**Walesca de Melo Avila**

# Mamadeira e aleitamento materno como fatores de risco para cárie dentária na dentição decídua: revisão sistemática e meta-análise.

Belo Horizonte

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# Mamadeira e aleitamento materno como fatores de risco para cárie dentária na dentição decídua: revisão sistemática e meta-análise.

Dissertação apresentada ao Programa de Pós-Graduação da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial à obtenção do título de Mestre em Odontologia.

Área de concentração: Odontopediatria

Orientadora: Prof. Dra. Carolina Castro Martins
Coorientadora: Prof. Dra. Isabela Almeida Pordeus

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# FOLHA DE APROVAÇÃO

**UNIVERSIDADE FEDERAL DE MINAS GERAIS**

**PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA**

## FOLHA DE APROVAÇÃO

**Aleitamento materno e uso de mamadeira como fatores de risco para cárie dentária: revisão sistemática e meta-análise.**

**WALESCA DE MELO AVILA**

Dissertação submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em ODONTOLOGIA, como requisito para obtenção do grau de Mestre em ODONTOLOGIA, área de concentração ODONTOPEDIATRIA.

Aprovada em 26 de junho de 2015, pela banca constituída pelos membros:

Prof(a). Carolina de Castro Martins - Orientador
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Prof(a). Isabela Almeida Pordeus
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Prof(a). Meire Coelho Ferreira
UniCeuma

Prof(a). Sheyla Marcia Auad
UFMG

Belo Horizonte, 26 de junho de 2015.

# ATA

**UNIVERSIDADE FEDERAL DE MINAS GERAIS**

**PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA**

## ATA DA DEFESA DA DISSERTAÇÃO DA ALUNA **WALESCA DE MELO AVILA**

Realizou-se, no dia 26 de junho de 2015, às 14:00 horas, Faculdade de Odontologia, da Universidade Federal de Minas Gerais, a defesa de dissertação, intitulada *Aleitamento materno e uso de mamadeira como fatores de risco para cárie dentária: revisão sistemática e meta-análise.*, apresentada por WALESCA DE MELO AVILA, número de registro 2013711250, graduada no curso de ODONTOLOGIA, como requisito parcial para a obtenção do grau de Mestre em ODONTOLOGIA, à seguinte Comissão Examinadora: Prof(a). Carolina de Castro Martins - Orientador (UFMG), Prof(a). Isabela Almeida Pordeus (UFMG), Prof(a). Meire Coelho Ferreira (UniCeuma), Prof(a). Sheyla Marcia Auad (UFMG).

A Comissão considerou a dissertação:

(X) Aprovada

( ) Reprovada

Finalizados os trabalhos, lavrei a presente ata que, lida e aprovada, vai assinada por mim e pelos membros da Comissão.
Belo Horizonte, 26 de junho de 2015.

Prof(a). Carolina de Castro Martins ( Doutora )

Prof(a). Isabela Almeida Pordeus ( Doutora )

Prof(a). Meire Coelho Ferreira ( Doutora )

Prof(a). Sheyla Marcia Auad ( Doutora )

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“Sempre me pareceu estranho que todos aqueles que estudam seriamente esta ciência acabam tomados de uma espécie de paixão pela mesma. Em verdade, o que proporciona o máximo de prazer não é o conhecimento, e sim a aprendizagem; não é a posse, mas sim a aquisição; não é a presença, mas o ato de atingir a meta.”

*Carl Friedrich Gauss*

## RESUMO

**Mamadeira e aleitamento materno como fatores de risco para cárie dentária na dentição decídua: revisão sistemática e meta-análise.**

Entender o papel do aleitamento materno e uso de mamadeira na experiência de cárie dentária é essencial para auxiliar dentistas e famílias em sua prevenção, além de aprimorar o desenvolvimento de políticas públicas adequadas. Entretanto, a relação do aleitamento materno e uso de mamadeira na etiologia da cárie ainda é controversa. O objetivo desta revisão sistemática e meta-análise foi avaliar a evidência científica disponível para a seguinte pergunta clínica: Crianças que usaram mamadeira apresentam mais lesões de cárie dentária na dentição decídua comparadas com crianças amamentadas no peito? A busca foi realizada em sete bases de dados eletrônicas e literatura cinzenta. Dois revisores independentes selecionaram os estudos, extraíram os dados e avaliaram o risco de viés por meio da análise de qualidade metodológica. A meta-análise foi realizada e foram calculados *odds ratio* (OR) e intervalo de confiança de 95% (IC95%). Sete estudos foram incluídos: cinco transversais, um caso-controle e uma coorte. A meta-análise de quatro estudos transversais não mostrou diferença estatisticamente significativa entre crianças aleitadas no peito e que usaram mamadeira em relação à cárie dentária (OR: 1,16; 95%IC: 0,60-2,23). Os resultados individuais de quatro estudos mostraram que crianças que fizeram uso da mamadeira apresentaram mais lesões cariosas ($p<0,05$) enquanto outros três estudos não mostraram essa associação ($p>0,05$). Apesar de a evidência científica ser fraca para fazer afirmações sobre o papel do tipo de alimentação para a cárie dentária nos primeiros anos da infância, os benefícios do aleitamento materno para a saúde geral fazem com que a melhor recomendação continue sendo o aleitamento materno exclusivo até os seis meses de vida. Estudos prospectivos observacionais do tipo coorte são necessários para obter novas evidências.



**Palavras-chave:** Revisão Sistemática, Aleitamento materno, Cárie dentária, meta-análise, mamadeira.

## ABSTRACT

**Bottle feeding and breastfeeding as risk factors for dental caries in deciduous teeth: systematic review and meta-analysis.**

Studies of the role of breastfeeding and bottle feeding in the occurrence of dental caries during childhood are important to help dentists and parents prevent caries, and also for the creation of public health policies. However, no consensus has yet been reached in literature regarding the issue. The aim of the present systematic review and meta-analysis was to seek scientific evidence relating to the clinical question: Do bottle fed children have more dental caries in primary dentition than children that were breastfed? Seven electronic databases and grey literature were searched. Two independent reviewers selected the studies, extracted data and evaluated risk of bias by quality assessment. Meta-analysis was conducted and the summary risk measure (odds ratio-OR) and 95% confidence intervals (95%CI) were calculated. Seven studies were included in the review: five cross-sectional, one case-control and one cohort study. Meta-analysis of the four cross-sectional studies did not reveal a statistically significant association between dental caries and whether the child was breast or bottle fed (OR: 1.16; 95%CI: 0.60-2.23). Four studies showed that bottle fed children had more dental caries than breast fed children ($p<0.05$), while three studies did not find an association ($p>0.05$). Scientific evidence regarding the role of breastfeeding and bottle feeding in the occurrence of dental caries during childhood is weak. Until new evidence is found, breastfeeding is recommended until up to six months of age, due to the fact that it has major benefits for the systematic health of babies. Further prospective observational cohort studies are needed to obtain new evidence.



**Keywords:** Meta-analysis, Systematic Review, Breast feeding, Dental caries.

## LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| **AAPD** | *American Academy of Pediatric Dentistry* |
| **ceo-d** | Dentes decíduos cariados, extraídos, obturados devido à cárie dentária |
| **CPI** | Cárie precoce na infância |
| **CPSI** | Cárie precoce e severa na infância |
| **ICDAS** | *International Caries Detection and Assessment System* |
| **OMS** | Organização Mundial de Saúde |
| **OR** | *Odds ratio* |
| **PRISMA** | *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* |
| **SB Brasil** | Saúde bucal Brasil |
| **S-ECC** | *Severe early childhood caries* |
| **WHO** | *World Health Organization* |

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## SUMÁRIO

# 1 INTRODUÇÃO

## 1 INTRODUÇÃO

A cárie dentária é resultante da desmineralização da superfície dentária pelos ácidos produzidos por bactérias, que ao longo do tempo metabolizaram os açúcares que permaneceram na superfície do dente (Loesche,1986). A cárie precoce da infância (CPI) é caracterizada pela presença de um ou mais dentes cariados, extraídos por cárie ou restaurados em qualquer superfície em crianças menores de 71 meses (American Academy of Pediatric Dentistry, 2014-2015).

Um dos primeiros trabalhos sobre cárie dentária em crianças foi publicado em 1927, quando médicos notaram um grande número de bebês com extensas lesões de cárie (Lancet, 1927). Apesar de nesta época ainda não haver pesquisas relacionando a etiologia da cárie dentária com o tipo de alimentação, posteriormente, vários autores mostraram resultados ambíguos a respeito da relação entre amamentação e uso de mamadeira com a cárie dentária (Hong *et al*., 2014; Chaffee *et al.*, 2014).

Os benefícios do aleitamento materno para a saúde geral são bem conhecidos, principalmente na redução da morbidade infantil e incidência de doenças infecciosas (Horta, Victora, 2013). Por outro lado, uma revisão sistemática de literatura observou que o aleitamento materno parece não trazer benefícios para o desenvolvimento normal da oclusão (Hermont *et al.*, 2015). O aleitamento materno exclusivo é recomendado pela Organização Mundial de Saúde (OMS) até os seis meses de idade. A partir desta idade e até dois anos, deve ser complementada com alimentos sólidos (Organização Mundial de Saúde, 2013). Entretanto, aspectos culturais e sociais podem afetar diretamente a prática do aleitamento materno bem como a sua duração (Martin-Bautista *et al.*, 2010).

Há medidas que possivelmente ajudam a reduzir a incidência de cárie dentária nas crianças, principalmente em relação ao aleitamento ou uso de mamadeira durante a primeira infância. Essas medidas precisam ser discutidas e disseminadas com a ajuda de todos os profissionais de saúde (Caplan *et al.*, 2008).

Alguns autores não identificaram o aleitamento materno como fator de risco para cárie dentária (Roberts *et al.*, 1994; Du *et al.*, 2007; Perera *et al.*, 2014), enquanto outro estudo encontrou esta associação, especialmente relacionada à sua duração (Corrêa-Faria *et al.*, 2013). Em relação ao uso de mamadeira, alguns autores o colocam como fator de risco para a cárie dentária (Plonka *et al*., 2013; Majorana *et al.*, 2014; Qadri *et al.*, 2012), mas resultado contrário já foi encontrado (Declerck *et al.*, 2008). A falta de consenso sobre o assunto torna evidente a necessidade de mais estudos (Al-Jewair, Leak, 2010).

Uma única revisão sistemática sobre a relação entre o aleitamento materno e cárie dentária foi publicada no ano 2000, e na época, não obteve respostas conclusivas sobre a questão (Valaitis *et al.*, 2000). Após quinze anos, esta questão ainda não foi totalmente compreendida. Diante da importância da alimentação na infância na etiologia da cárie dentária, o esclarecimento sobre o assunto faz-se necessário. O melhor entendimento sobre o tema possibilitará cirurgiões-dentistas a darem orientações mais adequadas aos pais. Responsáveis melhores orientados podem agir de maneira mais cuidadosa com a saúde bucal de seus filhos. Como consequência, crianças livres de alterações dentárias, dor e inflamação apresentam melhor qualidade de vida.

A cárie dentária na infância é um assunto que deve ser debatido, visto que afeta o bem estar, crescimento (Sheiham, 2006) e qualidade de vida de crianças e suas famílias (Ramos-Jorge *et al.*, 2014). Apesar do declínio da prevalência de cárie dentária em países desenvolvidos (Beaglehole *et al.*, 2009) e em desenvolvimento (Narvai *et al.*, 2006), a prevalência de cárie dentária em crianças de cinco anos de idade ao redor do planeta permanece alta: Inglaterra com 27,9% (Public Health England, 2013); Brasil com 46,6% (Brasil, 2010) e nos Estados Unidos da América varia entre 11,0-53,0% (Tyagi, 2008).

O objetivo desta revisão sistemática com meta-análise foi procurar por evidências científicas sobre a associação entre uso de mamadeira, amamentação e cárie dentária em crianças com dentição decídua. A pergunta cínica foi (PICO question): Pacientes: crianças com dentição exclusivamente decídua; Intervenção/Exposição ao fator de risco: uso de mamadeira; Comparação: aleitamento materno; Desfecho: cárie dentária.

# 2 CONSIDERAÇÕES INICIAIS

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## 2.1 A Odontologia Baseada em Evidências

A Prática Baseada em Evidência pode ser definida como o uso consciente, explícito e judicioso da melhor evidência na tomada de decisões sobre o cuidado de saúde dos pacientes (Sackett *et al.*, 1996). O objetivo principal é a aplicação mais válida da abordagem baseada em evidência para a prática odontológica. Além disso, busca encorajar o cirurgião dentista focado nos cuidados primários de saúde a basear sua conduta clínica nas evidências científicas disponíveis (Richards, Lawrence, 1995).

A prática da Odontologia Baseada em Evidência implica na integração da experiência clínica individual com a melhor evidência científica. A revisão sistemática é importante porque proporciona uma ampla discussão da evidência disponível. Ela pode tornar claro o conhecimento sobre determinado assunto por meio de um posicionamento crítico sobre o que foi feito e o que deve ser feito. Em Odontologia, é crescente o número de revisões sistemáticas com e sem meta-análise publicadas nos últimos anos. Há uma grande demanda que deve ser suprida por meio da pesquisa de dados secundários e seu agrupamento, visando a tomada de decisões em saúde baseada em evidências científicas.

## 2.2 Cárie precoce na infância: nomenclatura e dados epidemiológicos

Desde a década de 60, a definição da cárie precoce na infância (CPI) tem sido controversa. Várias nomenclaturas e definições apareceram: cárie de mamadeira, cárie rampante, feeding bottle syndrome, nursing caries, nursing bottle mouth, todas relacionadas à forma de alimentação e não levavam em consideração toda a etiologia multifatorial da cárie dentária. Em 2003, a American Academy of Pediatric Dentistry (AAPD) adotou uma nova definição de cárie precoce na infância (CPI), que pode ser definida como a presença de uma ou mais superfícies cariadas (cavitadas ou não), perdidas ou restauradas em crianças de até 71 meses de idade. Já a cárie precoce e severa na infância

(CPSI) foi definida em casos em que houvesse qualquer superfície dental cariada, perdida ou restaurada em crianças com até três anos de idade (AAPD, 2013; Borutta *et al.*, 2010; Drury *et al.*, 1999).

Apesar de a prevalência de cárie dentária continuar elevada em grupos populacionais mais vulneráveis (Arora *et al.*, 2011), tem havido uma redução de sua prevalência no Brasil (Tyagi, 2008; Brasil, 2004), bem como em outros países desenvolvidos, como Austrália, Reino Unido e Estados Unidos da América. Porém, ao utilizar-se o índice ICDAS (International Caries Detection and Assessment System) para levantamento da prevalência de cárie dentária em crianças colombianas, observou-se que esta ainda é alta ao considerar lesões de mancha branca (Cadavid *et al.*, 2010).

O levantamento epidemiológico do SB Brasil 2003 (Ministério da Saúde, Brasil, 2004) mostrou que 27% das crianças de 18 a 36 meses apresentavam pelo menos um dente cariado. Nas crianças com cinco anos de idade, essa proporção chegou a 60%. Houve uma redução na prevalência de cárie nos últimos sete anos, como pode ser visto no levantamento epidemiológico do SB Brasil 2010: crianças aos cinco anos de idade possuíam em média 2,43 dentes com experiência de cárie, correspondendo a 53,4% das crianças nesta idade com cárie dentária (Ministério da Saúde, Brasil, 2011; Ministério da Saúde, Brasil, 2004). Apesar da evidente redução da prevalência quando se compara os dois levantamentos, a cárie dentária continua a ser a doença bucal mais comum na infância.

## 2.3 Aleitamento materno

A OMS considera o leite humano como alimento ideal nos primeiros anos de vida do bebê, visto que seus benefícios são evidentes no desenvolvimento, prevenção e manutenção de sua saúde. O aleitamento materno traz inúmeros benefícios, tais como a redução da morbidade, da mortalidade, da diarreia e de infecções no trato respiratório inferior (Quigley *et al.*, 2007). A OMS recomenda o aleitamento materno exclusivo até os seis meses de idade, se estendendo até os dois anos de idade em adição a formas complementares de alimentação (OMS, 2003). A recomendação da OMS se

baseia em uma revisão sistemática de literatura (Kramer, Kakuma, 2012) que mostrou que o aleitamento materno exclusivo até os seis meses de idade diminui a morbidade, as doenças gastrointestinais e alérgicas nos primeiros anos de vida do bebê. Em contrapartida, não há evidência de benefícios do aleitamento materno para saúde bucal, por exemplo, na prevenção de má oclusão (Hermont *et al.*, 2015).

O aleitamento materno deve ser incentivado, tendo em vista todos os benefícios para a saúde sistêmica do bebê (Salone *et al.*, 2013). Porém, devido à falta de evidência científica que mostre uma relação entre aleitamento materno/ uso da mamadeira e cárie dentária, a prevenção deve ser enfatizada e mais pesquisas sobre o assunto devem ser realizadas.

## 2.4 Aleitamento materno, uso de mamadeira e a cárie dentária

Em um estudo realizado na Índia, composto por uma amostra de 1500 crianças de 8 a 48 meses, detectou-se que aquelas crianças que faziam uso de mamadeira com conteúdo adoçado ou aleitamento em livre demanda apresentavam aumento significativo de lesões cariosas. O grupo de crianças aleitadas exclusivamente no peito e em livre demanda apresentou uma prevalência de cárie de 29,6%, valor esse maior que a prevalência de cárie nas crianças que não amamentavam em livre demanda (26,7%). A prevalência de crianças com cárie que usavam mamadeira durante a noite foi ainda maior (40,7%) (Prakash *et al.*, 2012).

Outra pesquisa, realizada nos Estados Unidos da América, utilizando exame clínico em crianças de 1 a 5 anos de idade e entrevista com as mães, mostrou que o índice de dentes decíduos cariados, extraídos e restaurados devido a cárie dentária (ceo-d) aumentou conforme a duração do aleitamento materno aumentava. Crianças que usavam mamadeira por pelo menos 1,5 anos apresentavam mais lesões cariosas (Caplan *et al.*, 2008).

No Japão, um estudo transversal com 315 participantes mostrou que crianças que amamentaram por 18 meses ou mais apresentaram alto índice de CPI (OR: 2,70), e aquelas que usaram mamadeira com conteúdo adoçado apresentaram 2,63 vezes mais chance de apresentar alto índice de CPI

(IC=1,17-6,08). Os autores acreditam que o risco para cárie dentária foi aumentado em crianças com aleitamento prolongado, devido à alta concentração de lactose no leite humano, que é mais facilmente fermentado pelas bactérias. Outra possível explicação, seria de que mães que amamentam seus filhos por mais tempo, tendem a fazê-lo em livre demanda, o que também aumentaria o risco de desenvolvimento da cárie dentária (Tanaka *et al.*,2013).

Os estudos realizados sobre a relação entre o aleitamento materno e cárie dentária apresentam diferentes conclusões, alguns não mostram esta associação (Iida *et al.*, 2007), e outros observaram que a amamentação estava associada com a cárie dentária (Kato *et al.*, 2015). Uma revisão crítica de literatura (Ribeiro, Ribeiro, 2004) relatou informações conflitantes a respeito da cariogenicidade do leite materno. Apesar de o aleitamento materno prolongado ser a recomendação da OMS e da AAPD (AAPD, 2013), o aleitamento como fator de risco para a cárie dentária permanece um assunto sem consenso.

A única revisão sistemática publicada não encontrou tendência forte e consistência suficiente quanto à associação entre aleitamento materno e cárie dentária (Valaitis *et al.*, 2000). A maior parte dos estudos incluídos foram do tipo casos-controle, num total total de vinte e quatro, os demais estudos foram três séries de casos e um transversal. Nenhum dos estudos incluídos foi considerado de forte qualidade metodológica, e apenas três foram classificados medianos, sendo que apresentavam baixo rigor no desenho de estudo.

Tendo em vista a mudança do quadro epidemiológico da doença bem como as possíveis alterações no método de alimentação, torna-se importante uma nova revisão sobre o tema.

Desta forma, esta revisão sistemática poderá contribuir para a atualização do assunto, identificar quais aspectos na pesquisa científica do tema avançaram e quais ainda precisam avançar. Por meio dos dados obtidos, poderá auxiliar no estabelecimento de condutas de profissionais e na elaboração de políticas públicas de saúde. Além da revisão sistemática resultante da análise da comparação do aleitamento materno e uso de mamadeira no desenvolvimento de cárie dentária, também foi realizada a meta-análise. Este trabalho é fruto da inclusão de estudos dos tipos coorte, transversal e caso-controle.

# 3 OBJETIVOS

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## 3.1 Objetivo Geral

Verificar as evidências científicas da relação entre o aleitamento materno, o uso da mamadeira e a presença de lesão de cárie dentária.

## 3.2 Objetivos Específicos

Avaliar a qualidade metodológica dos estudos realizados sobre o tema.

Estabelecer a relação entre aleitamento materno, uso da mamadeira e cárie precoce na infância.

Estabelecer em quais áreas as futuras pesquisas precisam avançar.

# 4 ARTIGO CIENTÍFICO

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# Breast and bottle feeding as risk factors for dental caries: a systematic review and meta-analysis

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**Abstract**

Understanding the role that breastfeeding and bottle feeding play in the development of dental caries during childhood is essential in helping dentists and parents and care providers prevent the disease, and also for the development of effective public health policies. However, the issue is not yet fully understood. The aim of this systematic review and meta-analysis was to search for scientific evidence in response to the question: Do bottle fed children have more dental caries in primary dentition than breastfed children? Seven electronic databases and grey literature were used in the search. The protocol number of the study is PROSPERO CRD 42014006534. Two independent reviewers selected the studies, extracted data and evaluated risk of bias by quality assessment. A random effect model was used for meta-analysis, and the summary effect measure were calculated by odds ratio (OR) and 95% CI. Seven studies were included: five cross-sectional, one case-control and one cohort study. Meta-analysis for the cross-sectional studies and did not find a statistically significant difference between breast and bottle fed children regarding dental caries (OR: 1.17; 95%CI: 0.61-2.24). Four studies showed that bottle fed children had more dental caries ($p<0.05$), while three studies found no such association ($p>0.05$). Although the scientific evidence for statements about the role of breastfeeding and bottle feeding in dental caries during childhood is weak, the benefits of breastfeeding until age two is recommended by WHO/UNICEF guidelines. Further prospective observational cohort studies are needed to strengthen the evidence.

## Introduction

Early childhood caries (ECC) are defined as the presence of one or more decayed, missing or filled tooth surface in any primary tooth of children aged under 71 months [1].

One of the first published reports into dental caries in babies was performed in 1927[2], when doctors noticed that a large number of babies had extensive caries in tooth surfaces. Although no research into the role of breastfeeding and bottle feeding in the etiology of ECC existed at this time, many studies since then have revealed ambiguous results with respect to feeding habits and dental caries [3,4].

The benefits of breastfeeding for systemic health, such as the reduction of morbidity, infectious disease and low weight in newborns [5], are well known. The PROBIT trial emphasized the importance of breastfeeding, as it decreased the risk of gastrointestinal infections and inflammatory skin conditions [6]. Although it seems the practice does not benefit the development of normal occlusion [7]. Exclusive breastfeeding is recommended by the World Health Organization (WHO) until the age of six months, and breastfeeding complemented with food intake is suggested until two years old [8]. However, cultural and social factors directly affect knowledge of how long a child should be breastfed for [9].

The issue of whether bottle feeding is more cariogenic than breastfeeding remains unresolved even today. Some authors have not found an association between breastfeeding and dental caries [10-12], while other study have reported the existence of such an association[13]. Some authors have stated that bottle feeding is a risk factor for dental caries [14-16], while another author did not find such an association [17]. Due to the disagreement between these findings, further studies are needed to clarify the existence of this association [18].

A systematic review of studies investigating the relationship between breastfeeding and dental caries was published in 2000 and included twenty four case-control studies, three case series and one cohort. The systematic review could not confirm that breastfeeding was a risk factor of dental caries. However, it did not report comparisons between breastfeeding and bottle feeding [19]. Another review [20] identified three factors related to breastfeeding and/or bottle feeding as risk factors for dental caries: duration of breastfeeding greater than 18 months, used to feed or

stop crying during the night, and to put the child to sleep. However, none of these reviews compared bottle feeding vs. breastfeeding in relation to dental caries, and as such it has not been confirmed whether bottle feeding is more associated with dental caries in primary dentition than is breast feeding. Fifteen years later, the issue of whether bottle feeding can contribute to an increased risk of dental caries compared to breastfeeding remains unclear, as none of the reviews aimed to answer this clinical question. Therefore, this systematic review is the first to compare the rate of caries in different type of feeding practices: breastfeeding and bottle feeding.

Greater understanding of the subject is important, however, as improved knowledge can help dentists provide more appropriate instructions and lead to healthier children. The presence of dental caries in childhood is an important theme, which should be exhaustively discussed and treated as it affects well-being, growth [21] and quality of life [22]. Despite a decrease in the prevalence of dental caries in both developed [23] and developing countries [24], worldwide prevalence in five-year-old children remains high, with a level of 27.9% in England [25] ; 46.6% in Brazil [26], between 11.0 and 53.0% in the USA [27] and 23% in American children aged 2-3 years old [28] .

The aim of this study was to systematically review the scientific evidence relating to the association between feeding practice (breastfeeding vs. bottle feeding) and dental caries in childhood. The clinical question is (PICO): Patients: children with exclusively primary dentition; Intervention / Exposure to risk factor: bottle feeding; Comparison: breast feeding; Outcome: dental caries.

**Material and Methods**

The present systematic review was undertaken in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [29] (protocol number: PROSPERO CRD 42014006534).

This systematic review included observational cross-sectional, case-control, and cohort studies, together with clinical trials of children with exclusively primary dentition (age ≤ 71 months), which compared breastfeeding and bottle feeding in association with dental caries, and included statistical data comparing bottle to breast feeding. Statistical data could be: *odds ratio* (OR), *relative risk* (RR), *prevalence ratio* (PR), confidence intervals (95%CI), p-values, or studies that

reported frequency or an absolute number of events/total number of individuals per group.

Seven electronic databases were searched in March 2014: Pubmed (www.pubmed.gov); Cochrane Library (http://www.cochrane.org/index.html); Web of Science (http://www.isiknowledge.com); Controlled-trials Database of Clinical Trials (http://www.controlled-trials.com); Clinical Trials – US National Institute of Health (http://www.clinicaltrials.gov); National Institute for Health and Clinical Excellence (http://www.nice.org.uk); Lilacs (www.bireme.br) without restriction of date of publication. The search was updated in March 2015.

The following search strategy was used for the Pubmed, Cochrane Library and Web of Science databases: ((caries OR dental caries OR dental decay OR decay OR DMF index OR DMF Indices OR decayed teeth OR tooth decay) AND (bottle feeding OR bottlefeedings OR bottlefeed* OR breastfed* OR breast fed OR breastfeeding)).

The controlled-trials Database of Clinical Trials, Clinical Trials, National Institute for Health and Clinical Excellence, Lilacs were searched using the following combined keywords: dental caries AND breast feeding AND bottle feeding. A manual search was conducted in the reference lists of the included studies.

The online search identified a total of 1033 papers (Figure 1). After duplicate references were removed, a total of 784 studies were entered in the Reference Manager® program (Reference Manager, Thomson Reuters, version 12.0.3). The list provided by the reference manager was analyzed, and articles were selected based on abstracts and/or title by two independent reviewers (WMA and an undergraduate student). The independent reviewers were calibrated in accordance with inclusion/exclusion criteria using a sample of 20% of the retrieved studies, and agreement between reviewers was found to be good (K=0.79). The inclusion and exclusion criteria were applied independently to the remainder of the studies and any disagreement was resolved by consensus with a third reviewer (CCM).

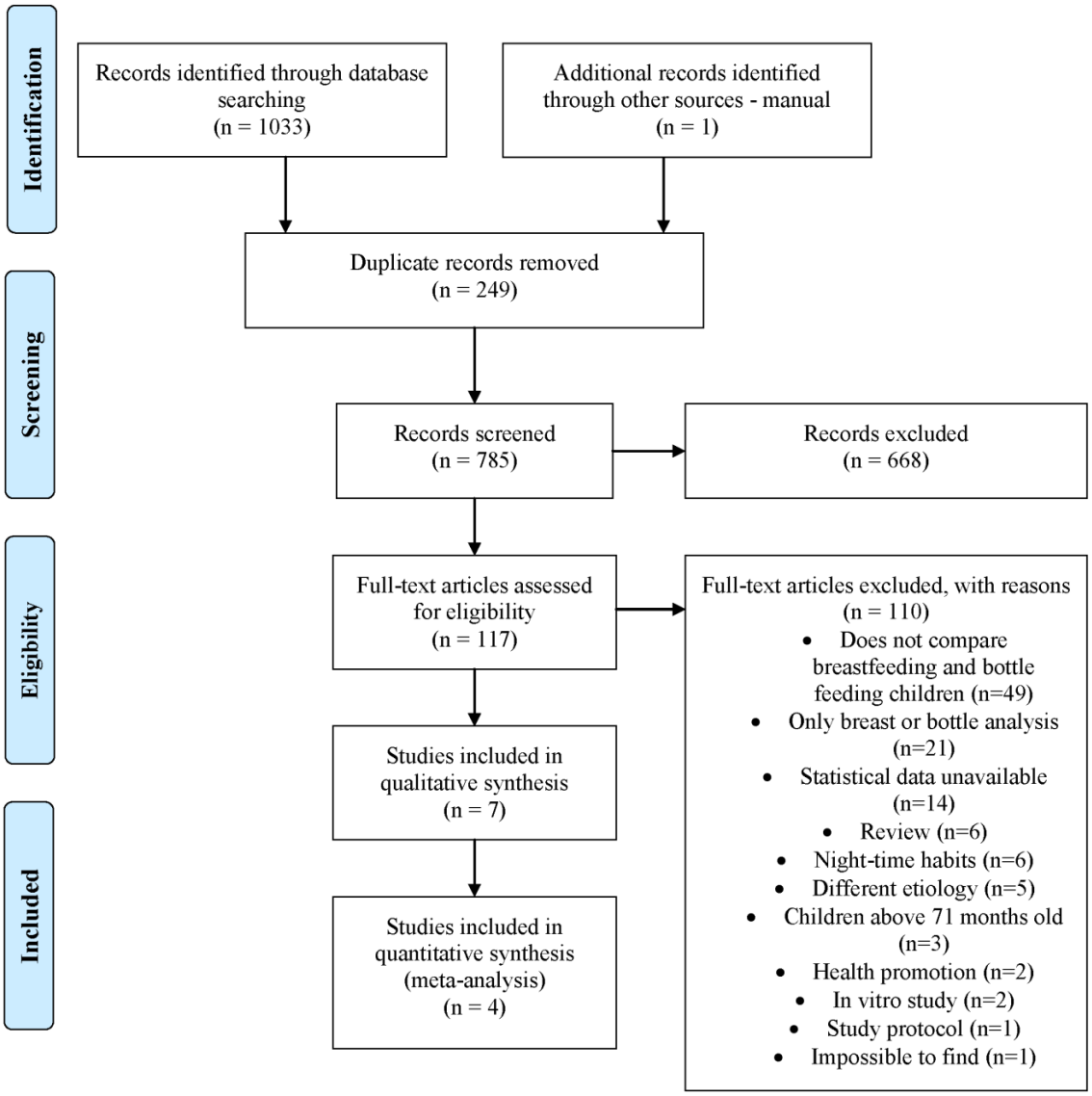


**Figure 1. Screening of articles.** Four-phase PRISMA flow-diagram for study collection, showing number of studies identified, screened, eligible, included in review and meta-analysis [26].

The exclusion criteria were: literature review, letters to the editor, editorials, patient handout, case report or case series, in vitro studies, etiology other than breast or bottle feeding, treatment of dental caries, health promotion, outcome other than dental caries (eg. malocclusion, dental hypoplasia, and others), other feeding habits, study protocol, studies reporting only bottle or breastfeeding, animal studies, studies of quality of life, language other than English.

A total of 667 studies were excluded after title/abstract analysis and 117 were selected for full text analysis. Where the studies could not be found, authors were

personally contacted by e-mail (for a list of excluded abstracts and/or title, see S1 Appendix). After full text analysis, 109 studies were excluded (for a list of excluded studies, see S2 Appendix). These studies were excluded for several reasons, such as: investigation of only one type of feeding practice (only breastfeeding or only bottle feeding), absence of comparison of breastfeeding and bottle feeding, investigation of other issues such as night-time feeding or weaning time, absence of statistical data, other etiology, in vitro study, case report, children above 71 months old. Grey literature was searched using abstracts presented in meetings, and a manual search was conducted from a reference list of included studies.

**Data extraction**

Descriptive data of clinical and methodological factors such as country, local setting, initial and final sample, dental examination, feeding habit evaluation, statistics, outcome and study design were extracted. In case of missing or misunderstood data, the authors were personally contacted by e-mail.

**Methodological quality assessment**

Quality assessment was performed by using the Newcastle-Ottawa Scale [30], which measures the methodological quality of a study by the number of points the study received. For case-control and cohort studies, the original scale was used. For cross-sectional studies, a modified version of the case-control study scale was used (Figure 2). Risk of bias was evaluated for each question. For each question-based entry the judgment was: “Yes, for low risk of bias” and a point was allocated (*), and “No, for high risk of bias” and a point was not allocated [31]. The questions evaluated in each study were based on the following criteria from the Newcastle-Ottawa scale: exposition/non-exposition and case/control definition; representativeness of the sample (evaluated by the methods of generation of samples, allocation concealment and sample calculation); sample selection (e.g., community, hospital, etc.), adjustment for confounders, blindness, acquisition of data on the dependent variable, description of bias, non-response rate (Figure 2).

| | *Definition /diagnosis of dental caries*[1] | *Definition for caries-free children*[2] | *Ascertainment of feeding habits*[3] | *Dental caries absence at start of study*[3] | *Sample selection*[4]† | *Representativeness*[4] | *Comparability*[4]† | *Exposure/Outcome*[4]†† |
|---|---|---|---|---|---|---|---|---|
| **Roberts *et al.*, 1994** | * | * | NR | NR | ** | | * | ** |
| **Al-Dashti *et al.*, 1995** | * | NR | NR | NR | * | | | ** |
| **Du *et al.*, 2000** | * | NR | NR | NR | * | | * | ** |
| **Du *et al.*, 2007** | * | NR | NR | NR | * | * | * | * |
| **Qadri *et al.*, 2012** | * | NR | NR | NR | * | * | | * |
| **Perera *et al.*, 2014** | * | NR | NR | NR | * | | | * |
| **Majorana *et al.*, 2014** | NR | NR | | * | * | | * | *** |

**Figure 2. Newcastle-Ottawa quality assessment** summary. [1]For cross-sectional and case-control studies. [2]For case-control study only. [3]For cohort study only. [4]For all study designs. †This item was allocated a maximum of 2 points. †† This item was allocated a maximum of 2 point for cross-sectional and 3 points for cohort and case-control studies. NR = not rated.

The representativeness criteria was evaluated through the sampling methods. The presence of a random component in the sequence generation was judged as low risk of bias. Allocation concealment was also used as a criteria for assessing representativeness. Thus, any method that precluded participants and researchers from foreseeing assignment was judged as low risk of bias.

## Data synthesis

The Comprehensive Meta-Analysis software program (version 2) was used for meta-analysis [32]. Heterogeneity among the studies was evaluated using $I^2$ statistics and a sensitivity test was used to test consistency of data. Fixed effect model was used for low heterogeneity and random effect model for high heterogeneity. As values exceeding 50% can be considered to be of notable heterogeneity [33], the random effect model was used for these cases. [34]. For categorical data, risk measures, odds ratio (OR), 95% confidence intervals (CI) and p-values were calculated in a forest plot.

The studies featured different weaning ages or breastfeeding duration, different study designs and differences in statistical tests. Meta-analysis was conducted only for those studies featuring variables that could be grouped. Data was extracted for the categorical variable feeding habit (breastfeeding vs. bottle feeding). For other studies a narrative synthesis of the data was conducted. Publication bias was not quantitatively evaluated by Egger test or funnel plot, as there were not enough studies to be grouped in a funnel plot [35].

## Results

### Study characteristics

Seven studies were included in this systematic review (four in meta-analysis): five cross-sectional [11, 12, 16, 36, 37], one case-control [10], and one cohort [15] (Table 1). Three studies recruited children from kindergartens [12, 16, 36] and four recruited children from hospital and health centers [10, 11, 15, 37]. The age of patients ranged from 18 months to 60 months. The sample size of the studies ranged from 218 to 2395 children. Only two studies used a representative sample and both collected the sample from kindergartens, one in one of the largest cities in Syria [15] and the other in two provinces of China [12, 16].

**Table 1**. Characteristics of studies included in systematic review.

| Authors (year) | Country, design | Local setting | Initial Sample (final) | Children with caries (total) | Child's age at dental examination | Dental examination (calibration) | Feeding habit evaluation | Statistics (adjusted for confounder) | Outcomes (OR, 95% CI) or (p-value) |
|---|---|---|---|---|---|---|---|---|---|
| **Al-Dashti *et al.* (1995)** | Kuwait, cross-sectional | One hospital and one health center | 227 | 82(179) were breastfed. 23 (30) had both feeding habits. 12(15) were bottlefed | 18-48 months | 2 dentists | Interview | Chi-square (no) | Breastfed children were affected by caries less frequently than bottle fed children ($p<0.05$); breastfed and mixed-fed (bottle+breast) children were less often affected by caries than bottle fed children |

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| | | | | | | | | | (<0.05); breastfed children were less affected by caries than bottle fed and mixed fed children (p<0.01). |
| **Du *et al.* (2000)** | China, cross-sectional | Kindergartens in a suburban area | 426 | 17(34) children bottle fed. 136 (392) children breast fed. | 24-48 months | 3 examiners (k=0.81-0.86) | Questionnaire for the mothers | Chi-square and Logistic regression (yes) | Bottle fed children were associated with rampant caries ($OR_{adj}$: 5.27; 95%CI: 2.16-12.89; p=0.003). Bottle fed children associated with incisor caries ($OR_{adj}$: 2.38; 95%CI: 1.03- |

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| | | | | | | | | | 4.76; p=0.042)<br>Bottle fed children were not associated with dental caries ($OR_{adj}$: 0.53; 95%CI: 0.26-1.09; p=0.08) |
| **Du *et al.* (2007)** | China, cross-sectional | Two provinces in China. Kindergartens in city and countryside. | 2014 (1621) | 59(130) bottle fed only ; 604(1070) children breast fed and 218(421) both feeding habits. | 36-60 months | 3 examiners (k = 0.85 for interexaminer agreement) | Questionnaire for the mothers (urban) and interview (rural). | Chi-square and multivariate regression analysis: logistic and linear regression (yes) | Logistic regression: no significance between feeding habit and dental caries (p>0.05). |
| **Qadri *et al*. (2012)** | Syria, cross- | Kindergartens | 400 | 121(192) children | 36-60 months | 1 pediatric dentist (NR) | Interview with parents | Chi-square, Z statistic, | Breastfed children were |

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| | sectional | | | were bottle fed. 71 were breastfed. | | | | Logistic regression (yes) | less associated with ECC* ($OR_{adj}$: 0.27; 95%CI: 0.18-0.41; p<0.001) and less associated with dmft† (OR:0.61; 95%CI: 0.39-0.97; p=0.038). Higher number of teeth affected by ECC in bottle fed children (p=0.036) |
| **Perera *et al.* (2014)** | Sri Lanka, cross-sectional | Pediatric Unit at the University Hospital | 300 (285) | 88(176) were exclusively breastfed. 48(109) were non exclusively | 36-60 months | 2 medical graduates | Interview | Odds ratio and student t test (no) | The mean DEFT did not reveal a statistically significant difference between |

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| | | | | breastfed. | | | | | breastfed children and bottle fed children (p=0.28). Breastfed children had a higher prevalence of caries than bottle fed children (OR = 1.27; 95% CI = 0.79-2.05). |
| **Roberts *et al.* (1994)** | South Africa, case-control | Health centers | 109 cases 109 controls | 34(75) were breastfed. 21(34) were bottlefed | 12-48 months | Examiner (K=0.95 for intra and interexaminer agreement) | Interview | Chi-square and Wilcoxon test (yes) | No statistically significant difference was found between breastfed children and bottle fed children |

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| | | | | | | | | | (p>0.05). |
| **Majorana *et al.* (2014)** | Italy, cohort | Obstetric ward of the city hospital | 2517 (2395) | ‡348(588); ǁ563(735); ⁑ 492 (534); ¤ 533(538) | 24-30 months | 2 examiners (K=0.84 for intra examiner agreement) | Questionnaire for the mothers at birth and then with 6, 9 and 12 months, including dietary diary. One clinical examination by the age of 24-30 months. | Ordered logistic regression (yes) | Comparison between exclusively breastfed‡; moderate-high mixed fedǁ, low mixed fed⁑, exclusive artificial formula¤ and caries severity - ICDAS score. Children with a higher proportion of breast milk had a lower ICDAS score (p<0.01, log likelihood=-1956.14, OR (Standard Error) = 6.75 |

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| | (0.40), 95% CI = 6.00-7.58). |

$OR_{adj}$ = Odds ratio adjusted

ECC = Early childhood caries

† Dmft= decayed tooth, decayed tooth indicated for extraction, filled tooth

‡Exclusive breast milk = 100% breast milk.

ǁModerate-High mixed feeding = 58-99% breast milk.

•Low mixed feeding = 1-57% breast milk.

¤Exclusive use of formula = 0% breast milk.

All studies included assessment of feeding habits by questionnaire [15, 36], interview [10, 11, 16, 37] or both, where an interview was used for the rural population and a questionnaire for the urban population [12]. The sample of the case-control study was drawn from a main study group of 1263 children in South African communities [38]. In this study, children aged one to four years were randomly selected from the birth records of every child of the community, targeting 300 children from each geographical area. First, children with dental caries were segregated from the main sample, giving a total of 109. These were matched with 109 children without dental caries for age, gender, race and social class.

The cohort study [15] analyzed children from a hospital from birth to up to 30 months of age. Feeding habits were identified through a questionnaire applied at birth, and then again at 6, 9 and 12 months. After feeding assessment, one clinical examination was conducted by two examiners between 24 and 30 months.

**Diagnosis of dental caries**

Most studies used WHO criteria[11, 12, 36, 37], ICDAS [15] or specific definition [10] for diagnosis of dental caries, while one study used three different criteria (those were ICDAS, WHO and Nyvad) [16]. One author [36] divided the presence of caries presence into three classifications: caries; rampant caries and incisor caries. The “with caries” group was defined according to WHO criteria [39], rampant caries was defined as two or more upper deciduous incisors with carious labial or palatal surfaces, while incisor caries considered only this tooth group.

**Feeding habits**

All studies considered categorical data regarding the presence and absence of breastfeeding, bottle feeding or mixed feeding, although the criteria used to define types of feeding differed between studies. One author considered breast feeding or bottle feeding at birth [37]; two authors considered feeding habits up to 6 months or more [11, 15], one author considered exclusive breastfeeding up to 12 months [10], and others considered feeding habits during infancy [12, 16, 36].

**Meta-analysis**

Meta-analysis was conducted in four cross sectional studies [11, 12, 36, 37], which presented categorical variables that could be grouped (breastfeeding vs. bottle

feeding). There was no significant association between feeding habit and dental caries (OR: 1.17, 95%CI: 0.61-2.24, $I^2$: 85.95%) (Figure 3).

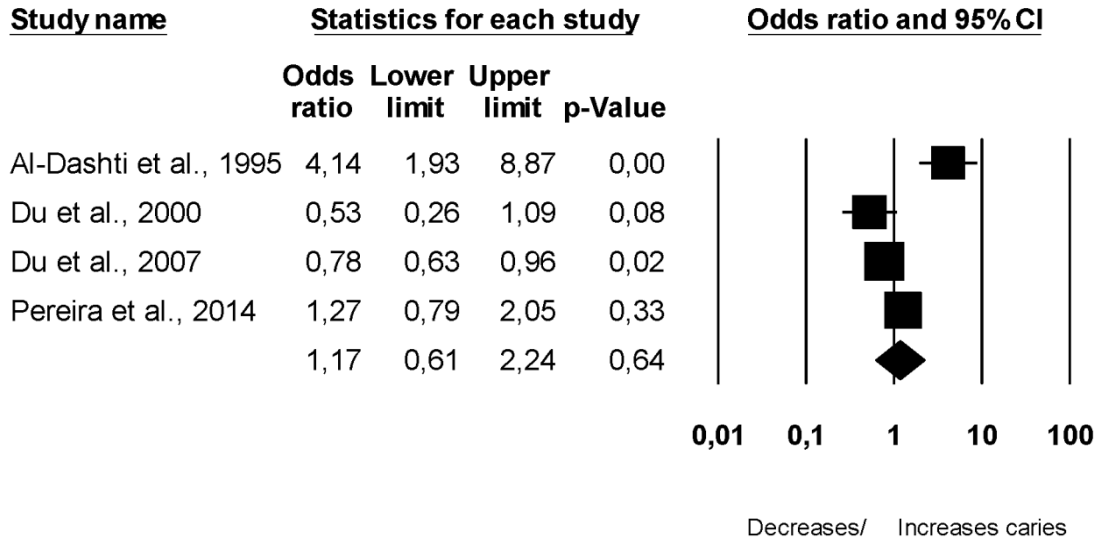


**Figure 3. Forest plot of meta-analysis for four cross-sectional studies.** Evaluates bottle or breast feeding practices and dental caries (outcome: presence of dental caries vs. absence of dental caries). Pooled effect measures [odds ratio (OR) and 95% confidence interval (CI)] indicated no statistically significant difference between breast and bottle fed children. $I^2$=85.95%. Random effect model used.

### Methodological Quality Assessment

The summary of quality assessment is summarized in Figure 2. A high risk of bias was obtained when the item did not fulfill the Newcastle-Ottawa criteria, and the response given for the item was ‘no, the item has high risk of bias” [31]. Four items were judged as having a high risk of bias in a number of studies: failure to adjust for any confounding variables [11, 16, 37], representativeness [10, 11, 15, 36, 37] and ascertainment for feeding habits [15]. The confounding variables were searched for in the Methods and Results section and in the tables of the published papers.

## Discussion

### Methodological Quality Assessment

The diversity of study designs in this review was analyzed using an adapted version of the Newcastle-Ottawa scale for assessing the quality of studies. The process was

made complex [40] due to the heterogeneity of studies and differences in feeding habits and dental caries classification.

While most of studies used WHO criteria [11, 12, 16, 36, 37] for diagnosing dental caries, the cohort study [15] used ICDAS criteria. Besides the diagnostic criteria, the authors of this study divided the practice of feeding into a gradative scale of exclusively breast/bottle feeding and mixed feeding.

Some studies had high risk of bias for comparability of variables. Adjustment for confounders in cross-sectional studies was performed only for social class [12, 36]. The case-control study [10] matched cases and controls for social class in order to reduce confounding bias. However, the study did not adjust the confounders in a multivariate model. Adjustment was made for social class but in respect of the severity of caries in the cohort study. This study defined one of the outcomes (dependent variable) as severity of caries, as the authors used the ICDAS scale to measure severity of dental caries [15]. None analyzed bottle content during bottle feeding. As none of the studies were adjusted for all the confounding factors, all are susceptible to residual confounding. Confounding variables can include social class, hygiene and sugar in bottle content, ethnicity, early preventive dental visits, water fluoridation and on-demand feeding at night. Some of these variables such as sugar in bottle content and on-demand feeding at night can contribute to an increase in the risk of dental caries, while others can act as protective factors (water fluoridation, early preventive dental visits). These variables should be considered during data collection and should be adjusted in proper multivariate models to control the confounders.

Confounding factors have the power to mask an association or even falsely indicate an apparent association. The presence of plausible confounding makes it difficult to establish a causal link between a risk factor and outcome [41]. This makes evaluation of the role of feeding habits in the etiology of dental caries. Adjustment for major confounders such as social class, hygiene and sugar in bottle content is extremely important, as these are known to be etiological factors of dental caries [42-44].

One common reason for the decrease in quality was the absence of blindness during the ascertainment of bottle/breast feeding in relation to dental caries (exposure/outcome). Only examiners from one study [37] were unaware of the

responses of mothers about feeding practices when the clinical examination for dental caries was performed. Risk of bias assessment emphasized selection bias because of inadequate or unclear allocation sequence and concealment. Lack of or unclear blinding statement can generate detection bias.

Attrition bias was low risk as all studies declared the withdrawal of participants, which did not exceed 20% (exposure/outcome). A low risk of reporting bias was observed as most of studies adequately reported outcome through a validated dental caries diagnosis index. However, observer bias may be present, as there was a lack of inter- and intra- examiner statistical measurement, such as kappa. Additionally, memory bias is inherent to the ascertainment of feeding habits, as mothers are required to report the food intake of their children. Cohort designs with real time investigation of feeding habits [15] can minimize memory bias.

Only two studies were allocated points for representativeness criteria [12, 16]. Both of these used stratified random sampling of kindergartens before randomized sampling was used to select children. The locations for sample selection were kindergartens, which were created for children whose parents worked outside the home [45]. Samples from these locations may favor specific social classes, leading to selection bias. Furthermore, many children may not be enrolled at kindergartens and can be cared for at home by a childminder or mother, leading to selecting of the sample. Moreover, there was no mention of whether these were public or private kindergartens. For this reason, the generalizability of these studies is limited.

Inter- and intra-examiner reproducibility of recordings was not evaluated in all of the studies. Studies evaluated inter-examiner agreement [12, 36]; intra-examiner agreement by Cohen's Kappa Coefficient [15]; or both [10]. Some studies did not report any calibration testing [11] [16, 37].The lack of a kappa statistic is also a critical issue in the studies [11, 16, 37], as this test is considered the most reliable way to assess the agreement of researchers during data collection [46, 47]. The absence of this assessment may produce bias and produce unreliable data and in consequence, unreliable results.

Data relating to feeding habits was collected through interviews with carers or mothers of children. This type of data collection may be subject to bias due to forgetfulness or inability to provide more precise information, called information bias.

All but one of the studies assessed feeding habits through questionnaires or interviews, while the remaining study [15] used a dietary diary for data collection in an attempt to reduce memory bias. However, it is important to clarify that this was only possible because it was a cohort study. A dietary diary consists of an individual writing down his or her entire food intake during a day. If this procedure is repeated regularly during a study, it could capture a more realistic view of the subject's feeding habits.

Information bias could not be measured quantitatively due to the imprecise information regarding feeding habits given by carers. Based on their knowledge of the importance of breastfeeding, mothers may overestimate the duration of breastfeeding. For this reason, information bias regarding feeding habit may have influenced the meta-analysis. Furthermore, psychological aspects are important in the decision of when to wean from the breast [48].

**Strength of evidence**

Randomized clinical trials were not found. This was expected because of the ethical questions related to the issue. Three cross-sectional [16, 36, 37] studies and the cohort [15] study showed that breastfed children were significantly less frequently affected by caries than bottle fed children. While the cross-sectional design features a lower level of evidence and may not give a cause-and-effect relationship [46], the cohort design may indicate a temporal sequence between exposure and outcome and allow the incidence of disease to be calculated [47]. Furthermore, such studies have a higher level of evidence.

Meta-analysis did not find a difference between dental caries and feeding practices. This finding was in accordance with two cross-sectional [11, 12] and the case-control study [10]. While case-control studies have an intermediate level of evidence, these studies, together with cohort studies, had a low risk of bias [10, 15].

Meta-analysis regarding breastfeeding duration could not be performed due to the impossibility of extracting this data. Studies showed clinical heterogeneity as the duration of breastfeeding varied from one study to another.

The studies that were included in the meta-analysis were all cross-sectional and statistically heterogeneous ($I^2$=85.95%). Moreover, there was a lack of adjustment for

all confounders among studies, with two adjusting for social class only [12, 36]. Representativeness was also lacking [11, 36, 37]. Two studies [12, 36] were conducted in the same cities, although with different samples. More studies of different populations makes meta-analysis results more representative. In addition, meta-analysis may be affected by information bias, since all of the studies collected feeding habits data from the reports of carers and parents.

This systematic review involved a search of multiple electronic databases, with no year of publication restriction. Efforts were made to try to find unpublished studies through grey literature. Some shortcomings of this systematic review are the presence of many Asian studies, and the exclusion of studies written in other language than English. These points can imply some publication bias, although the search of grey literature may reduce its impact [44]. These shortcomings limit the global extrapolation of these conclusions, as the concentration of Asian studies may lead to an unrepresentative sample of studies [45].

Current scientific evidence has not been able to confirm that bottle feeding is a risk factor for dental caries. The same conclusion was reached regarding breastfeeding and dental caries, as the methodological approach was considered inconsistent [18]. Although this review is the first to attempt to compare the rate of dental caries rate in breastfed and bottle fed children, statements about the effect of these feeding habits on dental caries could not be made. However, breast feeding benefits the systemic health of children [6, 49] and for this reason, the breastfeeding of children for at least six months is prudent [8].

## Conclusion

The available scientific evidence is too weak to make statements about the role of breastfeeding and bottle feeding in dental caries during childhood. The heterogeneity of study designs and the absence of controlling confounders made it impossible to determine the relationship between feeding practices in childhood and dental caries. Further prospective cohort studies with follow ups during childhood, blinding during dental examination, and control of confounders are suggested for future studies. Thus, breastfeeding should be encouraged and practiced by all children up to two years of age, in accordance with the WHO/UNICEF recommendation.

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## Supporting Information Captions

**S1 Appendix.** List of all titles and abstracts for analysis and reasons for exclusion.

**S2 Appendix.** List of titles selected for full text analysis and the reasons for exclusion.

**S3 Checklist.** PRISMA 2009 Checklist.

# 5 CONSIDERAÇÕES FINAIS

## 5 CONSIDERAÇÕES FINAIS

A evidência científica é fraca para fazer qualquer afirmação sobre o papel do aleitamento materno e do uso de mamadeira durante a infância na etiologia da cárie dentária. A heterogeneidade dos desenhos de estudo e a falta de controle para confundidores principais na etiologia da cárie dentária, como higiene bucal, classe social e presença de açúcar no conteúdo da mamadeira, dificultam a determinação da real relação entre hábitos de sucção nutritivos na infância e cárie dentária. Para futuros estudos são necessários e recomendados mais estudos prospectivos do tipo coorte com acompanhamento durante a infância; com cegamento durante o exame clínico, além de controle de confundidores.

É recomendada a manutenção dos hábitos nutritivos indicados pela Organização de Saúde, como aleitamento materno exclusivo até os seis meses de vida, e então, a introdução gradativa de alimentação complementar. Esta recomendação se baseia nos benefícios à saúde sistêmica do bebê. Além disso, a consulta com o dentista ou odontopediatra deve acontecer, de preferência no primeiro ano de vida, para que os responsáveis pelas crianças sejam orientados sobre a higienização bucal, a fim de prevenir o desenvolvimento de cárie dentária.

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# ANEXOS

# Anexo A – Registro PROSPERO

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

## PROSPERO International prospective register of systematic reviews

### Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Breast and bottle feeding as risk factors for dental caries: a systematic review and meta-analysis.

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.
Aleitamento materno e uso de mamadeira como fatores de risco para cárie dentária: revisão sistemática e meta-análise.

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
01/01/2014

4 Anticipated completion date
Give the date by which the review is expected to be completed.
31/07/2015

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started ×

| Review stage | Started | Completed |
|---|---|---|
| Preliminary searches | Yes | Yes |
| Piloting of the study selection process | Yes | Yes |
| Formal screening of search results against eligibility criteria | Yes | Yes |
| Data extraction | Yes | Yes |
| Risk of bias (quality) assessment | Yes | Yes |
| Data analysis | Yes | Yes |

Provide any other relevant information about the stage of the review here.

### Review team details

6 Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Walesca Avila

7 Named contact email
Enter the electronic mail address of the named contact.
walesca@gmail.com

8 Named contact address
Enter the full postal address for the named contact.
105 Andaluzita St. 604. Carmo Sion. Belo Horizonte, Minas Gerais. Brasil.

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.
+553132255009

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed

as 'None' if the review is not affiliated to any organisation.
Universidade Federal de Minas Gerais - UFMG

Website address:
www.ufmg.br

11 Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

| Title | First name | Last name | Affiliation |
|---|---|---|---|
| Miss | Walesca | Avila | UFMG |
| Professor | Isabela | Pordeus | UFMG |
| Professor | Carolina | Martins | UFMG |

12 Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
CAPES PROEX

13 Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.
Are there any actual or potential conflicts of interest?
None known

14 Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

| Title | First name | Last name | Organisation details |
|---|---|---|---|

## Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
Bottle fed children with exclusively primary dentition have more dental caries than those breasfed?

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
There will be no restriction on publication period.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.
Dental caries is a chronic disease that affects well being and general health, and inconsequence influences the development and integrity of the child. Although the World Health Organization recommends breast feeding up to 24 months old, there is no consensus about this type of feeding with the bottle feeding, regarding dental caries.

19 Participants/population

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
Children with exclusively primary dentition.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
Children artificially bottle fed will be included as the exposure group. Dental caries is associated with nocturnal feeding, mostly because of the bottle feeding. The breast feeding is promoted by international organizations, because of the many benefits of this practice. The bottle is controversial in its benefits and should be investigated.

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Children breastfed.

22 Types of study to be included initially
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Observational cross-sectional, case-control, and cohort studies, together with clinical trials of children with exclusively primary dentition (age = 71 months), which compared breastfeeding and bottle feeding in association with dental caries, and included statistical data comparing bottle to breast feeding.

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.
The exclusion criteria were: literature review, letters to the editor, editorials, patient handout, case report or case series, in vitro studies, etiology other than breast or bottle feeding, treatment of dental caries, health promotion, outcome other than dental caries (eg. malocclusion, dental hypoplasia, and others), other feeding habits, study protocol, studies reporting only bottle or breastfeeding, animal studies, studies of quality of life, language other than English.

24 Primary outcome(s)
Give the most important outcomes.
Dental caries.

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
None.

Give information on timing and effect measures, as appropriate.

26 Data extraction, (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.
Two review authors will independently retrieve studies through using search strategy. The inclusion and exclusion criteria will be considered. In case of disagreement between them over the eligibility of some studies this will be resolved through discussion with a third reviewer. Two software packages, Reference Manager and Endnote, will be used to keep the data and the references. The software Access will be used for classification of the studies. A concordance level of 20% will be verified inter and intra review authors. It will be calculated thorough the kappa.

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.
A table with all the data will be created and it will be summarized by each author reviewer. In case of discrepancy, there will be a discussion about the study. The design of the study; location of the research; frequency and duration of the bottle fed; content of the bottle; drop-outs; measure of the outcome; number of the sample; odds-ratio and others will be considered.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.
The data synthesis will be done in a table with the primary data, for a posterior quantitative and non-quantitative analysis. If quantitative data are available, meta-analysis will be done, it will not be possible if the studies are too heterogeneous. A narrative synthesis about the aggregated data will be conducted.

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
None planned.

## Review general information

30 Type of review
Select the type of review from the drop down list.
Epidemiologic, Prevention

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English, Portuguese-Brazil

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Brazil

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
breastfeeding

dental caries

systematic review

dental caries

bottle feeding

meta-analysis

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Completed but not published

12/08/2015

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.

## Anexo B – Instruções para os autores Journal PlosOne

### Submission Guidelines

### Style and Format

| | |
|---|---|
| **File format** | Manuscript files can be in the following formats: DOC, DOCX, RTF, or PDF. Microsoft Word documents should not be locked or protected. LaTeX manuscripts must be submitted as PDFs. Read the LaTeX guidelines. |
| **Length** | Manuscripts can be any length. There are no restrictions on word count, number of figures, or amount of supporting information. We encourage you to present and discuss your findings concisely. |
| **Font** | Use any standard font and a standard font size. |
| **Headings** | Limit manuscript sections and sub-sections to 3 heading levels. Make sure heading levels are clearly indicated in the manuscript text. |
| **Layout** | Manuscript text should be double-spaced. Do not format text in multiple columns. |
| **Page and line numbers** | Include page numbers and line numbers in the manuscript file. |
| **Footnotes** | Footnotes are not permitted. If your manuscript contains footnotes, move the information into the main text or the reference list, depending on the content. |
| **Language** | Manuscripts must be submitted in English. You may submit translations of the manuscript or abstract as supporting information. Read the supporting information guidelines. |
| **Abbreviations** | Define abbreviations upon first appearance in the text. Do not use non-standard abbreviations unless they appear at least three times in the text. List all non-standard abbreviations (with definitions) in alphabetical order in a separate section at the beginning of the manuscript. Keep abbreviations to a minimum. |
| **Reference style** | PLOS uses “Vancouver” style, as outlined in the ICMJE sample references.<br><br>See reference formatting examples and additional instructions below. |
| **Equations** | We recommend using MathType for display and inline equations, as it will provide the most reliable outcome. If this is not possible, Equation Editor is acceptable.<br><br>Avoid using MathType or Equation Editor to insert single variables (e.g., $\mathcal{A}$ or $Q$z) in running text. Wherever possible, single symbols should be inserted as normal text with the correct Unicode |

(hex) values.

Do not use MathType or Equation Editor for only a portion of an equation. Rather, ensure that the entire equation is included. Avoid “hybrid” inline or display equations, in which part is text and part is MathType, or part is MathType and part is Equation Editor.

**Nomenclature** Use correct and established nomenclature wherever possible.

| | |
|---|---|
| *Units of measurement* | Use SI units. If you do not use these exclusively, provide the SI value in parentheses after each value. Read more about SI units. |
| *Drugs* | Provide the Recommended International Non-Proprietary Name (rINN). |
| *Species names* | Write in italics (e.g., *Homo sapiens*). Write out in full the genus and species, both in the title of the manuscript and at the first mention of an organism in a paper. After first mention, the first letter of the genus name followed by the full species name may be used (e.g., *H. sapiens*). |
| *Genes, mutations, genotypes, and alleles* | Write in italics. Use the recommended name by consulting the appropriate genetic nomenclature database (e.g., HUGO for human genes). It is sometimes advisable to indicate the synonyms for the gene the first time it appears in the text. Gene prefixes such as those used for oncogenes or cellular localization should be shown in roman typeface (e.g., v-fes, c-MYC). |

***Manuscript Organization***

Manuscripts should be organized as follows. Instructions for each element appear below the list.

**Beginning section** *The following elements are required, in order:*

Title page: List title, authors, and affiliations as first page of manuscript: Abstract; Introduction.

**Middle section** *The following elements can be renamed as needed and presented in any order:* Materials and Methods; Results; Discussion; Conclusions (optional).

**Ending section** *The following elements are required, in order:* Acknowledgments; References; Supporting Information Captions (if applicable).

**Other elements** Figure captions are inserted immediately after the first paragraph in which the figure is cited. Figure files are uploaded separately.Tables are inserted immediately after the first paragraph in which they are

cited. Supporting information files are uploaded separately.

Please refer to our downloadable sample files to make sure that your submission meets our formatting requirements: Download sample title, author list, and affiliations page (PDF). Download full manuscript sample (PDF)

**Parts of a Submission**

**Title**

Include a full title and a short title for the manuscript.

| **Title** | Length | Guidelines | Examples |
|---|---|---|---|
| **Full title** | 250 characters | Specific, descriptive, concise, and comprehensible to readers outside the field | Impact of Cigarette Smoke Exposure on Innate Immunity: A *Caenorhabditis elegans* Model<br><br>Solar Drinking Water Disinfection (SODIS) to Reduce Childhood Diarrhoea in Rural Bolivia: A Cluster-Randomized, Controlled Trial |
| **Short title** | 50 characters | State the topic of the study | Cigarette Smoke Exposure and Innate Immunity<br><br>SODIS and Childhood Diarrhoea |

Titles should be written in title case (all words capitalized except articles, prepositions, and conjunctions). Avoid specialist abbreviations if possible. For clinical trials, systematic reviews, or meta-analyses, the subtitle should include the study design.

**Author list**

Who belongs on the author list all authors must meet the criteria for authorship as outlined in the authorship policy. Read the policy.
Those who contributed to the work but do not meet the criteria for authorship can be mentioned in the Acknowledgments.Read more about Acknowledgments.

**Author names and affiliations**

Enter author names on the title page of the manuscript and in the online submission system. On the title page, write author names in the following order: First name (or initials, if used); Middle name (or initials, if used); Last name (surname, family name)

Each author on the list must have an affiliation. The affiliation includes department, university, or organizational affiliation and its location, including city, state/province (if applicable), and country. If an author has multiple affiliations, enter all affiliations on the title page only. In the submission system, enter only the preferred or primary affiliation. Author names will be published exactly as they appear in the manuscript file. Please double-check the information carefully to make sure it is correct.

**Corresponding author**

One corresponding author should be designated in the submission system as well as on the title page. One corresponding author should be designated in the submission system. However, this does not restrict the number of corresponding authors that

may be listed on the article in the event of publication. Whoever is designated as a corresponding author on the title page of the manuscript file will be listed as such upon publication. Include an email address for each corresponding author listed on the title page of the manuscript.

**Consortia and group authorship**

If a manuscript is submitted on behalf of a consortium or group, include the consortium or group name in the author list, and include the full list of members in the Acknowledgments or in a Supporting Information file. The corresponding author is responsible for making sure all authors approve the final manuscript before submission. *PLOS ONE* will contact all authors by email at submission to ensure that they are aware of the submission

**Cover letter**

Upload a cover letter as a separate file in the online system. The length limit is 1 page. The cover letter should include the following information: Summarize the study's contribution to the scientific literature; Relate the study to previously published work; Specify the type of article (for example, research article, systematic review, meta-analysis, clinical trial); Describe any prior interactions with PLOS regarding the submitted manuscript; Suggest appropriate Academic Editors to handle your manuscript (see the full list of Academic Editors); List any opposed reviewers.

IMPORTANT: Do not include requests to reduce or waive publication fees in the cover letter. This information will be entered separately in the online submission system.Read about publication fee assistance.

**Title page**

The title, authors, and affiliations should all be included on a title page as the first page of the manuscript file. Download sample title, author list, and affiliations page (PDF).

**Abstract**

The Abstract comes after the title page in the manuscript file. The abstract text is also entered in a separate field in the submission system. The Abstract should: Describe the main objective(s) of the study; Explain how the study was done, including any model organisms used, without methodological detail; Summarize the most important results and their significance; Not exceed 300 words. Abstracts should not include: Citations; Abbreviations, if possible;

**Introduction**

The introduction should: Provide background that puts the manuscript into context and allows readers outside the field to understand the purpose and significance of the study, Define the problem addressed and why it is important, Include a brief review of the key literature, Note any relevant controversies or disagreements in the field, Conclude with a brief statement of the overall aim of the work and a comment about whether that aim was achieved

**Materials and Methods**

The Materials and Methods section should provide enough detail to allow suitably skilled investigators to fully replicate your study. Specific information and/or protocols

for new methods should be included in detail. If materials, methods, and protocols are well established, authors may cite articles where those protocols are described in detail, but the submission should include sufficient information to be understood independent of these references. We encourage authors to submit detailed protocols for newer or less well-established methods as Supporting Information. Read the Supporting Information guidelines.

**Human or animal subjects and/or tissue or field sampling**

Methods sections describing research using human or animal subjects and/or tissue or field sampling must include required ethics statements. See the reporting guidelines for human research, clinical trials, animal research, and observational and field studies for more information.

**Data**

Methods sections of manuscripts using data that should be deposited in a publicly available database should specify where the data have been deposited and provide the relevant accession numbers and version numbers, if appropriate. Accession numbers should be provided in parentheses after the entity on first use.

If the accession numbers have not yet been obtained at the time of submission, please state that they will be provided during review. They must be provided prior to publication. A list of recommended repositories for different types of data can be found here.

Cell lines

Methods sections describing research using cell lines must state the origin of the cell lines used. See the reporting guidelines for cell line research for more information.

New taxon names

Methods sections of manuscripts adding new taxon names to the literature must follow the reporting guidelines below for a new zoological taxon, botanical taxon, or fungal taxon.

**Results**

The Results section should provide details of all of the experiments that are required to support the conclusions of the paper, including information on the number of replicates (if relevant to ensure replicability). There is no specific word limit for this section, but details of experiments that are peripheral to the main thrust of the article and that detract from the focus of the article should not be included. The section may be divided into subsections, each with a concise subheading. Large datasets, including raw data, should be submitted as supplemental files; these are published online alongside the accepted article. The Results section should be written in past tense.

**Results, Discussion, Conclusions**

These sections may all be separate, or may be combined to create a mixed Results/Discussion section (commonly labeled “Results and Discussion”) or a mixed Discussion/Conclusions section (commonly labeled “Discussion”). These sections may be further divided into subsections, each with a concise subheading, as

appropriate. These sections have no word limit, but the language should be clear and concise.

Together, these sections should describe the results of the experiments, the interpretation of these results, and the conclusions that can be drawn.

Authors should explain how the results relate to the hypothesis presented as the basis of the study and provide a succinct explanation of the implications of the findings, particularly in relation to previous related studies and potential future directions for research.

*PLOS ONE* editorial decisions do not rely on perceived significance or impact, so authors should avoid overstating their conclusions. See the *PLOS ONE* Criteria for Publication for more information.

Copyediting manuscripts

Prior to submission, authors who believe their manuscripts would benefit from professional editing are encouraged to use language-editing and copyediting services. Obtaining this service is the responsibility of the author, and should be done before initial submission. These services can be found on the web using search terms like "scientific editing service" or "manuscript editing service."

*Submissions are not copyedited before publication*.

Submissions that do not meet the *PLOS ONE* publication criterion for language standards may be rejected.

**Acknowledgments**

Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution.

Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named.

Do not include funding sources in the Acknowledgments or anywhere else in the manuscript file. Funding information should only be entered in the financial disclosure section of the online submission system.

**References**

Any and all available works can be cited in the reference list. Acceptable sources include: Published or accepted manuscripts, Manuscripts on pre-print servers, if the manuscript is submitted to a journal and also publicly available as a pre-print.

Do not cite the following sources in the reference list: Unavailable and unpublished work, including manuscripts that have been submitted but not yet accepted (e.g., "unpublished work," "data not shown"). Instead, include those data as supplementary material or deposit the data in a publicly available database.

Personal communications (these should be supported by a letter from the relevant authors but not included in the reference list)

References are listed at the end of the manuscript and numbered in the order that they appear in the text. In the text, cite the reference number in brackets. PLOS uses the numbered citation (citation-sequence) method and first six authors, et al.

Do not include citations in abstracts or author summaries.

Make sure the parts of the manuscript are in the correct order *before* ordering the citations.

Formatting references

PLOS uses the reference style outlined by the International Committee of Medical Journal Editors (ICMJE), also referred to as the “Vancouver” style. Example formats are listed below. Additional examples are in the ICMJE sample references.

Because all references will be linked electronically as much as possible to the papers they cite, proper formatting of the references is crucial.

Journal name abbreviations should be those found in the National Center for Biotechnology Information (NCBI) databases.

| **Source** | Format |
|---|---|
| **Published articles** | Hou WR, Hou YL, Wu GF, Song Y, Su XL, Sun B, et al. cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda (*Ailuropoda melanoleuca*). Genet Mol Res. 2011;10: 1576-1588.<br><br>Devaraju P, Gulati R, Antony PT, Mithun CB, Negi VS. Susceptibility to SLE in South Indian Tamils may be influenced by genetic selection pressure on TLR2 and TLR9 genes. Mol Immunol. 2014 Nov 22. pii: S0161-5890(14)00313-7. doi: 10.1016/j.molimm.2014.11.005<br><br>*Note: A DOI number for the full-text article is acceptable as an alternative to or in addition to traditional volume and page numbers.* |
| **Accepted, unpublished articles** | Same as published articles, but substitute “In press” for page numbers or DOI. |
| **Web sites or online articles** | Huynen MMTE, Martens P, Hilderlink HBM. The health impacts of globalisation: a conceptual framework. Global Health. 2005;1: 14. Available: http://www.globalizationandhealth.com/content/1/1/14. |
| **Books** | Bates B. Bargaining for life: A social history of tuberculosis. 1st ed. Philadelphia: University of Pennsylvania Press; 1992. |
| **Book chapters** | Hansen B. New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. AIDS and the historian. Bethesda: National Institutes of Health; 1991. pp. 21-28. |
| **Deposited articles (preprin** | Krick T, Shub DA, Verstraete N, Ferreiro DU, Alonso LG, Shub M, et al. Amino acid metabolism conflicts with protein diversity; 1991. |

| Source | Format |
|---|---|
| **ts, e-prints, or arXiv)** | Preprint. Available: arXiv:1403.3301v1. Accessed 17 March 2014. |
| **Published media (print or online newspapers and magazine articles)** | Fountain H. For Already Vulnerable Penguins, Study Finds Climate Change Is Another Danger. The New York Times. 29 Jan 2014. Available: http://www.nytimes.com/2014/01/30/science/earth/climate-change-taking-toll-on-penguins-study-finds.html. Accessed 17 March 2014. |
| **New media (blogs, web sites, or other written works)** | Allen L. Announcing PLOS Blogs. 2010 Sep 1 [cited 17 March 2014]. In: PLOS Blogs [Internet]. San Francisco: PLOS 2006 - . [about 2 screens]. Available: http://blogs.plos.org/plos/2010/09/announcing-plos-blogs/. |
| **Masters' theses or doctoral dissertations** | Wells A. Exploring the development of the independent, electronic, scholarly journal. M.Sc. Thesis, The University of Sheffield. 1999. Available: http://cumincad.scix.net/cgi-bin/works/Show?2e09 |
| **Databases and repositories (Figshare, arXiv)** | Roberts SB. QPX Genome Browser Feature Tracks; 2013. Database: figshare [Internet]. Accessed: http://figshare.com/articles/QPX_Genome_Browser_Feature_Tracks/701214. |
| **Multimedia (videos, movies, or TV shows)** | Hitchcock A, producer and director. Rear Window [Film]; 1954. Los Angeles: MGM. |

Supporting Information

Authors can submit essential supporting files and multimedia files along with their manuscripts. All Supporting Information will be subject to peer review. All file types can be submitted, but files must be smaller than 10 MB in size.

Authors may use almost any description as the item name for a Supporting Information file as long as it contains an “S” and number. For example, “S1 Appendix” and “S2 Appendix,” “S1 Table” and “S2 Table,” and so forth. Supporting files should be publication-ready, as they are not copyedited.

**Supporting Information captions**

List Supporting Information captions at the end of the manuscript file. Do not submit captions in a separate file.

The file number and name are required in a caption, and we highly recommend including a one-line title as well. You may also include a legend in your caption, but it is not required.

Example caption
S1 Text. Title is strongly recommended. Legend is optional.

In-text citations

We recommend that you cite Supporting Information in the manuscript text, but this is not a requirement. If you cite Supporting Information in the text, citations do not need to be in numerical order.

Read the Supporting Information guidelines for more details about submitting Supporting Information and multimedia files.

**Figures and tables**

**Figures**

Do not include figures in the main manuscript file. Each figure must be prepared and submitted as an individual file. Cite figures in ascending numeric order upon first appearance in the manuscript file. Read the guidelines for figures.

Figure captions

Figure captions must be inserted in the text of the manuscript, immediately following the paragraph in which the figure is first cited (read order). Do not include captions as part of the figure files themselves or submit them in a separate document. At a minimum, include the following in your figure captions:

A figure label with Arabic numerals, and “Figure” abbreviated to “Fig” (e.g. Fig 1, Fig 2, Fig 3, etc). Match the label of your figure with the name of the file uploaded at submission (e.g. a figure citation of “Fig 1” must refer to a figure file named “Fig1.tif”).

A concise, descriptive title

The caption may also include a legend as needed.

Read more about figure captions.

**Tables**

Cite tables in ascending numeric order upon first appearance in the manuscript file. Place each table in your manuscript file directly after the paragraph in which it is first cited (read order). Do not submit your tables in separate files.Tables require a label (e.g., “Table 1”) and brief descriptive title to be placed above the table. Place legends, footnotes, and other text below the table. Read the guidelines for tables.

**Data reporting**

All data and related metadata underlying the findings reported in a submitted manuscript should be deposited in an appropriate public repository, unless already provided as part of the submitted article. Read our policy on data availability.

Repositories may be either subject-specific (where these exist) and accept specific types of structured data, or generalist repositories that accept multiple data types. We recommend that authors select repositories appropriate to their field. Repositories may be subject-specific (e.g., GenBank for sequences and PDB for structures), general, or institutional, as long as DOIs or accession numbers are provided and the data are at least as open as CC BY. Authors are encouraged to select repositories that meet accepted criteria as trustworthy digital repositories, such as criteria of the Centre for Research Libraries or Data Seal of Approval. Large, international databases are more likely to persist than small, local ones.

To support data sharing and author compliance of the PLOS data policy, we have integrated our submission process with a select set of data repositories. The list is neither representative nor exhaustive of the suitable repositories available to authors. Current repository integration partners include Dryad and FlowRepository. Please contact data@plos.org to make recommendations for further partnerships.

Instructions for PLOS submissions with data deposited in an integration partner repository:

Deposit data in the integrated repository of choice.

Once deposition is final and complete, the repository will provide you with a dataset DOI (provisional) and private URL for reviewers to gain access to the data.

Enter the given data DOI into the full Data Availability Statement, which is requested in the Additional Information section of the PLOS submission form. Then provide the URL passcode in the Attach Files section.

If you have any questions, please email us.

Accession numbers

All appropriate datasets, images, and information should be deposited in public resources. Please provide the relevant accession numbers (and version numbers, if appropriate). Accession numbers should be provided in parentheses after the entity on first use.

Suggested databases include, but are not limited to:

ArrayExpress; BioModels Database; Database of Interacting Proteins; DNA Data Bank of Japan [DDBJ]; DRYAD; EMBL Nucleotide Sequence Database; GenBank; Gene Expression Omnibus [GEO]; Protein Data Bank; UniProtKB/Swiss-Prot; ClinicalTrials.gov.

In addition, as much as possible, please provide accession numbers or identifiers for all entities such as genes, proteins, mutants, diseases, etc., for which there is an entry in a public database, for example:

Ensembl; Entrez Gene; FlyBase; InterPro; Mouse Genome Database (MGD); Online Mendelian Inheritance in Man (OMIM); PubChem.

Providing accession numbers allows linking to and from established databases and integrates your article with a broader collection of scientific information.

Striking image

You can choose to upload a “Striking Image” that we may use to represent your article online in places like the journal homepage or in search results.

The striking image must be derived from a figure or supporting information file from the submission, i.e., a cropped portion of an image or the entire image. Striking images should ideally be high resolution, eye-catching, single panel images, and should ideally avoid containing added details such as text, scale bars, and arrows.

If no striking image is uploaded, we will designate a figure from the submission as the striking image.

Striking images should not contain potentially identifying images of people. Read our policy on identifying information.

The PLOS content license also applies to striking images. Read more about the content license.

Additional Information Requested at Submission

Funding statement

This information should not be in your manuscript file; you will provide it via our submission system.

This information will be published with the final manuscript, if accepted, so please make sure that this is accurate and as detailed as possible. You should not include this information in your manuscript file, but it is important to gather it prior to submission, because your financial disclosure statement cannot be changed after initial submission.

Your statement should include relevant grant numbers and the URL of any funder's web site. Please also state whether any individuals employed or contracted by the funders (other than the named authors) played any role in: study design, data collection and analysis, decision to publish, or preparation of the manuscript. If so, please name the individual and describe their role.

Read our policy on disclosure of funding sources.

Competing interests

This information should not be in your manuscript file; you will provide it via our submission system.

All potential competing interests must be declared in full. If the submission is related to any patents, patent applications, or products in development or for market, these details, including patent numbers and titles, must be disclosed in full.

Read our policy on competing interests.

Manuscripts disputing published work

For manuscripts disputing previously published work, it is *PLOS ONE* policy to invite input from the disputed author during the peer review process. This procedure is aimed at ensuring a thorough, transparent, and productive review process.

If the disputed author chooses to submit a review, it must be returned in a timely fashion and contain a full declaration of all competing interests. The Academic Editor will consider any such reviews in light of the competing interest.

Authors submitting manuscripts disputing previous work should explain the relationship between the manuscripts in their cover letter, and will be required to confirm that they accept the conditions of this review policy before the manuscript is considered further.

Related manuscripts

Upon submission, authors must confirm that the manuscript, or any related manuscript, is not currently under consideration or accepted elsewhere. If related

work has been submitted to *PLOS ONE* or elsewhere, authors must include a copy with the submitted article. Reviewers will be asked to comment on the overlap between related submissions.

We strongly discourage the unnecessary division of related work into separate manuscripts, and we will not consider manuscripts that are divided into “parts.” Each submission to *PLOS ONE* must be written as an independent unit and should not rely on any work that has not already been accepted for publication. If related manuscripts are submitted to *PLOS ONE*, the authors may be advised to combine them into a single manuscript at the editor's discretion.

Guidelines for Specific Study Types

Human subjects research

All research involving human participants must have been approved by the authors’ Institutional Review Board (IRB) or by equivalent ethics committee(s), and must have been conducted according to the principles expressed in the Declaration of Helsinki. Authors should be able to submit, upon request, a statement from the IRB or ethics committee indicating approval of the research. We reserve the right to reject work that we believe has not been conducted to a high ethical standard, even when formal approval has been obtained.

Subjects must have been properly instructed and have indicated that they consent to participate by signing the appropriate informed consent paperwork. Authors may be asked to submit a blank, sample copy of a subject consent form. If consent was verbal instead of written, or if consent could not be obtained, the authors must explain the reason in the manuscript, and the use of verbal consent or the lack of consent must have been approved by the IRB or ethics committee.

All efforts should be made to protect patient privacy and anonymity. Identifying information, including photos, should not be included in the manuscript unless the information is crucial and the individual has provided written consent by completing the Consent Form for Publication in a PLOS Journal (PDF). More information about patient privacy, anonymity, and informed consent can be found in the International Committee of Medical Journal Editors (ICMJE) Privacy and Confidentiality guidelines.

Manuscripts should conform to the following reporting guidelines:

Studies of diagnostic accuracy: STARD

Observational studies: STROBE

Microarray experiments: MIAME

Other types of health-related research: Consult the EQUATOR web site for appropriate reporting guidelines

Methods sections of papers on research using human subjects or samples must include ethics statements that specify:

The name of the approving institutional review board or equivalent committee(s). If approval was not obtained, the authors must provide a detailed statement explaining why it was not needed

Whether informed consent was written or oral. If informed consent was oral, it must be stated in the manuscript:

Why written consent could not be obtained

That the Institutional Review Board (IRB) approved use of oral consent

How oral consent was documented

For studies involving humans categorized by race/ethnicity, age, disease/disabilities, religion, sex/gender, sexual orientation, or other socially constructed groupings, authors should:

Explicitly describe their methods of categorizing human populations

Define categories in as much detail as the study protocol allows

Justify their choices of definitions and categories, including for example whether any rules of human categorization were required by their funding agency

Explain whether (and if so, how) they controlled for confounding variables such as socioeconomic status, nutrition, environmental exposures, or similar factors in their analysis

In addition, outmoded terms and potentially stigmatizing labels should be changed to more current, acceptable terminology. Examples: “Caucasian” should be changed to “white” or “of [Western] European descent” (as appropriate); “cancer victims” should be changed to “patients with cancer.”

For papers that include identifying, or potentially identifying, information, authors must download the Consent Form for Publication in a PLOS Journal (PDF), which the individual, parent, or guardian must sign once they have read the paper and been informed about the terms of PLOS open-access license. The signed consent form should not be submitted with the manuscript, but authors should securely file it in the individual's case notes and the methods section of the manuscript should explicitly state that consent authorization for publication is on file, using wording like:

The individual in this manuscript has given written informed consent (as outlined in PLOS consent form) to publish these case details.

For more information about *PLOS ONE* policies regarding human subjects research, see the Publication Criteria and Editorial Policies.

Clinical trials

Clinical trials are subject to all policies regarding human research. *PLOS ONE* follows the World Health Organization's (WHO) definition of a clinical trial:

*A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes [...] Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.*

All clinical trials must be registered in one of the publicly-accessible registries approved by the WHO or ICMJE (International Committee of Medical Journal Editors). Authors must provide the trial registration number. Prior disclosure of results

on a clinical trial registry site will not affect consideration for publication. We reserve the right to inform authors' institutions or ethics committees, and to reject the manuscript, if we become aware of unregistered trials.

*PLOS ONE* supports prospective trial registration (i.e. before participant recruitment has begun) as recommended by the ICMJE's clinical trial registration policy. Where trials were not publicly registered before participant recruitment began, authors must:

Register all related clinical trials and confirm they have done so in the Methods section

Explain in the Methods the reason for failing to register before participant recruitment

Clinical trials must be reported according to the relevant reporting guidelines, i.e. CONSORT for randomized controlled trials, TREND for non-randomized trials, and other specialized guidelines as appropriate. The intervention should be described according to the requirements of the TIDieR checklist and guide. Submissions must also include the study protocol as Supporting Information, which will be published with the manuscript if accepted.

Authors of manuscripts describing the results of clinical trials must adhere to the CONSORT reporting guidelines appropriate to their trial design, available on the CONSORT Statement web site. Before the paper can enter peer review, authors must:

Provide the registry name and number in the methods section of the manuscript

Provide a copy of the trial protocol as approved by the ethics committee and a completed CONSORT checklist as Supporting Information (which will be published alongside the paper, if accepted). This should be named S1 CONSORT Checklist.

Include the CONSORT flow diagram as the manuscript's “Fig 1”

Any deviation from the trial protocol must be explained in the paper. Authors must explicitly discuss informed consent in their paper, and we reserve the right to ask for a copy of the patient consent form.

The methods section must include the name of the registry, the registry number, and the URL of your trial in the registry database for each location in which the trial is registered.

Animal research

We work in consultation with the *PLOS ONE* Animal Research Advisory Group to develop policies. Animal Research Advisory Group members may also be consulted on individual submissions.

All research involving vertebrates or cephalopods must have approval from the authors' Institutional Animal Care and Use Committee (IACUC) or equivalent ethics committee(s), and must have been conducted according to applicable national and international guidelines. Approval must be received prior to beginning research.

If we note differences between an IACUC-approved protocol and the methods reported in a submitted manuscript, we may report these discrepancies to the relevant institution or committee.

Methods sections of manuscripts reporting results of animal research must include required ethics statements that specify:

The full name of the relevant ethics committee that approved the work, and the associated permit number(s). Where ethical approval is not required, the manuscript should include a clear statement of this and the reason why.

Relevant details for efforts taken to ameliorate animal suffering

Example ethics statement

*This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health. The protocol was approved by the Committee on the Ethics of Animal Experiments of the University of Minnesota (Permit Number: 27-2956). All surgery was performed under sodium pentobarbital anesthesia, and all efforts were made to minimize suffering.*

The organism(s) studied should always be stated in the abstract. Where research may be confused as pertaining to clinical research, the animal model should also be stated in the title.

Where unregulated animals are used or ethics approval is not required, authors should make this clear in submitted articles and explain why ethical approval was not required. Relevant regulations that grant exemptions should be cited in full. It is the authors' responsibility to understand and comply with all relevant regulations.

We reserve the right to reject work that the editors believe has not been conducted to a high ethical standard, even if authors have obtained formal approval or approval is not required under local regulations.

We encourage authors to follow the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) guidelines for all submissions describing laboratory-based animal research and to upload a completed ARRIVE Guidelines Checklist to be published as supporting information. Please note that inclusion of a completed ARRIVE Checklist may be a formal requirement for publication at a later date.

Non-human primates

Manuscripts describing research involving non-human primates must include details of animal welfare, including information about housing, feeding, and environmental enrichment, and steps taken to minimize suffering, including use of anesthesia and method of sacrifice if appropriate, in accordance with the recommendations of the Weatherall report, *The use of non-human primates in research* (PDF).

Humane endpoints

Manuscripts describing studies that use death as an endpoint will be subject to additional ethical considerations, and may be rejected if they lack appropriate justification for the study or consideration of humane endpoints.

Observational and field studies

Methods sections for submissions reporting on any type of field study must include ethics statements that specify:

Permits and approvals obtained for the work, including the full name of the authority that approved the study; if none were required, authors should explain why

Whether the land accessed is privately owned or protected

Whether any protected species were sampled

Full details of animal husbandry, experimentation, and care/welfare, where relevant

Paleontology and archaeology research

Manuscripts reporting paleontology and archaeology research must include descriptions of methods and specimens in sufficient detail to allow the work to be reproduced. Data sets supporting statistical and phylogenetic analyses should be provided, preferably in a format that allows easy re-use.

Specimen numbers and complete repository information, including museum name and geographic location, are required for publication. Locality information should be provided in the manuscript as legally allowable, or a statement should be included giving details of the availability of such information to qualified researchers.

If permits were required for any aspect of the work, details should be given of all permits that were obtained, including the full name of the issuing authority. This should be accompanied by the following statement:

*All necessary permits were obtained for the described study, which complied with all relevant regulations.*

If no permits were required, please include the following statement:

*No permits were required for the described study, which complied with all relevant regulations.*

Manuscripts describing paleontology and archaeology research are subject to the following policies:

Sharing of data and materials. Any specimen that is erected as a new species, described, or figured must be deposited in an accessible, permanent repository (i.e., public museum or similar institution). If study conclusions depend on specimens that do not fit these criteria, the article will be rejected under *PLOS ONE*'s data availability criterion.

Ethics. *PLOS ONE* will not publish research on specimens that were obtained without necessary permission or were illegally exported

Systematic reviews and meta-analyses

A systematic review paper, as defined by The Cochrane Collaboration, is a review of a clearly formulated question that uses explicit, systematic methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. These reviews differ substantially from narrative-based reviews or synthesis articles. Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies.

Reports of systematic reviews and meta-analyses must include a completed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist and flow diagram to accompany the main text. Blank templates are available here:

Checklist: PDF or Word document

Flow diagram: PDF or Word document

Authors must also state in their “Methods” section whether a protocol exists for their systematic review, and if so, provide a copy of the protocol as Supporting Information and provide the registry number in the abstract.

If your article is a systematic review or a meta-analysis you should:

State this in your cover letter

Select “Research Article” as your article type when submitting

Include the PRISMA flow diagram as Fig 1 (required where applicable)

Include the PRISMA checklist as Supporting Information

Meta-analysis of genetic association studies

Manuscripts reporting a meta-analysis of genetic association studies must report results of value to the field and should be reported according to the guidelines presented in *Systematic Reviews of Genetic Association Studies* by Sagoo *et al.*

On submission, authors will be asked to justify the rationale for the meta-analysis and how it contributes to the base of scientific knowledge in the light of previously published results. Authors will also be asked to complete a checklist (DOCX) outlining information about the justification for the study and the methodology employed. Meta-analyses that replicate published studies will be rejected if the authors do not provide adequate justification.

Cell lines

Authors reporting research using cell lines should state when and where they obtained the cells, giving the date and the name of the researcher, cell line repository, or commercial source (company) who provided the cells, as appropriate.

Authors must also include the following information for each cell line:

For *de novo* (new) cell lines, including those given to the researchers a gift, authors must follow our policies for human subjects research or animal research, as appropriate. The ethics statement must include:

Details of institutional review board or ethics committee approval; AND

For human cells, confirmation of written informed consent from the donor, guardian, or next of kin

For established cell lines, the Methods section should include:

A reference to the published article that first described the cell line; AND/OR

The cell line repository or company the cell line was obtained from, the catalogue number, and whether the cell line was obtained directly from the repository/company or from another laboratory

Authors should check established cell lines using the ICLAC Database of Cross-contaminated or Misidentified Cell Lines to confirm they are not misidentified or contaminated. Cell line authentication is recommended – e.g., by karyotyping, isozyme analysis, or short tandem repeats (STR) analysis – and may be required during peer review or after publication.

Blots and gels

Manuscripts reporting results from blots (including Western blots) and electrophoretic gels should follow these guidelines:

In accordance with our policy on image manipulation, the image should not be adjusted in any way that could affect the scientific information displayed, e.g. by modifying the background or contrast.

All blots and gels that support results reported in the manuscript should be provided.

Original uncropped and unadjusted blots and gels, including molecular size markers, should be provided in either the figures or the supplementary files.

Lanes should not be overcropped around the bands; the image should show most or all of the blot or gel. Any non-specific bands should be shown and an explanation of their nature should be given.

The image should include all relevant controls, and controls should be run on the same blot or gel as the samples.

A figure panel should not include composite images of bands originating from different blots or gels. If the figure shows non-adjacent bands from the same blot or gel, this should be clearly denoted by vertical black lines and the figure legend should provide details of how the figure was made.

Antibodies

Manuscripts reporting experiments using antibodies should include the following information:

The name of each antibody, a description of whether it is monoclonal or polyclonal, and the host species.

The commercial supplier or source laboratory.

The catalogue or clone number and, if known, the batch number.

The antigen(s) used to raise the antibody.

For established antibodies, a stable public identifier from the Antibody Registry.

The manuscript should also report the following experimental details:

The final antibody concentration or dilution.

A reference to the validation study if the antibody was previously validated. If not, provide details of how the authors validated the antibody for the applications and species used.

We encourage authors to consider adding information on new validations to a publicly available database such asAntibodypedia or CiteAb.

## Methods, software, databases, and tools

*PLOS ONE* will consider submissions that present new methods, software, or databases as the primary focus of the manuscript if they meet the following criteria:

### Utility

The tool must be of use to the community and must present a proven advantage over existing alternatives, where applicable. Recapitulation of existing methods, software, or databases is not useful and will not be considered for publication. Combining data and/or functionalities from other sources may be acceptable, but simpler instances (i.e. presenting a subset of an already existing database) may not be considered. For software, databases, and online tools, the long-term utility should also be discussed, as relevant. This discussion may include maintenance, the potential for future growth, and the stability of the hosting, as applicable.

### Validation

Submissions presenting methods, software, databases, or tools must demonstrate that the new tool achieves its intended purpose. If similar options already exist, the submitted manuscript must demonstrate that the new tool is an improvement over existing options in some way. This requirement may be met by including a proof-of-principle experiment or analysis; if this is not possible, a discussion of the possible applications and some preliminary analysis may be sufficient.

### Availability

Software should be open source, deposited in an appropriate archive, and conform to the Open Source Definition. Databases must be open-access and hosted somewhere publicly accessible, and any software used to generate a database should also be open source. If relevant, databases should be open for appropriate deposition of additional data. Dependency on commercial software such as Mathematica and MATLAB does not preclude a paper from consideration, although complete open source solutions are preferred. Authors should provide a direct link to the deposited software or the database hosting site from within the paper.

## Software submissions

Manuscripts describing software should provide full details of the algorithms designed. Describe any dependencies on commercial products or operating system. Include details of the supplied test data and explain how to install and run the software. A brief description of enhancements made in the major releases of the software may also be given. Authors should provide a direct link to the deposited software from within the paper.

## Database submissions

For descriptions of databases, provide details about how the data were curated, as well as plans for long-term database maintenance, growth, and stability. Authors should provide a direct link to the database hosting site from within the paper.

## New taxon names

## Zoological names

When publishing papers that describe a new zoological taxon name, PLOS aims to comply with the requirements of the International Commission on Zoological Nomenclature (ICZN). Effective 1 January 2012, the ICZN considers an online-only publication to be legitimate if it meets the criteria of archiving and is registered in ZooBank, the ICZN's official registry.

For proper registration of a new zoological taxon, we require two specific statements to be included in your manuscript.

In the Results section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

*Anochetus boltoni Fisher sp. nov. urn:lsid:zoobank.org:act:B6C072CF-1CA6-40C7-8396-534E91EF7FBB*

You will need to contact Zoobank to obtain a GUID (LSID). Please do this as early as possible to avoid delay of publication upon acceptance of your manuscript. It is your responsibility to provide us with this information so we can include it in the final published paper.

Please also insert the following text into the Methods section, in a sub-section to be called “Nomenclatural Acts”:

The electronic edition of this article conforms to the requirements of the amended International Code of Zoological Nomenclature, and hence the new names contained herein are available under that Code from the electronic edition of this article. This published work and the nomenclatural acts it contains have been registered in ZooBank, the online registration system for the ICZN. The ZooBank LSIDs (Life Science Identifiers) can be resolved and the associated information viewed through any standard web browser by appending the LSID to the prefix “http://zoobank.org/”. The LSID for this publication is: urn:lsid:zoobank.org:pub: XXXXXXX. The electronic edition of this work was published in a journal with an ISSN, and has been archived and is available from the following digital repositories: PubMed Central, LOCKSS [author to insert any additional repositories].

All PLOS articles are deposited in PubMed Central and LOCKSS. If your institute, or those of your co-authors, has its own repository, we recommend that you also deposit the published online article there and include the name in your article.

Botanical names

When publishing papers that describe a new botanical taxon, PLOS aims to comply with the requirements of the International Code of Nomenclature for algae, fungi, and plants (ICN). The following guidelines for publication in an online-only journal have been agreed such that any scientific botanical name published by us is considered effectively published under the rules of the Code. Please note that these guidelines differ from those for zoological nomenclature, and apply only to seed plants, ferns, and lycophytes.

Effective January 2012, the description or diagnosis of a new taxon can be in either Latin or English. This does not affect the requirements for scientific names, which are still to be Latin.

Also effective January 2012, the electronic PDF represents a published work according to the ICN for algae, fungi, and plants. Therefore the new names contained in the electronic publication of PLOS article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

Additional information describing recent changes to the Code can be found here.

For proper registration of the new taxon, we require two specific statements to be included in your manuscript.

In the Results section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

Solanum aspersum S.Knapp, sp. nov. [urn:lsid:ipni.org:names:77103633-1] Type: Colombia. Putumayo: vertiente oriental de la Cordillera, entre Sachamates y San Francisco de Sibundoy, 1600-1750 m, 30 Dec 1940, J. Cuatrecasas 11471 (holotype, COL; isotypes, F [F-1335119], US [US-1799731]).

Journal staff will contact IPNI to obtain the GUID (LSID) after your manuscript is accepted for publication, and this information will then be added to the manuscript during the production phase

In the Methods section, include a sub-section called “Nomenclature” using the following wording:

The electronic version of this article in Portable Document Format (PDF) in a work with an ISSN or ISBN will represent a published work according to the International Code of Nomenclature for algae, fungi, and plants, and hence the new names contained in the electronic publication of a PLOS article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

In addition, new names contained in this work have been submitted to IPNI, from where they will be made available to the Global Names Index. The IPNI LSIDs can be resolved and the associated information viewed through any standard web browser by appending the LSID contained in this publication to the prefix http://ipni.org/. The online version of this work is archived and available from the following digital repositories: [INSERT NAMES OF DIGITAL REPOSITORIES WHERE ACCEPTED MANUSCRIPT WILL BE SUBMITTED (PubMed Central, LOCKSS etc)].

All PLOS articles are deposited in PubMed Central and LOCKSS. If your institute, or those of your co-authors, has its own repository, we recommend that you also deposit the published online article there and include the name in your article.

Fungal names

When publishing papers that describe a new botanical taxon, PLOS aims to comply with the requirements of the International Code of Nomenclature for algae, fungi, and plants (ICN). The following guidelines for publication in an online-only journal have been agreed such that any scientific botanical name published by us is considered

effectively published under the rules of the Code. Please note that these guidelines differ from those for zoological nomenclature.

Effective January 2012, the description or diagnosis of a new taxon can be in either Latin or English. This does not affect the requirements for scientific names, which are still to be Latin.

Also effective January 2012, the electronic PDF represents a published work according to the ICN for algae, fungi, and plants. Therefore the new names contained in the electronic publication of PLOS article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

Additional information describing recent changes to the Code can be found here.

For proper registration of the new taxon, we require two specific statements to be included in your manuscript.

In the Results section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

*Hymenogaster huthii.* Stielow et al. 2010, sp. nov. [urn:lsid:indexfungorum.org:names:518624]

You will need to contact either Mycobank or Index Fungorum to obtain the GUID (LSID). Please do this as early as possible to avoid delay of publication upon acceptance of your manuscript. It is your responsibility to provide us with this information so we can include it in the final published paper. Effective January 2013, all papers describing new fungal species must reference the identifier issued by a recognized repository in the protologue in order to be considered effectively published.

In the Methods section, include a sub-section called “Nomenclature” using the following wording (this example is for taxon names submitted to MycoBank; please substitute appropriately if you have submitted to Index Fungorum):

The electronic version of this article in Portable Document Format (PDF) in a work with an ISSN or ISBN will represent a published work according to the International Code of Nomenclature for algae, fungi, and plants, and hence the new names contained in the electronic publication of a PLOS article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

In addition, new names contained in this work have been submitted to MycoBank from where they will be made available to the Global Names Index. The unique MycoBank number can be resolved and the associated information viewed through any standard web browser by appending the MycoBank number contained in this publication to the prefix http://www.mycobank.org/MB/. The online version of this work is archived and available from the following digital repositories: [INSERT NAMES OF DIGITAL REPOSITORIES WHERE ACCEPTED MANUSCRIPT WILL BE SUBMITTED (PubMed Central, LOCKSS etc)].

All PLOS articles are deposited in PubMed Central and LOCKSS. If your institute, or those of your co-authors, has its own repository, we recommend that you also deposit the published online article there and include the name in your article.

Qualitative research

Qualitative research studies use non-quantitative methods to address a defined research question that may not be accessible by quantitative methods, such as people's interpretations, experiences, and perspectives. The analysis methods are explicit, systematic, and reproducible, but the results do not involve numerical values or use statistics. Examples of qualitative data sources include, but are not limited to, interviews, text documents, audio/video recordings, and free-form answers to questionnaires and surveys.

Qualitative research studies should be reported in accordance to the Consolidated criteria for reporting qualitative research (COREQ) checklist. Further reporting guidelines can be found in the Equator Network's Guidelines for reporting qualitative research.

# APÊNDICES

## Apêndice A - S1 Appendix. List of all titles and abstracts for analysis and reasons for exclusion.

| Reference | Classification |
|---|---|
| 1. Carrasco M, Arriagada C, Gomez S. Early childhood caries and prolonged night breast feeding. Journal of Dental Research 2003; 82:302. | Wrong reference. This paper does not exist in this journal. |
| 2. Olojugba OO, Hardwick JL. Relationship of Breast-Feeding and Bottle-Feeding During Infancy to Caries Experience in Nigerian Children. Caries Research 1979; 13(2):101-102. | Text could not be found |
| 3. Abbey LM. Breast-Feeding and Caries - Reply. Journal of the American Dental Association 1979; 99(1):12 | Letter to the editor |
| 4. Campbell OA. Breast-Feeding and Caries. Journal of the American Dental Association 1979; 98(5):691-692. | Letter to the editor |
| 5. Does breastfeeding increase risk of early childhood caries? J Can Dent Assoc 2013; 79:d123. | Guideline |
| 6. Staskiewicz T. [Analysis of the influence of some factors on the intensity of early childhood caries]. Ann Acad Med Stetin 2012; 58(2):36-39. | Language other than English other than English |
| 7. Smilematters patient fact sheet. February is National Children's Dental Health Month. J Mich Dent Assoc 2011; 93(2):15. | Patient's guide |
| 8. Zhong ZQ. [The relationship between the infant nursing bottle caries and the feeding patterns, oral health behavior and parents' oral health information]. Shanghai Kou Qiang Yi Xue 2009; 18(6):588-591.. | Language other than English other than English |
| 9. ODA patient's page. Baby bottle syndrome. J Okla Dent Assoc 2009; 100(9):7. | Patient's guide |
| 10. Ribeiro NM, Ribeiro MA. Breastfeeding and early childhood caries: a myth that survives. J Pediatr (Rio J ) 2009; 85(5):464-465. | Letter to the editor |
| 11. Jigjid B, Ueno M, Shinada K, Kawaguchi Y. Early childhood caries and related risk factors in Mongolian children. Community Dent Health 2009; 26(2):121-128. | Does not compare breastfeeding and bottlefeeding |
| 12. Khamadeeva AM, Demina RR, Bagdasarova OA, Nogina n. [Role of behaviorial risk factors in developing dental caries of temporary teeth in infancy]. Stomatologiia (Mosk) 2008; 87(5):68-71. | Language other than English |
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| 14. Menghini G, Steiner M, Imfeld T. [Early childhood caries--facts and prevention]. Ther Umsch 2008; 65(2):75-82. | Language other than English |
| 15. van Palenstein Helderman WH, Holmgren CJ. Research into factors which might contribute to the prevalence and severity of dental caries. Caries Res 2008; 42(2):155-156. | Letter to the editor |
| 16. Faye M, Ba AA, Yam AA, Ba I. [Caries patterns and diet in early childhood caries]. Dakar Med 2006; 51(2):72-77. | Language other than English other than English |
| 17. Abdoll GS. Report on the nursing bottle caries campaign launched by the Free State Oral Health Services. SADJ 2001; 56(1):32-33. | Different outcome, not dental caries |
| 18. Baginska J, Stokowska W. [Dietary habits and early childhood caries intensity among young children]. Wiad Lek 2006; 59(1-2):5-9. | Language other than English other than English |
| 19. Bringing up baby's teeth. CDS Rev 2005; 98(7):29. | Patient educational hand out |
| 20. Policy on dietary recommendations for infants, children, and adolescents. Pediatr Dent 2005; 27(7 Suppl):36-37. | Guideline |
| 21. Policy on early childhood caries (ECC): classifications, consequences, and preventive strategies. Pediatr Dent 2005; 27(7 Suppl):31-33. | Guideline |
| 22. Ge XJ, Zhang BS, Li B, Zhao LJ, Zhao B, Ren XY et al. [The effects of feeding methods on deciduous caries.]. Shanghai Kou Qiang Yi Xue 2004; 13(5):365-366. | Language other than English other than English |
| 23. Ye W, Feng XP, Liu YL. [An epidemiological study of risk factors of rampant caries in Shanghai children]. Shanghai Kou Qiang Yi Xue 2001; 10(2):166-169. | Language other than English other than English |
| 24. Mizoguchi K, Kurumado K, Tango T, Minowa M. [Study on factors for caries and infant feeding characteristics in children aged 1.5-3 years in a Kanto urban area]. Nihon Koshu Eisei Zasshi 2003; 50(9):867-878. | Language other than English other than English |
| 25. Ramezani GH, Norozi A, Valael N. The prevalence of nursing caries in | Does not compare |

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| 18 to 60 months old children in Qazvin. J Indian Soc Pedod Prev Dent 2003; 21(1):19-26. | breastfeeding and bottlefeeding |
| 26. Wyne AH, Chohan AN, al-Begomi R. Feeding and dietary practices of nursing caries children in Riyadh, Saudi Arabia. Odontostomatol Trop 2002; 25(100):37-42. | Prevalence feeding habits |
| 27. Hallett KB, O'Rourke PK. Early childhood caries and infant feeding practice. Community Dent Health 2002; 19(4):237-242. | Does not compare breastfeeding and bottlefeeding |
| 28. Sayegh A, Dini EL, Holt RD, Bedi R. Caries prevalence and patterns and their relationship to social class, infant feeding and oral hygiene in 4-5-year-old children in Amman, Jordan. Community Dent Health 2002; 19(3):144-151. | Does not compare breastfeeding and bottlefeeding |
| 29. Acs G, Ng MW. Early childhood caries and well being. Pediatr Dent 2002; 24(4):288. | Letter to the editor |
| 30. Greer MH, Tendan SL. Early childhood dental caries in Hawai'i. Hawaii Dent J 1998; 29(2):10, 14. | Title not interest |
| 31. Erickson PR, Nickman JD. Early childhood caries: etiology, risk assessment, and prevention. Northwest Dent 1999; 78(6):27-32. | Review |
| 32. Hallett KB. Early childhood caries--a new name for an old problem. Ann R Australas Coll Dent Surg 2000; 15:268-275. | Title not interest |
| 33. Creedon MI, O'Mullane DM. Factors affecting caries levels amongst 5-year-old children in County Kerry, Ireland. Community Dent Health 2001; 18(2):72-78. | Does not compare breastfeeding and bottlefeeding |
| 34. Davies GM, Blinkhorn FA, Duxbury JT. Caries among 3-year-olds in greater Manchester. Br Dent J 2001; 190(7):381-384. | Prevalence |
| 35. Behrendt A, Sziegoleit F, Muler-Lessmann V, Ipek-Ozdemir G, Wetzel WE. Nursing-bottle syndrome caused by prolonged drinking from vessels with bill-shaped extensions. ASDC J Dent Child 2001; 68(1):47-50, 12. | Different ethiology |
| 36. Usatine R. Severe caries in a child. West J Med 2001; 174(3):167-168. | Case report |
| 37. Peretz B, Eidelman E. ["Baby bottle tooth decay"--a risk to the teeth of babies and young infants]. Harefuah 1998; 134(9):731-734. | Language other than English |
| 38. Ye W, Feng XP, Liu YL. Epidemiological study of the risk factors of rampant caries in Shanghai children. Chin J Dent Res 1999; 2(2):58-62. | Does not compare breastfeeding and bottlefeeding |
| 39. Ramos-Gomez FJ, Tomar SL, Ellison J, Artiga N, Sintes J, Vicuna G. Assessment of early childhood caries and dietary habits in a population of migrant Hispanic children in Stockton, California. ASDC J Dent Child 1999; 66(6):395-403, 366. | Does not compare breasfeeding and bottlefeeding |
| 40. Sinton J, Valaitis R, Passarelli C, Sheehan D, Hesch R. A systematic overview of the relationship between infant feeding caries and breast-feeding. Ont Dent 1998; 75(9):23-27. | Review |
| 41. Quartey JB, Williamson DD. Prevalence of early childhood caries at Harris County clinics. ASDC J Dent Child 1999; 66(2):127-31, 85. | Prevalence |
| 42. Erickson PR, Mazhari E. Investigation of the role of human breast milk in caries development. Pediatr Dent 1999; 21(2):86-90. | Different ethiology |
| 43. Smith PJ, Moffatt ME. Baby-bottle tooth decay: are we on the right track? Int J Circumpolar Health 1998; 57 Suppl 1:155-162. | Review |
| 44. Ollila P, Niemela M, Uhari M, Larmas M. Prolonged pacifier-sucking and use of a nursing bottle at night: possible risk factors for dental caries in children. Acta Odontol Scand 1998; 56(4):233-237. | Does not compare breastfeeding and bottlefeeding |
| 45. Maupome G. An introspective qualitative report on dietary patterns and elevated levels of dental decay in a deprived urban population in northern Mexico. ASDC J Dent Child 1998; 65(4):276-85, 230. | Prevalence |
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| 47. Weerheijm KL, Uyttendaele-Speybrouck BF, Euwe HC, Groen HJ. Prolonged demand breast-feeding and nursing caries. Caries Res 1998; 32(1):46-50. | Does not compare breastfeeding and bottlefeeding |
| 48. Harrison R, Wong T, Ewan C, Contreras B, Phung Y. Feeding practices and dental caries in an urban Canadian population of Vietnamese preschool children. ASDC J Dent Child 1997; 64(2):112-117. | Does not compare breastfeeding and bottlefeeding |
| 49. Henry RJ. Why do 20% of our children experience 80% of the decay? An update on the status of childhood caries. Tex Dent J 1997; 114(1):10-14. | Review |
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| Dent 1997; 19(1):22-27. | bottlefeeding |
| 51. Holt RD, Winter GB, Downer MC, Bellis WJ, Hay IS. Caries in pre-school children in Camden 1993/94. Br Dent J 1996; 181(11-12):405-410. | Prevalence |
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| 53. Moynihan PJ, Holt RD. The national diet and nutrition survey of 1.5 to 4.5 year old children: summary of the findings of the dental survey. Br Dent J 1996; 181(9):328-332. | Prevalence |
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| 62. Tsubouchi J, Tsubouchi M, Maynard RJ, Domoto PK, Weinstein P. A study of dental caries and risk factors among Native American infants. ASDC J Dent Child 1995; 62(4):283-287. | Prevalence |
| 63. Duperon DF. Early childhood caries: a continuing dilemma. J Calif Dent Assoc 1995; 23(2):15-2. | Review |
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| 664. Wagner Y, Heinrich-Weltzien R. Pediatrians' oral health recommendations from 0-to- 3-years-old children: results of a survey in Thuringya, Germany. BMC Oral Health. 2014 May 1;14:44. doi: 10.1186/1472-6831-14-44. | Title not interest. |
| 665. Zhang S, Liu J, Lo EC, Chu CH. Dental caries status of Bulang preschool children in Southwest China. BMC Oral Health. 2014 Mar 4;14:16. doi: 10.1186/1472-6831-14-16. | Only bottle feeding. |
| 666. Congiu G, Campus G, Sale S, Spano G, Cagetti MG, Lugliè PF. Early childhood caries and associated determinants: a cross-sectional study on Italian preschool children. J Public Health Dent. 2014 Spring;74(2):147-52. doi: 10.1111/jphd.12038. | Does not compare breastfeeding and bottlefeeding. |
| 667. Nakayama Y, Mori M. Association between nocturnal breastfeeding and snacking habits and the risk of early childhood caries in 18- to 23-month-old Japanese children. J Epidemiol. 2015 Feb 5;25(2):142-7. doi: 10.2188/jea.JE20140097. | Does not compare breastfeeding and bottlefeeding. |
| 668. Verrips GH, Frencken JE, Kalsbeek H, ter Horst G, Filedt Kok-Weimar TL. Risk indicators and potential risks for caries in 5-years-old of different ethnic groups in Amsterdam. Community Dent Oral Epidemiol. 1992; 20: 256-260. | Different etiology. |

## Apêndice B - S2 Appendix. List of titles selected for full text analysis and the reasons for exclusion.

| Reference | Classification |
|---|---|
| 1. Aminabadi NA, Ghoreishizadeh A, Ghoreishizadeh M, Oskouei SG, Ghojazadeh M. Can Child Temperament Be Related to Early Childhood Caries? Caries Research 2014; 48(1):3-12. | NOT SELECTED. Does not compare breastfeeding with bottle feeding. |
| 2. Correa-Faria P, Martins PA, Vieira-Andrade RG, Marques LS, Ramos-Jorge ML. Factors associated with the development of early childhood caries among Brazilian preschoolers. Brazilian Oral Research 2013; 27(4):356-362. | NOT SELECTED. Statistical data unavailable. |
| 3. Aimutis WR. Lactose cariogenicity with an emphasis on childhood dental caries. International Dairy Journal 2012; 22(2):152-158. | NOT SELECTED. Review |
| 4. Arora A, Scott JA, Bhole S, Do L, Schwarz E, Blinkhorn AS. Early childhood feeding practices and dental caries in preschool children: a multi-centre birth cohort study. Bmc Public Health 2011; 11. | NOT SELECTED. Study protocol |
| 5. Helderman WV, Soe W, van't Hof MA. Risk factors of early childhood caries in a southeast Asian population. Journal of Dental Research 2006; 85(1):85-88. | NOT SELECTED. Only breastfeeding. |
| 6. Azevedo TDPL, Bezerra ACB, de Toledo OA. Feeding habits and severe early childhood caries in Brazilian an preschool children. Pediatric Dentistry 2005; 27(1):28-33. | NOT SELECTED. Breastfeeding during night. |
| 7. Del Valle LL, Velazquez-Quintana Y, Weinstein P, Domoto P, Leroux B. Early childhood caries and risk factors in rural Puerto Rican children. Journal of Dentistry for Children 1998; 65(2):132-+. | NOT SELECTED. Only bottle feeding. |
| 8. Olojugba OO, Hardwick JL. Relationship of Breast-Feeding and Bottle-Feeding During Infancy to Caries Experience in Nigerian Children. Caries Research 1979; 13(2):101-102. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 9. Nobile CG, Fortunato L, Bianco A, Pileggi C, Pavia M. Pattern and severity of early childhood caries in Southern Italy: a preschool-based cross-sectional study. Bmc Public Health 2014; 14(1):206. | NOT SELECTED. Statistical data unavailable. |
| 10. Prakasha SS, Vinit GB, Giri KY, Alam S. Feeding practices and early childhood caries: a cross-sectional study of preschool children in kanpur district, India. ISRN Dent 2013; 2013:275193. | NOT SELECTED. Statistical data unavailable. |
| 11. Nazar H, Al-Mutawa S, Ariga J, Soparkar P, Mascarenhas AK. Caries prevalence, oral hygiene, and oral health habits of kuwaiti infants and toddlers. Med Princ Pract 2014; 23:125-128. | NOT SELECTED. Only bottle feeding. |
| 12. Boka V, Trikaliotis A, Kotsanos N, Karagiannis V. Dental caries and oral health-related factors in a sample of Greek preschool children. Eur Arch Paediatr Dent 2013; 14(6):363-368. | NOT SELECTED. Only bottle feeding. |
| 13. Congiu G, Campus G, Sale S, Spano G, Cagetti MG, Luglie PF. Early childhood caries and associated determinants: a cross-sectional study on Italian preschool children. J Public Health Dent 2014(2):147-152. | NOT SELECTED. Only bottle feeding. |
| 14. Bissar A, Schiller P, Wolff A, Niekusch U, Schulte AG. Factors contributing to severe early childhood caries in south-west Germany. Clin Oral Investig 2014. | NOT SELECTED. Statistical data unavailable. |
| 15. Skrivele S, Care R, Berzina S, Kneist S, de Moura-Sieber V, de MR et al. Caries and its risk factors in young children in five different countries. Stomatologija 2013; 15(2):39-46. | NOT SELECTED. Only bottle feeding. |
| 16. Gaidhane AM, Patil M, Khatib N, Zodpey S, Zahiruddin QS. Prevalence and determinant of early childhood caries among the children attending the Anganwadis of Wardha district, India. Indian J Dent Res 2013; 24(2):199-205 | NOT SELECTED. Does not compare breastfeeding with bottle feeding. |
| 17. Tanaka K, Miyake Y, Sasaki S, Hirota Y. Infant feeding practices and risk of dental caries in Japan: the Osaka Maternal And Child Health Study. Pediatr Dent 2013; 35(3):267-271. | NOT SELECTED. Does not compare breastfeeding with bottle feeding. |
| 18. Bahuguna R, Younis KS, Jain A. Influence of feeding practices on dental caries. A case-control study. Eur J Paediatr Dent 2013; 14(1):55-58. | NOT SELECTED. Does not compare breastfeeding with |

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| | bottle feeding. |
| 19. Folayan MO, Sowole CA, Kola-Jebutu A, Owotade FJ. Risk factors for rampant caries in children from southwestern Nigeria. Afr J Med Med Sci 2012; 41(3):249-255. | NOT SELECTED. Statistical data unavailable. |
| 20. Hong CH, Bagramian RA, Hashim Nainar SM, Straffon LH, Shen L, Hsu CY. High caries prevalence and risk factors among young preschool children in an urban community with water fluoridation. Int J Paediatr Dent 2014; 24(1):32-42. | NOT SELECTED. Only breastfeeding |
| 21. Masumo R, Bardsen A, Mashoto K, Astrom AN. Feeding practice among 6-36 months old in Tanzania and Uganda: reliability and relationship with early childhood caries, ECC. Acta Odontol Scand 2013; 71(5):1309-1318. | NOT SELECTED. Only breastfeeding. |
| 22. Sankeshwari RM, Ankola AV, Tangade PS, Hebbal MI. Feeding habits and oral hygiene practices as determinants of early childhood caries in 3- to 5-year-old children of Belgaum City, India. Oral Health Prev Dent 2012; 10(3):283-290. | NOT SELECTED. Does not compare breastfeeding with bottle feeding. |
| 23. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. Cochrane Database Syst Rev 2012; 8:CD003517. | NOT SELECTED. Only breastfeeding. |
| 24. Masumo R, Bardsen A, Mashoto K, Astrom AN. Prevalence and socio-behavioral influence of early childhood caries, ECC, and feeding habits among 6-36 months old children in Uganda and Tanzania. Bmc Oral Health 2012; 12:24. | NOT SELECTED. Only breastfeeding. |
| 25. Nunes AM, Alves CM, Borba de AF, Ortiz TM, Ribeiro MR, Silva AA et al. Association between prolonged breast-feeding and early childhood caries: a hierarchical approach. Community Dent Oral Epidemiol 2012; 40(6):542-549. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 26. Retnakumari N, Cyriac G. Childhood caries as influenced by maternal and child characteristics in pre-school children of Kerala-an epidemiological study. Contemp Clin Dent 2012; 3(1):2-8. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 27. Prakash P, Subramaniam P, Durgesh BH, Konde S. Prevalence of early childhood caries and associated risk factors in preschool children of urban Bangalore, India: A cross-sectional study. Eur J Dent 2012; 6(2):141-152. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 28. Arora A, Bedros D, Bhole S, Do LG, Scott J, Blinkhorn A et al. Child and family health nurses' experiences of oral health of preschool children: a qualitative approach. J Public Health Dent 2012; 72(2):149-155. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 29. Bankel M, Robertson A, Kohler B. Carious lesions and caries risk predictors in a group of Swedish children 2 to 3 years of age. One year observation. Eur J Paediatr Dent 2011; 12(4):215-219. | NOT SELECTED. Health promotion. |
| 30. Tanaka K, Miyake Y. Association between breastfeeding and dental caries in Japanese children. J Epidemiol 2012; 22(1):72-77. | NOT SELECTED. Only breastfeeding. |
| 31. Kumarihamy SL, Subasinghe LD, Jayasekara P, Kularatna SM, Palipana PD. The prevalence of Early Childhood Caries in 1-2 yrs olds in a semi-urban area of Sri Lanka. BMC Res Notes 2011; 4:336. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 32. Ozer S, Sen TE, Bayrak S, Egilmez T. Evaluation of certain risk factors for early childhood caries in Samsun, Turkey. Eur J Paediatr Dent 2011; 12(2):103-106. | NOT SELECTED. Does not compare breastfeeding and bottle feeding |
| 33. Begzati A, Berisha M, Meqa K. Early childhood caries in preschool children of Kosovo - a serious public health problem. Bmc Public Health 2010; 10:788. | NOT SELECTED. Only bottle feeding. |
| 34. Feldens CA, Giugliani ER, Vigo A, Vitolo MR. Early feeding practices and severe early childhood caries in four-year-old children from southern Brazil: a birth cohort study. Caries Res 2010; 44(5):445-452. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 35. Folayan MO, Sowole CA, Owotade FJ, Sote E. Impact of infant feeding practices on caries experience of preschool children. J Clin Pediatr Dent 2010; 34(4):297-301. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 36. Johansson I, Holgerson PL, Kressin NR, Nunn ME, Tanner AC. Snacking habits and caries in young children. Caries Res 2010; 44(5):421-430. | NOT SELECTED. Feeding habits at night. |
| 37. Slabsinskiene E, Milciuviene S, Narbutaite J, Vasiliauskiene I, | NOT SELECTED. Does |

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| | Andruskeviciene V, Bendoraitiene EA et al. Severe early childhood caries and behavioral risk factors among 3-year-old children in Lithuania. Medicina (Kaunas ) 2010; 46(2):135-141. | not compare breastfeeding and bottle feeding. |
| 38. | Feldens CA, Giugliani ER, Duncan BB, Drachler ML, Vitolo MR. Long-term effectiveness of a nutritional program in reducing early childhood caries: a randomized trial. Community Dent Oral Epidemiol 2010; 38(4):324-332. | NOT SELECTED. Health promotion – intervention programme. |
| 39. | Jigjid B, Ueno M, Shinada K, Kawaguchi Y. Early childhood caries and related risk factors in Mongolian children. Community Dent Health 2009; 26(2):121-128. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 40. | Aldy D, Siregar H, Liwijaya SG, Tanyati S. A comparative study of caries formation in breast-fed and bottle-fed children. Pediatr Indones 1979; 19(11-12): 308-312. | NOT SELECTED. Not found by COMUT. |
| 41. | Mohebbi SZ, Virtanen JI, Vahid-Golpayegani M, Vehkalahti MM. Feeding habits as determinants of early childhood caries in a population where prolonged breastfeeding is the norm. Community Dent Oral Epidemiol 2008; 36(4):363-369. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 42. | Tyagi R. The prevalence of nursing caries in Davangere preschool children and its relationship with feeding practices and socioeconomic status of the family. J Indian Soc Pedod Prev Dent 2008; 26(4):153-157. | NOT SELECTED. Night-time breastfeeding. |
| 43. | Werneck RI, Lawrence HP, Kulkarni GV, Locker D. Early childhood caries and access to dental care among children of Portuguese-speaking immigrants in the city of Toronto. J Can Dent Assoc 2008; 74(9):805. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 44. | White V. Breastfeeding and the risk of early childhood caries. Evid Based Dent 2008; 9(3):86-88. | NOT SELECTED. Systematic review. |
| 45. | Mohamed N, Barnes J. Characteristics of children under 6 years of age treated for early chidhood caries in South Africa. J Clin Pediatr Dent 2008; 32(3):247-252. | NOT SELECTED. Statistical data unavailable. |
| 46. | Qin M, Li J, Zhang S, Ma W. Risk factors for severe early childhood caries in children younger than 4 years old in Beijing, China. Pediatr Dent 2008; 30(2):122-128. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 47. | Weber-Gasparoni K, Kanellis MJ, Levy SM, Stock J. Caries prior to age 3 and breastfeeding: a survey of La Leche League members. J Dent Child (Chic ) 2007; 74(1):52-61. | NOT SELECTED. Night-time feeding habits. |
| 48. | Caplan LS, Erwin K, Lense E, Hicks J, Jr. The potential role of breast-feeding and other factors in helping to reduce early childhood caries. J Public Health Dent 2008; 68(4):238-241. | NOT SELECTED. Statistical data not available. |
| 49. | Vazquez-Nava F, Vazquez RE, Saldivar GA, Beltran GF, Almeida AV, Vazquez RC. Allergic rhinitis, feeding and oral habits, toothbrushing and socioeconomic status. Effects on development of dental caries in primary dentition. Caries Res 2008; 42(2):141-147. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 50. | Campus G, Solinas G, Sanna A, Maida C, Castiglia P. Determinants of ECC in Sardinian preschool children. Community Dent Health 2007; 24(4):253-256. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 51. | Robke FJ. Effects of nursing bottle misuse on oral health. Prevalence of caries, tooth malalignments and malocclusions in North-German preschool children. J Orofac Orthop 2008; 69(1):5-19. | NOT SELECTED. Only bottle feeding. |
| 52. | Barge K. Breast-feeding doesn't contribute to dental caries. J Dent Hyg 2007; 81(4):69. | NOT SELECTED. Review |
| 53. | Nishimura M, Oda T, Kariya N, Matsumura S, Shimono T. Using a caries activity test to predict caries risk in early childhood. J Am Dent Assoc 2008; 139(1):63-71. | NOT SELECTED. Statistical data unavailable. |
| 54. | Iida H, Auinger P, Billings RJ, Weitzman M. Association between infant breastfeeding and early childhood caries in the United States. Pediatrics 2007; 120(4):e944-e952. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 55. | Kramer MS, Vanilovich I, Matush L, Bogdanovich N, Zhang X, Shishko G et al. The effect of prolonged and exclusive breast-feeding on dental caries in early school-age children. New evidence from a large randomized trial. Caries Res 2007; 41(6):484-488. | NOT SELECTED. Children above 71 months. |

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| 56. Tiberia MJ, Milnes AR, Feigal RJ, Morley KR, Richardson DS, Croft WG et al. Risk factors for early childhood caries in Canadian preschool children seeking care. Pediatr Dent 2007; 29(3):201-208. | NOT SELECTED. Different etiology: weaning. |
| 57. Livny A, Assali R, Sgan-Cohen HD. Early Childhood Caries among a Bedouin community residing in the eastern outskirts of Jerusalem. Bmc Public Health 2007; 7:167. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 58. Yonezu T, Yotsuya K, Yakushiji M. Characteristics of breast-fed children with nursing caries. Bull Tokyo Dent Coll 2006; 47(4):161-165. | NOT SELECTED. Only breastfeeding. |
| 59. Yonezu T, Ushida N, Yakushiji M. Longitudinal study of prolonged breast- or bottle-feeding on dental caries in Japanese children. Bull Tokyo Dent Coll 2006; 47(4):157-160. | NOT SELECTED. Different etiology: weaning |
| 60. Ollila P, Larmas M. A seven-year survival analysis of caries onset in primary second molars and permanent first molars in different caries risk groups determined at age two years. Acta Odontol Scand 2007; 65(1):29-35. | NOT SELECTED. Does not compare breastfeeding children and bottle feeding children. |
| 61. Ersin NK, Eronat N, Cogulu D, Uzel A, Aksit S. Association of maternal-child characteristics as a factor in early childhood caries and salivary bacterial counts. J Dent Child (Chic ) 2006; 73(2):105-111. | NOT SELECTED. In vitro study |
| 62. Spitz AS, Weber-Gasparoni K, Kanellis MJ, Qian F. Child temperament and risk factors for early childhood caries. J Dent Child (Chic ) 2006; 73(2):98-104. | NOT SELECTED. Different etiology: children temperament |
| 63. Martens L, Vanobbergen J, Willems S, Aps J, De MJ. Determinants of early childhood caries in a group of inner-city children. Quintessence Int 2006; 37(7):527-536. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 64. Hallett KB, O'Rourke PK. Pattern and severity of early childhood caries. Community Dent Oral Epidemiol 2006; 34(1):25-35. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 65. Moura LF, de Moura MS, de Toledo OA. Dental caries in children that participated in a dental program providing mother and child care. J Appl Oral Sci 2006; 14(1):53-60. | NOT SELECTED. Children above 71 months old. |
| 66. van Palenstein Helderman WH, Soe W, van 't Hof MA. Risk factors of early childhood caries in a Southeast Asian population. J Dent Res 2006; 85(1):85-88. | NOT SELECTED. Only breastfeeding. |
| 67. Singh P, King T. Infant and child feeding practices and dental caries in 6 to 36 months old children in Fiji. Pac Health Dialog 2003; 10(1):12-16. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 68. Schroth RJ, Moffatt ME. Determinants of early childhood caries (ECC) in a rural Manitoba community: a pilot study. Pediatr Dent 2005; 27(2):114-120. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 69. Zeng X, Luo Y, Du M, Bedi R. Dental caries experience of preschool children from different ethnic groups in Guangxi Province in China. Oral Health Prev Dent 2005; 3(1):25-31. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 70. Azevedo TD, Bezerra AC, de Toledo OA. Feeding habits and severe early childhood caries in Brazilian preschool children. Pediatr Dent 2005; 27(1):28-33. | NOT SELECTED. Different etiology: nocturnal breastfeeding and bottle during the day. |
| 71. Sayegh A, Dini EL, Holt RD, Bedi R. Oral health, sociodemographic factors, dietary and oral hygiene practices in Jordanian children. J Dent 2005; 33(5):379-388. | NOT SELECTED. Does not compare breastfeeding and bottle feeding children. |
| 72. Schroth RJ, Smith PJ, Whalen JC, Lekic C, Moffatt ME. Prevalence of caries among preschool-aged children in a northern Manitoba community. J Can Dent Assoc 2005; 71(1):27. | NOT SELECTED. Statistical data unavailable. |
| 73. Rosenblatt A, Zarzar P. Breast-feeding and early childhood caries: an assessment among Brazilian infants. Int J Paediatr Dent 2004; 14(6):439-445. | NOT SELECTED. Different etiology: bottle content. |
| 74. Gaffney KE, Farrar-Simpson MA, Claure D, Davilla G. Prolonged | NOT SELECTED. |

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| | baby bottle feeding: a health risk factor. Pediatr Nurs 2004; 30(3):242-245. | Review/Case report. |
| 75. | Vachirarojpisan T, Shinada K, Kawaguchi Y, Laungwechakan P, Somkote T, Detsomboonrat P. Early childhood caries in children aged 6-19 months. Community Dent Oral Epidemiol 2004; 32(2):133-142. | NOT SELECTED. Statistical data unavailable. |
| 76. | Bray KK, Branson BG, Williams K. Early childhood caries in an urban health department: an exploratory study. J Dent Hyg 2003; 77(4):225-232. | NOT SELECTED. Statistical data unavailable. |
| 77. | King NM, Wu II, Tsai JS. Caries prevalence and distribution, and oral health habits of zero- to four-year-old children in Macau, China. J Dent Child (Chic ) 2003; 70(3):243-249. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 78. | Dye BA, Shenkin JD, Ogden CL, Marshall TA, Levy SM, Kanellis MJ. The relationship between healthful eating practices and dental caries in children aged 2-5 years in the United States, 1988-1994. J Am Dent Assoc 2004; 135(1):55-66. | NOT SELECTED. Only bottle feeding. |
| 79. | Jose B, King NM. Early childhood caries lesions in preschool children in Kerala, India. Pediatr Dent 2003; 25(6):594-600. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 80. | Olmez S, Uzamis M, Erdem G. Association between early childhood caries and clinical, microbiological, oral hygiene and dietary variables in rural Turkish children. Turk J Pediatr 2003; 45(3):231-236. | NOT SELECTED. In vitro study. |
| 81. | Jin BH, Ma DS, Moon HS, Paik DI, Hahn SH, Horowitz AM. Early childhood caries: prevalence and risk factors in Seoul, Korea. J Public Health Dent 2003; 63(3):183-188. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 82. | Carino KM, Shinada K, Kawaguchi Y. Early childhood caries in northern Philippines. Community Dent Oral Epidemiol 2003; 31(2):81-89. | NOT SELECTED. Children above 71 months old. |
| 83. | Rosenblatt A, Zarzar P. The prevalence of early childhood caries in 12- to 36-month-old children in Recife, Brazil. ASDC J Dent Child 2002; 69(3):319-24, 236. | NOT SELECTED. Statistical data unavailable. |
| 84. | Huntington NL, Kim IJ, Hughes CV. Caries-risk factors for Hispanic children affected by early childhood caries. Pediatr Dent 2002; 24(6):536-542. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 85. | Hallett KB, O'Rourke PK. Early childhood caries and infant feeding practice. Community Dent Health 2002; 19(4):237-242. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 86. | Olmez S, Uzamris M. Risk factors of early childhood caries in Turkish children. Turk J Pediatr 2002; 44(3):230-236. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 87. | Santos AP, Soviero VM. Caries prevalence and risk factors among children aged 0 to 36 months. Pesqui Odontol Bras 2002; 16(3):203-208. | NOT SELECTED. Night-time breastfeeding. |
| 88. | Chan SC, Tsai JS, King NM. Feeding and oral hygiene habits of preschool children in Hong Kong and their caregivers' dental knowledge and attitudes. Int J Paediatr Dent 2002; 12(5):322-331. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 89. | Ngatia EM, Imungi JK, Muita JW, Nganga PM. Dietary patterns and dental caries in nursery school children in Nairobi, Kenya. East Afr Med J 2001; 78(12):673-677 | NOT SELECTED. Only bottle feeding. |
| 90. | Lulic-Dukic O, Juric H, Dukic W, Glavina D. Factors predisposing to early childhood caries (ECC) in children of pre-school age in the city of Zagreb, Croatia. Coll Antropol 2001; 25(1):297-302. | NOT SELECTED. Only bottle feeding. |
| 91. | Fraiz FC, Walter LR. Study of the factors associated with dental caries in children who receive early dental care. Pesqui Odontol Bras 2001; 15(3):201-207. | NOT SELECTED. Only bottle feeding. |
| 92. | Wyne A, Darwish S, Adenubi J, Battata S, Khan N. The prevalence and pattern of nursing caries in Saudi preschool children. Int J Paediatr Dent 2001; 11(5):361-364. | NOT SELECTED. Only bottle feeding. |
| 93. | Tsai AI, Johnsen DC, Lin YH, Hsu KH. A study of risk factors associated with nursing caries in Taiwanese children aged 24-48 | NOT SELECTED. Does not study breastfeeding |

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| months. Int J Paediatr Dent 2001; 11(2):147-149. | and bottle feeding. |
| 94. Tada A, Ando Y, Hanada N. Caries risk factors among three-year old children in Chiba, Japan. Asia Pac J Public Health 1999; 11(2):109-112. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 95. Douglass JM, Tinanoff N, Tang JM, Altman DS. Dental caries patterns and oral health behaviors in Arizona infants and toddlers. Community Dent Oral Epidemiol 2001; 29(1):14-22. | NOT SELECTED. Night-time habits. |
| 96. Petti S, Cairella G, Tarsitani G. Rampant early childhood dental decay: an example from Italy. J Public Health Dent 2000; 60(3):159-166. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 97. Milgrom P, Riedy CA, Weinstein P, Tanner AC, Manibusan L, Bruss J. Dental caries and its relationship to bacterial infection, hypoplasia, diet, and oral hygiene in 6- to 36-month-old children. Community Dent Oral Epidemiol 2000; 28(4):295-306. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 98. Dini EL, Holt RD, Bedi R. Caries and its association with infant feeding and oral health-related behaviours in 3-4-year-old Brazilian children. Community Dent Oral Epidemiol 2000; 28(4):241-248. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 99. Ismail AI, Sohn W. A systematic review of clinical diagnostic criteria of early childhood caries. J Public Health Dent 1999; 59(3):171-191. | NOT SELECTED. Review |
| 100. Oulis CJ, Berdouses ED, Vadiakas G, Lygidakis NA. Feeding practices of Greek children with and without nursing caries. Pediatr Dent 1999; 21(7):409-416. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 101. al Ghanim NA, Adenubi JO, Wyne AA, Khan NB. Caries prediction model in pre-school children in Riyadh, Saudi Arabia. Int J Paediatr Dent 1998; 8(2):115-122. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 102. Mattos-Graner RO, Zelante F, Line RC, Mayer MP. Association between caries prevalence and clinical, microbiological and dietary variables in 1.0 to 2.5-year-old Brazilian children. Caries Res 1998; 32(5):319-323. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 103. Wyne AH, Adenubi JO, Shalan T, Khan N. Feeding and socioeconomic characteristics of nursing caries children in a Saudi population. Pediatr Dent 1995; 17(7):451-454. | NOT SELECTED. Statistical data unavailable. |
| 104. Hallonsten AL, Wendt LK, Mejare I, Birkhed D, Hakansson C, Lindvall AM et al. Dental caries and prolonged breast-feeding in 18-month-old Swedish children. Int J Paediatr Dent 1995; 5(3):149-155. | NOT SELECTED. Only breastfeeding. |
| 105. Roberts GJ, Cleaton-Jones PE, Fatti LP, Richardson BD, Sinwel RE, Hargreaves JA et al. Patterns of breast and bottle feeding and their association with dental caries in 1- to 4-year-old South African children. 1. Dental caries prevalence and experience. Community Dent Health 1993; 10(4):405-413. | NOT SELECTED. Statistical data unavailable. |
| 106. Serwint JR, Mungo R, Negrete VF, Duggan AK, Korsch BM. Child-rearing practices and nursing caries. Pediatrics 1993; 92(2):233-237. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 107. Babeely K, Kaste LM, Husain J, Behbehani J, al-Za'abi F, Maher TC et al. Severity of nursing-bottle syndrome and feeding patterns in Kuwait. Community Dent Oral Epidemiol 1989; 17(5):237-239. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 108. Broderick E, Mabry J, Robertson D, Thompson J. Baby bottle tooth decay in Native American children in Head Start centers. Public Health Rep 1989; 104(1):50-54. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |
| 109. Schroth RJ, Halchuk S, Star L. Prevalence and risk factors of caregiver reported Severe Early Childhood Caries in Manitoba First Nations children: results from the RHS Phase 2 (2008-2010). Int J Circumpolar Health. 2013 Aug 5;72. | NOT SELECTED. Does not compare breastfeeding and bottle feeding. |

## Apêndice C - S3 Checklist. PRISMA 2009 Checklist.

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | #1-2 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | #13-30 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | #34-59 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | #60-64 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | #68 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | #69-72 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | #73-78 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | #79-86 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | #99-104 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | #87-95 #112-115 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | #71-74 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | #117-127 |

| | | | |
|---|---|---|---|
| Summary measures | 1 | State the principal summary measures (e.g., risk ratio, difference in means). | #112-115 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | #133-138 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | #117-#128 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | - |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Table 1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Figure 2 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | Figure 3 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | #182-185 Figure 3 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | #192-#194 Figure 2 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | - |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | #201-254 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | #273-279 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | #287-289 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | - |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

# PRODUÇÃO INTELECTUAL DESENVOLVIDA DURANTE O CURSO

## Resumos de trabalhos publicados em anais de eventos científicos

- Avila WM, Scarpelli AC, Ramos-Jorge J, Ramos-Jorge ML, Paiva SM, Martins CC, Pordeus IA. Análise do ICDAS para detecção de cárie dentária em estágio inicial: resultados preliminares de uma revisão sistemática. In: Congresso Latino-Americano ALOP/Congresso Paulista APO, 2014, São Paulo, São Paulo, Brasil.

- Avila WM, Scarpelli AC, Ramos-Jorge J, Ramos-Jorge ML, Paiva SM, Martins CC, Pordeus IA. Avaliação do ICDAS para detecção de lesões iniciais de cárie dentária: resultados preliminares de uma revisão sistemática. In: Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica, 2014, Águas de Lindóia, São Paulo, Brasil. Brazilian Oral Research, 2014;28:363.

- Pacheco RTCA, Avila WM, Pordeus IA, Zina LG, Martins CC. Aleitamento materno e risco de má oclusão na dentição mista e permanente: revisão sistemática. In: 31ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica, 2014, Águas de Lindóia, São Paulo, Brasil. Brazilian Oral Research, 2014;28:99.

- Avila WM, Fonseca L, Bonanato K, Reis J, Drugowick R, Imparato JCP. Influência de fatores sócio familiares na ansiedade da criança antes do tratamento odontológico. In: 12º Encontro Científico da Faculdade de Odontologia da UFMG/10º Encontro Mineiro das Faculdades de Odontologia, 2014, Belo Horizonte, Minas Gerais, Brasil. Arquivos em Odontologia, 2014;50(Suppl 1):9.

## Apresentação de trabalhos em eventos científicos

- Apresentação de pôster na 31ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica, 2014.

  Avila WM, Scarpelli AC, Ramos-Jorge J, Ramos-Jorge ML, Paiva SM, Martins CC, Pordeus IA. Avaliação do ICDAS para detecção de lesões iniciais de cárie dentária: resultados preliminares de uma revisão sistemática. In: 31ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica, 2014, Águas de Lindóia, São Paulo, Brasil.

- Apresentação de pôster no 17º Congresso Latino-Americano ALOP / 6º Congresso Paulista APO, 2014.

  Avila WM, Scarpelli AC, Ramos-Jorge J, Paiva SM, Martins CC, Pordeus IA. Análise do ICDAS para detecção de cárie dentária em estágio inicial: resultados preliminares de uma revisão sistemática. In: 17º Congresso Latino-Americano ALOP/6º Congresso Paulista APO, 2014, São Paulo, São Paulo, Brasil.