was provided by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute on Deafness and Other Communication Disorders, the Centers for Disease Control and Prevention, and the Association of Teachers of Preventive Medicine. Funding for the German Sudden Infant Death Syndrome Study was provided by Germany's Federal Ministry for Science and Education. Funding for The Scottish Cot Death Trust Study was provided by The Scottish Cot Death Trust. Funding for the European Concerted Action on Sudden Infant Death Syndrome was provided by the European Union and the Foundation for the Study of Infant Deaths (now called the Lullaby Trust). Funding for the Irish Study of Infant Death was provided by Ireland's Department of Health and Children. Funding for the Confidential Enquiry into Stillbirth and Deaths in Infancy was provided by the National Advisory Body for the Confidential Enquiry into Stillbirths and Deaths in Infancy, the Foundation for the Study of Infant Deaths (now called the Lullaby Trust), and Babes in Arms. Funding for the South-West England Infant Sleep Study was provided by the Foundation for the Study of Infant Deaths (now called the Lullaby Trust), Babes in Arms, and The Charitable Trusts of University Hospitals Bristol.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Ip S, Chung M, Raman G, Trikalinos TA, Lau J. A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries. *Breastfeed Med*. 2009;4(suppl 1):S17–S30
2. Vennemann MM, Bajanowski T, Brinkmann B, et al; GeSID Study Group. Does breastfeeding reduce the risk of sudden infant death syndrome? *Pediatrics*. 2009;123(3). Available at: www.pediatrics.org/cgi/content/full/123/3/e406
3. Hauck FR, Thompson JM, Tanabe KO, Moon RY, Vennemann MM. Breastfeeding and reduced risk of sudden infant death syndrome: a meta-analysis. *Pediatrics*. 2011;128(1):103–110
4. Mitchell EA, Taylor BJ, Ford RP, et al. Four modifiable and other major risk factors for cot death: the New Zealand study. *J Paediatr Child Health*. 1992;28(suppl 1):S3–S8
5. Hauck FR, Herman SM, Donovan M, et al. Sleep environment and the risk of sudden infant death syndrome in an urban population: the Chicago Infant Mortality Study. *Pediatrics*. 2003;111(5, pt 2):1207–1214
6. Vennemann MM, Findeisen M, Butterfass-Bahloul T, et al; GeSID Group. Modifiable risk factors for SIDS in Germany: results of GeSID. *Acta Paediatr*. 2005;94(6):655–660
7. Tappin D, Brooke H, Ecob R, Gibson A. Used infant mattresses and sudden infant death syndrome in Scotland: case-control study. *BMJ*. 2002;325(7371):1007–1012
8. Carpenter RG, Irgens LM, Blair PS, et al. Sudden unexplained infant death in 20 regions in Europe: case control study. *Lancet*. 2004;363(9404):185–191
9. McGarvey C, McDonnell M, Chong A, O'Regan M, Matthews T. Factors relating to the infant's last sleep environment in sudden infant death syndrome in the Republic of Ireland. *Arch Dis Child*. 2003;88(12):1058–1064
10. Matthews T, McDonnell M, McGarvey C, Loftus G, O'Regan M. A multivariate "time based" analysis of SIDS risk factors. *Arch Dis Child*. 2004;89(3):267–271
11. Fleming PJ, Blair PS, Pollard K, et al; CESDI SUDI Research Team. Pacifier use and sudden infant death syndrome: results from the CESDI/SUDI case control study. *Arch Dis Child*. 1999;81(2):112–116
12. Blair PS, Sidebotham P, Evason-Coombe C, Edmonds M, Heckstall-Smith EM, Fleming P. Hazardous cosleeping environments and risk factors amenable to change: case-control study of SIDS in south west England. *BMJ*. 2009;339:b3666
13. World Health Organization/UNICEF. *Global Nutrition Targets 2025: Breastfeeding Policy Brief (WHO/NMH/NHD/14.7)*. Geneva, Switzerland: World Health Organization; 2014
14. Paine SM, Jacques TS, Sebire NJ. Review: neuropathological features of unexplained sudden unexpected death in infancy: current evidence and controversies. *Neuropathol Appl Neurobiol*. 2014;40(4):364–384
15. Franco P, Scaillet S, Wermenbol V, Valente F, Groswasser J, Kahn A. The influence of a pacifier on infants' arousals from sleep. *J Pediatr*. 2000;136(6):775–779
16. Horne RS, Parslow PM, Ferens D, Watts AM, Adamson TM. Comparison of evoked arousability in breast and formula fed infants. *Arch Dis Child*. 2004;89(1):22–25
17. Ball HL. Breastfeeding, bed-sharing, and infant sleep. *Birth*. 2003;30(3):181–188
18. Blair PS, Ball HL. The prevalence and characteristics associated with parent-infant bed-sharing in England. *Arch Dis Child*. 2004;89(12):1106–1110
19. Duijts L, Jaddoe VW, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. *Pediatrics*. 2010;126(1). Available at: www.pediatrics.org/cgi/content/full/126/1/e18
20. Heinig MJ. Host defense benefits of breastfeeding for the infant. Effect of breastfeeding duration and exclusivity. *Pediatr Clin North Am*. 2001;48(1):105–123, ix
21. Kramer MS, Guo T, Platt RW, et al. Infant growth and health outcomes associated with 3 compared with 6 mo of exclusive breastfeeding. *Am J Clin Nutr*. 2003;78(2):291–295
22. Kinney HC, Brody BA, Finkelstein DM, Vavter GF, Mandell F, Gilles FH. Delayed central nervous system

- myelination in the sudden infant death syndrome. *J Neuropathol Exp Neurol*. 1991;50(1):29–48
23. Byard RW, Makrides M, Need M, Neumann MA, Gibson RA. Sudden infant death syndrome: effect of breast and formula feeding on frontal cortex and brainstem lipid composition. *J Paediatr Child Health*. 1995;31(1):14–16
24. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries. *Evid Rep Technol Assess (Full Rep)*. 2007;(153):1–186
25. Moon RY; Task Force on Sudden Infant Death Syndrome. SIDS and other sleep-related infant deaths: expansion of recommendations for a safe infant sleeping environment. *Pediatrics*. 2011;128(5):1030–1039
26. Public Health Agency of Canada. Joint statement on safe sleep: preventing sudden infant deaths in Canada. 2012. Available at: http://www.phac-aspc.gc.ca/hp-ps/dca-dea/stages-etapes/childhood-enfance_0-2/sids/pdf/jsss-ecss2011-eng.pdf. Accessed June 1, 2017
27. Blair P, Inch S. *The Health Professional's Guide to: "Caring for Your Baby at Night"*. London, England: UNICEF UK Baby Friendly Initiative; 2012
28. OECD Social Policy Division. Directorate of employment, labour and social affairs, OECD family database. Available at: <https://www.oecd.org/els/family>. Accessed June 1, 2017
29. Chen A, Rogan WJ. Breastfeeding and the risk of postneonatal death in the United States. *Pediatrics*. 2004;113(5). Available at: www.pediatrics.org/cgi/content/full/113/5/e435

Duration of Breastfeeding and Risk of SIDS: An Individual Participant Data Meta-analysis

John M.D. Thompson, Kawai Tanabe, Rachel Y. Moon, Edwin A. Mitchell, Cliona McGarvey, David Tappin, Peter S. Blair and Fern R. Hauck

Pediatrics 2017;140;

DOI: 10.1542/peds.2017-1324 originally published online October 30, 2017;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/140/5/e20171324
Supplementary Material	Supplementary material can be found at: http://pediatrics.aappublications.org/content/suppl/2017/10/16/peds.2017-1324.DCSupplemental
References	This article cites 25 articles, 12 of which you can access for free at: http://pediatrics.aappublications.org/content/140/5/e20171324.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Fetus/Newborn Infant http://classic.pediatrics.aappublications.org/cgi/collection/fetus:newborn_infant_sub SIDS http://classic.pediatrics.aappublications.org/cgi/collection/sids_sub Nutrition http://classic.pediatrics.aappublications.org/cgi/collection/nutrition_sub Breastfeeding http://classic.pediatrics.aappublications.org/cgi/collection/breastfeeding_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: https://shop.aap.org/licensing-permissions/
Reprints	Information about ordering reprints can be found online: http://classic.pediatrics.aappublications.org/content/reprints

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Duration of Breastfeeding and Risk of SIDS: An Individual Participant Data Meta-analysis

John M.D. Thompson, Kawai Tanabe, Rachel Y. Moon, Edwin A. Mitchell, Cliona
McGarvey, David Tappin, Peter S. Blair and Fern R. Hauck

Pediatrics 2017;140;

DOI: 10.1542/peds.2017-1324 originally published online October 30, 2017;

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/140/5/e20171324>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

