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[Intervention Review]

Infant pacifiers for reduction in risk of sudden infant death syndrome

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ABSTRACT

Background

Sudden infant death syndrome (SIDS) has been most recently defined as the sudden unexpected death of an infant less than one year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including the performance of a complete autopsy and a review of the circumstances of death and clinical history. Despite the success of several prevention campaigns, SIDS remains a leading cause of infant mortality. In 1994, a 'triple risk model' for SIDS was proposed that described SIDS as an event that results from the intersection of three factors: a vulnerable infant; a critical development period in homeostatic control (age related); and an exogenous stressor. The association between pacifier (dummy) use and reduced incidence of SIDS has been shown in epidemiological studies since the early 1990s. Pacifier use, given its low cost, might be a cost-effective intervention for SIDS prevention if it is confirmed effective in randomised controlled trials.

Objectives

To determine whether the use of pacifiers during sleep versus no pacifier during sleep reduces the risk of SIDS.

Search methods

We used the standard search strategy of the Cochrane Neonatal Review Group to search the Cochrane Central Register of Controlled Trials (CENTRAL 2016, Issue 2), MEDLINE via PubMed, Embase, and CINAHL to 16 March 2016. We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomised controlled trials and quasi-randomised trials.

Selection criteria

Published and unpublished controlled trials using random and quasi-random allocations of infants born at term and at preterm (less than 37 weeks' gestation) or with low birth weight (< 2500 g). Infants must have been randomised by one month' postmenstrual age. We planned to include studies reported only by abstracts, and cluster and cross-over randomised trials.

Data collection and analysis

Two review authors independently reviewed studies from searches. We found no eligible studies.

Main results

We identified no randomised controlled trials examining infant pacifiers for reduction in risk of SIDS.

Authors' conclusions

We found no randomised control trial evidence on which to support or refute the use of pacifiers for the prevention of SIDS.

PLAIN LANGUAGE SUMMARY**Infant pacifiers for reduction in risk of sudden infant death syndrome****Review question**

Does the use of infant pacifiers (dummies) reduce the risk of sudden infant death syndrome?

Background

Sudden unexpected death of an infant generally occurs during sleep from birth to one year of age but mainly occurs between one and four months of age. Despite the success of several prevention campaigns, sudden infant death syndrome remains a leading cause of infant mortality (death). A variety of factors have been identified as increasing the risk of sudden infant death syndrome such as male sex, preterm (before the due date) birth, overheating, exposure to cigarette smoke, and infants lying on their stomachs. Pacifier use has been proposed as a non-invasive intervention to reduce the risk of SIDS. This review was undertaken to examine whether infant pacifiers can reduce the risk of SIDS.

Study characteristics

We searched medical databases for clinical trials of SIDS in infants born at their due date or earlier (less than 37 weeks of pregnancy) or with low birth weight (less than 2500 g) using pacifiers or not using pacifiers up to one year of age. We found no well-designed clinical trials meeting our inclusion criteria.

Results

No well-designed clinical trials met our inclusion criteria.

BACKGROUND

Description of the condition

Sudden infant death syndrome (SIDS) has been most recently defined as the sudden unexpected death of an infant less than one year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including the performance of a complete autopsy and a review of the circumstances of death and clinical history (Krous 2004). The incidence of SIDS has varied over time, and between nations. For example, the incidence of SIDS per 1000 live births in 2004 in the Netherlands was 0.09, in Japan 0.19, in Canada 0.24, in England and Wales 0.32, in the USA 0.55, in Argentina 0.47 and in Australia 0.22 (Hauck 2009). According to Australian Social Trends 2007 statistics, death from SIDS in Australia between 1985 and 2005 declined by 83%, from 523 deaths in 1985 to 87 in 2005 (Linacre 2007). Of the 297,900 births in Australia in 2010, there were 81 cases of SIDS reported (SIDS 2012). This decline is strongly associated with a public health campaign launched by SIDS and Kids, formerly the National SIDS Council of Australia (Linacre 2007). However, there has been no similar reduction in the rate of SIDS among Aboriginal and Torres Strait Islander (ATSI) infants. Between 2002 and 2006, infants from an ATSI background were five times more likely to die from SIDS than non-indigenous infants (AHMAC 2008).

Despite the success of several prevention campaigns, SIDS remains a leading cause of infant mortality. Deaths classified as SIDS occur unexpectedly from birth to one year of age, but predominantly occur between one and four months of age (Page 2000). Reported risk factors for SIDS include male sex, preterm birth, low birth weight, poor antenatal medical care, low socioeconomic status of the family, young age of parents, parental low educational level, short periods between pregnancies, multiple pregnancy, drug intake by pregnant woman, winter months, prone sleeping, bed sharing, exposure to cigarette smoke during pregnancy and after birth, overheating, head covering and infection (Harper 2000). Despite the identification of major risk factors that increase an infant's chance of dying of SIDS, the underlying mechanism by which infants die remains unknown.

Read 1984 first suggested a model for SIDS consisting of the vulnerable infant (prematurity, state of arousal), subtle neurological impairment (in pregnancy) and an external precipitating factor, to provide a research framework for use with the then key known risk factors. A variety of theories relating to the mechanisms by which SIDS occurs have been proposed, including: airway obstruction during sleep and the subsequent rebreathing of expired gases on arousal leading to hypoxic coma (Kahn 2003); undiagnosed infections and genetic abnormalities (Panigrahy 2000; Opdal 2004) that may affect brainstem-mediated control of respiratory and autonomic function (Hunt 2005; Weese-Mayer 2008); and cardiac arrhythmia and genetic disorders such as cardiac ion channel mutations (Klaver 2011). Other genetic factors such as immunological polymorphisms, and autonomic and metabolic disorders have been identified (Klaver 2011). It has been hypothesised that pregnancy-related factors, such as low birth weight, preterm birth and maternal smoking, may alter cardiovascular function and control of autonomic, behavioural and homeostatic function in the infant (Schellscheidt 1998; Cohen 2009; Cohen 2010; Franco 2010). The effect of genetic or pregnancy-related factors causes the failure of normal 'protective' reflexes

during normal stresses that may occur in sleep (Malloy 2004). Filiano 1994 proposed a 'triple risk model' that describes SIDS as an event that results from the intersection of three factors: a vulnerable infant; a critical development period in homeostatic control (age related) and an exogenous stressor.

Few theories have been tested. One that has is the role of gastro-oesophageal reflux, which can be a major cause of cardiorespiratory events in early postnatal life, especially via the triggering of the laryngeal chemoreflex (LCR). Response to LCR stimulation in mature infants and adults results in short apnoea, laryngeal closure, expiratory reflex, cough and swallowing, as well as arousal if it occurs during sleep. In contrast, an immature response to LCR results in life-threatening apnoea, bradycardia and oxygen desaturation. These have been observed in many mammalian species, especially in preterm newborn infants, the reflex becoming rapidly attenuated with postnatal age. Studies in human infants and piglets have suggested that the coexistence of reflux to the level of the pharynx during sleep, together with impaired swallowing, depressed arousal or both, is one mechanism that may lead to an age-limited, sudden and fatal apnoea (Jeffery 1995). Hence, the occurrence of gastro-oesophageal reflux to the level of the pharynx during sleep, an infrequent event that is usually innocuous, could be converted to a fatal event if swallowing is impaired and arousal depressed by a variety of mediating factors such as prone sleeping, preterm birth, sedatives, seizures or upper respiratory tract infections (Jeffery 1999; Page 2000; McKelvey 2001). The LCR is both sleep and age related (vulnerable infant), and apnoea may be worsened by hypoxia or infection (neurological impairment) and any external factor that decreases airway protection by reducing swallowing or arousal. Other researchers have suggested that the LCR does not cause SIDS as such, but acts as a trigger, perhaps as a component of the 'triple risk model', ultimately leading to death if the multiple recovery mechanisms, such as arousal and anoxic gasping, fail (Marom 2012).

Description of the intervention

A pacifier or dummy is a device that is placed in the mouth to stimulate non-nutritive sucking behaviour. Non-nutritive sucking is considered a natural reflex to satisfy a child's need for contact and may include unrestricted sucking on a breast, digit, pacifier or other object (Foster 2016). A pacifier is usually similar in material and shape to a feeding teat and is attached to a broad flat disc of plastic that covers the child's mouth to prevent ingestion (Schwartz 2008).

Worldwide pacifier use in early childhood is very common, especially in low- to middle-income countries, where mothers believe pacifier use satisfies their infants' natural need to suck (Moimaz 2008). Use of pacifiers in low- to middle-income countries is controversial due to conflicting evidence regarding the potential for increased infantile infection (Rossit 2007; Alrifai 2010). Historically, the pacifier has been used to soothe or calm a distressed infant or to prevent an infant sucking on its hands. Pacifiers are used for other purposes, such as non-nutritive sucking for the management of painful procedures (Stevens 2016). One Cochrane review found non-nutritive sucking to be effective for pain and pain-related regulation in neonates and preterm infants (Pillai Riddell 2015). In addition, pacifier use has been proposed as a protective intervention for SIDS (Schwartz 2008).

It has been proposed that pacifier use reduces rates of breastfeeding; however, several randomised controlled trials (RCTs) and a Cochrane Review have disputed this claim (Kramer 2001; Collins 2004; Jaafar 2016). Collins 2004 found that pacifier use had no impact on prevalence or duration of breastfeeding at six months while Kramer 2001 found that, rather than being the cause of breastfeeding difficulties, the use of a pacifier by a mother was a marker of breastfeeding difficulties. One systematic review concluded that pacifier use in healthy term breastfeeding infants started from birth or after lactation was established did not significantly affect the prevalence or duration of exclusive and partial breastfeeding up to four months of age (Jaafar 2016). Importantly, Collins 2004 explored pacifier use in preterm infants and found that pacifier use in this population had no significant effect on the proportion of infants who were being fully or partly breastfed. An increased risk of otitis media associated with pacifier use has been demonstrated but the incidence of otitis media is generally lower in the first year of life, especially for the first six months when the risk of SIDS is the highest (Darwazeh 1995; Jackson 1999; North 1999; Daly 2000). Gastrointestinal infections and oral colonisation are more common among infants who use a pacifier (Niemela 1994; Darwazeh 1995; Uhari 1996; North 1999; Daly 2000).

How the intervention might work

There has been significant debate around the use of pacifiers by infants, particularly when pacifiers are given to the infant prior to sleeping, and the role that this plays in the prevention of SIDS. There have been a number of theories put forward to explain why pacifiers may reduce SIDS. The use of a pacifier may result in improved autonomic control of breathing and cardiovascular stability, may maintain airway patency in infants during sleep in the first year of life, or both (Franco 2004). An alternative hypothesis is the possibility that the infant's sleeping environment is altered by the pacifier's external handle, which may in turn change the configuration of the airway passage around the area of the mouth and nose. The altered airway passage could help prevent accidental hypoxia resulting from, for example, smothering by a blanket or soft bedding (Li 2006). The pacifier may also prevent the infant from rolling into the prone position (Franco 2004). One case-control study showed that sucking a pacifier enhanced neural pathway development, which controls the patency around the upper airway (Li 2006). The sensory input from the pacifier is important for upper airway muscle tone in the infant, which helps maintain upper airway patency by keeping the tongue forward via its active protrusion (Mitchell 1993; Weiss 2001).

Several arousal states are usually recognised in infants: active sleep (rapid eye-movement sleep, REM); quiet sleep (non-REM, NREM, or slow-wave sleep); indeterminate sleep; and waking (sometimes separated into crying, active and quiet) (Read 1984). The rate, depth and regularity of breathing in infants is closely related to behavioural state (Read 1984). Read 1984 proposed that various breathing patterns may reflect altered central nervous system activity. Breathing is regular in quiet sleep and irregular in active sleep. The rate and depth cycles are of larger amplitude and are in-phase, leading to marked swings in minute ventilation in active sleep. Infants have small oxygen stores in their lungs in relation to their metabolic oxygen consumption, resulting in an instability in arterial oxygen tension. Further instability would be expected in active sleep, since lung volume is reduced and metabolic rate is

increased (Read 1984). Jeffery 1991 found oesophageal pH readings to be stable, between pH 5 and 7, in preterm infants during quiet sleep, whereas in active sleep, reflux occurred, with a significant decrease in oesophageal pH. One study of term infants at 10 weeks of age showed these infants had increased cardiac sympathovagal balance during sucking sleep periods, whereas lower sympathetic activity together with high parasympathetic tone were associated with non-sucking sleep periods (Franco 2004; Horne 2010).

Defects in normal arousal mechanisms have long been theorised to cause SIDS, and gene mutations affecting the development of the autonomic nervous system appear in as many as 15% of cases (Weese-Mayer 2004). Pacifier use possibly creates a lower arousal threshold in infants, which may result in increased sensitivity to critical situations such as cardiac arrhythmia, obstructive apnoea or external conditions leading to asphyxia or hypoxia (Franco 2000). Even if the pacifier becomes dislodged from the mouth as the infant falls asleep, habitual use of the pacifier appears to still protect against SIDS. The reason for this remains unclear and more research is needed in this area (Franco 2001; Hanzer 2010). One RCT was undertaken to determine the effects of pacifier use on spontaneous arousability in infants sleeping both prone and supine over the first six months of life (Odoi 2014). This study demonstrated no difference in either the total spontaneous arousals/hour of sleep, or in the duration of either subcortical arousals or cortical arousals in either sleep state or position between pacifier users and non-users (Odoi 2014).

Several authors have reported a link between sleep states, movement, and the incidence and duration of gastro-oesophageal reflux episodes (Jeffery 1983; Kahn 1990). Infants reportedly experience increased incidence and longer duration of gastro-oesophageal reflux during states of wakefulness and active sleep as opposed to quiet sleep (Jeffery 1991). Reflexes that protect the airway against aspiration and provide respiratory defence against asphyxia are also depressed in active sleep compared with quiet sleep (Jeffery 1991). A theory that the decrease in SIDS among non-nutritive sucking infants is due to its effect in decreasing the rate of gastro-oesophageal reflux disease has been proposed (Mitchell 1993; Mitchell 2009); the mechanism being that use of pacifiers allows for non-nutritive sucking during sleep, which potentially helps acid neutralisation by increasing sucking and swallowing, and therefore assisting the clearance of refluxed gastric contents (Jeffery 1991; Page 2000; Hanzer 2010). This may contribute to a protective effect of pacifiers against SIDS. However, Page 2000 noted different responses to acid gastro-oesophageal reflux between term and preterm infants. Similar to the response to acid gastro-oesophageal reflux found in adults, term infants responded with increased swallowing that in turn led to increased primary peristalsis. However, preterm infants did not increase pharyngeal swallowing, but rather increased propagated peristalsis. Both responses, however, help clear acid reflux.

Why it is important to do this review

Pacifier use is a non-invasive intervention that may have the potential to reduce the risk of SIDS (Niemela 1994; Darwazeh 1995; Uhari 1996; Jackson 1999; North 1999; Daly 2000). This review examined the current evidence for infant pacifier use for the reduction of SIDS and their associated risks. This review aimed to provide guidance to clinicians and parents as to whether pacifier use is an effective and safe strategy in reducing SIDS.

OBJECTIVES

To determine whether the use of pacifiers during sleep versus no pacifier during sleep reduces the risk of SIDS.

METHODS

Criteria for considering studies for this review

Types of studies

We considered all published and unpublished RCTs and quasi-RCTs eligible for inclusion in this review. Studies reported only in abstract form were eligible for inclusion. Cluster and cross-over randomised trials were eligible for inclusion in this review.

Types of participants

We included infants born at term and at preterm (less than 37 weeks' gestation) or with low birth weight (less than 2500 grams). Infants must have been randomised by one month of postmenstrual age.

Types of interventions

Pacifier use (when infant placed down to sleep, for all sleep events) versus no pacifier use up to one year of age. Pacifier use was defined as sucking on a pacifier before, during or after feeding by a nasogastric or orogastric tube; or outside of feeding times. A pacifier is a device that is placed in the mouth to stimulate non-nutritive sucking behaviour. A pacifier is usually similar in material and shape to a feeding teat and is attached to a broad flat disc of plastic that covers the child's mouth to prevent ingestion (Schwartz 2008).

Types of outcome measures

Primary outcomes

- Deaths attributed to SIDS during the course of the study.

Secondary outcomes

- Episodes of otitis media during the course of the study up to 18 months of age.
- Episodes of oral candidiasis during the course of the study up to 18 months of age.
- Episodes of gastrointestinal infection during the course of the study (laboratory confirmed) up to 18 months of age.
- Incidence of breastfeeding at six months of age.
- Incidence of breastfeeding at 12 months of age.
- All-cause mortality during the course of the study up to 18 months of age.

Search methods for identification of studies

We used the criteria and standard methods of Cochrane and the Cochrane Neonatal Review Group (CNRG) (see [the Cochrane Neonatal Group search strategy for specialized register](#)).

Electronic searches

We used the criteria and standard methods of Cochrane and the CNRG (see [the Cochrane Neonatal Group search strategy for specialized register](#)).

We conducted a comprehensive search including: Cochrane Central Register of Controlled Trials (CENTRAL 2016, Issue 2); MEDLINE via PubMed (1966 to 16 March 2016); Embase (1980 to 16 March 2016) and CINAHL (1982 to 16 March 2016) using the following search terms: (non-nutritive sucking OR non nutritive sucking OR NNS OR dummy OR dummies OR pacifier OR soother OR comforter) AND (SIDS OR sudden infant death OR cot death), plus database-specific limiters for RCTs and neonates (see [Appendix 1](#) for the full search strategies for each database). We applied no language restrictions.

We searched clinical trials registries for ongoing or recently completed trials ([clinicaltrials.gov](#); the World Health Organization International Trials Registry and Platform [www.who.int/ictrp/search/en/](#), and the [ISRCTN Registry](#)).

Three review authors (KP, JF and NP) independently performed the electronic database searches.

Searching other resources

We communicated with expert informants and searched bibliographies of reviews and trials for references to other trials. We also searched previous reviews including cross-references, abstracts, and the conference and symposia proceedings of the Perinatal Society of Australia and New Zealand, and other paediatric academic societies (American Pediatric Society/Society for Pediatric Research and European Society for Paediatric Research) from 1990 to 2015. If we had identified any unpublished trials, we would have contacted the corresponding investigator for information. We would have considered unpublished studies and studies reported only as abstracts as eligible for review if the author confirmed the methods and data. We intended to contact the corresponding authors of identified RCTs for additional information about their studies if we required further data.

Data collection and analysis

We used the standard methods of Cochrane, as documented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and proposed by the CNRG.

Quality of evidence

We planned to use the GRADE approach to assess the quality of evidence for the following (clinically relevant) outcomes (Schünemann 2013): deaths attributed to SIDS during the course of the study; episodes of otitis media during the course of the study up to 18 months of age; episodes of oral candidiasis during the course of the study up to 18 months of age; episodes of gastrointestinal infection during the course of the study (laboratory confirmed) up to 18 months of age; incidence of breastfeeding at six months of age, incidence of breastfeeding at 12 months of age, and all-cause mortality during the course of the study up to 18 months of age.

Review authors planned to assess the quality of the evidence for each of the outcomes independently ([Primary outcomes](#); [Secondary outcomes](#)). We planned to consider evidence from RCTs as high quality but to downgrade the evidence one level for serious (or two levels for very serious) limitations based upon the following: design (risk of bias), consistency across studies, directness of the evidence, precision of estimates and presence of publication bias. We planned to use the [GRADEpro 2014](#) Guideline Development Tool to create a 'Summary of findings' table to report the quality of the evidence.

The GRADE approach results in an assessment of the quality of a body of evidence in one of four grades.

- High: we are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- Very low: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Selection of studies

Review authors independently assessed all the potential studies identified as a result of the search strategy for inclusion. We intended to resolve disagreement through discussion.

Specifically, we intended to:

- merge search results using reference management software and removed duplicate records of the same report;
- examine titles and abstracts to remove irrelevant reports;
- retrieve the full text of the potentially relevant reports;
- link multiple reports of the same study;
- examine full-text reports for compliance of studies with eligibility criteria;
- correspond with investigators, when appropriate, to clarify study eligibility;
- note, at all stages, reasons for inclusion and exclusion of articles; resolve disagreements through consensus;
- make final decisions on study inclusion;
- resolve all discrepancies through a consensus process.

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- correspond with investigators, when appropriate, to clarify study eligibility;
- note, at all stages, reasons for inclusion and exclusion of articles; resolve disagreements through consensus;
- make final decisions on study inclusion;
- resolve all discrepancies through a consensus process.

Data extraction and management

We designed a form intended for data extraction. However, we identified no eligible RCTs.

Assessment of risk of bias in included studies

We planned to assess risk of bias for included studies using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We planned to complete a 'Risk of bias' table addressing the following methodological issues.

The items planned for appraisal were:

- random sequence generation (biased allocation to interventions) due to inadequate generation of a randomised sequence;
- allocation concealment: selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment;
- blinding of participants and personnel: performance bias due to knowledge of the allocated interventions by participants and personnel during the study;
- blinding of outcome assessment: detection bias due to knowledge of the allocated interventions by outcome assessors;
- Incomplete outcome data: attrition bias due to amount, nature or handling of incomplete outcome data;
- selective reporting: reporting bias due to selective outcome reporting;
- other bias: bias due to problems not covered elsewhere.

See [Appendix 2](#) for more detailed description of risk of bias for each domain.

Measures of treatment effect

We planned to analyse treatment effects using Review Manager 5 (RevMan 2014). We intended to report the risk ratio (RR), risk difference (RD), number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH) derived from 1/RD for dichotomous outcomes and mean difference for continuous outcomes with the 95% confidence intervals (CI). We planned to use standardised mean difference where trials reported continuous outcomes using different measurement scales.

Data synthesis

We planned to perform data synthesis using the standard methods of the CNRG. If sufficient studies were located and deemed to be appropriate to group for analysis, the review authors planned to use a fixed-effect model. For the analysis of cluster trials, we intended to use the inverse variance method. The inverse variance method assumes that the individual cluster trial had been correctly analysed (e.g. the unit of analysis is the cluster not individuals and the analysis takes into account the correlation between clusters). We planned to obtain professional statistical advice as required to conduct these analyses.

Subgroup analysis and investigation of heterogeneity

We identified the following subgroups for analysis a priori:

- postmenstrual age (less than 28 weeks; 28 to 32 weeks; 32 to 37 weeks);

- exclusively breastfed; not exclusively breastfed;
- pacifier use (placed in mouth only versus pacifier replaced if dislodged from mouth).

RESULTS

Description of studies

We found no RCT or quasi-RCTs that met the inclusion criteria ([Figure 1](#)).

Figure 1. Study flow diagram.

Risk of bias in included studies

We found no studies.

Effects of interventions

We found no studies.

DISCUSSION

We found no studies that met the inclusion criteria.

We found two meta-analyses reporting an association between SIDS and lack of soother or pacifier use ([Hauck 2005](#); [Mitchell 2006](#)). The first meta-analysis pooled data of seven case-control studies of SIDS among pacifier users compared to the control group, using the last sleep as the reference sleep ([Hauck 2005](#)). Five studies provided data for both usual and last/reference-sleep pacifier use, and two studies provided data for last/reference sleep. When univariate odds ratios (OR) were analysed, usual pacifier use was associated with a non-significant decrease in risk of SIDS (summary odds ratio (SOR) 0.90, 95% CI 0.79 to 1.03). However, based on the four studies that used multivariate ORs controlling for a variety of factors including sleeping position, usual pacifier use was associated with a significant reduced risk of SIDS (SOR 0.71, 95% CI 0.59 to 0.85). All ORs provided for last sleep use indicated a lower risk of SIDS on both univariate and multivariate analysis. The SORs calculated for both univariate and multivariate ORs, reported by seven studies, were 0.47 (95% CI 0.40 to 0.55) for univariate and 0.39 (95% CI 0.31 to 0.50) for multivariate. These authors consequently recommended the use of pacifiers as a potential risk reduction strategy for SIDS.

Despite using essentially the same studies as [Hauck 2005](#), [Mitchell 2006](#) reached different conclusions and recommendations for practice. [Mitchell 2006](#) pooled data from seven case-control studies and examined routine pacifier use and SIDS. An increased prevalence of pacifier use among the control infants compared with the case infants demonstrated a significant reduced risk of SIDS with routine pacifier use (OR 0.83, 95% CI 0.75 to 0.93). [Mitchell 2006](#) also pooled data from eight case-control studies which examined pacifier use for the last sleep. All studies showed a reduced risk of SIDS (pooled OR 0.48, 95% CI 0.43 to 0.54). Despite these findings, [Mitchell 2006](#) suggested that pacifier use may be a marker for a yet unmeasured variable, and questioned the potential negative impact of dummies on breastfeeding. These authors concluded that discouraging the use of pacifiers would be inappropriate.

A number of observational studies found an association between pacifier use and reduction in the risk of SIDS ([Mitchell 1993](#);

[Arnestad 1997](#); [L'Hoir 1998](#); [Fleming 1999](#); [McGarvey 2003](#); [Hauck 2003](#); [Vennemann 2005](#); [Li 2006](#); [Blair 2009](#); [Moon 2011](#)). However, because observational studies do not demonstrate causation, this evidence of the protective effect of pacifiers in reducing the risk of SIDS remains controversial. Many of the interventions for the prevention of SIDS, including avoidance of prone sleeping, have not been tested in RCTs ([Gilbert 2005](#)).

While adequately powered RCTs on infant pacifiers for reduction in risk of SIDS would be ideal, such trials would require large sample sizes (i.e. with significance level of 95% and power of 80%, a minimum of 9894 infants). In addition, given the existing lower level evidence of the effectiveness of pacifier use in numerous case-control studies, and support for pacifier use by some professional bodies it may be difficult to recruit participants into such a trial. For example, the American Academy of Pediatrics (AAP) recommends pacifier use as a strategy for SIDS reduction by stating "Until evidence dictates otherwise, the AAP Task Force on Sudden Infant Death recommends use of a pacifier throughout the first year of life according to the following procedures: The pacifier should be used when placing the infant down for sleep and not be reinserted once the infant falls asleep. If the infant refuses the pacifier, he or she should not be forced to take it; Pacifiers should not be coated in any sweet solution; Pacifiers should be cleaned often and replaced regularly, and for breastfed infants, delay pacifier introduction until 1 month of age to ensure that breastfeeding is firmly established and possible concern in allocating babies to a control group" ([AAP 2005](#), p.1252).

AUTHORS' CONCLUSIONS

Implications for practice

We found no randomised controlled trial evidence on which to support or refute the use of pacifiers for the prevention of sudden infant death syndrome (SIDS).

Implications for research

Until the protective mechanism by which pacifier use for SIDS is better understood, and in the absence of quality randomised controlled trials, we are unable to support or refute the use of pacifiers for reduction in risk of SIDS.

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APPENDICES

Appendix 1. Standard search methodology

PubMed: ((infant, newborn[MeSH] OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or infan* or neonat*) AND (randomised controlled trial [pt] OR controlled clinical trial [pt] OR Clinical Trial[ptyp] OR randomised [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh]))

Embase: (infant, newborn or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW or Newborn or infan* or neonat*) AND (human not animal) AND (randomised controlled trial or controlled clinical trial or randomised or placebo or clinical trials as topic or randomly or trial or clinical trial)

CINAHL: (infant, newborn OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or Newborn or infan* or neonat*) AND (randomised controlled trial OR controlled clinical trial OR randomised OR placebo OR clinical trials as topic OR randomly OR trial OR PT clinical trial)

Cochrane Library: (infant or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW)

Appendix 2. Assessment of risk of bias in included studies

Random sequence generation

Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.

Criteria for the judgement of 'low risk' bias:

- referred to a random number table;
- used a computer random number generator;
- coin tossing;
- shuffling cards or envelopes;
- throwing dice;
- drawing of lots;
- minimisation.

Minimisation may be implemented without a random element and this is considered to be equivalent to being random.

Criteria for the judgement of 'high risk' bias:

The investigators described a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example:

- sequence generated by odd or even date of birth;
- sequence generated by some rule based on date (or day) of admission;
- sequence generated by some rule based on hospital or clinic record number.

Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorisation of participants, for example:

- allocation by judgement of the clinician;
- allocation by preference of the participant;
- allocation based on the results of a laboratory test or a series of tests;
- allocation by availability of the intervention.

Criteria for the judgement of 'unclear risk' of bias:

Insufficient information about the sequence generation process to permit judgement of 'low risk' or 'high risk'.

Allocation concealment

Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.

Criteria for the judgement of 'low risk' of bias:

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation:

- central allocation (including telephone, web-based and pharmacy-controlled randomisation);
- sequentially numbered drug containers of identical appearance;
- sequentially numbered, opaque, sealed envelopes.

Criteria for the judgement of 'high risk' of bias:

Participants or investigators enrolling participants could have possibly foresee assignments and thus introduced selection bias, such as allocation based on:

- using an open random allocation schedule (e.g. a list of random numbers);
- assignment envelopes were used without appropriate standards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered);
- alternation or rotation;
- date of birth;
- case record number;
- any other explicitly unconcealed procedure.

Criteria for the judgement of 'unclear risk' of bias:

Insufficient information to permit judgement of 'low risk' or 'high risk'. This is usually the case if the method of concealment was not described or not described in sufficient detail to allow a definite judgement; for example, if the use of assignment envelopes was described, but it remained unclear whether envelopes were sequentially numbered, opaque and sealed.

Blinding of outcome assessment

Detection bias due to knowledge of the allocated interventions by outcome assessors.

Criteria for the judgement of 'low risk' of bias:

Either of the following:

- no blinding of outcome assessment, but the review authors judged that the outcome measurement was not likely to be influenced by lack of blinding;
- blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.

Criteria for the judgement of 'high risk' of bias:

Either of the following:

- no blinding of outcome assessment, and the outcome measurement was likely to be influenced by the lack of blinding;
- blinding of outcome assessment but likely that the blinding could not have been broken, and the outcome measurement was likely to be influenced by lack of blinding.

Criteria for the judgement of 'unclear risk' of bias:

Either of the following:

- insufficient information to permit judgement of 'low risk' or 'high risk';
- the study did not address this outcome.

Incomplete outcome data

Attrition bias due to amount, nature or handling of incomplete data.

Criteria for the judgement of 'low risk' of bias:

Any one of the following:

- no missing outcome data;
- reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias);
- missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups;
- for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate;
- for continuous outcome data, plausible effect size (difference in means or standard difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size;
- missing data were imputed using appropriate methods.

Criteria for the judgement of 'high risk' of bias:

Any one of the following:

- reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups;
- for dichotomous outcome data, the proportion of missing outcomes compared with the observed event risk enough to induce clinically relevant bias in intervention effect estimate;
- for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size;
- 'as treated' analysis done with substantial departure of the intervention received from that assigned at randomisation;
- potentially inappropriate application of simple imputation.

Criteria for the judgement of 'unclear risk' of bias:

Either of the following:

- insufficient reporting of attrition/exclusions to permit judgement of 'low risk' or 'high risk' (e.g. number randomised not stated, no reasons for missing data provided);
- study did not address this outcome.

Selective reporting

Reporting bias due to selective outcome reporting.

Criteria for the judgement of 'low risk' of bias:

Either of the following:

- the study protocol was available and all the study's prespecified (primary and secondary) outcomes that were of interest in the review were reported in the prespecified way;
- the study protocol was not available but it was clear that the published reports included all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).

Criteria for the judgement of 'high risk' of bias:

Any one of the following:

- not all the study's prespecified primary outcomes were reported

- one or more primary outcomes was reported using measurements, analysis methods or subjects of the data (e.g. subscales) that were not prespecified;
- one or more reported primary outcomes were not prespecified (unless clear justification for their reporting was provided, such as an unexpected adverse effect);
- one or more outcomes of interest in the review were reported incompletely so that they could not be entered in a meta-analysis;
- the study report failed to include results for a key outcome that would be expected to have been reported for such a study.

Criteria for the judgement of 'unclear risk' of bias:

Insufficient information to permit judgement of 'low risk' or 'high risk'. It is likely that the majority of studies will fall into this category.

Other bias

Bias due to problems not covered elsewhere in the table.

Criteria for the judgement of 'low risk' of bias:

The study appeared to be free of other sources of bias.

Criteria for the judgement of 'high risk' bias:

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used or
- had been claimed to have been fraudulent or
- had some other problem.

Criteria for the judgement of 'unclear risk' of bias:

There may be a risk of bias, but there was either:

- insufficient information to assess whether an important risk of bias existed; or
- insufficient rationale or evidence that an identified problem introduced bias.

CONTRIBUTIONS OF AUTHORS

All review authors (KP, JF, NP, HJ) contributed to the writing of the protocol and review.

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None.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added the methodology and plan for the 'Summary of findings' tables and GRADE recommendations, which were not included in the original protocol. These will be applied to future updates.

INDEX TERMS**Medical Subject Headings (MeSH)**

*Pacifiers; Infant, Premature; Sudden Infant Death [*prevention & control]; Term Birth

MeSH check words

Humans; Infant; Infant, Newborn