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The relationship between exclusive breastfeeding and motor development in children: a protocol for a systematic review and meta-analysis.

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Protocol manuscript

The relationship between exclusive breastfeeding and motor development in children: a protocol for a systematic review and meta-analysis.

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ABSTRACT

Introduction:

The recommendations of most scientific societies encourage mothers to keep breastfeeding for at least 6 months, due to the numerous immunologic, cognitive developmental and motor skill benefits that breastfeeding confers. Although the influence of breastfeeding on motor development during childhood has been extensively studied, the findings are inconsistent, and some studies have even reported no effect. This manuscript presents a protocol for a systematic review and meta-analysis, with the aim of reviewing the relationship between breastfeeding and motor skill development in children; in terms of duration, exclusivity or non-exclusivity of breastfeeding, based on data from published observational studies.

Methods and analysis:

To identify relevant studies, the search will be conducted using MEDLINE (via PubMed), EMBASE, Web of Science and Cochrane Library. Observational studies (Cross-sectional and follow up studies) written in English or Spanish that investigate the association between breastfeeding and motor development in children will be included. This systematic review and meta-analysis protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). A Critical Appraisal Checklist for Analytical Cross-Sectional Studies and The Newcastle-Ottawa Quality Assessment Scale for longitudinal studies will be used to assess the quality of included studies. The effect of breastfeeding on motor skill development will be calculated as the primary outcome. Subgroup analyses will be carried out based on the characteristics of motor skill development and the population included.

Ethics and dissemination

Ethical approval is not required because the data used for will be obtained from published studies and there will be no concerns about privacy. The findings from this study will be relevant information regarding the association of breastfeeding and motor development in children, and could be used encourage to improve breastfeeding rates. The results will be published in a peer-reviewed journal.

Trial registration number: PROSPERO CRD42018093706. (24/04/2018)

Keywords: breastfeeding, motor development, motor skills, children.

Strengths and limitations of this study

- This review will present a comprehensive and standardised methodology, according to an established framework, to identify relevant studies that analyse the effect of breastfeeding on motor skills.
- Analysis of different sources of heterogeneity and the assessment of risk of bias of the included studies will be performed independently by two researchers.
- To identify studies that aim to determine the association between breastfeeding and motor development, an exhaustive literature search will be carried out.
- This study could be limited by the quality of available studies, insufficient methodological rigor and statistical heterogeneity.
- Different methods used for measuring breastfeeding and motor development from observational studies may be another limitation to the quality of evidence of this study.

INTRODUCTION

The first two years of a child's life is a critical period for health, growth and development; all of which are affected by nutritional status. It is well documented that breastfeeding provides many important health benefits to children and mothers, and this is considered the gold standard in infant feeding.^{1,2}

The World Health Organization (WHO) recommends exclusive breastfeeding for the first 6 months of life as an ideal feed, and continuation of breastfeeding for at least the first and second years to supplement the introduction of complementary feed. There is no evidence against this recommendation,^{1,2,3,4} which is also supported by many scientific and practitioner associations.^{5,6,7} The World Health Assembly, as part of its Global Strategy for the Feeding of Infants and Young Children, encouraged Member States to promote exclusive breastfeeding for 6 months as a global public health recommendation which provides many benefits to babies, reduces the risk of diseases and helps to promote good physical and cognitive growth.^{8,9}

However, the rates of breastfeeding at 6 months of age remain low in Europe; and even in countries where initial rates are high, there is a marked decrease by the sixth month.^{10,11,12} Early cessation of breastfeeding and the introduction of solids before 4 months can have considerable adverse effects on the health of women and children.^{12,13,14,15} Therefore, it is important to consider what is causing the failure to comply with recommendations, and there is a need for greater efforts to disseminate the benefits of breastfeeding and create a social environment that favours it.

Although infant development is a process that is influenced by several factors, breastfeeding in the first months of life is a key determinant for optimal growth and adequate cognitive and motor development. Additionally, breastfeeding prevents gastrointestinal infection and decreases the risk of diseases later in life such as allergies, asthma, obesity and celiac disease.^{2,3,7,9,12,16,17}

Thus, motor development and cognitive function represent indicators of overall development during the first years.^{18,19} Although consistent evidence of the positive effects of extended breastfeeding on cognitive function has been reported,²⁰ few studies have focused on motor development. The relationship between motor development and breastfeeding is difficult to analyse because incomplete control for confounders is reported in the current literature, even when various assessments of motor milestones are

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3 considered across studies. To date, no clear associations between the duration of
4 breastfeeding and motor development have been reported.^{21,22,23,24}
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7 The purpose of this study protocol is to provide a clear methodology to review the effects
8 of breastfeeding practices on motor development in children, in terms of duration and
9 exclusive or not exclusive breastfeeding.
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15 **OBJECTIVE**

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17 The aim of this protocol study is to present an objective and transparent methodology
18 with which to conduct a systematic review and meta-analysis aimed to increase
19 knowledge and understanding of the associations between the duration and exclusivity of
20 breastfeeding and motor development in early childhood.
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28 **METHODS AND ANALYSIS**

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30 The methodology of this protocol was developed in accordance with the Preferred
31 Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P)²⁵.
32 The Meta-analysis of observational studies in epidemiology: a proposal for reporting
33 (MOOSE²⁶), PRISMA and Cochrane Collaboration Handbook²⁷ will be used to guide the
34 review methods. This protocol was registered with PROSPERO, (Registration number
35 CRD42018093706) on 24 April 2018.
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45 **Inclusion/exclusion criteria for study selection**

46 Studies will be retrieved from the literature by searching for studies which measure the
47 effects of breastfeeding duration and exclusivity, and report any type of measure of motor
48 development. To be considered inclusion, studies will be required to meet the following
49 criteria: (i) participants, children who have not received supplementation in feeding; (ii)
50 exposure, studies that measure the effect of breastfeeding in terms of duration and
51 exclusivity and report any type of measure; (iii) outcome, studies in which motor
52 development is an outcome measured using standardised tests; and (iv) study design,
53 observational studies (cross-sectional or longitudinal design) that are written in English
54 or Spanish.
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3 Studies will be excluded when: (i) they include infants born in multiple pregnancies with
4 congenital infections or special circumstances requiring intensive care or hospitalization
5 during the neonatal period or children with mental disorders or any detected delay in
6 communication, cognition or motor skills (ii) studies where breast milk has been
7 supplemented and (iii) studies which have already been used in other similar reviews.
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13 **Search methods for the identification of studies**

14 **Search strategy**

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17 The literature search will be conducted in MEDLINE (via PubMed), EMBASE, Web of
18 Science and Cochrane Library. The searches will be reviewed immediately prior to the
19 final analysis in order to identify further potential studies. Study records will be managed
20 using the Mendeley reference manager. The following search terms will be combined to
21 conduct the search: breastfeeding, feeding, 'exclusive breastfeeding', breastfed, 'breast
22 suckling', suckling, 'motor skill', 'psychomotor performance', 'motor development',
23 'psychomotor development', 'development milestones', children, child, infant,
24 childhood, 'observational study', 'cohort study', 'population-based' and 'cross sectional'
25 (Table 1). Previous reviews and meta-analyses will be screened, as well as the reference
26 lists of the selected studies.
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Table 1 Search strategy for MEDLINE database

Breastfeeding	AND	'motor skills'	AND	children	AND	'observational
OR		OR		OR		study'
feeding		'psychomotor		child		OR
OR		performance'		OR		'cohort study'
'exclusive		OR		infant		OR
breastfeeding'		'motor		OR		'population-
OR		development'		childhood		based'
breastfed		OR				OR
OR		'psychomotor				'cross
'breast suckling'		development'				sectional'
OR		OR				
'suckling'		'motor				
		development				
		milestones'				

Selection of studies and data extraction

Two researchers will screen all relevant titles and abstracts of the retrieved publications to identify eligible studies. Inclusion and exclusion criteria will be applied to full texts to identify all potentially eligible articles. Inconsistencies in data collection will be solved by consensus. A third reviewer will be consulted when disagreements persist. The process of identifying, screening and including/excluding articles will be illustrated using the PRISMA²⁵ flow chart (Figure 1).

Finally, information about the main characteristics of the identified studies will be extracted, including the following data: i) first author's name, ii) publication year, iii) country, iv) study design, v) characteristics of the study population (sample size, age of children at evaluation, gender and number of participants in each group), vi) breastfeeding category (as defined in Table 2) and vii) test used for assessment of motor development (Table 2). The authors of the included studies will be contacted to request any missing data.

Table 2 Characteristics of studies included in the systematic review and/or meta-analysis

Reference	Country	Study design	Population		Breastfeeding		Outcome MD	
			Sample size	Sample age	Categories	n	Tool	Measurement
First author's name and year of publication	Country	Design of the study	Number of participants	Age of participants (years)	Duration periods of exclusive breastfeeding /any breastfeeding	Number participants in each breastfeeding category	Instrument used to measure MD	Measure used to express MD

Key: MD, Motor Development

Assessment of risk of bias

Two independent researchers will be blinded to the authors, titles and years of publication of the included studies to evaluate the risk of bias of each included study. The Critical Appraisal Checklist for Analytical Cross-Sectional Studies from The Joanna Briggs Institute will be used.²⁸ This tool evaluates the risk of bias according to eight items which are scored as “Yes”, “No”, “Unclear” or “Not applicable”.

The Newcastle-Ottawa Quality Assessment Scale²⁹ will be used to assess the risk of bias of longitudinal studies, including case control and cohort studies. This tool evaluates the risk of bias according to eight items which are grouped in three categories: selection, comparability and exposure or outcome (for case control or cohort studies, respectively). Each study can be awarded one star for each item within the selection and exposure categories, and a maximum of two stars in the comparability category. Any disagreements over the assessment of quality will be solved by consensus. A third researcher will be consulted if a consensus is not reached.

Statistical analysis

After data extraction, the reviewers will determine whether meta-analysis is possible. At least four studies addressing the association between breastfeeding and motor development will be required in order to conduct a meta-analysis. If meta-analysis is possible, STATA V.15 software will be used to compute the pooled effect size (ES) estimates with 95% confidence intervals (CIs). The standardized mean difference will be

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3 calculated for each breastfeeding category as an estimate of ES,³⁰ using Cohen's d index
4 as the ES statistic. We will compare the level of motor development in children who have
5 never been breastfed, as a reference group, with children who have been exclusively
6 breastfed or breastfed for any length of time. If possible, a comparison between children
7 breastfed for at least 6 months and children breastfed for less than 6 months will also be
8 carried out.
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14 A fixed-effects model³¹ will be used in the case of no heterogeneity; otherwise, a random-
15 effects model³² will be used. Heterogeneity will be assessed by computing the I² statistic
16 to quantify inconsistencies and variability within the meta-analysis.³³ The values of I²
17 will be considered as follows: 0%–40% might not be important, 30%–60% may represent
18 moderate heterogeneity, 50%–90% may represent substantial heterogeneity and 75%–
19 100% represents considerable heterogeneity.
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25 Linear meta-analysis regression models will be used to explore the impact of covariates,
26 directed by the results of heterogeneity analysis. Finally, publication bias will be
27 evaluated using a funnel plot according to the method proposed by Egger.³⁴ When a meta-
28 analysis is not feasible, we will perform a narrative synthesis.
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33 *Subgroup analysis and meta-regression*

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36 If enough studies are available, subgroup analysis will be conducted. Subgroup and meta-
37 regression analyses will be carried out on the main factors causing heterogeneity, such as
38 the type of motor development assessment (i.e., gross or fine motor), gender, age of study
39 participants, birth weight, breastfeeding classification (never, less than 6 months or more
40 than 6 months) and aspects related to motor skills such as the type of measure used.
41 Furthermore, the design and risk of bias scores of the studies will be considered for
42 additional subgroup analysis. Additional potential moderating variables may be identified
43 after reviewing the literature.
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52 *Sensitivity analysis*

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54 We will perform sensitivity analysis to assess whether the findings are robust over the
55 assumptions made. These analyses will be conducted by removing studies one by one
56 from the main analysis.
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No patient and Public Involvement

Existing databases will be used for the purpose of this study. Patients and public will not be involved in the design of this study. This review will assess the effect of breastfeeding on motor developmental outcomes in infants. Insights provided by this study could be used in clinical practice to ameliorate outcomes; specifically, motor development; of children in the population.

DISCUSSION

The aim of this study is to present an objective and transparent methodology with which to conduct a systematic review and meta-analysis investigating whether the duration of breastfeeding is associated with motor development and the child's developmental status.

Many studies have examined whether breastfeeding in early life, a critical phase of development, could affect later cognitive function and motor development in children.^{18,19,20} Infant development is a complex process, which encompasses several factors that allow the acquisition of skills that will contribute to a child's full participation in activities and will help to establish a direct relationship with the environment.¹⁸

Motor function is an accepted indicator of development during the first years of life.^{35,36,37} It directly contributes to and reflects the relationship that the child establishes with the physical and social environments. In addition, motor development plays an important role in other areas of development, such as physical growth and cardiorespiratory fitness, the latter being a powerful and effective indicator of cardiovascular health.^{38,39,40} Poor motor development performance may incline children towards activity avoidance and sedentary behaviours, which are linked to increased risk of chronic disease in adulthood.⁴¹

There is considerable evidence about the long- and short-term benefits of breastfeeding for infant health.^{16,17} However, no consensus has been reached about the effects of breastfeeding on motor development, and the results and conclusions of existing studies are controversial.^{19,23,24} The complexity of child development makes it difficult to evaluate these effects, and certain aspects of infant development are influenced by psychosocial and socioeconomic factors, which could contribute to some of the observed differences. The scientific evidence regarding the benefits of breastfeeding in terms of

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3 motor development outcomes is weak, and the strength of this association is controversial
4 because most studies lack adequate control for potential confounders. Furthermore,
5 previous studies have measured infant development using different standardised tests.
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9 Potential limitations of this research could include publication bias, information bias, lack
10 of consultation of grey literature, inclusion of articles in English and Spanish only,
11 analysis of cross-sectional studies as this does not allow a causal association to be
12 evaluated (breastfeeding always precedes motor development), poor statistical analysis
13 and inadequate reporting of methods and findings of the primary studies. To overcome
14 these limitations, the study will be conducted and reported by two independent reviewers,
15 and inconsistencies in data collection will be solved by consensus. Furthermore; existing
16 guidelines, the MOOSE statement, PRISMA, and Cochrane Collaboration Handbook
17 recommendations will be followed.
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21 To summarise, we will carry out a systematic review and meta-analysis with the objective
22 of reviewing existing literature on the relationship between breastfeeding and motor
23 development. Despite the fact that some aspects of motor development appear to be
24 controversial, if this study confirms the positive effects of breastfeeding on motor skill
25 development through analysis of the evidence, it could encourage greater interest in
26 breastfeeding within the areas of public and child health.
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30 This situation highlights the need for guidelines or recommendations that are based on
31 rigorous and updated bibliographical review of the best available scientific evidence, for
32 use in daily practice to improve the quality and effectiveness of interventions. This could
33 lead to an improvement in the health status and development of children worldwide.
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36 37 38 39 40 41 42 43 44 45 46 **ETHICS AND DISSEMINATION**

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48 The data included in this project will be provide by the original studies; therefore, ethical
49 approval and informed consent of patients will not be required.
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52 This protocol provides a clear and structured procedure to extract relevant information on
53 the association of breastfeeding and motor milestones. This study will have clinical and
54 public health implications, because it could provide support for recommendations of
55 breastfeeding, which might help to prevent low rates of breastfeeding and early
56 abandonment. Suggestions for future research will be made according to the findings of
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3 this systematic review and meta-analysis, and evidence-based recommendations to
4 improve breastfeeding rates will be offered, due to the involvement of this practice in
5 children's development.
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8 9 **Contributors:**

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11 BN-P and MH-L designed the study. BN-P was the principal investigator and guarantor.
12
13 BN-P and MH-L were the main coordinators of the study. DPP-C, CA-B, CB-C, VM-V
14 and BN-P conducted the study. MH-L, DPP-C and VM-V gave statistical and
15 epidemiological support. MH-L wrote the article with the support of CB-C, VM-V and
16 BN-P. All authors reviewed and approved the final version of the manuscript.
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20 21 **Competing interests:**

22
23 All authors have completed the ICMJE uniform disclosure form at
24 www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the
25 submitted work; no financial relationships with any organisations that might have an
26 interest in the submitted work in the previous three years; no other relationships or
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31 32 **Funding statement:**

33
34 This work was not supported by any external grants or funding.
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37 38 **Data sharing:**

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40 Extra data is available by emailing: celia.alvarezbueno@uclm.es
41

42 43 **Transparency**

44
45 The manuscripts guarantor (BN-P) affirms that the manuscript is an honest, accurate, and
46 transparent account of the study being reported; that no important aspects of the study
47 have been omitted; and that any discrepancies from the study as planned have been
48 explained.
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39 neurodevelopmental disorders: a meta-analysis. *BMC Pediatr*. 2016;16:193.
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45 TABLES LEGENDS

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47 **Table 1.** Search strategy for the MEDILINE database.
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50 **Table 2.** Characteristics of studies included in the systematic review and/or meta-
51 analysis.
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53 FIGURE LEGENDS

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56 **Figure 1.** PRISMA (Preferred Reporting Items for Systematic Review and Meta-
57 Analysis) flow diagram of identification, screening, eligibility and inclusion of studies
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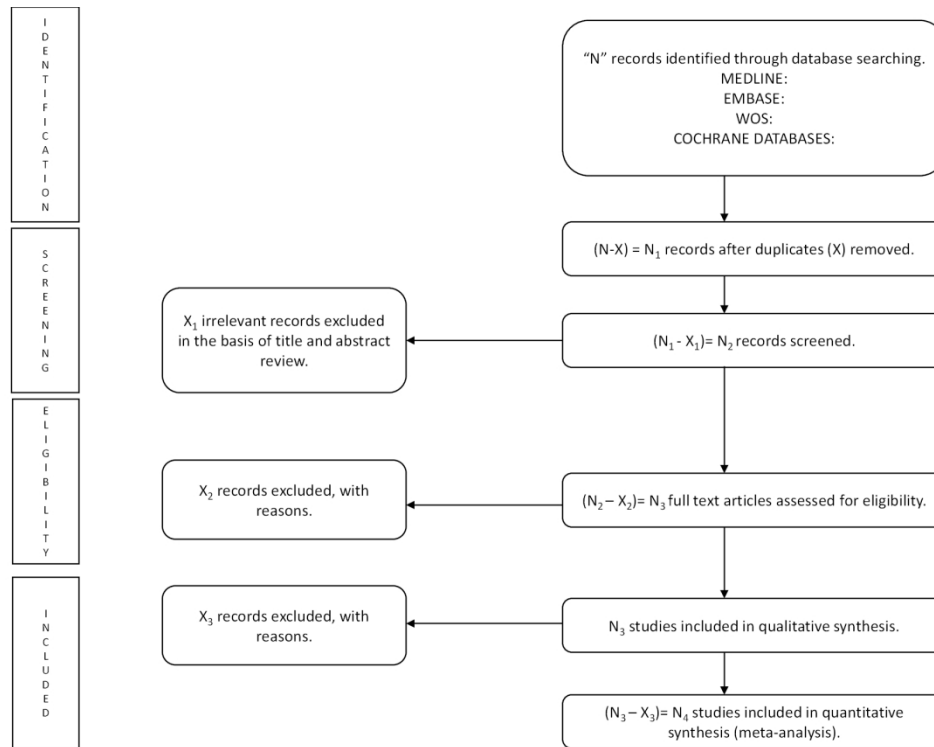


Figure 1 Literature search Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram of identification, screening, eligibility and inclusion of studies.

169x127mm (300 x 300 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration: p. 2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors: pp. 1, 13		
Contact: p. 1	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p. 13	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support: NA		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: pp 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: pp. 5, 6	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources: p. 6	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 6, 7	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records: pp. 7, 8		
Data management: p. 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

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3	Selection process: p. 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
4			
5	Data collection process: p. 7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
6			
7	Data items: pp 7, 10	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
8			
9			
10	Outcomes and prioritization: pp. 7, 8	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
11			
12	Risk of bias in individual studies: p. 8	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
13			
14	Data synthesis: pp 9, 10	15a	Describe criteria under which study data will be quantitatively synthesised
15		15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)
16		15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
17		15d	If quantitative synthesis is not appropriate, describe the type of summary planned
18			
19	Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
20			
21	Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)
22			

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

The relationship between breastfeeding and motor development in children: a protocol for a systematic review and meta-analysis.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-029063.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Jun-2019
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Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	General practice / Family practice
Keywords:	breastfeeding, motor development, motor skills, children

SCHOLARONE™
Manuscripts

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3 **1 Protocol manuscript**
4

5 2 The relationship between breastfeeding and motor development in children: a protocol
6 3 for a systematic review and meta-analysis.
7
8

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40 **17 Word count: 2562**
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3 **19 ABSTRACT**
4

5 **20 Introduction:**
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8 The recommendations of most health organizations encourage mothers to keep exclusive
9 breastfeeding during the first 6 months and combining breastfeeding with the
10 complementary feed at least the first and second years, due to the numerous immunologic,
11 23 complementary feed at least the first and second years, due to the numerous immunologic,
12 24 cognitive developmental and motor skill benefits that breastfeeding confers. Although the
13 25 influence of breastfeeding on motor development during childhood has been studied, the
14 26 findings are inconsistent, and some studies have even reported no effect. This manuscript
15 27 presents a protocol for a systematic review and meta-analysis, with the aim of reviewing
16 28 the relationship between breastfeeding and motor skill development in children; in terms
17 29 of duration, exclusivity or non-exclusivity of breastfeeding.
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24 **30 Methods and analysis:**
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26 To identify relevant studies, the search will be conducted using MEDLINE (via PubMed),
27 32 EMBASE, Web of Science and Cochrane Library from inception to December 2019.
28 33 Observational studies (Cross-sectional and follow up studies) written in English or
29 34 Spanish that investigate the association between breastfeeding and motor development in
30 35 children will be included. This systematic review and meta-analysis protocol follows the
31 36 Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
32 37 (PRISMA-P). A Critical Appraisal Checklist for Analytical Cross-Sectional Studies and
33 38 The Newcastle-Ottawa Quality Assessment Scale for longitudinal studies will be used to
34 39 assess the quality of included studies. The effect of breastfeeding on motor skill
35 40 development will be calculated as the primary outcome. Subgroup analyses will be carried
36 41 out based on the characteristics of motor skill development and the population included.
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46 **42 Ethics and dissemination**
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48 Ethical approval is not required because the data used for will be obtained from published
49 44 studies and there will be no concerns about privacy. The findings from this study will be
50 45 relevant information regarding the association of breastfeeding and motor development
51 46 in children and could be used encourage to improve breastfeeding rates. The results will
52 47 be published in a peer-reviewed journal.
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58 **48 Trial registration number:** PROSPERO CRD42018093706. (24/04/2018)

59 **49 Keywords:** breastfeeding, motor development, motor skills, children.
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Strengths and limitations of this study

- This review will present a comprehensive and standardised methodology, according to an established framework, to identify relevant studies that analyse the effect of breastfeeding on motor skills.
- Analysis of different sources of heterogeneity and the assessment of risk of bias of the included studies will be performed independently by two researchers.
- To identify studies that aim to determine the association between breastfeeding and motor development, an exhaustive literature search will be carried out.
- This study could be limited by the quality of available studies, insufficient methodological rigor and statistical heterogeneity.
- Different methods used for measuring breastfeeding and motor development from observational studies may be another limitation to the quality of evidence of this study.

77 INTRODUCTION

78 The first two years of a child's life is a critical period for health, growth and development;
79 all of which are affected by nutritional status. It is well documented that breastfeeding
80 provides many important health benefits to children and mothers and is considered the
81 gold standard in infant feeding.^{1,2}

82 The World Health Organization (WHO) recommends exclusive breastfeeding for the first
83 6 months of life as an ideal feed, and continuation of breastfeeding for at least the first
84 and second years, which is also supported by many health organizations.¹⁻⁶ However, the
85 European Society for Paediatric Gastroenterology, Hepatology and Nutrition
86 (ESPGHAN) differs in the recommendation of the age when complementary feed should
87 be included because of the risk of food allergies.⁷ The World Health Assembly, as part
88 of its Global Strategy for the Feeding of Infants and Young Children, encouraged Member
89 States to promote exclusive breastfeeding for 6 months as a global public health
90 recommendation which provides many benefits to babies, reduces the risk of diseases and
91 helps to promote good physical and cognitive growth.^{8,9}

92 However, the rates of breastfeeding at 6 months remain low in Europe; and even in
93 countries where initial rates are high, there is a marked decrease by the sixth month.¹⁰⁻¹¹
94 Early cessation of breastfeeding and the introduction of solids before 4 months could have
95 considerable adverse effects on the children and women's health.¹²⁻¹⁵ Therefore, it is
96 important to elucidate what are the reasons behind the failure to achieve the
97 recommendations, and there is a need for greater efforts to disseminate the benefits of
98 breastfeeding and create a social environment that could favour it.

99 Although infant development is a process that is influenced by several factors,
100 breastfeeding in the first months of life is a key determinant for optimal growth and
101 adequate cognitive and motor development. Additionally, breastfeeding provides quality
102 nutrients improvement (higher proportion of unsaturated fatty acids), prevents
103 gastrointestinal infection and decreases the risk of diseases later in life such as allergies,
104 asthma, obesity and celiac disease.^{2,3,7,9,12,16-19}

105 Thus, motor development and cognitive function represent indicators of overall
106 development during the first years. Motor development allows the acquisition of skills
107 that will contribute to a child's full participation in activities, avoiding sedentary
108 behaviours and will help to establish a direct and active relationship with the

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3 109 environment.^{20,21} Although consistent evidence of the positive effects of extended
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5 110 breastfeeding on cognitive function has been reported,²² few studies have focused on
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7 111 motor development. The relationship between motor development and breastfeeding is
8
9 112 difficult to analyse because incomplete control for confounders is reported in the current
10
11 113 literature, even when various assessments of motor milestones are considered across
12
13 114 studies. To date, no clear associations between the duration of breastfeeding and motor
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15 115 development have been reported.²³⁻²⁶

16 116 The purpose of this study protocol is to provide a clear methodology to review the effects
17
18 117 of breastfeeding practices on motor development in children, in terms of duration and
19
20 118 exclusive or not exclusive breastfeeding.

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23 24 120 **OBJECTIVE**

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26 121 The aim of this protocol study is to present an objective and transparent methodology to
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28 122 conduct a systematic review and meta-analysis aimed to increase knowledge and
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30 123 understanding of the associations between the duration and exclusivity of breastfeeding
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32 124 and motor development in children age 0 to 10 years old.

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35 36 126 **METHODS AND ANALYSIS**

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39 127 The methodology of this protocol was reported in accordance with the Preferred
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41 128 Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P)²⁷.
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43 129 The Meta-analysis of observational studies in epidemiology: a proposal for reporting
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45 130 (MOOSE²⁸), the Preferred Reporting Items for Systematic Reviews and Meta-analyses
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47 131 (PRISMA) and Cochrane Collaboration Handbook²⁹ will be used to report and guide the
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49 132 review methods. This protocol was registered with PROSPERO, (Registration number
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51 133 CRD42018093706) on 24 April 2018.

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54 135 **Inclusion/exclusion criteria for study selection**

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56 136 Studies will be retrieved from the literature by searching for studies which measure the
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58 137 effects of breastfeeding duration and type (exclusivity, even if it is little, or no exclusive
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60 138 breastfeeding), and report any type of measure of motor development. To be considered

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3 139 for inclusion, studies will be required to meet the following criteria: (i) children age 0 to
4 140 10 years old (ii) exposure, breastfeeding in terms of duration and type (exclusivity or non-
5 141 exclusivity) and reported any type of measure; (iii) outcome, motor development
6 142 measured using standardised tests; and (iv) studies written in English or Spanish.

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10 143 Studies will be excluded when: (i) include infants born in multiple pregnancies, with
11 144 congenital infections or special circumstances requiring intensive care or hospitalization
12 145 during the neonatal period; (ii) include children with mental disorders or any detected
13 146 delay in communication, cognition or motor skills; (ii) breast milk has been
14 147 supplemented, (iii) multiple publication derived from a single study; and (iv) do not adjust
15 148 for confounding variates such as socioeconomic status and home environment.

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22 150 **Search methods for the identification of studies**

23 151 **Search strategy**

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27 152 The literature search will be conducted in MEDLINE (via PubMed), EMBASE (via
28 153 Scopus), Web of Science and Cochrane Library from inception to December 2019.
29 154 Searches for unpublished studies will be conducted at: OPEN GRAY, ProQuest
30 155 dissertations & Thesis Global, Theseo, Networked digital library of theses and
31 156 dissertations (NDLTD), and Google Scholar. A search of ClinicalTrials.gov and EudraCT
32 157 clinical trial records will also be conducted. The searches will be reviewed immediately
33 158 prior to the final analysis in order to identify further potential studies. Study records will
34 159 be managed using the Mendeley reference manager.

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40 160 The following search terms will be combined: breastfeeding, feeding, 'exclusive
41 161 breastfeeding', breastfed, 'breast suckling', suckling, 'motor skill', 'psychomotor
42 162 performance', 'motor development', 'psychomotor development', 'development
43 163 milestones', children, child, infant, childhood (Table 1). Previous reviews and meta-
44 164 analyses will be screened, as well as the reference lists of the selected studies to complete
45 165 the literature search.

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Table 1 Search strategy for MEDLINE database

Breastfeeding	AND	'motor skills'	AND	children
OR		OR		OR
feeding		'psychomotor		child
OR		performance'		OR
'exclusive		OR		infant
breastfeeding'		'motor development'		OR
OR		OR		childhood
breastfed		'psychomotor		
OR		development'		
'breast suckling'		OR		
OR		'motor development		
'suckling'		milestones'		

173 Selection of studies and data extraction

174 Two researchers will screen all relevant titles and abstracts of the retrieved publications
 175 to identify eligible studies. Inclusion and exclusion criteria will be applied to full texts to
 176 identify all potentially eligible articles. Inconsistencies in data collection will be solved
 177 by consensus. A third reviewer will be consulted when disagreements persist. The process
 178 of identifying, screening and including/excluding articles will be illustrated using the
 179 PRISMA²⁷ flow chart (Figure 1).

180 Finally, information about the main characteristics of the identified studies will be
 181 extracted, including the following data: i) first author's name, ii) publication year, iii)
 182 country, iv) study design, v) characteristics of the study population (sample size, age of
 183 children at evaluation, gender and number of participants in each group), vi) breastfeeding
 184 category (as defined in Table 2) and vii) test used for assessment of motor development,
 185 vii (Table 2). The authors of the included studies will be contacted to request any missing
 186 data.

Table 2 Characteristics of studies included in the systematic review and/or meta-analysis

Reference	Country	Study design	Population		Breastfeeding		Outcome MD	
			Sample size	Sample age	Categories	n	Tool	Measurement
First author's name and year of publication	Country	Design of the study	Number of participants	Age of participants (years)	Duration periods of exclusive breastfeeding /any breastfeeding	Number participants in each breastfeeding category	Instrument used to measure MD	Mean value (SD)

189 Key: MD, Motor Development; SD: Standard Deviation

190

191 **Assessment of risk of bias**

192 Two independent researchers will be blinded to the authors, titles and years of publication
 193 of the included studies to evaluate the risk of bias of each included study. The Critical
 194 Appraisal Checklist for Analytical Cross-Sectional Studies from The Joanna Briggs
 195 Institute will be used.³⁰ This tool evaluates the risk of bias according to eight items that
 196 could be scored as “Yes”, “No”, “Unclear” or “Not applicable”.

197 The Newcastle-Ottawa Quality Assessment Scale³¹ will be used to assess the risk of bias
 198 of longitudinal studies, including case control and cohort studies. This tool evaluates the
 199 risk of bias according to eight items which could be grouped in three categories: selection,
 200 comparability and exposure or outcome (for case control or cohort studies, respectively).
 201 Each study can be awarded one star for each item within the selection and exposure
 202 categories, and a maximum of two stars in the comparability category.

203 Any disagreements over the assessment of quality will be solved by consensus. A third
 204 researcher will be consulted if a consensus is not reached.

205

206 **Statistical analysis**

207 After data extraction, the reviewers will determine whether meta-analysis is possible. At
 208 least four studies addressing the association between breastfeeding and motor
 209 development will be required in order to conduct the meta-analysis. If meta-analysis is
 210 possible, STATA V.15 software will be used. The standardized mean difference will be

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3 211 calculated for each study reporting the association between breastfeeding category and
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5 212 motor development using Cohen's d index.³² To compute the pooled effect size (ES)
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7 213 estimates with 95% confidence intervals (CIs) fixed-effects models³³ will be used in the
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9 214 case of no heterogeneity; otherwise, random-effects model^{34,35} will be used We will
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11 215 compare the level of motor development in children who have been exclusively breastfed
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13 216 or breastfed for any length of time, as a reference group, with the motor development of
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15 217 those who have never been breastfed. If possible, a comparison between children
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17 218 breastfed for at least 6 months and children breastfed for less than 6 months will also be
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19 219 carried out.

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21 220 Heterogeneity will be assessed by computing the I² statistic.³⁶ The values of I² will be
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23 221 considered as follows: 0%–40% might not be important, 30%–60% may represent
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25 222 moderate heterogeneity, 50%–90% may represent substantial heterogeneity and 75%–
26
27 223 100% represents considerable heterogeneity.

28
29 224 Linear meta-analysis regression models will be used to explore whether covariates could
30
31 225 be associated with the magnitude of the effect and could explain the observed statistical
32
33 226 heterogeneity.³⁶ Finally, publication bias will be evaluated using a funnel plot according
34
35 227 to the method proposed by Egger.³⁷ When a meta-analysis is not feasible, we will perform
36
37 228 a narrative synthesis.

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230 *Subgroup analysis and meta-regression*

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41 231 If enough studies are available, subgroup analysis will be conducted. Several meta-
42
43 232 regressions will be performed on study and sample characteristics including the type of
44
45 233 motor development assessment (i.e., gross or fine motor), gender, age of study
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47 234 participants, birth weight, breastfeeding classification (never, less than 6 months or more
48
49 235 than 6 months) and aspects related to motor . Furthermore, the design and risk of bias
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51 236 scores of the studies will be considered for additional subgroup analysis. Additional
52
53 237 potential moderating variables may be identified after reviewing the literature.

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239 *Sensitivity analysis*

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57 240 We will perform sensitivity analysis by removing studies one by one from the main
58
59 241 analysis to assess the robustness of the findings.

242 **No patient and Public Involvement**

243 Existing databases will be used for the purpose of this study. Patients and public will not
244 be involved in the design of this study. This review will assess the effect of breastfeeding
245 on motor developmental outcomes in infants. Insights provided by this study could be
246 used in clinical practice to ameliorate outcomes; specifically, motor development; of
247 children in the population.

249 **DISCUSSION**

250 The aim of this study is to present an objective and transparent methodology to conduct
251 a systematic review and meta-analysis investigating whether the duration of
252 breastfeeding is associated with motor development.

253 Many studies have examined whether breastfeeding in early life, a critical phase of
254 development, could affect later cognitive function and motor development in
255 children.²⁰⁻²² Infant development is a complex process, which encompasses several
256 factors allowing the acquisition of skills that will contribute to the child's full
257 participation in activities and help to establish a direct relationship with the
258 environment.²⁰

259 Motor function is an accepted indicator of development during the first years of life.³⁸⁻⁴⁰
260 It directly contributes to and reflects the relationship that the child establishes with the
261 physical and social environments. In addition, motor development plays an important role
262 in other areas of development, such as physical growth and cardiorespiratory fitness, the
263 latter being a powerful and effective indicator of cardiovascular health.⁴¹⁻⁴³ Poor motor
264 development performance may incline children towards activity avoidance and sedentary
265 behaviours, which are linked to increased risk of chronic disease in adulthood.⁴⁴

266 There is considerable evidence about the long- and short-term benefits of breastfeeding
267 for infant health.¹⁶⁻¹⁹ However, no consensus has been reached about the effects of
268 breastfeeding on motor development, and the results and conclusions of existing studies
269 are controversial.^{21,25,26} The complexity of child development makes it difficult to
270 evaluate these effects, and certain aspects of infant development are influenced by
271 psychosocial and socioeconomic factors, which could contribute to some of the observed
272 differences. The scientific evidence regarding the benefits of breastfeeding in terms of

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3 273 motor development outcomes is weak, and the strength of this association is controversial
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5 274 because most studies lack adequate control for potential confounders. Furthermore,
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7 275 previous studies have measured infant development using different standardised tests.

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9 276 Potential limitations of this research could include publication bias, information bias,
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11 277 inclusion of articles in English and Spanish only, analysis of cross-sectional studies as
12
13 278 this does not allow a causal association to be evaluated (breastfeeding always precedes
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15 279 motor development), poor statistical analysis and inadequate reporting of methods and
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17 280 findings of the primary studies. To overcome these limitations, the systematic review and
18
19 281 meta-analysis will be conducted and reported by two independent reviewers and a third
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21 282 researcher will be consulted if inconsistencies exist in data collection or consensus is not
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23 283 reached. However, despite these strategies, is not possible to ensure the lack of risk of
24
25 284 bias. Furthermore; existing guidelines, the MOOSE statement, PRISMA, and Cochrane
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27 285 Collaboration Handbook recommendations will be followed.

28
29 286 To summarise, we will carry out a systematic review and meta-analysis with the objective
30
31 287 of reviewing existing literature on the relationship between breastfeeding and motor
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33 288 development. Despite the fact that some aspects of motor development appear to be
34
35 289 controversial, if this study confirms the positive effects of breastfeeding on motor skills
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37 290 development, it could encourage greater interest in breastfeeding within the areas of
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39 291 public and child health.

40
41 292 The lack of evidence on the effect of breastfeeding and motor skills development
42
43 293 highlights the need for guidelines or recommendations based on rigorous and updated
44
45 294 reviews summarizing the available scientific evidence, to be used in daily practice in
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47 295 order to improve the quality and effectiveness of interventions. The findings of this
48
49 296 review could lead to an improvement in the health status and development of children
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51 297 worldwide.

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54 299 **ETHICS AND DISSEMINATION**

55
56 300 The data included in this project will be provide by the original studies; therefore, ethical
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58 301 approval and informed consent of patients will not be required.

59
60 302 This protocol provides a clear and structured procedure to extract relevant information on
303 the association of breastfeeding and motor skills. This study will have clinical and public

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3 304 health implications, because it could provide support for recommendations on
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5 305 breastfeeding, which might help to prevent low rates of breastfeeding and early
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7 306 abandonment. Suggestions for future research will be made according to the findings of
8
9 307 this systematic review and meta-analysis, and evidence-based recommendations to
10
11 308 improve breastfeeding rates will be offered. Moreover, longitudinal studies will be
12
13 309 needed to confirm the duration effect of breastfeeding better associate with children's
14
15 310 motor development.

16 311

17
18 312 **Contributors:**

19
20 313 BN-P and MH-L designed the study. BN-P was the principal investigator and guarantor.
21
22 314 BN-P and MH-L were the main coordinators of the study. DPP-C, CA-B, CB-C, VM-V
23
24 315 and BN-P conducted the study. MH-L, DPP-C and VM-V gave statistical and
25
26 316 epidemiological support. MH-L wrote the article with the support of CB-C, VM-V and
27
28 317 BN-P. All authors reviewed and approved the final version of the manuscript.

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30 318 **Competing interests:**

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32 319 All authors have completed the ICMJE uniform disclosure form at
33
34 320 www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the
35
36 321 submitted work; no financial relationships with any organisations that might have an
37
38 322 interest in the submitted work in the previous three years; no other relationships or
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40 323 activities that could appear to have influenced the submitted work.

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42
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44
45 326 **Data sharing:**

46
47 327 Extra data is available by emailing: celia.alvarezbuena@uclm.es

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49 328 **Transparency**

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51 329 The manuscripts guarantor (BN-P) affirms that the manuscript is an honest, accurate, and
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53 330 transparent account of the study being reported; that no important aspects of the study
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55 331 have been omitted; and that any discrepancies from the study as planned have been
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57 332 explained.
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456 TABLES LEGENDS

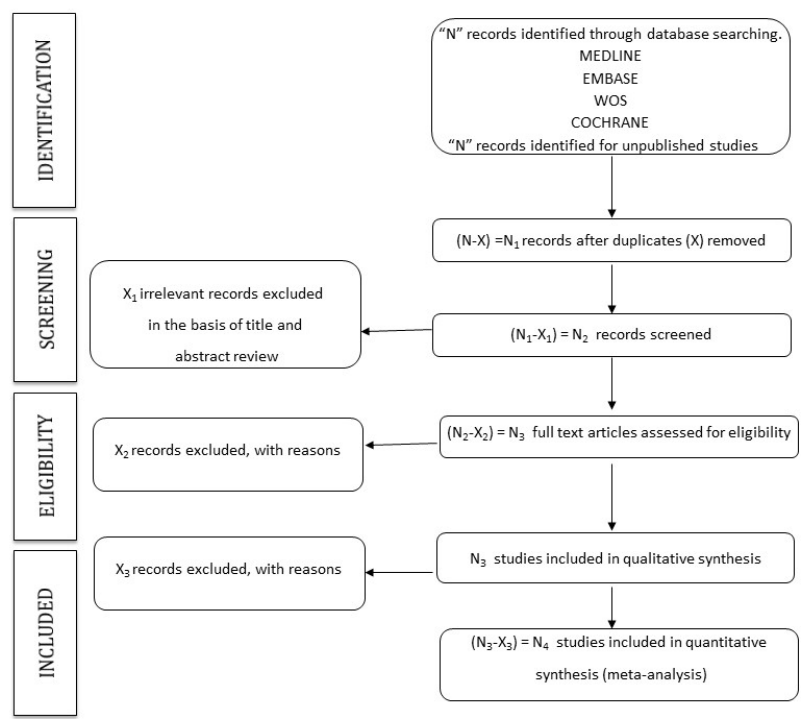
457 **Table 1.** Search strategy for the MEDILINE database.

458 **Table 2.** Characteristics of studies included in the systematic review and/or meta-
459 analysis.

460 FIGURE LEGENDS

461 **Figure 1.** PRISMA (Preferred Reporting Items for Systematic Review and Meta-
462 Analysis) flow diagram of identification, screening, eligibility and inclusion of studies

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254x190mm (96 x 96 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration: p. 2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors: pp. 1, 13		
Contact: p. 1	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p. 13	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support: NA		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: pp 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: pp. 5, 6	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources: p. 6	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 6, 7	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records: pp. 7, 8		
Data management: p. 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

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Selection process: p. 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: p. 7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: pp 7, 10	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: pp. 7, 8	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p. 8	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp 9, 10	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I ² , Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

The relationship between breastfeeding and motor development in children: a protocol for a systematic review and meta-analysis.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-029063.R2
Article Type:	Protocol
Date Submitted by the Author:	05-Aug-2019
Complete List of Authors:	Hernández Luengo, Monserrat; Universidad de Castilla-La Mancha, Social and Health Care Research Center Álvarez-Bueno, Celia; Universidad de Castilla-La Mancha, Social and Health Care Research Center Pozuelo-Carrascosa, Diana P; Universidad de Castilla-La Mancha, Social and Health Care Research Center Berlanga-Macías, Carlos; Universidad de Castilla-La Mancha, Social and Health Care Research Center Martinez-Vizcaino, Vicente; Universidad de Castilla-La Mancha, Centro de Estudios Sociosanitarios Notario-Pacheco, Blanca; Universidad de Castilla-La Mancha, Faculty of Nursing
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	General practice / Family practice
Keywords:	breastfeeding, motor development, motor skills, children

SCHOLARONE™
Manuscripts

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3 **1 Protocol manuscript**
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5 2 The relationship between breastfeeding and motor development in children: a protocol
6 3 for a systematic review and meta-analysis.
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10 **4 Authors and affiliations:**

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40 **17 Word count: 2562**
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3 19 **ABSTRACT**
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5 20 **Introduction:**
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8 21 The recommendations of most health organizations encourage mothers to keep exclusive
9 22 breastfeeding during the first 6 months and combining breastfeeding with the
10 23 complementary feed at least the first and second years, due to the numerous immunologic,
11 24 cognitive developmental and motor skill benefits that breastfeeding confers. Although the
12 25 influence of breastfeeding on motor development during childhood has been studied, the
13 26 findings are inconsistent, and some studies have even reported no effect. This manuscript
14 27 presents a protocol for a systematic review and meta-analysis, with the aim of reviewing
15 28 the relationship between breastfeeding and motor skill development in children; in terms
16 29 of duration, exclusivity or non-exclusivity of breastfeeding.
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24 30 **Methods and analysis:**
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26 31 To identify relevant studies, the search will be conducted using MEDLINE (via PubMed),
27 32 EMBASE, Web of Science and Cochrane Library from inception to December 2019.
28 33 Observational studies (Cross-sectional and follow up studies) written in English or
29 34 Spanish that investigate the association between breastfeeding and motor development in
30 35 children will be included. This systematic review and meta-analysis protocol follows the
31 36 Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
32 37 (PRISMA-P). A Critical Appraisal Checklist for Analytical Cross-Sectional Studies and
33 38 The Newcastle-Ottawa Quality Assessment Scale for longitudinal studies will be used to
34 39 assess the quality of included studies. The effect of breastfeeding on motor skill
35 40 development will be calculated as the primary outcome. Subgroup analyses will be carried
36 41 out based on the characteristics of motor skill development and the population included.
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46 42 **Ethics and dissemination**
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48 43 Ethical approval is not required because the data used for will be obtained from published
49 44 studies and there will be no concerns about privacy. The findings from this study will be
50 45 relevant information regarding the association of breastfeeding and motor development
51 46 in children and could be used encourage to improve breastfeeding rates. The results will
52 47 be published in a peer-reviewed journal.
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58 48 **Trial registration number:** PROSPERO CRD42018093706. (24/04/2018)

59 49 **Keywords:** breastfeeding, motor development, motor skills, children.
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Strengths and limitations of this study

- This review will present a comprehensive and standardised methodology, according to an established framework, to identify relevant studies that analyse the effect of breastfeeding on motor skills.
- Analysis of different sources of heterogeneity and the assessment of risk of bias of the included studies will be performed independently by two researchers.
- To identify studies that aim to determine the association between breastfeeding and motor development, an exhaustive literature search will be carried out.
- This study could be limited by the quality of available studies, insufficient methodological rigor and statistical heterogeneity.
- Different methods used for measuring breastfeeding and motor development from observational studies may be another limitation to the quality of evidence of this study.

77 INTRODUCTION

78 The first two years of a child's life is a critical period for health, growth and development;
79 all of which are affected by nutritional status. It is well documented that breastfeeding
80 provides many important health benefits to children and mothers and is considered the
81 gold standard in infant feeding.^{1,2}

82 The World Health Organization (WHO) recommends exclusive breastfeeding for the first
83 6 months of life as an ideal feed, and continuation of breastfeeding for at least the first
84 and second years, which is also supported by many health organizations.¹⁻⁶ However, the
85 European Society for Paediatric Gastroenterology, Hepatology and Nutrition
86 (ESPGHAN) differs in the recommendation of the age when complementary feed should
87 be included because of the risk of food allergies.⁷ The World Health Assembly, as part
88 of its Global Strategy for the Feeding of Infants and Young Children, encouraged Member
89 States to promote exclusive breastfeeding for 6 months as a global public health
90 recommendation which provides many benefits to babies, reduces the risk of diseases and
91 helps to promote good physical and cognitive growth.^{8,9}

92 However, the rates of breastfeeding at 6 months remain low in Europe; and even in
93 countries where initial rates are high, there is a marked decrease by the sixth month.¹⁰⁻¹¹
94 Early cessation of breastfeeding and the introduction of solids before 4 months could have
95 considerable adverse effects on the children and women's health.¹²⁻¹⁵ Therefore, it is
96 important to elucidate what are the reasons behind the failure to achieve the
97 recommendations, and there is a need for greater efforts to disseminate the benefits of
98 breastfeeding and create a social environment that could favour it.

99 Although infant development is a process that is influenced by several factors,
100 breastfeeding in the first months of life is a key determinant for optimal growth and
101 adequate cognitive and motor development. Additionally, breastfeeding provides quality
102 nutrients improvement (higher proportion of unsaturated fatty acids), prevents
103 gastrointestinal infection and decreases the risk of diseases later in life such as allergies,
104 asthma, obesity and celiac disease.^{2,3,7,9,12,16-19}

105 Thus, motor development and cognitive function represent indicators of overall
106 development during the first years. Motor development allows the acquisition of skills
107 that will contribute to a child's full participation in activities, avoiding sedentary
108 behaviours and will help to establish a direct and active relationship with the

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3 109 environment.^{20,21} Although consistent evidence of the positive effects of extended
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5 110 breastfeeding on cognitive function has been reported,²² few studies have focused on
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7 111 motor development. The relationship between motor development and breastfeeding is
8
9 112 difficult to analyse because incomplete control for confounders is reported in the current
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11 113 literature, even when various assessments of motor milestones are considered across
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13 114 studies. To date, no clear associations between the duration of breastfeeding and motor
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15 115 development have been reported.²³⁻²⁶

16 116 The purpose of this study protocol is to provide a clear methodology to review the effects
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18 117 of breastfeeding practices on motor development in children, in terms of duration and
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20 118 exclusive or not exclusive breastfeeding.

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23 24 120 **OBJECTIVE**

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26 121 The aim of this protocol study is to present an objective and transparent methodology to
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28 122 conduct a systematic review and meta-analysis aimed to increase knowledge and
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30 123 understanding of the associations between the duration and exclusivity of breastfeeding
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32 124 and motor development in children age 0 to 10 years old.

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35 36 126 **METHODS AND ANALYSIS**

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39 127 The methodology of this protocol was reported in accordance with the Preferred
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41 128 Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P)²⁷.
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43 129 The Meta-analysis of observational studies in epidemiology: a proposal for reporting
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45 130 (MOOSE²⁸), the Preferred Reporting Items for Systematic Reviews and Meta-analyses
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47 131 (PRISMA) and Cochrane Collaboration Handbook²⁹ will be used to report and guide the
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49 132 review methods. This protocol was registered with PROSPERO, (Registration number
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51 133 CRD42018093706) on 24 April 2018.

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54 135 **Inclusion/exclusion criteria for study selection**

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56 136 Studies will be retrieved from the literature by searching for studies which measure the
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58 137 effects of breastfeeding duration and type (exclusivity, even if it is little, or no exclusive
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60 138 breastfeeding), and report any type of measure of motor development. To be considered

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3 139 for inclusion, studies will be required to meet the following criteria: (i) children age 0 to
4 140 10 years old (ii) exposure, breastfeeding in terms of duration and type (exclusivity or non-
5 141 exclusivity) and reported any type of measure; (iii) outcome, motor development
6 142 measured using standardised tests; and (iv) studies written in English or Spanish.

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10 143 Studies will be excluded when: (i) include infants born in multiple pregnancies, with
11 144 congenital infections or special circumstances requiring intensive care or hospitalization
12 145 during the neonatal period; (ii) include children with mental disorders or any detected
13 146 delay in communication, cognition or motor skills; (ii) breast milk has been
14 147 supplemented, (iii) multiple publication derived from a single study; and (iv) do not adjust
15 148 for confounding variates such as socioeconomic status and home environment.

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22 150 **Search methods for the identification of studies**

23 151 **Search strategy**

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27 152 The literature search will be conducted in MEDLINE (via PubMed), EMBASE (via
28 153 Scopus), Web of Science and Cochrane Library from inception to December 2019.
29 154 Searches for unpublished studies will be conducted at: OPEN GRAY, ProQuest
30 155 dissertations & Thesis Global, Theseo, Networked digital library of theses and
31 156 dissertations (NDLTD), and Google Scholar. A search of ClinicalTrials.gov and EudraCT
32 157 clinical trial records will also be conducted. The searches will be reviewed immediately
33 158 prior to the final analysis in order to identify further potential studies. Study records will
34 159 be managed using the Mendeley reference manager.

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40 160 The following search terms will be combined: breastfeeding, feeding, 'exclusive
41 161 breastfeeding', breastfed, 'breast suckling', suckling, 'motor skill', 'psychomotor
42 162 performance', 'motor development', 'psychomotor development', 'development
43 163 milestones', children, child, infant, childhood (Table 1). Previous reviews and meta-
44 164 analyses will be screened, as well as the reference lists of the selected studies to complete
45 165 the literature search.

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Table 1 Search strategy for MEDLINE database

Breastfeeding	AND	'motor skills'	AND	children
OR		OR		OR
feeding		'psychomotor		child
OR		performance'		OR
'exclusive		OR		infant
breastfeeding'		'motor development'		OR
OR		OR		childhood
breastfed		'psychomotor		
OR		development'		
'breast suckling'		OR		
OR		'motor development		
'suckling'		milestones'		

173 Selection of studies and data extraction

174 Two researchers will screen all relevant titles and abstracts of the retrieved publications
 175 to identify eligible studies. Inclusion and exclusion criteria will be applied to full texts to
 176 identify all potentially eligible articles. Inconsistencies in data collection will be solved
 177 by consensus. A third reviewer will be consulted when disagreements persist. The process
 178 of identifying, screening and including/excluding articles will be illustrated using the
 179 PRISMA²⁷ flow chart (Figure 1).

180 Finally, information about the main characteristics of the identified studies will be
 181 extracted, including the following data: i) first author's name, ii) publication year, iii)
 182 country, iv) study design, v) characteristics of the study population (sample size, age of
 183 children at evaluation, gender and number of participants in each group), vi) breastfeeding
 184 category (as defined in Table 2) and vii) test used for assessment of motor development,
 185 vii (Table 2). The authors of the included studies will be contacted to request any missing
 186 data.

Table 2 Characteristics of studies included in the systematic review and/or meta-analysis

Reference	Country	Study design	Population		Breastfeeding		Outcome MD	
			Sample size	Sample age	Categories	n	Tool	Measurement
First author's name and year of publication	Country	Design of the study	Number of participants	Age of participants (years)	Duration periods of exclusive breastfeeding /any breastfeeding	Number participants in each breastfeeding category	Instrument used to measure MD	Mean value (SD)

189 Key: MD, Motor Development; SD: Standard Deviation

190

191 **Assessment of risk of bias**

192 Two independent researchers will be blinded to the authors, titles and years of publication
 193 of the included studies to evaluate the risk of bias of each included study. The Critical
 194 Appraisal Checklist for Analytical Cross-Sectional Studies from The Joanna Briggs
 195 Institute will be used.³⁰ This tool evaluates the risk of bias according to eight items that
 196 could be scored as “Yes”, “No”, “Unclear” or “Not applicable”.

197 The Newcastle-Ottawa Quality Assessment Scale³¹ will be used to assess the risk of bias
 198 of longitudinal studies, including case control and cohort studies. This tool evaluates the
 199 risk of bias according to eight items which could be grouped in three categories: selection,
 200 comparability and exposure or outcome (for case control or cohort studies, respectively).
 201 Each study can be awarded one star for each item within the selection and exposure
 202 categories, and a maximum of two stars in the comparability category.

203 Any disagreements over the assessment of quality will be solved by consensus. A third
 204 researcher will be consulted if a consensus is not reached.

205

206 **Statistical analysis**

207 After data extraction, the reviewers will determine whether meta-analysis is possible. At
 208 least four studies addressing the association between breastfeeding and motor
 209 development will be required in order to conduct the meta-analysis. If meta-analysis is
 210 possible, STATA V.15 software will be used. The standardized mean difference will be

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3 211 calculated for each study reporting the association between breastfeeding category and
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5 212 motor development using Cohen's d index.³² To compute the pooled effect size (ES)
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7 213 estimates with 95% confidence intervals (CIs) fixed-effects models³³ will be used in the
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9 214 case of no heterogeneity; otherwise, random-effects model^{34,35} will be used. We will
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11 215 compare the level of motor development in children who have been exclusively breastfed
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13 216 or breastfed for any length of time, as a reference group, with the motor development of
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15 217 those who have never been breastfed. If possible, a comparison between children
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17 218 breastfed for at least 6 months and children breastfed for less than 6 months will also be
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19 219 carried out.

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21 220 We also will provide further information on the main confounders for our research. Some
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23 221 confounders we will require in order to get full points of the quality assessment of the
24
25 222 published studies, are social class, mother's and father's education level, maternal age,
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27 223 home stimulation and maternal smoking during pregnancy.

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29 224 Heterogeneity will be assessed by computing the I² statistic.³⁶ The values of I² will be
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31 225 considered as follows: 0%–40% might not be important, 30%–60% may represent
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33 226 moderate heterogeneity, 50%–90% may represent substantial heterogeneity and 75%–
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35 227 100% represents considerable heterogeneity.

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37 228 Linear meta-analysis regression models will be used to explore whether covariates could
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39 229 be associated with the magnitude of the effect and could explain the observed statistical
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41 230 heterogeneity.³⁶ Finally, publication bias will be evaluated using a funnel plot according
42
43 231 to the method proposed by Egger.³⁷ When a meta-analysis is not feasible, we will perform
44
45 232 a narrative synthesis.

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48 234 *Subgroup analysis and meta-regression*

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50 235 If enough studies are available, subgroup analysis will be conducted. Several meta-
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52 236 regressions will be performed on study and sample characteristics including the type of
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54 237 motor development assessment (i.e., gross or fine motor), gender, age of study
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56 238 participants, birth weight, breastfeeding classification (never, less than 6 months or more
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58 239 than 6 months) and aspects related to motor. If possible, the method of breast milk feeding
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60 240 will be investigated by subgroup analysis. Furthermore, the design and risk of bias scores
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242 of the studies will be considered for additional subgroup analysis. Additional potential
moderating variables may be identified after reviewing the literature.

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5 244 *Sensitivity analysis*

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8 245 We will perform sensitivity analysis by removing studies one by one from the main
9 246 analysis to assess the robustness of the findings.

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12 247 **Patient and Public Involvement**

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14 248 Existing databases will be used for the purpose of this study. Patients and public will not
15 249 be involved in the design of this study. This review will assess the effect of breastfeeding
16 250 on motor developmental outcomes in infants. Insights provided by this study could be
17 251 used in clinical practice to ameliorate outcomes; specifically, motor development; of
18 252 children in the population.

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25 254 **DISCUSSION**

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28 255 The aim of this study is to present an objective and transparent methodology to conduct
29 256 a systematic review and meta-analysis investigating whether the duration of
30 257 breastfeeding is associated with motor development.

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33 258 Many studies have examined whether breastfeeding in early life, a critical phase of
34 259 development, could affect later cognitive function and motor development in
35 260 children.²⁰⁻²² Infant development is a complex process, which encompasses several
36 261 factors allowing the acquisition of skills that will contribute to the child's full
37 262 participation in activities and help to establish a direct relationship with the
38 263 environment.²⁰

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44 264 Motor function is an accepted indicator of development during the first years of life.³⁸⁻⁴⁰
45 265 It directly contributes to and reflects the relationship that the child establishes with the
46 266 physical and social environments. In addition, motor development plays an important role
47 267 in other areas of development, such as physical growth and cardiorespiratory fitness, the
48 268 latter being a powerful and effective indicator of cardiovascular health.⁴¹⁻⁴³ Poor motor
49 269 development performance may incline children towards activity avoidance and sedentary
50 270 behaviours, which are linked to increased risk of chronic disease in adulthood.⁴⁴

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57 271 There is considerable evidence about the long- and short-term benefits of breastfeeding
58 272 for infant health.¹⁶⁻¹⁹ However, no consensus has been reached about the effects of

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3 273 breastfeeding on motor development, and the results and conclusions of existing studies
4 are controversial.^{21,25,26} The complexity of child development makes it difficult to
5 274 evaluate these effects, and certain aspects of infant development are influenced by
6 275 psychosocial and socioeconomic factors, which could contribute to some of the observed
7 276 differences. The scientific evidence regarding the benefits of breastfeeding in terms of
8 277 motor development outcomes is weak, and the strength of this association is controversial
9 278 because most studies lack adequate control for potential confounders. Furthermore,
10 279 previous studies have measured infant development using different standardised tests.
11 280

12 281 Potential limitations of this research could include publication bias, information bias,
13 282 inclusion of articles in English and Spanish only, analysis of cross-sectional studies as
14 283 this does not allow a causal association to be evaluated (breastfeeding always precedes
15 284 motor development), poor statistical analysis and inadequate reporting of methods and
16 285 findings of the primary studies. To overcome these limitations, the systematic review and
17 286 meta-analysis will be conducted and reported by two independent reviewers and a third
18 287 researcher will be consulted if inconsistencies exist in data collection or consensus is not
19 288 reached. However, despite these strategies, is not possible to ensure the lack of risk of
20 289 bias. Furthermore; existing guidelines, the MOOSE statement, PRISMA, and Cochrane
21 290 Collaboration Handbook recommendations will be followed.

22 291 To summarise, we will carry out a systematic review and meta-analysis with the objective
23 292 of reviewing existing literature on the relationship between breastfeeding and motor
24 293 development. Despite the fact that some aspects of motor development appear to be
25 294 controversial, if this study confirms the positive effects of breastfeeding on motor skills
26 295 development, it could encourage greater interest in breastfeeding within the areas of
27 296 public and child health.

28 297 The lack of evidence on the effect of breastfeeding and motor skills development
29 298 highlights the need for guidelines or recommendations based on rigorous and updated
30 299 reviews summarizing the available scientific evidence, to be used in daily practice in
31 300 order to improve the quality and effectiveness of interventions. The findings of this
32 301 review could lead to an improvement in the health status and development of children
33 302 worldwide.

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3 305 **ETHICS AND DISSEMINATION**
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5 306 The data included in this project will be provide by the original studies; therefore, ethical
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7 307 approval and informed consent of patients will not be required.
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10 308 This protocol provides a clear and structured procedure to extract relevant information on
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12 309 the association of breastfeeding and motor skills. This study will have clinical and public
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14 310 health implications, because it could provide support for recommendations on
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16 311 breastfeeding, which might help to prevent low rates of breastfeeding and early
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18 312 abandonment. Suggestions for future research will be made according to the findings of
19
20 313 this systematic review and meta-analysis, and evidence-based recommendations to
21
22 314 improve breastfeeding rates will be offered. Moreover, longitudinal studies will be
23
24 315 needed to confirm the duration effect of breastfeeding better associate with children's
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26 316 motor development.
27

28 317
29 318 **Contributors:**

30 319 BN-P and MH-L designed the study. BN-P was the principal investigator and guarantor.
31
32 320 BN-P and MH-L were the main coordinators of the study. DPP-C, CA-B, CB-M, VM-V
33
34 321 and BN-P conducted the study. MH-L, DPP-C and VM-V gave statistical and
35
36 322 epidemiological support. MH-L wrote the article with the support of CB-M, VM-V and
37
38 323 BN-P. All authors reviewed and approved the final version of the manuscript.
39

40 324 **Competing interests:**

41
42 325 None declared. All authors have completed the ICMJE uniform disclosure form at
43
44 326 www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the
45
46 327 submitted work; no financial relationships with any organisations that might have an
47
48 328 interest in the submitted work in the previous three years; no other relationships or
49
50 329 activities that could appear to have influenced the submitted work.

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52
53
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55
56 332 **Data sharing:**

57
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59 333 Extra data is available by emailing: celia.alvarezbueno@uclm.es
60

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2
3 334 **Transparency**
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5 335 The manuscripts guarantor (BN-P) affirms that the manuscript is an honest, accurate, and
6
7 336 transparent account of the study being reported; that no important aspects of the study
8
9 337 have been omitted; and that any discrepancies from the study as planned have been
10
11 338 explained.

12
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462 TABLES LEGENDS

463 **Table 1.** Search strategy for the MEDILINE database.

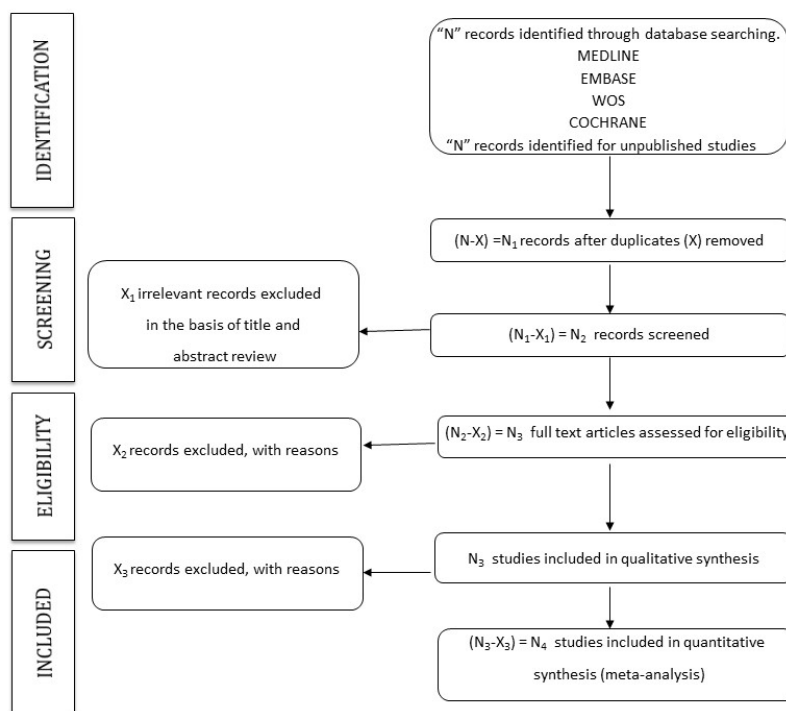
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3 464 **Table 2.** Characteristics of studies included in the systematic review and/or meta-
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5 465 analysis.
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7 466 **FIGURE LEGENDS**
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10 467 **Figure 1.** PRISMA (Preferred Reporting Items for Systematic Review and Meta-
11 468 Analysis) flow diagram of identification, screening, eligibility and inclusion of studies
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For peer review only



254x190mm (96 x 96 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification: p. 1	1a	Identify the report as a protocol of a systematic review
Update: NA	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration: p. 2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors: pp. 1, 13		
Contact: p. 1	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions: p. 13	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments: NA	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support: NA		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale: pp 4, 5	6	Describe the rationale for the review in the context of what is already known
Objectives p. 5	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria: pp. 5, 6	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources: p. 6	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy: pp. 6, 7	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records: pp. 7, 8		
Data management: p. 7	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process: p. 7	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process: p. 7	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items: pp 7, 10	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization: pp. 7, 8	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies: p. 8	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis: pp 9, 10	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es): NA	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence: NA	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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