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Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.

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Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.

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Abstract

Introduction: Several techniques have been proposed to manage Dental Fear/Dental Anxiety (DF/DA) in children and adolescents undergoing dental procedures. To our knowledge, no widely available compendium of therapies to manage DF/DA exists. We propose a study protocol to assess the evidence regarding pharmacological and non-pharmacological interventions to relieve dental anxiety in children and adolescents.

Methods and analysis: In our systematic review, we will include Randomised Controlled Trials (RCT), Controlled Clinical Trials (CCT) and Systematic Reviews (SR) of RCTs and CCTs that investigated the effects of pharmacological and non-pharmacological interventions to decrease dental anxiety in children and adolescents. We will search The Cochrane Database of Systematic Reviews (CDSR), The Cochrane Database of Abstracts of Reviews of Effects (DARE), The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, PsycINFO, CINAHL and the Web of Science for relevant studies. Pairs of authors will independently review all titles, abstracts, and full-texts identified by the specific literature search, and extract data using a structured data extraction form. For each study, information will be extracted on the study report (e.g., author, year of publication), the study design (e.g., the methodology and, for SRs, the types and number of studies included), the population characteristics, the intervention(s), the outcome measures and the results. The quality of SRs will be assessed using the AMSTAR (A Measurement Tool to Assess Reviews) instrument, while the quality of the retrieved RCTs and CCTs will be evaluated using the Cochrane Handbook for Systematic Reviews of Interventions criteria. A narrative description of all the included studies will be provided.

Ethics and dissemination: Approval from an ethics committee is not required, as no primary data will be collected. Results will be disseminated through a peer-reviewed publication and conference presentations.

Strengths and limitations of this study

- The strength of this study is its extensive, comprehensive systematic reviews concerning pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DF/DA) in children and adolescents undergoing dental procedures as well as an assessment of the quality of evidence of the included studies will be performed in this review.
- A limitation of the study is that we will not perform, for a reason of time, a systematic review of the concurrent literature.

Introduction

Dental Fear (DF) usually indicates a normal unpleasant emotional reaction to specific threatening stimuli occurring in situations associated with dental treatment, while Dental Anxiety (DA) is an excessive and unreasonable negative emotional state experienced by dental patients. These psychological states consist of apprehension that something dreadful is going to happen in relation to dental treatment. In the scientific literature DF and DA often are used indistinctly.[1] DF/DA has been identified as a significant and common problem in children and adolescents, with a mean prevalence ranging between 10% and 20%, being particularly high in the earliest ages.[2] There is a general agreement on the consequences of DA Dental avoidance, which is the failure to attend dental clinics, is a major consequence to DA.[3] The measurement of anxiety is a vital step towards the management of the existing anxiety in dental settings. Four measures are generally used to assess the level of DA: (a) “behavioural rating scale”, in which the dental team or researchers are asked to rate both the emotional and behavioral reactions shown by the children during the treatment; (b) “psychometric assessment” in which the children or one of their parents have to complete a questionnaire, usually before the treatment, to indicate the child’s level of anxiety associated with various common dental situations; (c) “physiological response analysis” in which the variations linked to the manifestation of anxiety are measured, such as salivary cortisol levels and (d) “projective test” based on psychological interpretation of children pictures concerning elements of dental setting.[4-6] Anxiety during dental treatment prevent the patient from cooperating fully with the dentist resulting in loss of time, increasing difficulty in performing dental procedures and unsatisfactory results.[7-11] In order to contain the anxiety of children and adolescents, both pharmacological (e.g., conscious sedation, nitrous oxide, general anaesthesia) and non-pharmacological techniques (e.g., voice control, positive reinforcement, distraction, non verbal communication and hypnosis) have been proposed.[12] While many examples of approaches and techniques to reduce DF/DA exist, to date there is no widely used compendium of pharmacological and non-pharmacological therapies for the management of DF/DA in children and adolescents. This might contribute to the underuse of effective techniques to reduce DF/DA in clinical practice.

To fill this knowledge gap we propose a protocol for the assessment of the evidence of pharmacological and non-pharmacological interventions for relieving anxiety in children and adolescents undergoing dental procedures.

Objective

The primary objective of this review is to assess the efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients undergoing dental procedures.

Methods

Criteria for considering studies for this review

Types of studies

Systematic Reviews (SRs) of Randomised Controlled Trials and/or Controlled Clinical Trials, Randomised Controlled Trials (RCT) and Controlled Clinical Trials (CCT) assessing the effects of pharmacological and non-pharmacological interventions aimed to decrease the levels of dental anxiety in children and adolescents will be considered. Publications written in languages other than English language will be excluded.

Types of participants

Children and adolescents between the ages of 0 and 18 years attending a dental centre for dental visit/treatment.

Types of interventions

Any pharmacological and non-pharmacological intervention aimed at reducing levels of DA. This should include -but is not limited to- the list of the American Academy of Pediatric Dentistry: mild sedation, medium sedation, deep sedation, general anaesthesia, voice control, positive reinforcement, distraction, non verbal communication, tell- show-do, and physical restraint. Furthermore, children and adolescents, receiving a mixed intervention will be included. We will consider studies comparing the intervention(s) of interest versus the following controls:

- no intervention or placebo;
- other type of pharmacological and/or non-pharmacological intervention.

Types of outcome measures

Primary outcomes

- Anxiety levels measured by a validated behavioral rating scale;
- Anxiety levels measured by a validated physiological measure,
- Anxiety levels measured by a validated questionnaire;
- Anxiety levels measured by a validated projective test;
- Completion of dental treatment (yes/no);
- Adverse events associated with the intervention.

Secondary outcomes

- Operator preference/fatigue in operator;
- Patient satisfaction;
- Parental satisfaction;
- Time taken to undertake the intervention;

- Duration of dental treatment.

Search methods for identification of SRs

We will attempt to identify all relevant SRs providing data on the issue, published in English between 2000 and 31th December 2016. Publications written in a language other than English, will not be included.

Electronic searches

To identify the records of interest we will use the following terms to formulate specific search strategy: *dental fear, dental anxiety*, *dental phobia and odontophobia.*

The search string will be used in the following databases:

- Cochrane Database of Systematic Reviews (CDSR);
- Cochrane Database of Abstracts of Reviews of Effects (DARE);
- PubMed;
- Embase;
- Psychology & Behavioral Sciences Collection;
- CINAHL;
- Web Of Science.

All eligible studies retrieved from the searches will be checked for relevant references.

Study selection

Two authors will independently assess SRs as being 'for exclusion', for 'inclusion', or 'potentially eligible' on the basis of title and abstract. Two criteria will be considered for further evaluation of an abstract: a) a publication defined as a review or meta-analysis, b) the mention of any pharmacological or non-pharmacological intervention for dental anxiety management. Subsequently, full-texts of relevant abstracts will be obtained and screened to identify SRs of interest based on the following inclusion criteria:

1. The use of at least one medical literature database;
2. The inclusion of at least one primary study (RCT or CCT);
3. The use of at least one pharmacological or non-pharmacological intervention for the management of dental anxiety in children and adolescents between the ages of 0 and 18 years old attending a dental centre for dental visit/treatment;
4. Two independent authors will judge their suitability for inclusion against the inclusion criteria. Disagreement will be resolved by discussion and, if necessary, by a third independent reviewer.

The process of published study selection will be presented in a PRISMA flow diagram (Figure 1)[13]. Studies that will be excluded at this stage will be placed in a detailed excluded studies table along with reasons for their exclusion.

Data extraction and management

Two review authors will independently and in duplicate extract data from included SRs, and disagreements will be resolved by a consensus meeting with a third review author.

The data extracted will provide information on the following review criteria: study information (author, year of publication, country), database used, types and number of studies included, population characteristics, intervention(s) description, outcome(s) measures used and results. If the review contains meta-analyses we will extract pooled results. Funding and author's conflict of interest will be extracted, too.

If any information from the review is unclear or missing, we will access the published reports of the individual trials and contact individual researchers.

Search methods for identification of RCTs and CCTs

We will attempt to identify any relevant clinical trial providing data on the efficacy and safety of interventions to decrease DF/DA published in English between 1990 and [31] December 2016. Papers written in a language other than English will not be included**.**

Electronic searches

To identify the records of interest we will use the following terms to formulate specific search strategy: *dental fear, dental anxiety*, *dental phobia and odontophobia*.

This search strategy will be used in the following database:

- Cochrane Central Register of Controlled Trials (CENTRAL);
- PubMed;
- Embase;
- Psychology & Behavioral Sciences Collection;
- CINAHL;
- Web Of Science.

Searching other resources

We will check the bibliographies of included studies in order to identify further relevant studies.

Study selection

The titles and abstracts resulting from the searches will be independently screened by two review authors to select potentially relevant studies. These studies will be obtained in full text and their

inclusion assessed independently and in duplicate. Any discrepancies with respect to the inclusion or suitability of the papers will be resolved by discussion and, if necessary, by a third independent reviewer. Primary studies already contained in the included SRs will not be considered. The process of published study selection will be presented in a PRISMA flow diagram (Figure 2)[13]. Studies excluded at this stage will be recorded in a table along with detailed information on reasons for their exclusion.

Data extraction and management

Two researchers will independently and in duplicate extract data from primary studies, and disagreements will be resolved by consensus with a third researcher.

The data extracted will provide information on the following study characteristics: study information (author, year of publication, country), study design, population characteristics, intervention(s) description, outcome(s) measures used and results. Funding and author's conflict of interest will also be extracted.

Assessing the methodological quality of evidence in included studies

Quality of evidence for included SRs

We will assess the methodological quality of each systematic review using the AMSTAR (A Measurement Tool to Assess Reviews) instrument to appraise the quality.[14] AMSTAR appraises the quality of reviews using the following 11 items: duplicate study selection and data extraction, comprehensive searching of the literature, provision of a list of included and excluded studies, provision of characteristics of included studies, assessment of methodological quality of included studies, appropriate methods for combining results of studies and for assessing publication bias, and consideration of conflict of interest statement.[14] Two reviewers will independently evaluate the quality of the SRs and disagreement will be resolved by consensus. Where there are multiple reviews that answer the same clinical question, the reviews with the highest score will be prioritised in the evidence retrieval and assessment.

Quality of evidence for RCTs and CCTs

The quality of evidence for retrieved RCTs and CCTs will be assessed using the criteria from the Cochrane Handbook for Systematic Reviews of Interventions.[15,16] We will assess studies according to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other potential items that can be a source of bias. We will assign risk of bias to one of three categories on the basis of the reviewer's judgement, that is, low risk, unclear risk and high risk. Given that participants and personnel might not always be blinded due to the nature of the non-

pharmacological interventions, performance bias will usually not be used for downgrading the level of evidence within the risk of bias assessment.

Data Synthesis

We will present narrative descriptions of the evidence for the included individual studies.

Ethics and dissemination

Approval from an ethics committee is not required as no primary data will be collected. Results will be disseminated through a peer-reviewed publication and conference presentations.

Acknowledgements The authors acknowledge the contribution of Silvano Gallus for his precious hints.

Contributors SC, LP, RG, AM and EL conceived, drafted and approved the final version of the protocol.

Funding This study is funded by the National Centre for Disease Prevention and Control - Ministry of Health, (Grant CCM 2015). The study sponsor is not involved in the study design and collection, analysis, and interpretation of data, or the writing of the article or the decision to submit it for publication. The authors are independent from study sponsors.

Data sharing statement The findings of this systematic review will be disseminated via peer-reviewed publications and conference presentations. All the data will be available.

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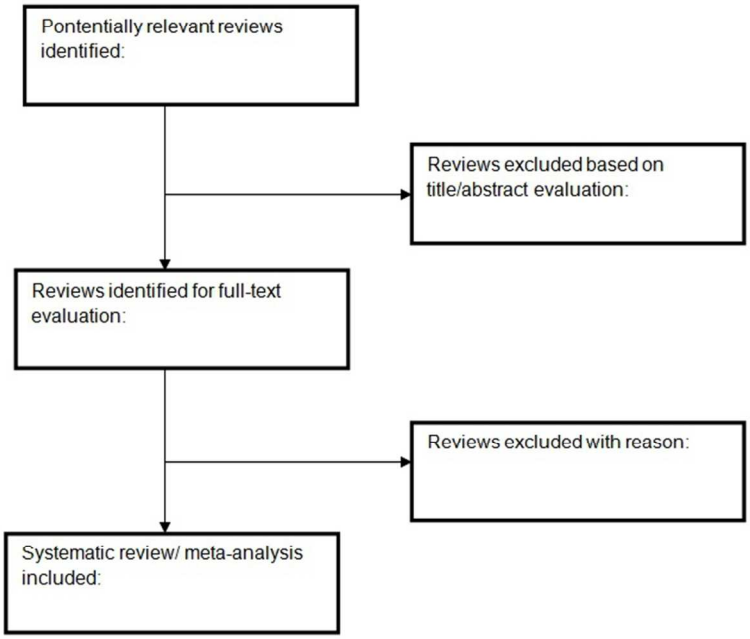
References

1. Klingberg G, Broberg AG. Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children 2007;17(6):391-406.
2. Porritt J, Buchanan H, Hall M, et al. Assessing children's dental anxiety: a systematic review of current measures. Community Dent Oral Epidemiol 2013;41(2):130-42.
3. Winer GA. A review and analysis of children's fearful behavior in dental settings. Child Dev. 1982 Oct;53(5):1111-33;
4. Ter Horst G, de Wit CA. Review of behavioural research in dentistry 1987-1992: dental anxiety, dentist-patient relationship, compliance and dental attendance. Int Dent J. 1993 Jun;43(3 Suppl 1):265-78.;
5. Wong HM, Humphris GM, Lee GT. Preliminary validation and reliability of the Modified Child Dental Anxiety Scale. Psychol Rep. 1998 Dec;83(3 Pt 2):1179-86;
6. Aartman I, Van Everdingen T, Hoogstraten J, Schuurs A. Appraisal of behavioural measurement techniques fors assessing dental anxiety and fear in children: A review. J Psychopathol Behav 1996;18:153-71;
7. Wogelius P, Poulsen S, Sorensen HT. Prevalence of dental anxiety and behavior management problems among six to eight years old Danish children. Acta Odontol Scand 2003;61(3):178-83;
8. Kyritsi MA, Dimou G, Lygidakis NA. Parental attitudes and perceptions affecting children's dental behaviour in Greek population. A clinical study. Eur Arch Paediatr Dent 2009;10(1):29-32;
9. Gustafsson A, Arnrup K, Broberg AG, et al. Child dental fear as measured with the Dental Subscale of the Children's Fear Survey Schedule: the impact of referral status and type of informant (child versus parent). Community Dent Oral Epidemiol 2010;38(3):256-66;
10. Salem K, Kousha M, Anissian A, et al. Dental Fear and Concomitant Factors in 3-6 Year-old Children. J Dent Res Dent Clin Dent Prospects 2012;6(2):70-4;
11. Moore R, Brodsgaard I. Dentists' perceived stress and its relation to perceptions about anxious patients. Community Dent Oral Epidemiol 2001;29(1):73-80;
12. American Association of Pediatric Dentristry, Guideline on Behavior Guidance for the Pediatric Dental Patient 2004;
13. BMJ (OPEN ACCESS) Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. BMJ 2009;339:b2535;

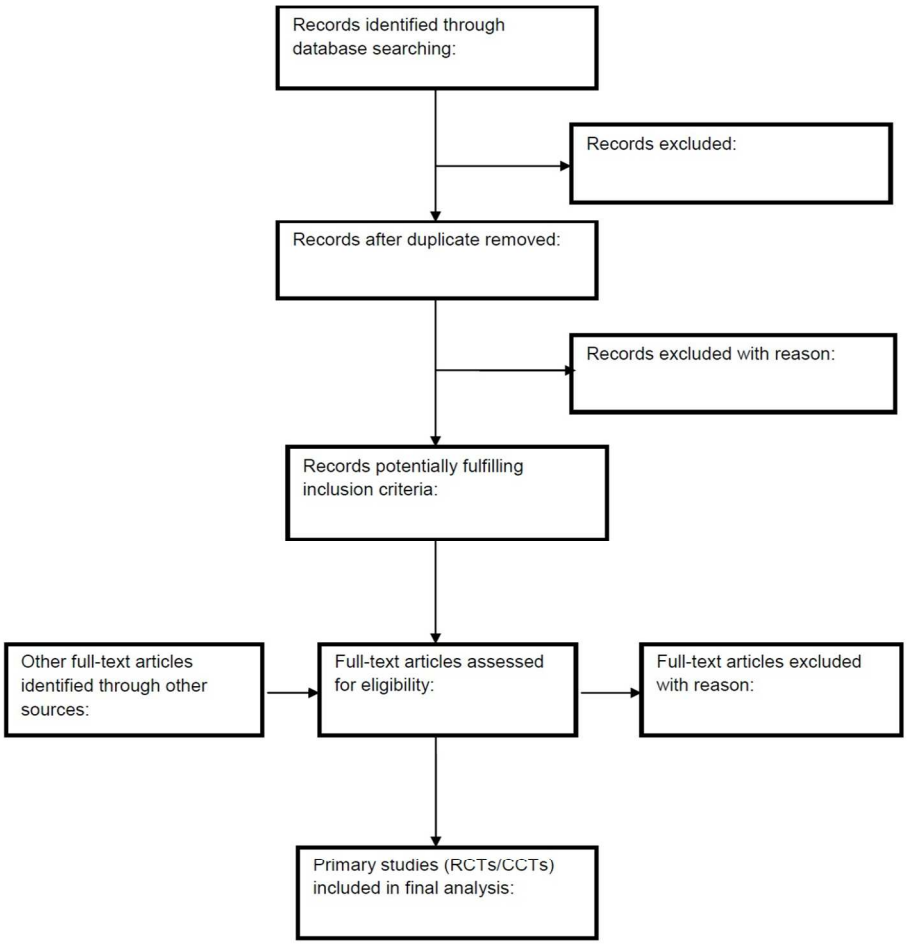
14. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. (2007) Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 7: 10;
15. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011;
16. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group.; Cochrane Statistical Methods Group.. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18;343:d5928.

Figure 1: PRISMA flow diagram for Systematic Reviews (SRs).



71x59mm (300 x 300 DPI)

Figure 2: PRISMA flow diagram for Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs).



125x133mm (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	On page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Prospero-CRD42016052591
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	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:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	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	4
Information sources	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	5

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	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)	5
Data collection process	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
Data items	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	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	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	7
Data synthesis	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	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	
Confidence in cumulative evidence	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

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Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Paediatrics
Keywords:	ORAL MEDICINE, Anxiety disorders < PSYCHIATRY, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.

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Abstract

Introduction: Several techniques have been proposed to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. To our knowledge, no widely available compendium of therapies to manage DFA exists. We propose a study protocol to assess the evidence regarding pharmacological and non-pharmacological interventions to relieve dental anxiety in children and adolescents.

Methods and analysis: In our systematic review, we will include Randomised Controlled Trials (RCTs), Controlled Clinical Trials (CCTs) and Systematic Reviews (SRs) of RCTs and CCTs that investigated the effects of pharmacological and non-pharmacological interventions to decrease dental anxiety in children and adolescents. We will search The Cochrane Database of Systematic Reviews (CDSR), The Cochrane Database of Abstracts of Reviews of Effects (DARE), The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, PsycINFO, CINAHL and the Web of Science for relevant studies. Pairs of authors will independently review all titles, abstracts, and full-texts identified by the specific literature search, and extract data using a structured data extraction form. For each study, information will be extracted on the study report (e.g., author, year of publication), the study design (e.g., the methodology and, for SRs, the types and number of studies included), the population characteristics, the intervention(s), the outcome measures and the results. The quality of SRs will be assessed using the AMSTAR (A Measurement Tool to Assess Reviews) instrument, while the quality of the retrieved RCTs and CCTs will be evaluated using the Cochrane Handbook for Systematic Reviews of Interventions criteria.

Ethics and dissemination: Approval from an ethics committee is not required, as no primary data will be collected. Results will be disseminated through a peer-reviewed publication and conference presentations.

Strengths and limitations of this study

- We anticipate our study to be the first comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures as well as an assessment of the quality of evidence of the included studies will be performed in this review.
- The findings of this study have the potential to inform and influence clinical decision-making and guideline development.
- There may be language bias as only studies published in English will be included, so relevant studies in other languages may be missed.
- There may be significant heterogeneity due to the different types of interventions and duration and frequency of practice.

Introduction

Dental Fear (DF) usually indicates a normal unpleasant emotional reaction to specific threatening stimuli occurring in situations associated with dental treatment, while Dental Anxiety (DA) is an excessive and unreasonable negative emotional state experienced by dental patients. These psychological states consist of apprehension that something dreadful is going to happen in relation to dental treatment.[1-2] In the scientific literature DF and DA often are used indistinctly.[1] The term dental fear and anxiety (DFA) will be used throughout this review when we refer to strong negative emotions associated with dental treatment among children and adolescents. DFA has been identified as a significant and common problem in children and adolescents, with a mean prevalence ranging between 10% and 20%, being particularly high in the earliest ages.[2] There is a general agreement on the consequences of DFA and dental avoidance, which is the failure to attend dental clinics, is a major consequence to DFA.[3] The measurement of anxiety is a vital step towards the management of the existing anxiety in dental settings. Three measures are generally used to assess the level of DFA: (a) “psychometric assessment” in which the children or one of their parents have to complete a questionnaire, usually before the treatment, to indicate the child’s level of anxiety associated with various common dental situations; (b) “physiological response analysis” in which the variations linked to the manifestation of anxiety are measured, such as salivary cortisol levels and (c) “projective test” based on psychological interpretation of children pictures concerning elements of dental setting.[4-6] Anxiety during dental treatment prevent the patient from cooperating fully with the dentist resulting in loss of time, increasing difficulty in performing dental procedures and unsatisfactory results.[7-11] In order to allay the anxiety of children and increase the compliance to dental treatment, the American Academy of Pediatric Dentistry has proposed various techniques, both pharmacological and non-pharmacological, namely: voice control, tell-show-do, positive reinforcement, distraction, non-verbal communication, hand over mouth, physical restraint, conscious sedation, nitrous oxide, and general anaesthesia.[12] Others have advocated additional methods to reduce anxiety such as the use of contingent distraction, modelling, and contingent escape. The etiology for dental anxiety is multifactorial, and hence there is no monotherapy for management. Proper evaluation of the patient and identifying their source and level of anxiety can enable the dentist in deciding a proper treatment plan.

The dentist should identify the factors that may influence DFA, so they may select the most appropriate behaviour management interventions, either non-pharmacological or pharmacological, to minimise DFA, and deliver high-quality dentistry, whilst also helping the the child develop a positive attitude towards dental health and treatment.[13]

While many examples of approaches and techniques to reduce DFA exist, to date there is no widely used compendium of pharmacological and non-pharmacological therapies for the management of DFA in children and adolescents. This might contribute to the underuse of effective techniques to reduce DFA in clinical practice.

To fill this knowledge gap, we propose a review for the assessment of the evidence of all pharmacological and non-pharmacological interventions for relieving anxiety in children and adolescents undergoing dental procedures.

Objective

The primary objective of this review is to assess the efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients undergoing dental procedures.

Methods

Criteria for considering studies for this review

Types of studies

Systematic Reviews (SRs) of Randomised Controlled Trials and/or Controlled Clinical Trials, Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs) assessing the effects of pharmacological and non-pharmacological interventions aimed to decrease the levels of dental anxiety in children and adolescents will be considered. Publications written in languages other than English language will be excluded.

Types of participants

Children and adolescents between the ages of 0 and 18 years attending a dental centre for dental visit/treatment.

Types of interventions

Any pharmacological and non-pharmacological intervention aimed at reducing levels of DFA. This should include -but is not limited to- the list of the American Academy of Pediatric Dentistry. Furthermore, children and adolescents, receiving a mixed intervention will be included. We will consider studies comparing the intervention(s) of interest versus the following controls:

- no intervention or placebo;
- other type of pharmacological and/or non-pharmacological intervention.

Types of outcome measures

Primary outcomes

- Anxiety levels measured by a validated physiological measure,
- Anxiety levels measured by a validated questionnaire;
- Anxiety levels measured by a validated projective test;

- Completion of dental treatment (yes/no);
- Adverse events associated with the intervention.

Secondary outcomes

- Dental avoidance;
- Operator preference/fatigue in operator;
- Patient satisfaction;
- Parental satisfaction;
- Time taken to undertake the intervention;
- Duration of dental treatment.

Search methods for identification of SRs

We will attempt to identify all relevant SRs providing data on the issue, published in English between 1990 and 31th December 2016. Publications written in a language other than English, will not be included.

Electronic searches

To identify the records of interest we will use the following terms to formulate specific search strategy: *dental fear, dental anxiety*, *dental phobia and odontophobia.*

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- Psychology & Behavioral Sciences Collection;
- CINAHL;
- Web of Science.

All eligible studies retrieved from the searches will be checked for relevant references.

Study selection

Two authors will independently assess SRs as being 'for exclusion', for 'inclusion', or 'potentially eligible' on the basis of title and abstract. Two criteria will be considered for further evaluation of an abstract: a) a publication defined as a review or meta-analysis, b) the mention of any pharmacological or non-pharmacological intervention for dental anxiety management. Subsequently, full-texts of relevant abstracts will be obtained and screened to identify SRs of interest based on the following inclusion criteria:

1. The use of at least one medical literature database;
2. The inclusion of at least one primary study (RCTs or CCTs);

3. The use of at least one pharmacological or non-pharmacological intervention for the management of dental anxiety in children and adolescents between the ages of 0 and 18 years old attending a dental centre for dental visit/treatment;
4. Two independent authors will judge their suitability for inclusion against the inclusion criteria. Disagreement will be resolved by discussion and, if necessary, by a third independent reviewer.

The process of published study selection will be presented in a PRISMA flow diagram (Figure 1).[14] Studies that will be excluded at this stage will be placed in a detailed excluded studies table along with reasons for their exclusion.

Data extraction and management

Two review authors will independently and in duplicate extract data from included SRs, and disagreements will be resolved by a consensus meeting with a third review author.

The data extracted will provide information on the following review criteria: study information (author, year of publication, country), database used, types and number of studies included, population characteristics, intervention(s) description, control or comparison intervention, outcome(s) measures used and results. If the review contains meta-analyses we will extract pooled results. Funding and author's conflict of interest will be extracted, too.

If any information from the review is unclear or missing, we will access the published reports of the individual trials and contact individual researchers.

Search methods for identification of RCTs and CCTs

We will attempt to identify any relevant clinical trial providing data on the efficacy and safety of interventions to decrease DFA published in English between 1990 and 31th December 2016. Papers written in a language other than English will not be included.

Electronic searches

To identify the records of interest we will use the following terms to formulate specific search strategy: *dental fear, dental anxiety*, *dental phobia and odontophobia*.

This search strategy will be used in the following database:

- Cochrane Central Register of Controlled Trials (CENTRAL);
- PubMed;
- Embase;
- Psychology & Behavioral Sciences Collection;
- CINAHL;
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Searching other resources

We will check the bibliographies of included studies in order to identify further relevant studies.

Study selection

The titles and abstracts resulting from the searches will be independently screened by two review authors to select potentially relevant studies. These studies will be obtained in full text and their inclusion assessed independently and in duplicate. Any discrepancies with respect to the inclusion or suitability of the papers will be resolved by discussion and, if necessary, by a third independent reviewer. Primary studies already contained in the included SRs will not be considered. The process of published study selection will be presented in a PRISMA flow diagram (Figure 2).[14] Studies excluded at this stage will be recorded in a table along with detailed information on reasons for their exclusion.

Data extraction and management

Two researchers will independently and in duplicate extract data from primary studies, and disagreements will be resolved by consensus with a third researcher.

The data extracted will provide information on the following study characteristics: study information (author, year of publication, country), study design, population characteristics, intervention(s) description, control or comparison intervention, outcome(s) measures used and results. Funding and author's conflict of interest will also be extracted.

Assessing the methodological quality of evidence in included studies

Quality of evidence for included SRs

We will assess the methodological quality of each systematic review using the AMSTAR (A Measurement Tool to Assess Reviews) instrument to appraise the quality.[15] AMSTAR appraises the quality of reviews using the following 11 items: duplicate study selection and data extraction, comprehensive searching of the literature, provision of a list of included and excluded studies, provision of characteristics of included studies, assessment of methodological quality of included studies, appropriate methods for combining results of studies and for assessing publication bias, and consideration of conflict of interest statement.[15] Two reviewers will independently evaluate the quality of the SRs and disagreement will be resolved by consensus. Where there are multiple reviews that answer the same clinical question, the reviews with the highest score will be prioritised in the evidence retrieval and assessment.

Quality of evidence for RCTs and CCTs

The quality of evidence for retrieved RCTs and CCTs will be assessed using the criteria from the Cochrane Handbook for Systematic Reviews of Interventions.[16-18] We will assess studies according to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other potential items that can be a source of bias. We will assign risk of bias to one of three categories on the basis of the reviewer's judgement, that is, low risk, unclear risk and high risk. Given that participants and personnel might not always be blinded due to the nature of the non-pharmacological interventions, performance bias will usually not be used for downgrading the level of evidence within the risk of bias assessment.

Data Synthesis

Where a number of primary studies are identified a meta-analysis will be performed. Dichotomous outcomes results will be expressed as risk ratio (RRs) with 95% confidence intervals (CIs). Where continuous scales of measurement are used to assess the effects of treatment, the mean difference (MD) will be used; the standardised mean difference (SMD) will be used if different scales have been used. For time to event data (survival, freedom from adverse events), hazard ratios will be used to calculate the magnitude of effect. The hazard ratio and variance corresponding to the published survival data will be used. Where this will not be directly available from the published version we will contact authors. Otherwise we will estimate hazard ratio and variance using log rank P-value, number randomised, events, or survival curves where available.[19] Where data are available cumulative event rate will be calculated. Analysis will be performed according to an intention-to-treat principle. For missing data, trial authors will be contacted or sensitivity analyses will be performed.[18] Heterogeneity will be evaluated using a Chi2 test with N-1 degrees of freedom, with an alpha of 0.10 used for statistical significance and with the I2 test.[17] Source of heterogeneity will be sought by assessing the participants, the intervention, the comparison group, and the outcomes and by visually assessing the forest plots. Review Manager (Revman 5.3) will be used for data synthesis. Data will be pooled using both the random-effects model and the fixed-effect model to ensure robustness.

Final consideration

Dental Fear represents a significant problem in paediatric dentistry, interesting about 2 children on 10. Pharmacological and non-pharmacological interventions represent useful instruments to treat children who suffer from Dental Fear. However, there has been no comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. Therefore, it is necessary to perform an objective systematic review to assess efficacy and safety

of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients.

Our review may provide evidence for researchers and be helpful for clinical practitioners in treating children with DFA.

Acknowledgements The authors acknowledge the contribution of Silvano Gallus for his precious hints.

Contributors SC, LP, RG, AM and EL conceived, drafted and approved the final version of the protocol.

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Competing interests None Declared.

Data sharing statement The findings of this systematic review will be disseminated via peer-reviewed publications and conference presentations. All the data will be available.

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Figure legends:

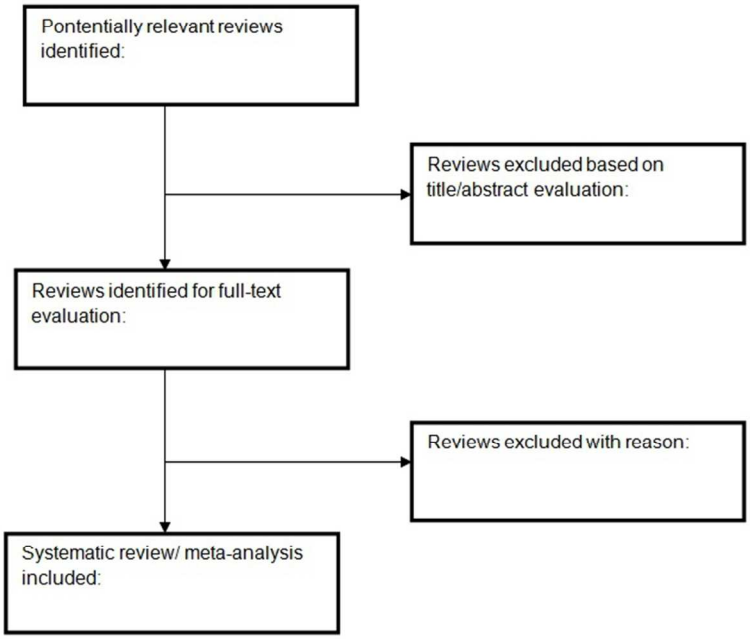
- Figure 1: PRISMA flow diagram for Systematic Reviews(SRs);
- Figure 2: PRISMA flow diagram for Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs).

References

1. Klingberg G, Broberg AG. Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children 2007;17(6):391-406;
2. Porritt J, Buchanan H, Hall M, et al. Assessing children's dental anxiety: a systematic review of current measures. Community Dent Oral Epidemiol 2013;41(2):130-42;
3. Winer GA. A review and analysis of children's fearful behavior in dental settings. Child Dev. 1982 Oct;53(5):1111-33;
4. Ter Horst G, de Wit CA. Review of behavioural research in dentistry 1987-1992: dental anxiety, dentist-patient relationship, compliance and dental attendance. Int Dent J. 1993 Jun;43(3 Suppl 1):265-78;
5. Wong HM, Humphris GM, Lee GT. Preliminary validation and reliability of the Modified Child Dental Anxiety Scale. Psychol Rep. 1998 Dec;83(3 Pt 2):1179-86;
6. Aartman I, Van Everdingen T, Hoogstraten J, Schuurs A. Appraisal of behavioural measurement techniques fors assessing dental anxiety and fear in children: A review. J Psychopathol Behav 1996;18:153-71;
7. Wogelius P, Poulsen S, Sorensen HT. Prevalence of dental anxiety and behavior management problems among six to eight years old Danish children. Acta Odontol Scand 2003;61(3):178-83;
8. Kyritsi MA, Dimou G, Lygidakis NA. Parental attitudes and perceptions affecting children's dental behaviour in Greek population. A clinical study. Eur Arch Paediatr Dent 2009;10(1):29-32;
9. Gustafsson A, Arnrup K, Broberg AG, et al. Child dental fear as measured with the Dental Subscale of the Children's Fear Survey Schedule: the impact of referral status and type of informant (child versus parent). Community Dent Oral Epidemiol 2010;38(3):256-66;
10. Salem K, Kousha M, Anissian A, et al. Dental Fear and Concomitant Factors in 3-6 Year-old Children. J Dent Res Dent Clin Dent Prospects 2012;6(2):70-4;
11. Moore R, Brodsgaard I. Dentists' perceived stress and its relation to perceptions about anxious patients. Community Dent Oral Epidemiol 2001;29(1):73-80;
12. American Association of Pediatric Dentristry, Guideline on Behavior Guidance for the Pediatric Dental Patient 2004;
13. Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. Clin Cosmet Investig Dent. 2016 Mar 10;8:35-50;
14. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. BMJ 2009;339:b2535;

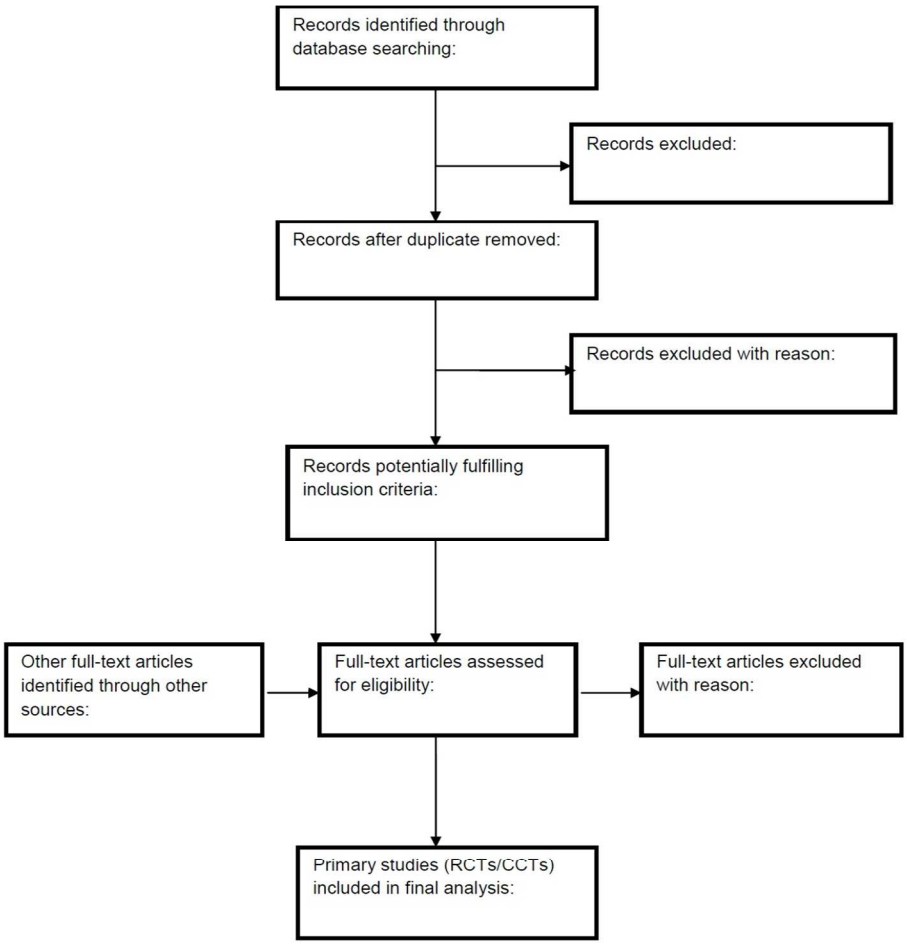
15. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. (2007) Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 7: 10;
16. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011;
17. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group.; Cochrane Statistical Methods Group.. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18;343:d5928;
18. Abraha I, Cozzolino F, Orso M, Marchesi M, Germani A, Lombardo G, Eusebi P, De Florio R, Luchetta ML, Iorio A, Montedori A. A systematic review found that deviations from intention-to-treat are common in randomized trials and systematic reviews. J Clin Epidemiol. 2017 Apr;84:37-46;
19. Tierney, J. F.L. A. StewartD. Ghersi (2007). "Practical methods for incorporating summary time-to-event data into meta-analysis." Trials 8: 16.

Figure 1: PRISMA flow diagram for Systematic Reviews (SRs).



71x59mm (300 x 300 DPI)

Figure 2: PRISMA flow diagram for Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs).



125x133mm (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	On page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Prospero-CRD42016052591
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	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:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	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	4
Information sources	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	5

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	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)	5
Data collection process	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
Data items	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	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	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	7
Data synthesis	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	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	
Confidence in cumulative evidence	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

Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.

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Primary Subject Heading:	Dentistry and oral medicine
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Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.

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Abstract

Introduction: Several techniques have been proposed to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. To our knowledge, no widely available compendium of therapies to manage DFA exists. We propose a study protocol to assess the evidence regarding pharmacological and non-pharmacological interventions to relieve dental anxiety in children and adolescents.

Methods and analysis: In our systematic review, we will include Randomised Controlled Trials (RCTs), Controlled Clinical Trials (CCTs) and Systematic Reviews (SRs) of RCTs and CCTs that investigated the effects of pharmacological and non-pharmacological interventions to decrease dental anxiety in children and adolescents. We will search The Cochrane Database of Systematic Reviews (CDSR), The Cochrane Database of Abstracts of Reviews of Effects (DARE), The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, PsycINFO, CINAHL and the Web of Science for relevant studies. Pairs of authors will independently review all titles, abstracts, and full-texts identified by the specific literature search, and extract data using a structured data extraction form. For each study, information will be extracted on the study report (e.g., author, year of publication), the study design (e.g., the methodology and, for SRs, the types and number of studies included), the population characteristics, the intervention(s), the outcome measures and the results. The quality of SRs will be assessed using the AMSTAR (A Measurement Tool to Assess Reviews) instrument, while the quality of the retrieved RCTs and CCTs will be evaluated using the Cochrane Handbook for Systematic Reviews of Interventions criteria.

Ethics and dissemination: Approval from an ethics committee is not required, as no primary data will be collected. Results will be disseminated through a peer-reviewed publication and conference presentations.

Strengths and limitations of this study

- We anticipate our study to be the first comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures as well as an assessment of the quality of evidence of the included studies will be performed in this review.
- The findings of this study have the potential to inform and influence clinical decision-making and guideline development.
- There may be language bias as only studies published in English will be included, so relevant studies in other languages may be missed.
- There may be significant heterogeneity due to the different types of interventions and duration and frequency of practice.

Introduction

Dental Fear (DF) usually indicates a normal unpleasant emotional reaction to specific threatening stimuli occurring in situations associated with dental treatment, while Dental Anxiety (DA) is an excessive and unreasonable negative emotional state experienced by dental patients. These psychological states consist of apprehension that something dreadful is going to happen in relation to dental treatment.[1-2] In the scientific literature DF and DA often are used indistinctly.[1] The term dental fear and anxiety (DFA) will be used throughout this review when we refer to strong negative emotions associated with dental treatment among children and adolescents. DFA has been identified as a significant and common problem in children and adolescents, with a mean prevalence ranging between 10% and 20%, being particularly high in the earliest ages.[2] There is a general agreement on the consequences of DFA and dental avoidance, which is the failure to attend dental clinics, is a major consequence to DFA.[3] The etiology for dental anxiety is multifactorial, and hence there is no monotherapy for management. Proper evaluation of the patient and identifying their source and level of anxiety can enable the dentist in deciding a proper treatment plan. Three measures are generally used to assess the level of DFA: (a) “psychometric assessment” in which the children or one of their parents have to complete a questionnaire, usually before the treatment, to indicate the child’s level of anxiety associated with various common dental situations; (b) “physiological response analysis” in which the variations linked to the manifestation of anxiety are measured, such as salivary cortisol levels and (c) “projective test” based on psychological interpretation of children pictures concerning elements of dental setting.[4-6] Anxiety during dental treatment prevent the patient from cooperating fully with the dentist resulting in loss of time, increasing difficulty in performing dental procedures and unsatisfactory results.[7-11]

In order to allay the anxiety of children and increase the compliance to dental treatment, various techniques have been proposed, both pharmacological and non-pharmacological.[12] Pharmacological interventions include all those agents that induce a state of sedation. Commonly used agents for sedation include the benzodiazepines, nitrous oxide or other agents. These agents are delivered by a large variety of methods (such as oral, rectal and nasal), in a bewildering variety of combinations and in varying doses. The other alternative pharmacological intervention is the use of general anaesthesia, though it is now recognized that it should be avoided wherever possible due to the associated rare risk of death. General anaesthesia is also very costly, it requires the use of specialist facilities and staff such as anaesthetists and specialist nurses.[13,14]

Non–pharmacological interventions, can be theoretically grouped into: (i) communication skills, rapport, and trust building (ii) behaviour-modification techniques (iii) cognitive behaviour therapy, and (iv) physical restraints.[15] The first group of non-pharmacological interventions include verbal and non verbal communication.[16] Behaviour-modifications techniques represent a heterogeneous group of interventions such as tell show do, voice control, signalling, distraction, hypnosis and others.[16-19] The cognitive behaviour therapy aims to alter and restructure the child’s negative

beliefs and expectations to reduce their dental anxiety and improve the control of negative thoughts. The use of cognitive behavior therapy (CBT) has been shown to be highly successful in the management of extremely anxious and phobic individuals.[15] Finally, physical restraints is a technique used in some countries and is characterized by a forced restricted movement of the patient. This approach should be limited to rare, critical clinical situations, where there are no other possibilities of intervention. [20]

While many examples of approaches and techniques for the management of DFA exist, to date there is no widely used compendium of pharmacological and non-pharmacological therapies for the management of DFA in children and adolescents. This might contribute to the underuse of effective techniques to reduce DFA in clinical practice.

To fill this knowledge gap, we propose a review for the assessment of the evidence of all pharmacological and non-pharmacological interventions for relieving anxiety in children and adolescents undergoing dental procedures.

Objective

The primary objective of this review is to assess the efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients undergoing dental procedures.

Methods

Criteria for considering studies for this review

Types of studies

Systematic Reviews (SRs) of Randomised Controlled Trials and/or Controlled Clinical Trials, Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs) assessing the effects of pharmacological and non-pharmacological interventions aimed to decrease the levels of dental anxiety in children and adolescents will be considered. Publications written in languages other than English language will be excluded.

Types of participants

Children and adolescents between the ages of 0 and 18 years attending a dental centre for dental visit/treatment.

Types of interventions

Any pharmacological and non-pharmacological intervention aimed at reducing levels of DFA. Furthermore, children and adolescents, receiving a mixed intervention will be included. We will consider studies comparing the intervention(s) of interest versus the following controls:

- no intervention or placebo;
- other type of pharmacological and/or non-pharmacological intervention.

Types of outcome measures

Primary outcomes

- Anxiety levels measured by a validated physiological measure,
- Anxiety levels measured by a validated questionnaire;
- Anxiety levels measured by a validated projective test;
- Completion of dental treatment (yes/no);
- Adverse events associated with the intervention.

Secondary outcomes

- Dental avoidance;
- Operator preference/fatigue in operator;
- Patient satisfaction;
- Parental satisfaction;
- Time taken to undertake the intervention;
- Duration of dental treatment.

Search methods for identification of SRs

We will attempt to identify all relevant SRs providing data on the issue, published in English between 1990 and 31th December 2016. Publications written in a language other than English, will not be included.

Electronic searches

To identify the records of interest we will use the following terms to formulate specific search strategy: *dental fear, dental anxiety*, *dental phobia and odontophobia.*

The search string will be used in the following databases:

- Cochrane Database of Systematic Reviews (CDSR);
- Cochrane Database of Abstracts of Reviews of Effects (DARE);
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All eligible studies retrieved from the searches will be checked for relevant references.

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1. The use of at least one medical literature database;
2. The inclusion of at least one primary study (RCTs or CCTs);
3. The use of at least one pharmacological or non-pharmacological intervention for the management of dental anxiety in children and adolescents between the ages of 0 and 18 years old attending a dental centre for dental visit/treatment;
4. Two independent authors will judge their suitability for inclusion against the inclusion criteria. Disagreement will be resolved by discussion and, if necessary, by a third independent reviewer.

The process of published study selection will be presented in a PRISMA flow diagram (Figure 1).[21] Studies that will be excluded at this stage will be placed in a detailed excluded studies table along with reasons for their exclusion.

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If any information from the review is unclear or missing, we will access the published reports of the individual trials and contact individual researchers.

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The quality of evidence for retrieved RCTs and CCTs will be assessed using the criteria from the Cochrane Handbook for Systematic Reviews of Interventions.[23-25] We will assess studies according to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other potential items that can be a source of bias. We will assign risk of bias to one of three categories on the basis of the reviewer's judgment, that is, low risk, unclear risk and high risk. Given that participants and personnel might not always be blinded due to the nature of the non-pharmacological interventions, performance bias will usually not be used for downgrading the level of evidence within the risk of bias assessment.

Data Synthesis

Where a number of primary studies are identified a meta-analysis will be performed. Dichotomous outcomes results will be expressed as risk ratio (RRs) with 95% confidence intervals (CIs). Where continuous scales of measurement are used to assess the effects of treatment, the mean difference (MD) will be used; the standardised mean difference (SMD) will be used if different scales have been used. For time to event data (survival, freedom from adverse events), hazard ratios will be used to calculate the magnitude of effect. The hazard ratio and variance corresponding to the published survival data will be used. Where this will not be directly available from the published version we will contact authors. Otherwise we will estimate hazard ratio and variance using log rank P-value, number randomised, events, or survival curves where available.[26] Where data are available cumulative event rate will be calculated. Analysis will be performed according to an intention-to-treat principle. For missing data, trial authors will be contacted or sensitivity analyses will be performed.[25] Heterogeneity will be evaluated using a Chi2 test with N-1 degrees of freedom, with an alpha of 0.10 used for statistical significance and with the I2 test.[24] Source of heterogeneity will be sought by assessing the participants, the intervention, the comparison group, and the outcomes and by visually assessing the forest plots. Review Manager

(Revman 5.3) will be used for data synthesis. Data will be pooled using both the random-effects model and the fixed-effect model to ensure robustness.

Final consideration

Dental Fear represents a significant problem in paediatric dentistry, interesting about 2 children on 10. Pharmacological and non-pharmacological interventions represent useful instruments to treat children who suffer from Dental Fear. However, there has been no comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. Therefore, it is necessary to perform an objective systematic review to assess efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients.

Our review may provide evidence for researchers and be helpful for clinical practitioners in treating children with DFA.

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Contributors SC, LP, RG, AM and EL conceived, drafted and approved the final version of the protocol.

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Competing interests None Declared**.**

Data sharing statement The findings of this systematic review will be disseminated via peer-reviewed publications and conference presentations. All the data will be available.

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Figure legends:

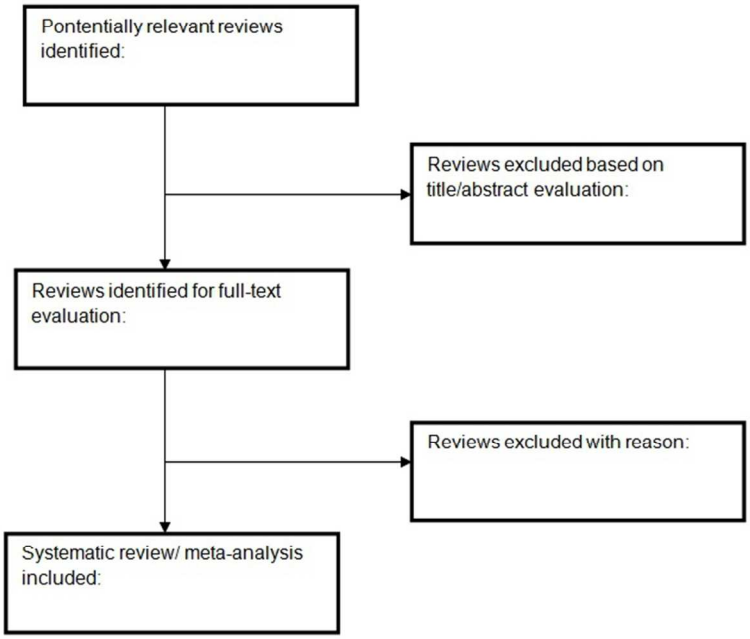
- Figure 1: PRISMA flow diagram for Systematic Reviews(SRs);
- Figure 2: PRISMA flow diagram for Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs).

References

1. Klingberg G, Broberg AG. Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children 2007;17(6):391-406;
2. Porritt J, Buchanan H, Hall M, et al. Assessing children's dental anxiety: a systematic review of current measures. Community Dent Oral Epidemiol 2013;41(2):130-42;
3. Winer GA. A review and analysis of children's fearful behavior in dental settings. Child Dev. 1982 Oct;53(5):1111-33;
4. Ter Horst G, de Wit CA. Review of behavioural research in dentistry 1987-1992: dental anxiety, dentist-patient relationship, compliance and dental attendance. Int Dent J. 1993 Jun;43(3 Suppl 1):265-78;
5. Wong HM, Humphris GM, Lee GT. Preliminary validation and reliability of the Modified Child Dental Anxiety Scale. Psychol Rep. 1998 Dec;83(3 Pt 2):1179-86;
6. Aartman I, Van Everdingen T, Hoogstraten J, Schuurs A. Appraisal of behavioural measurement techniques fors assessing dental anxiety and fear in children: A review. J Psychopathol Behav 1996;18:153-71;
7. Wogelius P, Poulsen S, Sorensen HT. Prevalence of dental anxiety and behavior management problems among six to eight years old Danish children. Acta Odontol Scand 2003;61(3):178-83;
8. Kyritsi MA, Dimou G, Lygidakis NA. Parental attitudes and perceptions affecting children's dental behaviour in Greek population. A clinical study. Eur Arch Paediatr Dent 2009;10(1):29-32;
9. Gustafsson A, Arnrup K, Broberg AG, et al. Child dental fear as measured with the Dental Subscale of the Children's Fear Survey Schedule: the impact of referral status and type of informant (child versus parent). Community Dent Oral Epidemiol 2010;38(3):256-66;
10. Salem K, Kousha M, Anissian A, et al. Dental Fear and Concomitant Factors in 3-6 Year-old Children. J Dent Res Dent Clin Dent Prospects 2012;6(2):70-4;
11. Moore R, Brodsgaard I. Dentists' perceived stress and its relation to perceptions about anxious patients. Community Dent Oral Epidemiol 2001;29(1):73-80;
12. Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. Clin Cosmet Investig Dent. 2016 Mar 10;8:35-50;
13. Lourenço-Matharu L, Ashley PF, Furness S. Sedation of children undergoing dental treatment. Cochrane Database Syst Rev. 2012 Mar 14;(3):CD003877;
14. Harbuz DK, O'Halloran M. Techniques to administer oral, inhalational, and IV sedation in dentistry. Australas Med J. 2016 Feb 29;9(2):25-32;

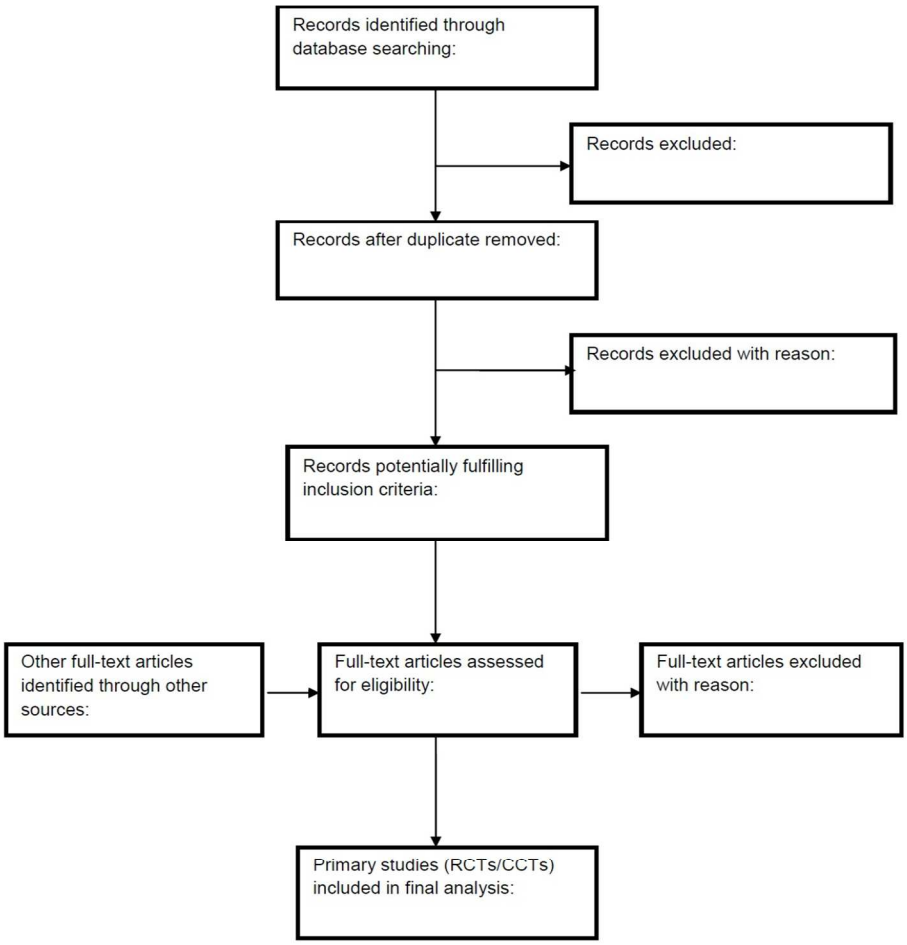
15. Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. Clin Cosmet Investig Dent. 2016;8:35-50. doi: 10.2147/CCIDE.S63626. eCollection 2016;
16. Greenbaum PE, Turner C, Cook EW 3rd, Melamed BG. Dentists' voice control: effects on children's disruptive and affective behavior. Health Psychol 1990;9:546–558;
17. Buchanan H, Niven N. Self-report treatment techniques used by dentists to treat dentally anxious children: a preliminary investigation. Int J Paediatr Dent 2003;13:9–12;
18. Armfield JM, Heaton LJ. Management of fear and anxiety in the dental clinic: a review. Aust Dent J. 2013 Dec;58(4):390-407; quiz 531;
19. Lynn SJ, Green JP, Kirsch I, Capafons A, Lilienfeld SO, Laurence JR, Montgomery GH. Grounding Hypnosis in Science: The "New" APA Division 30 Definition of Hypnosis as a Step Backward. Am J Clin Hypn. 2015 Apr;57(4):390-401;
20. Roberts JF, Curzon ME, Koch G, Martens LC. Review: behaviour management techniques in paediatric dentistry. EurArch Paediatr Dent 2010;11:166–174;
21. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. BMJ 2009;339:b2535;
22. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. (2007) Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 7: 10;
23. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011;
24. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group.; Cochrane Statistical Methods Group.. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18;343:d5928;
25. Abraha I, Cozzolino F, Orso M, Marchesi M, Germani A, Lombardo G, Eusebi P, De Florio R, Luchetta ML, Iorio A, Montedori A. A systematic review found that deviations from intention-to-treat are common in randomized trials and systematic reviews. J Clin Epidemiol. 2017 Apr;84:37-46;
26. Tierney, J. F.L. A. StewartD. Ghersi (2007). "Practical methods for incorporating summary time-to-event data into meta-analysis." Trials 8: 16.

Figure 1: PRISMA flow diagram for Systematic Reviews (SRs).



71x59mm (300 x 300 DPI)

Figure 2: PRISMA flow diagram for Randomised Controlled Trials (RCTs) and Controlled Clinical Trials (CCTs).



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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	On page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Prospero-CRD42016052591
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	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:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	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	4
Information sources	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	5

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	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)	5
Data collection process	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
Data items	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	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	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	7
Data synthesis	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	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	
Confidence in cumulative evidence	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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