National Institute for Health and Care Excellence

Draft

Periodontal treatment to improve diabetic control in children and young people with type 1 or type 2 diabetes

Evidence review C

NICE guideline NG18

Evidence reviews underpinning recommendations 1.2.1, 1.2.111 to 1.2.113, 1.3.3, and 1.3.41 to 1.3.43 and research recommendations in the NICE guideline

March 2022

Draft for Consultation

These evidence reviews were developed by NICE Guideline Development Team



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Evidence review on effectiveness of

periodontal treatment to improve diabetic

3 control in children and young people with

4 type 1 or type 2 diabetes

5 1.1 Review question

- 6 In children and young people with type 1 or type 2 diabetes, what is the effectiveness of
- 7 periodontal treatment to improve diabetic control?

1.1.1 Introduction

8

25

- 9 Diabetes mellitus represents an extremely significant health problem as it plays a pivotal role
- in the etiopathogenesis of long-term complications. Suboptimal diabetes control, typically
- 11 quantified by increased glycated haemoglobin (HbA1c), is a recognised risk factor for
- 12 periodontal diseases.
- 13 Periodontal disease is the sixth most common complication of diabetes that can manifest either
- as gingivitis or periodontitis. Gingivitis is the most prevalent inflammatory periodontal disease
- among children and young people with diabetes, which can be treated with simple non-surgical
- periodontal interventions such as debridement of root surfaces to remove bacterial plaque,
- biofilms, and mineralised plaque. Periodontal inflammation if left untreated or inadequately
- 18 controlled, does not only progress to periodontitis, but results in increased systemic
- 19 inflammatory burden, further worsening the glycaemic status and perpetual promotion of
- 20 associated complications of diabetes. Establishing the effectiveness of periodontal treatment
- 21 on diabetic control is important to help to reduce the harms associated with hyperglycaemia
- 22 and diabetes complications.
- 23 The aim of this review is to assess the effectiveness of periodontal treatment in improving
- 24 diabetic control in children and young people with type 1 or type 2 diabetes.

1.1.2 Summary of the protocol

26 Table 1 PICO table

	Children and young people with type 1 or type 2 diabetes and periodontal disease: Children under 5 years old School age children (6-12 years)
Population	Young people (>12 years)
Interventions	A non-surgical periodontal treatment such as subgingival instrumentation also known as scaling and root planing (SRP), which may include one or more of the following:
	 mechanical debridement which includes scaling and root planing subgingival curettage

	 antimicrobial therapy (antibacterials and antibiotics), either locally applied (including mouth rinses, gels, or dentifrices) or systemically administered other drug therapy with a possible benefit of improving the periodontal condition of the participant
	other novel interventions to manage periodontal disease
	Studies combining periodontal treatment with usual care or with antimicrobial therapy (antibacterial and antibiotics) will be grouped for the purpose of the analysis.
Comparator	Placebo
	 Usual care (defined as supragingival prophylaxis which can include scaling only or/and polish, oral hygiene instruction; education or support sessions to improve self-help or self- awareness of oral hygiene.)
Outcomes	All outcomes should be reported at least 90 days following the intervention. All outcomes will be sorted into 3 months, 6 months, 12 months following the intervention
	Primary outcomes
	Change in HbA1c
	Change in clinical attachment level (CAL)
	Change in periodontal probing pocket depth (PPD)
	Secondary outcomes
	 Quality of life (measured by validated tools e.g., hospital anxiety and depression scale (HADS), oral health-related quality of life (OHRQoL), health-related quality of life (HRQoL))
	Adverse events

1 1.1.3 Methods and process

- 2 This evidence review was developed using the methods and process described in <u>Developing</u>
- 3 NICE guidelines: the manual. Methods specific to this review question are described in the
- 4 review protocol in appendix A and the methods document.
- 5 Randomised controlled trials (RCTs), systematic reviews of RCTs, prospective and
- 6 retrospective cohort studies, non-randomised controlled trials, controlled before-and-after
- 7 studies and before-and-after studies were considered.
- 8 No studies were found that matched the inclusion criteria for the review.
- 9 Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

- 3 A systematic literature search was conducted for this review on effectiveness of periodontal
- 4 treatment in improving diabetic control in children and young people with type 1 or type 2
- 5 diabetes.

1

2

- The search after deduplication returned a total of 2070 results (see Appendix B for the
- 7 literature search strategy). Based on title and abstract screening against the review protocol,
- 8 21 potential references were ordered and reviewed against the inclusion criteria for full text
- 9 screening.
- 10 Of the 21 references screened as full texts, no studies met the inclusion criteria specified in
- 11 the review protocol for this question (Appendix A). The clinical evidence study selection is
- presented as a diagram in Appendix D.

13 1.1.4.2 Excluded studies

14 See Appendix K for excluded studies and reasons for exclusion.

1.1.5 Summary of studies included in the effectiveness evidence

16 Studies that met the inclusion criteria specified in the review protocol were not identified.

17 **1.1.6 Summary of the effectiveness evidence**

18 Studies that met the inclusion criteria specified in the review protocol were not found.

19 1.1.7 Economic evidence

20 1.1.7.1 Included studies

No relevant health economic studies were included.

22 **1.1.7.2 Excluded studies**

- No economic studies relating to this review question were identified.
- See the health economic study selection flow chart presented in Appendix H.

25 1.1.8 Summary of included economic evidence

There are no existing studies for this review question.

27 1.1.9 Economic model

29

No original economic modelling was completed for this review question.

1.1.11 The committee's discussion and interpretation of the evidence

1.1.11.1. The outcomes that matter most

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- 3 Based on the evidence from the periodontal treatment in improving diabetic control in adults
- 4 with type 1 and type 2 diabetes, the committee agreed that HbA1c, Clinical Attachment Level
- 5 (CAL), and Probing Pocket Depth (PPD) are important outcomes to assess the link and further
- 6 progression of diabetes and periodontal disease. The committee members also agreed that by
- 7 monitoring closely these indices, delay in the progression of diabetes complications and
- 8 periodontal disease later in life could be achieved. This would consequently result in improved
- 9 Quality of Life (QoL) which was considered a secondary outcome.
- 10 Adverse effects were thought to be less important as periodontal disease is not common
- among children and young people. In rare cases when required, conventional non-surgical
- techniques such as subgingival instrumentation / scaling and root planing cause only minor
- discomfort and tooth sensitivity that normally resolve after a few days.

15 **1.1.11.2** The quality of the evidence

- No studies were identified for the present evidence review.
- 17 The committee members agreed to extrapolate from the findings of the effectiveness of
- periodontal treatment in improving diabetic control in adults with type 1 and type 2 diabetes
- when compared to no active intervention or usual care. Two important factors influenced their
- decision. Firstly, the well documented biological link between diabetes and periodontal disease
- and the pathogenesis of diabetic-related complications was considered. Namely, research
- 22 shows that hyperglycaemia and resultant advanced glycation end-product formation
- 23 exaggerate immuno-inflammatory response to the bacterial challenge which initiate
- 24 periodontal disease. As a result of persistent hyperglycaemia, these advanced glycation end
- products accumulate in the plasma and tissue cells, causing more rapid periodontal tissue destruction and premature loss of the teeth. Because the degree of diabetes control ranges
- destruction and premature loss of the teeth. Because the degree of diabetes control ranges widely in children and young people, the susceptibility to gingival and periodontal inflammation
- 28 may vary. Consequently, although not all gingivitis proceeds into a destructive periodontal
- disease, the committee members thought that prevention of gingival inflammation should be
- emphasised, particularly in children and young with poorly controlled diabetes.
- 31 The second decision-making factor was the clinical evidence base for the adult population with
- 32 diabetes which had consistent and adequate volume of effectiveness to justify the
- 33 recommendations for children and young people with diabetes aimed at prevention and delay
- of the onset of periodontal disease.
- 35 Also, to support decision making, the committee referred to several other documents: care
- 36 standard (the Commissioning Standard: Dental Care for People with Diabetes), guideline (the
- 37 NICE's Guideline on Oral health promotion: general dental practice (NG30)) and consensus
- 38 papers (the European Federation of Periodontology (EFP) and the International Diabetes
- 39 Federation (IDF) joint workshop).
- 40 The above evidence combined with the clinical knowledge and experience of the dental
- 41 healthcare professionals co-opted to the committee was used as bases when drafting the
- 42 recommendations for the effectiveness of periodontal treatment in children and young people
- with type 1 and type 2 diabetes.

- 1 The link to the effectiveness of periodontal treatment in adults with type 1 and type 2 diabetes
- 2 review can be found here.
- 3 The committee did not suggest any recommendations for future research as periodontitis is a
- 4 rare condition among children and young people.

1.1.11.3 Benefits and harms

- 6 Studies that met the inclusion criteria specified in the review protocol were not found and the
- 7 committee members acknowledged the identified gap in evidence regarding children and
- young people diagnosed with type 1 and type 2 diabetes and periodontitis. They noted that the
- 9 possible explanation for the lack of evidence lies in the fact that periodontitis rarely develops
- in children and young people. Periodontal disease among children and young people consists
- mainly of gingivitis, the mildest form of periodontal disease. Gingivitis is a reversible and nondestructive form of periodontal disease which is characterised by plaque build-up, gingival
- redness, swelling, bleeding, and absence of periodontal attachment loss. However, if left
- untreated, it may progress to cause exposure of the roots, mobility, and premature loss of the
- 15 teeth.

5

- 16 The committee members acknowledged that children and young people with diabetes are at
- increased risk of developing periodontal diseases and stated that this should be routinely
- 18 discussed during diabetes consultations alongside eye disease and diabetes related foot
- 19 problems. Regular dental checks and oral health review to monitor plaque formation and
- 20 gingival inflammation was suggested.
- 21 Based on the evidence in adults, the committee agreed that successful periodontal treatment
- 22 can have a positive impact on metabolic control in people with type 1 and type 2 diabetes.
- Namely, the pooled effect of periodontal treatment when compared to no active intervention or
- 24 usual care demonstrated that the treatment of periodontitis via subgingival instrumentation /
- 25 scaling and root planing improved all primary outcomes (HbA1c, CAL and PPD) in the adult
- 26 population. The committee considered this indirect beneficial effect and agreed that if left
- 27 unattended, gingivitis in children and young people with type 1 and type 2 diabetes may
- progress to periodontitis which would further exacerbate diabetes outcomes.
- 29 Further extrapolating from the benefits of periodontal treatment evident in the adult diabetic
- 30 population, the committee acknowledged that early detection and treatment of periodontal
- 31 disease has the potential to improve quality of life in some aspects of living with diabetes in
- 32 adulthood. Due to the negligible side effects of subgingival instrumentation / scaling and root
- planing, no specific adverse events regarding the management of gingivitis were highlighted.
- 34 Overall, it was agreed that the benefits outweigh the possible minor side effects, and the
- 35 prevention and monitoring of periodontal disease should be recommended to improve diabetic
- 36 control in children and young people in the long term. As essential to the success of prevention
- and treatment of periodontal disease, maintaining good oral health hygiene and early diagnosis
- was emphasised.

39

1.1.11.4 Cost effectiveness and resource use

- The committee noted that no relevant published economic evaluations were identified, and no
- 41 additional economic analysis was undertaken for the cost-effectiveness of periodontal
- 42 treatment among children and young people with type 1 or type 2 diabetes. This is due to the
- fact that periodontal disease is extremely rare in people under the age of 18. Therefore, the
- 44 committee based the recommendations on the cost-effectiveness evidence of periodontal
- 45 treatments among adults with diabetes, along with their clinical knowledge and experience,

- 1 and existing NICE guidance. The new recommendations are mainly about preventive
- 2 measures and should have a minimal cost impact to the NHS in terms of extra healthcare
- 3 professionals' time. This may be offset by better health outcomes by improving the care and
- 4 quality of life of children and young people who may develop periodontal diseases when they
- 5 reach adulthood.

6 1.1.11.5 Other factors the committee took into account

- 7 The committee agreed that maintaining gingival health to help prevent or manage periodontal
- 8 disease in children and young people with diabetes requires promoting and supporting positive
- 9 oral health behaviours and regular dental prophylaxis. The provision of continuous educational
- 10 support to improve self-care by maintaining effective oral health hygiene and managing
- 11 lifestyle risk factors, such as smoking, diet and optimal diabetes control are essential to the
- 12 success of prevention and management of periodontal disease.
- 13 In addition, the committee wished to highlight the increased risk and the needs of certain
- 14 groups of children and young people with diabetes. The committee considered the needs of
- 15 certain disadvantaged groups such as children and young people with physical disability,
- mental health related or learning disability. These groups may also have limitations with their
- dexterity which can cause difficulties in using interdental and interproximal brushes to maintain
- 18 good oral hygiene and often do not engage during dental checks putting them into an increased
- risk of further progression towards periodontitis. Consideration for children and young people
- in secure settings was also given due to the limited access to interdental and/or interproximal
- brushes and other dental health care products for security reasons. In general, broader access
- 22 to dental treatment and adequate personal oral hygiene products combined with the enhanced
- 23 educational support has the potential to reduce inequalities among disadvantaged groups.
- Lastly, how the delivery of care for children and young people with diabetes is best integrated
- across healthcare settings was considered. Clear advice for the dental team, of what is
- 26 expected of them regarding diabetes dental care of children and young people and clear
- 27 pathways are necessary to enhance the quality of care across the continuum and improve
- service delivery. The committee members also discussed the uncertainty regarding the initial
- 29 increase in referrals of children and young people with diabetes for dental checks and oral
- 30 health review following the publication of this guidelines, as this will potentially impact on the
- 31 scarce NHS dental service. Current lack of access to NHS dentistry and gaps in periodontal
- 32 services and future provision of periodontal treatment was of a major concern.

1.1.12 Recommendations supported by this evidence review

- 34 This review supports recommendations 1.2.1, 1.2.111 to 1.2.113, 1.3.1, and 1.3.41 to 1.3.43
- of the Diabetes (type 1 and type 2) in children and young people: diagnosis and management
- 36 quideline.

33

37

1.1.13 References – included studies

38 **1.1.13.1 Effectiveness**

39 References that met the inclusion criteria specified in the review protocol were not found.

40 **1.1.13.2 Economic**

41 No relevant studies have been included as part of the economic evidence review.

- 1 1.1.13.3 Other
- 2 No other studies were included in this review.

Appendices

5

2 Appendix A – Review protocols

Review protocol for effectiveness of periodontal treatment in improving diabetic control in children and young people with type 1 or type 2 diabetes.

ID	Field	Content
0.	PROSPERO registration number	
1.	Review title	Periodontal treatment to improve diabetic control in children and young people with type 1 or type 2 diabetes.
2.	Review question	In children and young people with type 1 or type 2 diabetes, what is the effectiveness of periodontal treatment to improve diabetic control?
3.	Objective	Determine the effectiveness of periodontal treatment in improving diabetic control in children with type 1 or type 2 diabetes.
4.	Searches	The following databases will be searched: Clinical searches: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase DARE

	1		
		MEDLINE	
		MEDLINE In Process	
		MEDLINE ePubs	
		 PsycINFO 	
		Economic searches:	
		Econlit	
		Embase	
		HTA	
		MEDLINE	
		MEDLINE In Process	
		MEDLINE ePubs	
		NHS EED	
		PsycINFO	
		Searches will be restricted by:	
		English language	
		Study designs of RCTs, SRs and observational studies will be applied	
		Animal studies will be excluded from the search results	
		Conference abstracts will be excluded from the search results	
		There was no data limit set for these searches.	
		Other accomb as N/A	
		Other searches: N/A	
		The full search strategies for MEDLINE database will be published in the final review.	
		The full search strategies for Micheliae database will be published in the linal review.	
5.	Condition or domain being		
	studied	Type 1 or type 2 diabetes and periodontal disease in children and young people	

6.	Population	Inclusion: Children and young people with type 1 or type 2 diabetes and periodontal disease: • Children under 5 years old • School age children (6-12 years) • Young people (>12 years) Exclusion: Adults with type 1 or type 2 diabetes
7.	Intervention	A non-surgical periodontal treatment such as subgingival instrumentation also known as scaling and root planing (SRP), which may include one or more of the following: • mechanical debridement which includes scaling and root planing • subgingival curettage • antimicrobial therapy (antibacterials and antibiotics), either locally applied (including mouth rinses, gels, or dentifrices) or systemically administered • other drug therapy with a possible benefit of improving the periodontal condition of the participant • other novel interventions to manage periodontal disease Note: Studies combining periodontal treatment with usual care will be included. Usual care can include scale and polish, oral hygiene instruction; education or support sessions to improve self-help or self-awareness of oral hygiene. Note: Studies combining periodontal treatment with antimicrobial therapy (antibacterial and antibiotics) will be included. Each arm of the trial should be given identical antimicrobial therapy.
8.	Comparator	Placebo

		Usual care (which we defined as supragingival prophylaxis or oral hygiene instruction)		
		Note: Usual care can include scale and polish, oral hygiene instruction; education or support sessions to impreself-help or self-awareness of oral hygiene.		
9.	Types of study to be included	Randomised controlled trials (RCTs)		
		Systematic reviews of RCTs		
		If no or insufficient evidence from RCTs found, evidence from the following study designs will be sought:		
		Prospective cohort studies		
		Retrospective cohort studies		
		Non-randomised controlled trials		
		Controlled before-and-after studies		
		Before and after studies		
		Note: Only cohort studies that attempt to assess and adjust for baseline differences (e.g. through propensity		
		matching) or adjust for confounding (e.g. age, sex, ethnicity, education, smoking, time to follow up) in		
		multivariable analysis will be included.		
10.	Other exclusion criteria	Trials which followed up participants for less than 90 days after completion of treatment course		
		Split mouth and cross-over studies		
		Definition: Split mouth is a research design in which instead of randomising individuals, a mouth is divided into two or more experimental segments that are randomly assigned to different treatments.		

11.	Context	This review is part of an update of the NICE guideline on Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18) https://www.nice.org.uk/guidance/ng18 This update covers periodontal treatment in children and young people with type 1 or type 2 diabetes. This guideline will also cover all settings where NHS healthcare is provided or commissioned.
12.	Primary outcomes (critical	will also sever all settings where twile healthoare is provided or seminissioned.
	outcomes)	All outcomes will have to be reported at least 3 months following the intervention. Outcomes will be reported based
		on duration of follow up since the periodontal intervention e.g. 3 months, 6 months, 12 months etc.
		These include:
		Change in HbA1c
		Change in periodontal attachment level
		Periodontal pocket reduction
13.	Secondary outcomes (important outcomes)	 Quality of life (using validated tools e.g., hospital anxiety and depression scale (HADS), oral health-related quality of life (OHRQoL), health-related quality of life (HRQoL)) Adverse events
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and deduplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.
		The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.

		This review will make use of the priority screening functionality within the EPPI-reviewer software.		
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklists as described in Developing NICE guidelines: the manual.		
		Randomised control trials (individuals or cluster) will be assessed using the Cochrane risk of bias tool 2.0.		
		Non-randomised controlled trials (clinical controlled trials) will be assessed using the Cochrane ROBINS-I tool. Cohort studies will be assessed using the Cochrane ROBINS-I tool.		
		Assessment of the robustness of Controlled before-and-after studies will be performed using the Effective Practice and Organisation of Care (EPOC) RoB Tool (for before-and-after study)		
16.	Strategy for data synthesis	Meta-analysis will be conducted where data is available. Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) to combine the data given in all studies for each of the outcomes stated above.		
		A fixed effect meta-analysis, with weighted mean differences for continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome.		
		Heterogeneity between the studies in effect measures will be assessed using the I² statistic and visually inspected.		
		Where data is available sensitivity analyses will be conducted using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented using random effects.		
		GRADE will be used to assess the quality of each outcome, considering individual study quality and the meta- analysis results.		
		Where meta-analysis is not possible, data will be presented, and quality assessed individually per outcome.		

		Network meta-analysis and cost-effectiveness analysis of periodontal treatments on improving glucose control are not planned for this review.	
		For details, please see section 6 of <u>Developing NICE guidelines: the manual.</u>	
17.	Analysis of sub-groups	We plan to carry out the following subgroup analyses: Type of intervention and comparison (e.g. SRP, SRP plus antimicrobials, SRP plus antimicrobial mouth rinse vs supragingival scaling or usual care as the control	
		 Length of follow up since completion of treatment (e.g. 3,6, 12 months) Periodontal disease severity at baseline (e.g. chronic or aggressive periodontitis, necrotising ulcerative gingivitis, periodontal abscess) 	
		Should we find sufficient data, we will also consider the following groups for subgroup analyses:	
		Intensiveness of periodontal treatment (e.g. single intervention or a supportive care programme on 3-monthly basis)	
		Diabetes control - through categorisation of participants into good, fairly, and poorly controlled diabetes (mean HbA1c 7%, between 7% and 8.5% or >8.5% on the DCCT or equivalent scale)	
		Diabetes type (Type1 and Type 2)	
		Diabetes duration (since diagnosis)	
		 Age (children under 5 years old, school age children (6-12 years) and young people (>12 years Sex 	
		General health status (presence of other diabetes complications)	
		Presence of other medical conditions Plague central	
		 Plaque control Socioeconomic status/ health inequalities (ethnicity and social class) 	

		 Drug therapy Children with learning difficulties Children with disabilities Location (urban or rural) Children and young people in custody Eating disorders and disordered eating 			
18.	Type and method of review	☑ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)			
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	November 2021			
22.	Anticipated completion date	June 2022			
23.	Stage of review at time of this submission	Review stage	Started	Completed	
		Preliminary searches			

		Piloting of the study selection process		
		Formal screening of search results against eligibility criteria		
		Data extraction		
		Risk of bias (quality) assessment		
		Data analysis		
24.	Named contact	5a. Named contact Guideline Updates Team 5b Named contact e-mail Diabetesupdate@nice.org.uk 5c Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and NICE Guideline Updates Team		
25.	Review team members	From the guidelin Caroline Mulvi Teuta Gjuladir Miaoqing Yan	ihill n-Hellon	eam:

		 Steph Armstrong Kirsty Hounsell David Nicholls
26.	Funding sources/sponsor	This systematic review is being completed by the Centre for Guidelines which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual . Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10244
29.	Other registration details	None
30.	Reference/URL for published protocol	None
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

		notifying registered stakeholders of publication	
		publicising the guideline through NICE's newsletter and alerts	
		 issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social 	
			nedia channels, and publicising the guideline within NICE.
32.	Keywords		
		Periodontal disease, periodontal treatment, type 1 diabetes, type 2 diabetes, paediatric diabetes	
33.	Details of existing review of	Nisas	
	same topic by same authors	None	
34.	Current review status		Ongoing
0	Canoni review states		Crigoria
			Completed but not published
			Completed and published
			Completed, published and being updated
			Discontinued
35	Additional information	None	
36.	Details of final publication	www.nice	e.org.uk

1

Appendix B - Methods

Priority screening

The review undertaken for this guideline made use of the priority screening functionality with the EPPI-reviewer systematic reviewing software. This uses a machine learning algorithm (specifically, an SGD classifier) to take information on features (1, 2 and 3 word blocks) in the titles and abstract of papers marked as being 'includes' or 'excludes' during the title and abstract screening process, and re-orders the remaining records from most likely to least likely to be an include, based on that algorithm. This re-ordering of the remaining records occurs every time 25 additional records have been screened. As the number of records for screening was relatively small (2070 articles), a stopping criterion was not used when conducting screening. Therefore, all records were screened. Twenty-one potential studies were assessed at full-text stage.

Evidence of effectiveness of interventions

Evidence that met the inclusion criteria specified in the review protocol was not found.

Appendix C - Literature search strategies

Evidence review on effectiveness of periodontal treatment in improving diabetic control in children and young people with type 1 or type 2 diabetes.

Clinical literature search strategy

The search of the following databases was conducted on 8th November 2021: Medline, Medline In Process, Medline E-pub Ahead of print, PsycINFO, Embase (all via the Ovid platform), Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews (both via the both via the Wiley platform) and the Database of Abstracts of Reviews of Effect (via the CRD platform)

Intervention and population terms

Database: Medline, Medline in Process, Medline E-pub ahead of print

Database: Ovid MEDLINE(R) <1946 to November 04, 2021>

Search Strategy:

- 1 exp Diabetes Mellitus/ (459901)
- 2 diabet*.tw. (598976)
- 3 (DM adj4 ("type 1" or type1 or "type I" or "type one" or T1 or T-1 or TI or T-I)).tw. (1805)
- 4 lada.tw. (584)
- 5 (dm1 or iddm or t1d* or dka).tw. (21704)
- 6 (dm2 or t2d* or mody or niddm).tw. (38801)
- 7 (DM adj4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)).tw. (4731)
- 8 (DM adj4 (autoimmun* or auto immun* or brittle or labile or insulin depend* or insulin deficien*)).tw. (339)
- 9 (DM adj4 onset* adj4 (maturit* or adult* or slow*)).tw. (68)
- 10 (DM adj4 depend* adj4 (non-insulin* or non insulin* or noninsulin*)).tw. (94)
- 11 (DM adj4 (earl* or sudden onset or juvenile or child*)).tw. (933)
- 12 (DM adj4 (keto* or acidi* or gastropare*)).tw. (79)
- 13 or/1-12 (666209)
- 14 exp Dentistry/ (418443)
- 15 exp Periodontal Diseases/ (91107)
- 16 exp Dental Health Services/ (39024)
- 17 exp Dental Staff/ (2470)
- 18 exp Dentists/ (19914)
- 19 exp Dental Care for Chronically III/ (2873)
- 20 periodont*.tw. (71753)
- 21 ((root* or surface*) adj4 debrid*).tw. (624)
- 22 ((prevent* or prophyla*) adj4 (dent* or oral*)).tw. (18724)

23 ((scale* or scaling) adj4 polish*).tw. (311) 24 (root adj4 plan*).tw. (9386) 25 (SRP or RSD).tw. (18028) 26 (gingiv* or subgingiv*).tw. (50240) (gum* adj4 (diseas* or infect* or disord* or inflam* or sensitiv*)).tw. (731) 27 28 ((tooth or teeth or dental) adj4 (scaling or scale*)).tw. (1524) 29 Oral Health/ (18396) 30 ((dent* or oral*) adj4 (hygien* or health)).tw. (49576) or/14-30 (553994) 31 32 13 and 31 (6552) 33 exp Infant/ or Infant Health/ or Infant Welfare/ (1194655) (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (918750) exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (2030834) 35 36 Minors/ (2698) (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2603875) 37 exp pediatrics/ (61407) 39 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (947283) 40 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2136410) 41 Puberty/ (13798) 42 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or prepubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (474675) 43 Schools/ (44711) 44 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7423) (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (517556) 46 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (4540)

Database: EMBASE

47 or/33-46 (5581995) 48 32 and 47 (1512)

50 48 not 49 (1482)

49

Database: Embase <1974 to 2021 November 05>

animals/ not humans/ (4876857)

51 limit 50 to english language (1282)

Search Strategy:

.....

- 1 exp Diabetes Mellitus/ (1055455)
- 2 diabet*.tw. (1027761)
- 3 (DM adj4 ("type 1" or type1 or "type I" or "type one" or T1 or T-1 or TI or T-I)).tw. (4346)

- 4 lada.tw. (1093)
- 5 (dm1 or iddm or t1d* or dka).tw. (44711)
- 6 (dm2 or t2d* or mody or niddm).tw. (81908)
- 7 (DM adj4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)).tw. (11589)
- 8 (DM adj4 (autoimmun* or auto immun* or brittle or labile or insulin depend* or insulin deficien*)).tw. (800)
- 9 (DM adj4 onset* adj4 (maturit* or adult* or slow*)).tw. (118)
- 10 (DM adj4 depend* adj4 (non-insulin* or non insulin* or noninsulin*)).tw. (170)
- 11 (DM adj4 (earl* or sudden onset or juvenile or child*)).tw. (2029)
- 12 (DM adj4 (keto* or acidi* or gastropare*)).tw. (208)
- 13 or/1-12 (1254453)
- 14 exp dentistry/ (102820)
- 15 exp periodontal disease/ (105229)
- 16 exp dental procedure/ (182350)
- 17 exp dental staff/ (119)
- 18 exp dentist/ (26523)
- 19 periodont*.tw. (79890)
- 20 ((root* or surface*) adj4 debrid*).tw. (727)
- 21 ((prevent* or prophyla*) adj4 (dent* or oral*)).tw. (24139)
- 22 ((scale* or scaling) adj4 polish*).tw. (427)
- 23 (root adj4 plan*).tw. (11830)
- 24 (SRP or RSD).tw. (28871)
- 25 (gingiv* or subgingiv*).tw. (57593)
- 26 (gum* adj4 (diseas* or infect* or disord* or inflam* or sensitiv*)).tw. (1205)
- 27 ((tooth or teeth or dental) adj4 (scaling or scale*)).tw. (1859)
- 28 ((dent* or oral*) adj4 (hygien* or health)).tw. (57453)
- 29 or/14-28 (456775)
- 30 13 and 29 (10434)
- 31 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3694981)
- 32 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,ad,jw. (1306624)
- 33 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3979529)
- 34 exp pediatrics/ (115130)
- 35 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1814171)
- 36 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (114660)
- 37 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,ad,jw. (731363)
- school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (113074)
- 39 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (776739)
- 40 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (8614)

- 41 or/31-40 (6979762)
- 42 30 and 41 (2210)
- 43 nonhuman/ not human/ (4882166)
- 44 42 not 43 (2169)
- 45 limit 44 to english language (2005)
- 46 (conference abstract or conference paper or conference proceeding or "conference review").pt. (5015578)
- 47 45 not 46 (1668)

Database: Cochrane (CDSR/CENTRAL)

Search Name: GU diabetes _ periodontal treatment _ children and young people_T1 AND T2

Date Run: 05/11/2021 21:24:13

Comment: DN 05 11 2021

- ID Search Hits
- #1 MeSH descriptor: [Diabetes Mellitus] explode all trees 33584
- #2 diabet*:ti,ab,kw 101779
- #3 (DM near/4 ("type 1" or type1 or "type I" or "type one" or T1 or T-1)):ti,ab,kw 276
- #4 lada:ti,ab,kw 74
- #5 (dm1 or iddm or t1d* or dka):ti,ab,kw 3856
- #6 (dm2 or t2d* or mody or niddm):ti,ab,kw 12005
- #7 (DM near/4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)):ti,ab,kw
- #8 (DM near/4 (autoimmun* or auto immun* or brittle or labile or insulin depend* or insulin deficien*)):ti,ab,kw 550
- #9 (DM near/4 onset* near/4 (maturit* or adult* or slow*)):ti,ab,kw 0
- #10 (DM near/4 depend* near/4 (non-insulin* or non insulin* or noninsulin*)):ti,ab,kw 202
- #11 (DM near/4 (earl* or sudden onset or juvenile or child*)):ti,ab,kw 240
- #12 (DM near/4 (keto* or acidi* or gastropare*)):ti,ab,kw 13
- #13 {OR #1-#12} 103278
- #14 MeSH descriptor: [Dentistry] explode all trees 18363
- #15 MeSH descriptor: [Periodontal Diseases] explode all trees 6862
- #16 MeSH descriptor: [Dental Health Services] explode all trees 692
- #17 MeSH descriptor: [Dental Staff] explode all trees8
- #18 MeSH descriptor: [Dentists] explode all trees 102
- #19 MeSH descriptor: [Dental Care for Chronically III] explode all trees 53
- #20 periodont*:ti,ab,kw 11995
- #21 ((root* or surface*) near/4 debrid*):ti,ab,kw 234

```
#22
        ((prevent* or prophyla*) near/4 (dent* or oral*)):ti,ab,kw
                                                                       7945
#23
        ((scale* or scaling) near/4 polish*):ti,ab,kw
#24
        (root near/4 plan*):ti,ab,kw
#25
        (SRP or RSD):ti,ab,kw
                               1314
#26
        (gingiv* or subgingiv*):ti,ab,kw 10907
#27
        (gum* near/4 (diseas* or infect* or disord* or inflam* or sensitiv*)):ti,ab,kw
                                                                                       389
        ((tooth or teeth or dental) near/4 (scaling or scale*)):ti,ab,kw
#28
#29
        MeSH descriptor: [Oral Health] this term only
#30
        ((dent* or oral*) near/4 (hygien* or health)):ti,ab,kw
                                                               9076
#31
        {OR #14-#30} 39064
#32
       #13 and #31
                       1052
#33
        MeSH descriptor: [Infant] explode all trees
                                                       33690
#34
        MeSH descriptor: [Infant Health] this term only 58
#35
        MeSH descriptor: [Infant Welfare] this term only
                                                               83
#36
        (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or
perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*):ti,ab,kw
#37
        MeSH descriptor: [Child] explode all trees
                                                       58991
#38
        MeSH descriptor: [Child Behavior] explode all trees
                                                               2244
#39
        MeSH descriptor: [Child Health] this term only 136
#40
        MeSH descriptor: [Child Welfare] this term only 335
#41
        MeSH descriptor: [Minors] this term only
                                                       10
        (child* or minor or minors or boy* or girl* or kid or kids or young*):ti,ab,kw
#42
                                                                                       293576
#43
        MeSH descriptor: [Pediatrics] explode all trees 710
#44
        (pediatric* or paediatric* or peadiatric*):ti,ab,kw
                                                               37595
#45
        MeSH descriptor: [Adolescent] this term only
#46
        MeSH descriptor: [Adolescent Behavior] this term only 1445
#47
        MeSH descriptor: [Adolescent Health] this term only
#48
        MeSH descriptor: [Puberty] this term only
#49
        (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or
pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*):ti,ab,kw
        150522
#50
        MeSH descriptor: [Schools] this term only
                                                                       257
#51
        MeSH descriptor: [Child Day Care Centers] this term only
#52
        MeSH descriptor: [Nurseries, Infant] explode all trees
                                                               10
#53
        MeSH descriptor: [Schools, Nursery] this term only
                                                               40
#54
        (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or
pupil* or student*):ti,ab,kw
                               108683
        ("under 18" or "under eighteen" or "under 18s" or "under eighteens" or "under 25" or "under
#55
twenty five" or "under 25s" or "under twenty fives"):ti,ab,kw
                                                               16197
#56
        {OR #33-#46}
                      394024
#57
       #32 and #56
                       151
Couldn't find 'Nurseries' in the MeSH search in Cochrane, defaulted to Infant Nurseries
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Database: PsychINFO Database: APA PsycInfo <1806 to November Week 1 2021> Search Strategy: 1 exp Diabetes Mellitus/ (9212) 2 diabet*.tw. (34168) 3 (DM adj4 ("type 1" or type1 or "type I" or "type one" or T1 or T-1 or TI or T-I)).tw. (95) 4 lada.tw. (12) (dm1 or iddm or t1d* or dka).tw. (1193) 6 (dm2 or t2d* or mody or niddm).tw. (2019) (DM adj4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)).tw. (248) 8 (DM adj4 (autoimmun* or auto immun* or brittle or labile or insulin depend* or insulin deficien*)).tw. (12) (DM adj4 onset* adj4 (maturit* or adult* or slow*)).tw. (4) 10 (DM adj4 depend* adj4 (non-insulin* or non insulin* or noninsulin*)).tw. (4) (DM adj4 (earl* or sudden onset or juvenile or child*)).tw. (55) 12 (DM adj4 (keto* or acidi* or gastropare*)).tw. (7) 13 or/1-12 (34998) 14 exp Dentistry/ (451) 15 exp Dentists/ (486) periodont*.tw. (518) ((root* or surface*) adj4 debrid*).tw. (1) 17 18 ((prevent* or prophyla*) adj4 (dent* or oral*)).tw. (754) 19 ((scale* or scaling) adj4 polish*).tw. (140) 20 (root adj4 plan*).tw. (39) 21 (SRP or RSD).tw. (586) 22 (gingiv* or subgingiv*).tw. (247) 23 (gum* adj4 (diseas* or infect* or disord* or inflam* or sensitiv*)).tw. (47) 24 ((tooth or teeth or dental) adj4 (scaling or scale*)).tw. (154) 25 Oral Health/ (1302) 26 ((dent* or oral*) adj4 (hygien* or health)).tw. (2807) 27 or/14-26 (5266) 13 and 27 (152) 28 29 exp Infant/ or Infant Health/ or Infant Welfare/ (0) (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (158240) exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (10170) 31 32 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (1043485) 33 exp pediatrics/ (31987) (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (85431) 34 35 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (5023)

- 36 Puberty/ (2959)
- 37 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (372318)
- 38 Schools/ (29835)
- 39 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)
- 40 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (818185)
- 41 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (1140)
- 42 or/29-41 (1770729)
- 43 28 and 42 (52)

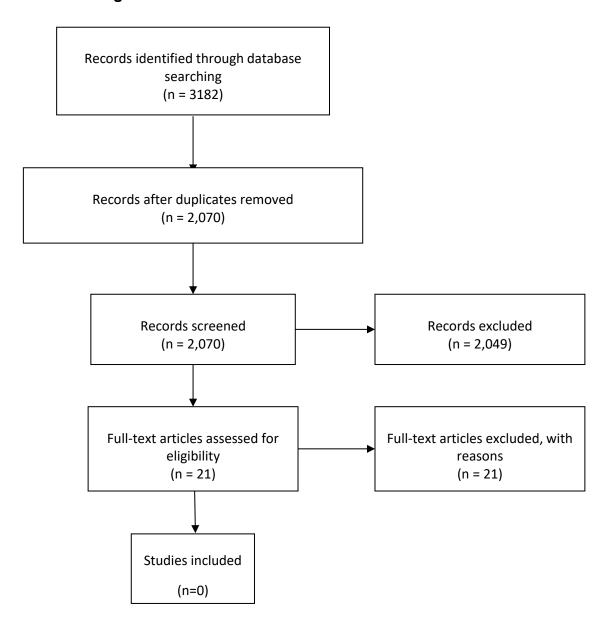
Database	: CRD (DARE)	
1	MeSH DESCRIPTOR Diabetes Mellitus EXPLODE ALL TREES	2444
2	(diabet*)	4478
3	((DM near4 ("type 1" or type1 or "type I" or "type one" or T1 or T-1 or TI or T-I)))	2
4	(lada)	1
5	((dm1 or iddm or t1d* or dka))	53
6	((dm2 or t2d* or mody or niddm))	83
7	((DM near4 ("type 2" or type2 or "type ii" or "type two" or T2 or T-2 or TII or T-II)))	4
8	((DM near4 (autoimmun* or auto immun* or brittle or labile or insulin depend* or insulin deficien*)))	0
9	((DM near4 onset* near4 (maturit* or adult* or slow*)))	0
10	((DM near4 depend* near4 (non-insulin* or non insulin* or noninsulin*)))	0
11	((DM near4 (earl* or sudden onset or juvenile or child*)))	1
12	((DM near4 (keto* or acidi* or gastropare*)))	0
13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	4525
14	MeSH DESCRIPTOR Dentistry EXPLODE ALL TREES	958
15	MeSH DESCRIPTOR Periodontal Diseases EXPLODE ALL TREES	303
16	MeSH DESCRIPTOR Dental Health Services EXPLODE ALL TREES	77

17	MeSH DESCRIPTOR Dental Staff EXPLODE ALL TREES	3
18	MeSH DESCRIPTOR Dentists EXPLODE ALL TREES	12
19	MeSH DESCRIPTOR Dental Care for Chronically III EXPLODE ALL TREES	7
20	(periodont*)	344
21	(((root* or surface*) near4 debrid*))	4
22	((((prevent* or prophyla*) near4 (dent* or oral*)))	238
23	(((scale* or scaling) near4 polish*))	5
24	((root near4 plan*))	49
25	((SRP or RSD))	12
26	((gingiv* or subgingiv*))	140
27	((gum* near4 (diseas* or infect* or disord* or inflam* or sensitiv*)))	8
28	(((tooth or teeth or dental) near4 (scaling or scale*)))	51
29	MeSH DESCRIPTOR Oral Health EXPLODE ALL TREES	37
30	(((dent* or oral*) near4 (hygien* or health)))	411
31	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30	1402
32	#13 AND #31	29
33	MeSH DESCRIPTOR Infant EXPLODE ALL TREES	2964
34	MeSH DESCRIPTOR Infant Health	0
35	MeSH DESCRIPTOR Infant Welfare	22
36	((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or newborn* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*))	5510
37	MeSH DESCRIPTOR Child EXPLODE ALL TREES	4935
38	MeSH DESCRIPTOR Child Behavior EXPLODE ALL TREES	64
39	MeSH DESCRIPTOR Child Health EXPLODE ALL TREES	2
40	MeSH DESCRIPTOR Child Welfare EXPLODE ALL TREES	90
41	MeSH DESCRIPTOR Minors EXPLODE ALL TREES	2
42	((child* or minor or minors or boy* or girl* or kid or kids or young*))	13575

43	MeSH DESCRIPTOR pediatrics EXPLODE ALL TREES	119
44	((pediatric* or paediatric* or peadiatric*))	2842
45	MeSH DESCRIPTOR Adolescent EXPLODE ALL TREES	4594
46	MeSH DESCRIPTOR Adolescent Behavior	94
47	MeSH DESCRIPTOR Adolescent Health	0
48	MeSH DESCRIPTOR Puberty	3
49	((adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*))	5621
50	MeSH DESCRIPTOR Schools EXPLODE ALL TREES	200
51	MeSH DESCRIPTOR Child Day Care Centers	12
52	MeSH DESCRIPTOR Schools, Nursery EXPLODE ALL TREES	3
53	((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*))	4454
54	(("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*"))	148
55	#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54	18461
56	#32 AND #55	3

Appendix D - Effectiveness evidence study selection

PRISMA diagram



Appendix E – Effectiveness evidence

Evidence that met the inclusion criteria specified in the review protocol was not found.

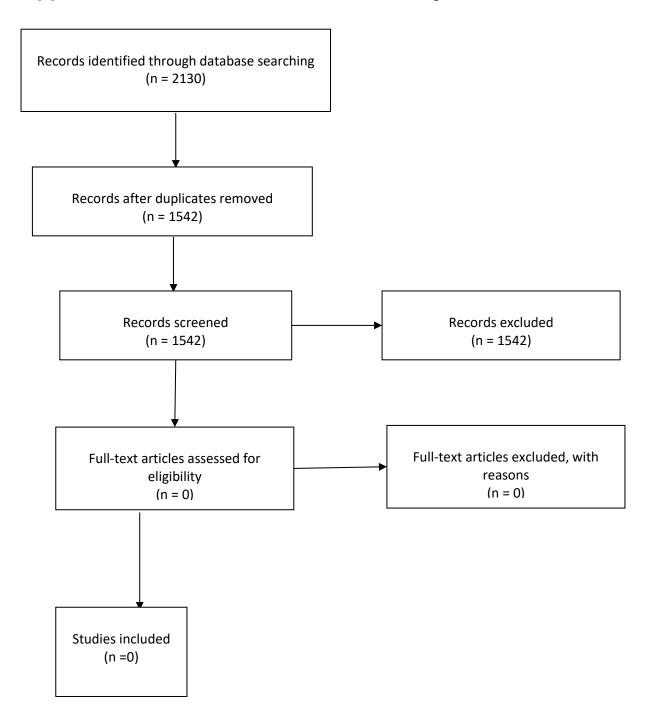
Appendix F - Forest plots

Evidence that met the inclusion criteria specified in the review protocol was not found, hence no data was available to generate forest plots.

Appendix G - GRADE tables

Studies that met the inclusion criteria specified in the review protocol were not found.

Appendix H - Economic evidence study selection



Appendix I – Economic evidence tables

There are no included studies in this review question.

Appendix J - Health economic model

There is no original modelling in this review question.

Appendix K - Excluded studies

Study	Reasons for exclusion
Aldridge, J P, Lester, V, Watts, T L et al. (1995) Single-blind studies of the effects of improved periodontal health on metabolic control in type 1 diabetes mellitus. Journal of clinical periodontology 22(4): 271-5	- Study does not contain a relevant intervention
Alpert, B (1966) Surgical treatment of chronic periapical abscesses in juvenile diabetic patients. Dental student 44(8): 651-3	- Full text paper not available
Baughman, R A (1973) Periodontal disease in the child patient. Florida dental journal 44(3): 11-21	- Not a relevant study design (opinion letter)
Calabrese, N, D'Aiuto, F, Calabrese, A et al. (2011) Effects of periodontal therapy on glucose management in people with diabetes mellitus. Diabetes & metabolism 37(5): 456-9	- Does not contain a population of children with diabetes (Adult population)
Cohen, D W, Friedman, L A, Shapiro, J et al. (1970) Diabetes mellitus and periodontal disease: two-year longitudinal observations. I. Journal of periodontology 41(12): 709-12	- Does not contain a population of children with diabetes (Adult female population)
Elheeny, A A H (2020) Determinants of oral-health related quality of life and overall quality of life among early adolescents with type-1 diabetes. Community dental health 37(3): 199-204	- Study does not contain a relevant intervention
Faizuddin, M; Prakasam, M K; Khan, K A (1987) Vascular changes in the gingiva of young insulin dependent diabetics. Journal of the Indian Dental Association 59(6789): 176-8	- No outcomes of relevance to this review
Hara, K; Imagawa, Y; Araya, S (1965) Carbohydrate in pus and exudate from gingival pockets. Including investigation with regard to relationship of blood sugar level to glucose concentration in gingival pocket fluid of periodontitis associated with diabetes mellitus. The Bulletin of Tokyo Medical and Dental University 12(3): 325-39	- Comparator in study does not match that specified in protocol (mixed population with or without diabetes (age 15-65))
Harrison, R and Bowen, W H (1987) Periodontal health, dental caries, and metabolic control in insulin-dependent diabetic children and adolescents. Pediatric dentistry 9(4): 283-6	- Comparator does not contain a population of children with diabetes (Adult population)

Study	Reasons for exclusion
Hills-Smith, H and Schuman, N J (1983) Antibiotic therapy in pediatric dentistry. II. Treatment of oral infection and management of systemic disease. Pediatric dentistry 5(1): 45-50	- Review article but not a systematic review
Hoge, H W and Kirkham, D B (1978) Juvenile diabetes and periodontitis. Dental survey 54(10): 27-9	- Not a relevant study design (cross-sectional study)
Hoshi, Adriano Tomio, Steffen, Priscila, Pawlak, Laiane Carla et al. (2018) The effect of chlorhexidine on glycemic and inflammation control in children with type 1 diabetes mellitus. Journal of Public Health (Germany) 26(1): 23-28	- Comparator in study does not match that specified in protocol (comparing mouth wash vs no mouth wash)
Kjellman, O, Henriksson, C O, Berghagen, N et al. (1970) Oral conditions in 105 subjects with insulin-treated diabetes mellitus. Svensk tandlakare tidskrift. Swedish dental journal 63(2): 99-110	- Comparator in study does not match that specified in protocol
Llambes, Fernando, Silvestre, Francisco-Javier, Hernandez-Mijares, Antonio et al. (2008) The effect of periodontal treatment on metabolic control of type 1 diabetes mellitus. Clinical oral investigations 12(4): 337-43	- Does not contain a population of children with diabetes (Adult population)
Mashimo, P.A.; Yamamoto, Y.; Slots, J. (1981) Subgingival microflora in insulin dependent diabetes mellitus (juvenile diabetes). Journal of Dental Research 60(speca)	- Not a relevant study design (split design RCT in adults)
Nagarajan, S and Chandra, R V (2012) Perception of oral health related quality of life (OHQoL-UK) among periodontal risk patients before and after periodontal therapy. Community dental health 29(1): 90-4	- Does not contain a population of children with diabetes (Adult population)
NCT03170089 (2017) Oral Health Awareness and Oral Hygiene in Insulin Dependent Diabetes Mellitus. https://clinicaltrials.gov/show/NCT03170089	Clinical trial protocol registration (status: not yet recruiting)
Ofilada, Edmund Julian L.; Jimeno, Cecilia; Barrera, Jerome (2015) Improvement in periodontitis following conservative periodontal treatment in a type 1 diabetic patient. Journal of the ASEAN Federation of Endocrine Societies 30(1): 59-63	- Not a relevant study design (Case report)

Study	Reasons for exclusion
Ringelberg, M L, Dixon, D O, Francis, A O et al. (1977) Comparison of gingival health and gingival crevicular fluid flow in children with and without diabetes. Journal of dental research 56(2): 108-11	- Comparator in study does not match that specified in protocol (<i>Diabetic vs non-diabetic children</i>)
Stein, G M and Nebbia, A A (1969) A chairside method of diabetic screening with gingival blood. Oral surgery, oral medicine, and oral pathology 27(5): 607-12	- Study does not contain a relevant intervention
Wolf, J (1977) Dental and periodontal conditions in diabetes mellitus. A clinical and radiographic study. Proceedings of the Finnish Dental Society. Suomen Hammaslaakariseuran toimituksia 73(46suppl): 1-56	- Comparator in study does not match that specified in protocol