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Detection and Treatment of Dental Problems on Chronic Disease Outcomes

Supplementary Materials

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Prepared for:
Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service
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VA | U.S. Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service

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SEARCH STRATEGIES

SYSTEMATIC REVIEW SEARCH: OVID MEDLINE (10-14-20)

Search for current systematic reviews MEDLINE Date Searched: 10-14-20		
#	**Search Statement**	**Results:**
1	exp Dental Care/ or Dental Care for Chronically Ill/ or Preventive Dentistry/ or exp Oral Hygiene/ or Oral Health/ or exp Periodontal Diseases/ or exp Dental Caries/	173818
2	(dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or oral health or dental hygiene or oral hygiene or periodont* or parodontos* or pyorrhea alveolaris or gingivitis or gingiva* or paradont* or dental decay or dental caries or carious dentin$1 or root decay).ti,ab.	172096
3	1 or 2	252602
4	exp Cardiovascular Diseases/ or exp Cerebrovascular Disorders/ or exp Diabetes Mellitus/ or exp Pulmonary Disease, Chronic Obstructive/	2761864
5	(((cardiovascular or heart) adj2 disease$1) or atheroscleros* or arterioscleros*).ti,ab.	447365
6	((cerebrovascular adj2 (disorder$1 or disease$1 or occlusion$1 or insufficienc*)) or intracranial vascular disease$1 or intracranial vascular disorder$1 or brain vascular disorder$1 or stroke).ti,ab.	276591
7	(diabetes or diabetic or glycemic control).ti,ab.	666350
8	(COPD or COAD or chronic obstructive airway disease or chronic obstructive lung disease or chronic obstructive pulmonary disease or chronic airflow obstruction).ti,ab.	70849
9	4 or 5 or 6 or 7 or 8	70849
10	3 and 9	12747
11	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or	445481

	overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.	
12	10 and 11	481
13	limit 12 to english language	460

SYSTEMATIC REVIEW SEARCH: COCHRANE DATABASE OF SYSTEMATIC REVIEWS (10-14-20)

Search for current systematic reviews
CDSR
Date Searched: 10-14-20

#	Search Statement	Results:
1	MeSH descriptor: [Dental Care] explode all trees	21
2	MeSH descriptor: [Dental Care for Chronically Ill] explode all trees	0
3	MeSH descriptor: [Preventive Dentistry] explode all trees	29
4	MeSH descriptor: [Oral Hygiene] explode all trees	23
5	MeSH descriptor: [Oral Health] explode all trees	15
6	MeSH descriptor: [Periodontal Diseases] explode all trees	32
7	MeSH descriptor: [Dental Caries] explode all trees	41
8	(dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or oral health or dental hygiene or oral hygiene or periodont* or parodontos* or pyorrhea alveolaris or gingivitis or gingiva* or paradont* or dental decay or dental caries or carious dentin$1 or root decay):ti,ab,kw	684
9		685
10	MeSH descriptor: [Cardiovascular Diseases] explode all trees	962
11	MeSH descriptor: [Cerebrovascular Disorders] explode all trees	307
12	MeSH descriptor: [Diabetes Mellitus] explode all trees	205
13	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	95
14	(((cardiovascular or heart) N2 disease$1) or atheroscleros* or arterioscleros*):ti.ab,kw	46
15	((cerebrovascular N2 (disorder$1 or disease$1 or occlusion$1	517

	or insufficienc*)) or intracranial vascular disease$1 or intracranial vascular disorder$1 or brain vascular disorder$1 or stroke):ti,ab,kw	
16	(diabetes or diabetic or glycemic control):ti,ab,kw	434
17	(COPD or COAD or chronic obstructive airway disease or chronic obstructive lung disease or chronic obstructive pulmonary disease or chronic airflow obstruction):ti,ab,kw	137
18	(OR #10-#17)	1544
19	#9 AND #18	97

PRIMARY STUDY GAP SEARCH: OVID MEDLINE (12-8-20)

Search for primary literature
MEDLINE
Date searched: 12-08-20

Search #1

#	Search Statement	Results
1	exp Cerebrovascular Disorders/ or exp Pulmonary Disease, Chronic Obstructive/ or ((cerebrovascular adj2 (disorder$1 or disease$1 or occlusion$1 or insufficienc*)) or intracranial vascular disease$1 or intracranial vascular disorder$1 or brain vascular disorder$1 or stroke or COPD or COAD or chronic obstructive airway disease or chronic obstructive lung disease or chronic obstructive pulmonary disease or chronic airflow obstruction).ti,ab.	584995
2	exp Dental Care/ or Dental Care for Chronically Ill/ or Preventive Dentistry/ or exp Periodontal Diseases/ or (dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	177113
3	1 AND 2	948
4	Limit 3 to English language	867

Search #2

#	Search Statement	Results
1	exp Cardiovascular Diseases/ or exp Diabetes Mellitus/ or (((cardiovascular or heart) adj2 disease$1) or atherosclerosis or arteriosclerosis or diabetes or diabetic or glycemic control).ti,ab.	3069969
2	exp Dental Care/ or Dental Care for Chronically Ill/ or Preventive Dentistry/ or exp Periodontal Diseases/ or (dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	177600
3	Patient Acceptance of Health Care/ or Health Care Costs/ or Quality of Life/ or Self Report/ or ((health?care adj1 (utilization or acceptance or acceptor$1 or seeking or costs$1)) or health cost$1 or treatment cost$1 or (quality adj1 life) or self?report$1 or (patient-reported adj2 symptom$1)).ti,ab.	338796
4	1 and 2 and 3	166
5	Limit 4 to English language	159

PRIMARY STUDY GAP SEARCH: CCRCT (12-14-20)

Search for primary literature
CCRCT
Date searched: 12-14-20

Search #1

#	Search Statement	Results
1	((cerebrovascular adj2 (disorder$1 or disease$1 or occlusion$1 or insufficienc*)) or intracranial vascular disease$1 or intracranial vascular disorder$1 or brain vascular disorder$1 or stroke or COPD or COAD or chronic obstructive airway disease or chronic obstructive lung disease or chronic obstructive pulmonary disease or chronic airflow obstruction).ti,ab.	75984
2	(Cerebrovascular Disorders or Pulmonary Disease, Chronic Obstructive).kw.	85
3	1 OR 2	76005
4	(dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	14433
5	(Dental Care or Dental Care for Chronically Ill or Preventive Dentistry or Periodontal Diseases).kw.	141
6	4 OR 5	14482
7	3 AND 6	70
8	Limit 7 to English language	45

Search #2

#	Search Statement	Results
1	(((cardiovascular or heart) adj2 disease$1) or atherosclerosis or arteriosclerosis or diabetes or diabetic or glycemic control).ti,ab.	128047
2	(Cardiovascular Disease or Diabetes Mellitus).kw.	36268
3	1 or 2	133483
4	(dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	14433
5	(Dental Care or Dental Care for Chronically Ill or Preventive Dentistry or Periodontal Diseases).kw.	141
6	4 or 5	14482
7	((health?care adj1 (utilization or acceptance or acceptor$1 or seeking or costs$1)) or health cost$1 or treatment cost$1 or (quality adj1 life) or self?report$1 or (patient-reported adj2 symptom$1)).ti,ab.	108801
8	(Patient Acceptance of Health Care or Health Care Costs or Quality of Life or Self Report).kw.	40851
9	7 or 8	119502
10	3 AND 6 AND 9	35
11	Limit 10 to English language	15

PRIMARY STUDY UPDATE SEARCH: OVID MEDLINE (2-5-21)

Ovid MEDLINE(R) ALL 1946 to February 03, 2021 Date Searched: 02-05-21		
#	**Search Statement**	**Results**
1	exp Cardiovascular Diseases/ or exp Diabetes Mellitus/ or (((cardiovascular or heart) adj2 disease$1) or atherosclerosis or arteriosclerosis or diabetes or diabetic or glycemic control).ti,ab.	3091462
2	exp Dental Care/ or Dental Care for Chronically Ill/ or Preventive Dentistry/ or exp Periodontal Diseases/ or (dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	178775
3	Chronic Disease Indicators/ or Glycated Hemoglobin A/ or exp Triglycerides/ or C-Reactive Protein/ or Interleukin-6/ or Cholesterol, HDL/ or Cholesterol, LDL/ or (clinical outcome$1 OR chronic disease indicator$1 OR HbA1c OR glycated hemoglobin OR fasting blood glucose OR total cholesterol OR triglycerides OR tricylglycerol$1 OR HDL OR LDL OR C-reactive protein OR IL-6 OR systematic inflammation OR endothelial function OR TNF-alpha OR blood pressure or hs?CRP or interleukin 6 or MGI-2 or cholesterol).ti,ab.	1118111
4	1 or 2 or 3	2048
5	Limit 4 to english language and yr=”2019-2020”)	263

PRIMARY STUDY UPDATE SEARCH: CCRCT (2-5-20)

EBM Reviews - Cochrane Central Register of Controlled Trials December 2020 Date Searched: 02-05-21		
#	Search Statement	Results
1	exp Cardiovascular Diseases/ or exp Diabetes Mellitus/ or (((cardiovascular or heart) adj2 disease$1) or atherosclerosis or arteriosclerosis or diabetes or diabetic or glycemic control).ti,ab.	216678
2	exp Dental Care/ or Dental Care for Chronically Ill/ or Preventive Dentistry/ or exp Periodontal Diseases/ or (dental health service$1 or dental care or dental practice or preventive dentistry or preventive dentistries or periodontal or periodontitis or parodontosis or pyorrhea alveolaris or gingivitis or gingiva or gingival or paradontal or paradontopathia or paradontosis).ti,ab.	16291
3	Chronic Disease Indicators/ or Glycated Hemoglobin A/ or exp Triglycerides/ or C-Reactive Protein/ or Interleukin-6/ or Cholesterol, HDL/ or Cholesterol, LDL/ or (clinical outcome$1 OR chronic disease indicator$1 OR HbA1c OR glycated hemoglobin OR fasting blood glucose OR total cholesterol OR triglycerides OR tricylglycerol$1 OR HDL OR LDL OR C-reactive protein OR IL-6 OR systematic inflammation OR endothelial function OR TNF-alpha OR blood pressure or hs?CRP or interleukin 6 or MGI-2 or cholesterol).ti,ab.	187811
4	1 or 2 or 3	388
5	Limit 4 to english language and yr=”2019-2020”)	23

INCLUSION/EXCLUSION CRITERIA

	Include	Exclude	Code
Population	Include adults with cardiovascular disease, cerebrovascular disease, diabetes, or COPD.	Exclude children; pregnant adults; adults without chronic diseases; adults with chronic diseases other than those listed	E1
Intervention	Include *SRs*- any preventive dental treatment *Primary studies*- periodontal treatment	Exclude patient brushing/flossing, treatment of rare or advanced conditions occurring outside the routine dental care setting	E2
Comparator	Include: no detection or treatment of dental problems	Exclude other active comparators such as alternative treatments, alternative timing of treatments, and alternative intensity of treatments	E3
Outcomes	Include ○ Clinical outcomes (*eg*, patient-reported symptoms, complications of chronic diseases) ○ Chronic disease indicators (*eg*, HbA1c, blood pressure, cholesterol, SpO2, other measures of chronic inflammation) ○ Quality of life (*eg*, oral health-related quality of life, overall quality of life) ○ Health care utilization (*eg*, emergency department visits for non-traumatic dental conditions or non-dental conditions, health care visits associated with chronic disease management, direct costs) ○ Harms (Any)	Exclude all other outcomes	E4
Timing	Include any timing	NA	E5
Setting	Include any setting	NA	E6
Study Design	Include *SRs*- Any that meet the following 4 criteria- • Explicit and adequate search • Application of predefined eligibility criteria to select studies • Risk of bias assessment for included studies • Synthesis of results *Primary studies*- Any study design	Exclude *SRs*- those that don't meet these 4 criteria *Primary studies*- NA	E7
Publication type	Include full-text studies	Exclude: Abstract only, protocol only, editorial, letter, narrative review, guidelines	E8
Outdated or ineligible SR	NA	Exclude systematic reviews that use outdated methods or were updated by another, published review	E9
Language	Include English	Exclude languages other than English	E10

LIST OF EXCLUDED STUDIES

Exclude reasons: 1=Ineligible population, 2=Ineligible intervention, 3=Ineligible comparator, 4=Ineligible outcome, 5=Ineligible timing, 6=Ineligible setting, 7=Ineligible study design, 8=Ineligible publication type, 9=Outdated or ineligible systematic review, 10=Not available in English

#	Citation	Exclude reason
1	Abduljabbar T, Javed F, Shah A, Samer MS, Vohra F, Akram Z. Role of lasers as an adjunct to scaling and root planing in patients with type 2 diabetes mellitus: a systematic review. Lasers in Medical Science. 2017;32(2):449-459.	E3
2	Alexander RE, Grogan DM. Management of dental patients with obstructive lung diseases. Texas Dental Journal. 2008;125(3):228-240.	E8
3	Al-Hamoudi N. Is antimicrobial photodynamic therapy an effective treatment for chronic periodontitis in diabetes mellitus and cigarette smokers: a systematic review and meta-analysis. Photodiagnosis & Photodynamic Therapy. 2017;19:375-382.	E3
4	Alim BA, Canturk E, Koksal C. The effect of treated apical periodontitis before heart valve surgery on C-reactive protein levels. Oral Diseases. 2020;24:24.	E1
5	Androsz-Kowalska O, Jankowski K, Rymarczyk Z, Kowalski J, Pruszczyk P, Gorska R. Correlation between clinical parameters of periodontal disease and mean platelet volume in patients with coronary artery disease: a pilot study. Kardiologia Polska. 2013;71(6):600-605.	E4
6	Brignardello-Petersen R. There seem to be no benefits from periodontal treatment on glycated hemoglobin levels of patients with uncontrolled diabetes mellitus 3 months after treatment. Journal of the American Dental Association. 2019;150(4):e43.	E7
7	Brignardello-Petersen R. There is still no high-quality evidence that periodontitis is a risk factor for hypertension or that periodontal treatment has beneficial effects on blood pressure. Journal of the American Dental Association. 2020;151(4):e31.	E7
8	Brown TT, Dela Cruz E, Brown SS. The effect of dental care on cardiovascular disease outcomes: an application of instrumental variables in the presence of heterogeneity and self-selection. Health Economics. 2011;20(10):1241-1256.	E2
9	Chandra S, Shashikumar P. Diode Laser - A Novel Therapeutic Approach in the Treatment of Chronic Periodontitis in Type 2 Diabetes Mellitus Patients: A Prospective Randomized Controlled Clinical Trial. Journal of Lasers in Medical Sciences. 2019;10(1):56-63.	E7
10	Chen ZY, Chiang CH, Huang CC, et al. The association of tooth scaling and decreased cardiovascular disease: a nationwide population-based study. American Journal of Medicine. 2012;125(6):568-575.	E1
11	Cortelli SC, Costa FO, Gargioni-Filho A, et al. Impact of gingivitis treatment for diabetic patients on quality of life related to periodontal objective parameters: A randomized controlled clinical trial. Archives of Oral Biology. 2018;86:80-86.	E2
12	Cotti E, Arrica M, Di Lenarda A, et al. The perioperative dental screening and management of patients undergoing cardiothoracic, vascular surgery and other cardiovascular invasive procedures: A systematic review. European Journal of Preventive Cardiology. 2017;24(4):409-425.	E7

#	Citation	Exclude reason
13	Czesnikiewicz-Guzik M, Osmenda G, Siedlinski M, et al. Causal association between periodontitis and hypertension: evidence from Mendelian randomization and a randomized controlled trial of non-surgical periodontal therapy. European Heart Journal. 2019;40(42):3459-3470.	E3
14	D'Aiuto F, Orlandi M, Gunsolley JC. Evidence that periodontal treatment improves biomarkers and CVD outcomes. Journal of Periodontology. 2013;84(4 Suppl):S85-S105.	E7
15	Darre L, Vergnes JN, Gourdy P, Sixou M. Efficacy of periodontal treatment on glycaemic control in diabetic patients: A meta-analysis of interventional studies. Diabetes & Metabolism. 2008;34(5):497-506.	E7
16	de Oliveira C, Watt R, Hamer M. Toothbrushing, inflammation, and risk of cardiovascular disease: results from Scottish Health Survey. BMJ. 2010;340:c2451.	E2
17	Engebretson S, Kocher T. Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis. Journal of Periodontology. 2013;84(4 Suppl):S153-169.	E7
18	Freitas CO, Gomes-Filho IS, Naves RC, et al. Influence of periodontal therapy on C-reactive protein level: a systematic review and meta-analysis. Journal of Applied Oral Science. 2012;20(1):1-8.	E1
19	Garcia R. Periodontal treatment could improve glycaemic control in diabetic patients. Evidence-Based Dentistry. 2009;10(1):20-21	E8
20	Garg A, Guez G. Study links oral care to lower diabetes costs. Dental Implantology Update. 2012;23(5):37-40.	E8
21	Henschel M, Keenan AV. Insufficient evidence of effect of periodontal treatment on prevention or management of cardiovascular disease. Evidence-Based Dentistry. 2015;16(1):17-18.	E8
22	Huang JL, Chen WK, Lin CL, et al. Association between intensive periodontal treatment and spontaneous intracerebral hemorrhage-a nationwide, population-based cohort study. Medicine. 2019;98(10):e14814.	E1
23	Improved Health and Lower Medical Costs: Why Good Dental Care is Important. Cigna. https://www.cigna.com/assets/docs/life-wall-library/Whygooddentalcareisimportant_whitepaper.pdf. Published 2020. Updated June 1, 2016. Accessed February 11, 2021.	E7
24	Ioannidou E, Malekzadeh T, Dongari-Bagtzoglou A. Effect of periodontal treatment on serum C-reactive protein levels: a systematic review and meta-analysis. J Periodontol. 2006 Oct;77(10):1635-42. doi: 10.1902/jop.2006.050443. PMID: 17032104.	E1
25	Irani FC, Wassall RR, Preshaw PM. Impact of periodontal status on oral health-related quality of life in patients with and without type 2 diabetes. Journal of Dentistry. 2015;43(5):506-511.	E3
26	Janket SJ. Scaling and root-planing (SRP) may improve glycemic control and lipid profile in patients with chronic periodontitis (CP) and type 2 diabetes (DM2) in a specific subgroup: a meta-analysis of randomized clinical trials. The Journal of Evidencebased Dental Practice. 2014;14(1):31-33	E8
27	Janket SJ, Wightman A, Baird AE, Van Dyke TE, Jones JA. Does periodontal treatment improve glycemic control in diabetic patients? A meta-analysis of intervention studies. Journal of Dental Research. 2005;84(12):1154-1159.	E7
28	Jeffcoat M, Hall M, Hedlund C. Periodontal treatment and medical costs in diabetes and cerebrovascular accident. Paper presented at: International Association for Dental Research Meeting, Miami, Florida2009.	E8

#	Citation	Exclude reason
29	Jones JA, Miller DR, Wehler CJ, et al. Does periodontal care improve glycemic control? The Department of Veterans Affairs Dental Diabetes Study. Journal of Clinical Periodontology. 2007;34(1):46-52.	E4
30	Jones JA, Miller DR, Wehler CJ, et al. Study design, recruitment, and baseline characteristics: the Department of Veterans Affairs Dental Diabetes Study. Journal of Clinical Periodontology. 2007;34(1):40-45.	E4
31	Kim HK, Kim YG, Cho JH, Lee SK, Lee JM. The effect of periodontal and prosthodontic therapy on glycemic control in patients with diabetes. The Journal of Advanced Prosthodontics. 2019;11(5):247-252.	E3
32	Kumar G, Ponnaiyan D, Parthasarathy H, Tadepalli A, Veeramani S. Evaluation of Endocan and Tumor Necrosis Factor-alpha as Inflammatory Biomarkers in Type 2 Diabetes and Periodontal Disease. Genetic Testing & Molecular Biomarkers. 2020;24(7):431-435.	E8
33	Lam OL, Zhang W, Samaranayake LP, Li LS, McGrath C. A systematic review of the effectiveness of oral health promotion activities among patients with cardiovascular disease. International Journal of Cardiology. 2011;151(3):261-267.	E7
34	Li C, Lv Z, Shi Z, et al. Periodontal therapy for the management of cardiovascular disease in patients with chronic periodontitis. Cochrane Database of Systematic Reviews. 2014(8):CD009197.	E9
35	Li C, Lv Z, Shi Z, et al. Periodontal therapy for the management of cardiovascular disease in patients with chronic periodontitis. Cochrane Database of Systematic Reviews. 2017;11:CD009197.	E9
36	Lin HW, Chen CM, Yeh YC, et al. Dental treatment procedures for periodontal disease and the subsequent risk of ischaemic stroke: A retrospective population-based cohort study. Journal of Clinical Periodontology. 2019;46(6):642-649.	E1
37	Luo H, Bell RA, Wright W, Wu Q, Wu B. Trends in annual dental visits among US dentate adults with and without self-reported diabetes and prediabetes, 2004-2014. Journal of the American Dental Association. 2018;149(6):460-469	E2
38	Madianos PN, Koromantzos PA. An update of the evidence on the potential impact of periodontal therapy on diabetes outcomes. Journal of Clinical Periodontology. 2018;45(2):188-195.	E7
39	Marano A, Hahn M, Hall M, Hedlund C, Sun C, R G. Appropriate Periodontal Therapy Associated with Lower Medical Utilization and Costs. Cigna. https://www.cigna.com/assets/docs/business/small-employers/853244_c_select_value_prop_final-6-9.pdf. Published 2013. Updated March 2013. Accessed February 11, 2021.	E8
40	Merchant AT. Will periodontal treatment prevent heart disease and stroke? The Journal of Evidencebased Dental Practice. 2012;12(4):212-215.	E8
41	Mirza S, Khan AA, Al-Kheraif AA, Khan SZ, Shafqat SS. Efficacy of adjunctive photodynamic therapy on the clinical periodontal, HbA1c and advanced glycation end product levels among mild to moderate chronic periodontal disease patients with type 2 diabetes mellitus: A randomized controlled clinical trial. Photodiagnosis & Photodynamic Therapy. 2019;28:177-182.	E3
42	Montenegro MM, Ribeiro IWJ, Kampits C, et al. Randomized controlled trial of the effect of periodontal treatment on cardiovascular risk biomarkers in patients with stable coronary artery disease: Preliminary findings of 3 months. Journal of Clinical Periodontology. 2019;46(3):321-331.	E3
43	Mori C, Hakuta C, Endo K, et al. The effects of professional oral health care on patients in the subacute stage of emergent neurosurgical disorders. Special Care in Dentistry. 2012;32(6):259-264.	E1

#	Citation	Exclude reason
44	Moura Foz A, Alexandre Romito G, Manoel Bispo C, et al. Periodontal therapy and biomarkers related to cardiovascular risk. Minerva Stomatologica. 2010;59(5):271-283.	E7
45	Munjal A, Jain Y, Kote S, et al. A study on the change in HbA1c levels before and after non-surgical periodontal therapy in type-2 diabetes mellitus in generalized periodontitis. Journal of Family Medicine & Primary Care. 2019;8(4):1326-1329.	E3
46	Munoz Aguilera E, Suvan J, Buti J, et al. Periodontitis is associated with hypertension: a systematic review and meta-analysis. Cardiovascular Research. 2020;116(1):28-39.	E7
47	Nishioka S, Maruyama K, Tanigawa T, et al. Effect of non-surgical periodontal therapy on insulin resistance and insulin sensitivity among individuals with borderline diabetes: A randomized controlled trial. Journal of Dentistry. 2019;85:18-24.	E1
48	Oates TW, Huynh-Ba G, Vargas A, Alexander P, Feine J. A critical review of diabetes, glycemic control, and dental implant therapy. Clinical Oral Implants Research. 2013;24(2):117-127.	E7
49	Obadan-Udoh E, Jordan S, Mudah O, Borgnakke W, Tavares M. Gap Analysis of Older Adults With Type 2 Diabetes Receiving Nonsurgical Periodontal Therapy. The Journal of Evidencebased Dental Practice. 2017;17(4):335-349.	E7
50	Orlandi M, Suvan J, Petrie A, et al. Association between periodontal disease and its treatment, flow-mediated dilatation and carotid intima-media thickness: a systematic review and meta-analysis. Atherosclerosis. 2014;236(1):39-46.	E7
51	Oates TW, Huynh-Ba G, Vargas A, Alexander P, Feine J. A critical review of diabetes, glycemic control, and dental implant therapy. Clinical Oral Implants Research. 2013;24(2):117-127.	E7
52	Paraskevas S, Huizinga JD, Loos BG. A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. Journal of Clinical Periodontology. 2008;35(4):277-290.	E1
53	Patil VA, Desai MH. Effect of periodontal therapy on serum C-reactive protein levels in patients with gingivitis and chronic periodontitis: a clinicobiochemical study. Journal of Contemporary Dental Practice [Electronic Resource]. 2013;14(2):233-237	E1
54	Parenti A, Paccosi S, Cairo F, Defraia E. Treatment of Periodontitis for the Prevention of Endothelial Dysfunction: A Narrative Review. Current Vascular Pharmacology. 2015;13(6):749-758.	E7
55	Park SY, Kim SH, Kang SH, et al. Improved oral hygiene care attenuates the cardiovascular risk of oral health disease: a population-based study from Korea. European Heart Journal. 2019;40(14):1138-1145.	E2
56	Pedersen PU, Uhrenfeldt L, Larsen P. Oral hygiene in patients with chronic obstructive pulmonary disease: a scoping review protocol. JBI Database Of Systematic Reviews And Implementation Reports. 2017;15(5):1236-1241.	E2
57	Polzer I, Schwahn C, Volzke H, Mundt T, Biffar R. The association of tooth loss with all-cause and circulatory mortality. Is there a benefit of replaced teeth? A systematic review and meta-analysis. Clinical Oral Investigations. 2012;16(2):333-351.	E1
58	Pohjamo L, Tervonen T, Knuuttila M, Nurkkala H. Adult diabetic and nondiabetic subjects as users of dental services. A longitudinal study. Acta Odontologica Scandinavica. 1995;53(2):112-114.	E3

#	Citation	Exclude reason
59	Ramirez JH, Arce RM, Contreras A. Periodontal treatment effects on endothelial function and cardiovascular disease biomarkers in subjects with chronic periodontitis: protocol for a randomized clinical trial. Trials [Electronic Resource]. 2011;12:46.	E4
60	Redd KT, Phillips ST, McMillian B, et al. PeRiodontal Treatment to Eliminate Minority Inequality and Rural Disparities in Stroke (PREMIERS): A Multicenter, Randomized, Controlled Study. International Journal of Cerebrovascular Disease & Stroke. 2019;2(2).	E4
61	Reichert S, Schlitt A, Beschow V, et al. Use of floss/interdental brushes is associated with lower risk for new cardiovascular events among patients with coronary heart disease. Journal of Periodontal Research. 2015;50(2):180-188.	E2
62	Roca-Millan E, Gonzalez-Navarro B, Sabater-Recolons MM, Mari-Roig A, Jane-Salas E, Lopez-Lopez J. Periodontal treatment on patients with cardiovascular disease: Systematic review and meta-analysis. Medicina Oral, Patologia Oral y Cirugia Bucal. 2018;23(6):e681-e690.	E7
63	Romero SS, Pinto EH, Longo PL, et al. Effects of periodontal treatment on exacerbation frequency and lung function in patients with chronic periodontitis: study protocol of a 1-year randomized controlled trial. BMC Pulmonary Medicine. 2017;17(1):23.	E4
64	Salvi GE, Carollo-Bittel B, Lang NP. Effects of diabetes mellitus on periodontal and peri-implant conditions: update on associations and risks. Journal of Clinical Periodontology. 2008;35(8 Suppl):398-409.	E7
65	Sanz M, Ceriello A, Buysschaert M, et al. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. Journal of Clinical Periodontology. 2018;45(2):138-149.	E8
66	Sanchez P, Salamonson Y, Everett B, George A. Barriers and Predictors Associated With Accessing Oral Healthcare Among Patients With Cardiovascular Disease in Australia. Journal of Cardiovascular Nursing. 2019;34(3):208-214.	E4
67	Seinost G, Wimmer G, Skerget M, et al. Periodontal treatment improves endothelial dysfunction in patients with severe periodontitis. American Heart Journal. 2005;149(6):1050-1054.	E1
68	Sen S, Giamberardino LD, Moss K, et al. Periodontal Disease, Regular Dental Care Use, and Incident Ischemic Stroke. Stroke. 2018;49(2):355-362.	E1
69	Seshima F, Nishina M, Namba T, Saito A. Periodontal Regenerative Therapy in Patient with Chronic Periodontitis and Type 2 Diabetes Mellitus: A Case Report. Bulletin of Tokyo Dental College. 2016;57(2):97-104.	E3
70	Sgolastra F, Severino M, Pietropaoli D, Gatto R, Monaco A. Effectiveness of periodontal treatment to improve metabolic control in patients with chronic periodontitis and type 2 diabetes: a meta-analysis of randomized clinical trials. Journal of Periodontology. 2013;84(7):958-973.	E9
71	Shen TC, Chang PY, Lin CL, et al. Periodontal Treatment Reduces Risk of Adverse Respiratory Events in Patients With Chronic Obstructive Pulmonary Disease: A Propensity-Matched Cohort Study. Medicine. 2016;95(20):e3735.	E3
72	Sheiham A. Claims that periodontal treatment reduces costs of treating five systemic conditions are questionable. *The Journal of Evidencebased Dental Practice.* 2015;15(1):35-36.	E8

#	Citation	Exclude reason
73	Skaar D, O'Connor H, Lunos S, Luepker R, Michalowicz BS. Dental procedures and risk of experiencing a second vascular event in a Medicare population. Journal of the American Dental Association. 2012;143(11):1190-1198	E2
74	Sun WL, Chen LL, Zhang SZ, Ren YZ, Qin GM. Changes of adiponectin and inflammatory cytokines after periodontal intervention in type 2 diabetes patients with periodontitis. Archives of Oral Biology. 2010;55(12):970-974.	E4
75	Syrjala AM, Kneckt MC, Knuuttila ML. Dental self-efficacy as a determinant to oral health behaviour, oral hygiene and HbA1c level among diabetic patients. Journal of Clinical Periodontology. 1999;26(9):616-621.	E2
76	Taylor GW. Periodontal treatment and its effects on glycemic control: a review of the evidence. Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics. 1999;87(3):311-316.	E7
77	Taylor GW. Bidirectional interrelationships between diabetes and periodontal diseases: an epidemiologic perspective. Annals of Periodontology. 2001;6(1):99-112.	E7
78	Teeuw WJ, Gerdes VE, Loos BG. Effect of periodontal treatment on glycemic control of diabetic patients: a systematic review and meta-analysis. Diabetes Care. 2010;33(2):421-427.	E1
79	Tonetti MS. Periodontitis and risk for atherosclerosis: an update on intervention trials. Journal of Clinical Periodontology. 2009;36 Suppl 10:15-19.	E6
80	Tonetti MS, D'Aiuto F, Nibali L, et al. Treatment of periodontitis and endothelial function. N Engl J Med. 2007;356(9):911-920.	E1
81	Vergnes JN. Treating periodontal disease may improve metabolic control in diabetics. Evidence-Based Dentistry. 2010;11(3):73-74	E8
82	Wang X, Han X, Guo X, Luo X, Wang D. The effect of periodontal treatment on hemoglobin a1c levels of diabetic patients: a systematic review and meta-analysis. PLoS ONE [Electronic Resource]. 2014;9(9):e108412.	E2
83	Watts T. Periodontal treatment and glycemic control in diabetic patients: the problem of a possible Hawthorne effect. Journal of Dental Research. 2006;85(4):294; author reply 294-295.	E8

SEVENTEEN INCLUDED BUT DE-PRIORITIZED SYSTEMATIC REVIEWS

Author Year	Reason de-prioritized
Cao 2019[1]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Jain 2019[2]	Included in Ata-Ali 2020
Hasuike 2017[3]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Manger 2017[4]	Did not find any studies on link between periodontal disease treatment & COPD
Botero 2016[5]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Faggion 2016[6]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Perez Losado 2016[7]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Teshome 2016[8]	PICOs covered by more recent review of reviews (Ata-Ali 2020)
Artese 2015[9]	PICOs covered by more recent reviews (systematic inflammation: Beza 2020 & Lima 2019) or more comprehensive review (harms: Simpson 2015).
Li 2015[10]	Included in Ata-Ali 2020
Mauri-Obradors 2015[11]	Included in Ata-Ali 2020
Schmitt 2015[12]	Only potentially relevant outcome measured among people with hypertension was “arterial stiffness” which was evaluated in a single study and has limited clinical relevance.
Sun 2014[13]	Included in Ata-Ali 2020
Wang 2014[14]	Included in Ata-Ali 2020
Corbella 2013[15]	PICOs covered by more recent review of reviews (Ata-Ali 2020)

Liew 2013[16]	Included in Ata-Ali 2020
Teeuw 2010[17]	Included in Ata-Ali 2020

EVIDENCE TABLES

DATA ABSTRACTION OF PRIORITIZED SYSTEMATIC REVIEWS

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
Ata-Ali 2020[18]	PubMed MEDLINE, Cochrane Library, Scopus and LILACS database. Database inception - Sep 2019 P: Pts with T2 diabetes I: Nonsurgical periodontal therapy C: No periodontal therapy O: HbA1c and/or fasting blood glucose T: 3+ months S: SRs: had to perform a meta-analysis; Primary studies: had to be RCTs	11 meta-analyses of 27 primary studies	N=1,341 pts with T2 diabetes in 11 RCTs from author's meta-analysis	Non-surgical periodontal therapy (*ie*, scaling and root planing with adjunctive treatments such as antibiotics or oral hygiene)	**HbA1c**: Eight meta-analyses found significant improvement in HbA1c and 2 found non-significant improvement in HbA1c. From meta-analysis of 11 RCTs conducted by review authors: periodontal treatment was associated with significant improvements in HbA1c compared to controls (Mean difference: -.32% [.5, -.15]). **FBG**: 1 meta-analysis found significant improvement in FBG compared to controls and 2 found a non-significant improvement. From meta-analysis of 6 RCTs conducted by review authors: periodontal treatment associated with significant improvements in FBG compared to controls (Mean difference: -11.59 [-15.2, -8.0]).
Baeza 2020[19]	PubMed MEDLINE, CENTRAL Database inception - Jul 2018 P: Pts with T2 diabetes and periodontitis I: Periodontal treatment (oral hygiene instruction and SRP with or without flap surgery C: No periodontal therapy O: HbA1c, C-reactive protein (CRP), adverse	9 RCTs	N=623 pts with T2 diabetes and periodontitis	8 RCTs looked at conventional periodontal treatment with nonsurgical SRP, one RCT included surgical debridement at 3 months	**HbA1c:** Meta-analysis indicted a significant reduction in %HbA1c from the beginning to the end of the follow-up in the intervention group [differences in means (DM)=0.56, 95% CI (0.36-0.75), p<0.00001]. **CRP:** the meta-analysis indicated a significant reduction from the start to the end of follow-up in favor of the intervention group [DM=1.89, 95% CI (1.70-2.08), p<0.00001]. **Adverse events**: None of the included studies reported the occurrence of adverse effects or complications related to periodontal treatment.

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
	events T: 3+ months S: RCTs				
Garde 2019[20]	PubMed, MEDLINE via Ovid, EMBASE via Ovid, Web of Science. Up to May 2019 P: Pts with T2 diabetes I: Anti-inflammatory surgical or non-surgical periodontal treatment C: no periodontal treatment or only supragingival scaling and polishing O: Lipid profiles T: NR S: Excluded cross-sectional studies, retrospective studies, and studies that didn't include pre-post data	7 studies	N= 707 pts with T2 diabetes	6 studies looked at non-surgical periodontal treatment, 1 looked at surgical + non-surgical periodontal treatment	**Total cholesterol:** Based on 4 studies of 235 ppts, periodontal therapy was associated with significant improvements in total cholesterol levels (mean difference -.47 mmol/L [-.75 to -.18 mmol/L], p=.001) compared to control group at 3 months. No differences between groups at 6 months based on 3 studies. **Triglycerides**: Based on 4 studies of 330 ppts, periodontal therapy was associated with significant improvements in triglycerides (mean difference -.2 mmol/L [-.24 to -.16 mmol/L], p=.00001) compared to control group at 3 months. No differences between groups at 6 months based on 3 studies. **LDL:** Based on 4 studies of 330 ppts, there was difference between intervention and control groups in terms of LDL at 3 months. No differences between groups at 6 months based on 3 studies. **HDL**: Based on 5 studies of 392 ppts, control groups were associated with significant improvements in HDL compared to periodontal therapy (mean difference .06 mmol/L [.03 to .08 mmol/L], p=.00001) at 3 months. No differences between groups at 6 months based on 3 studies.
Lima 2019[21]	PubMed, Web of Science, Scopus, MEDLINE Ovid, Lilacs. Up to Feb 2018	15 studies	N= 622 pts with T2 diabetes	15 studies looked at periodontal therapy	**IL-6:** Seven studies demonstrated periodontal therapy contributes to the reduction of serum IL-6, while 9 studies did not find any impact of periodontal intervention on IL-6.

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
	P: Pts with T2 diabetes I: Periodontal treatment C: No periodontal treatment O: Serum IL-6 levels T: NR S: Excluded cross-sectional and case-control studies				
Liu 2019[22]	Cochrane Oral Health's Trial Register, CENTRAL, MEDLINE Ovid, Embase Ovid, CINAHL EBSCO, OpenGrey, CBM, CNKI, and VIP, plus the US National Institutes of Health Trials Register and the WHO Clinical Trials Registry Platform and Sciencepaper Online. Up to Sep 2019 P: Pts with chronic periodontitis with or without CVD I: Periodontal therapy subgingival scaling and root planing, with or without systemic antibiotic or host modulation and other active remedies C: Maintenance therapy or no periodontal treatment, with or without same active remedies as	1 RCT of pts with CVD (secondary prevention)	N=303 ppts with ≥50% blockage of one coronary artery or have had a coronary event within the preceding 3 years	Oral hygiene instruction + full mouth scaling and root planing	**All-cause and CVD-related death**: NR **All cardiovascular events, blood test results, adverse events**: No useable data due to large loss to follow-up.

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
	intervention group O: All-cause and CVD-related death; all cardiovascular events (angina, myocardial infarction, stroke); modifiable CVD risk factors; blood test results; heart function parameters; revascularisation procedures; adverse events T: 1+ years S: RCTs				
D'Autio 2017[23]	Cochrane, PubMed, OVID Embase, OVID MEDLINE, and OVID PsycInfo. 2005 to 2015 P: NR I: NR C: NR O: Link between diabetes and oral health T: NR S: SRs and meta-analyses	8 SRs on periodontal therapy & glycemic control. 2 SRs on periodontal therapy & systemic inflammation.	Patients with type 1 or type 2 diabetes (N=NR)	Periodontal therapy involving scaling and root planing	**HbA1c**: One high-quality systematic review provides evidence that in patients with type 2 diabetes, intensive periodontal therapy involving scaling and root planing reduced HbA1c by 0.29% [3-4 mmol/l] for up to 3 months; however, after 6 months there was no evidence that this reduction was sustained. Modest improvements in glycemic control, as demonstrated by a reduction in Hb1Ac, are supported by 7 other moderate quality systematic reviews, while 1 was equivocal. **Systematic inflammation**: One high-quality review suggests that periodontal treatment reduced markers of systemic inflammation in patients with diabetes: serum levels of TNF- α and CRP. Another review found no significant improvements in lipid fractions (total cholesterol, triglycerides and high and low density lipoprotein cholesterol) in patients with diabetes and chronic periodontitis who received scaling and

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
					root planing.
Simpson 2015[24]	Cochrane Oral Health Group Trials Registry, CENTRAL, Ovid MEDLINE, Ovid Embase, CINAHL, LILACS, ISI Web of Knowledge, ZETOC. Database inception to Dec 2014 P: People 16+ years with T1 or T2 diabetes and periodontitis I: Periodontal treatments that could include oral hygiene instruction or education C: No treatment, usual care, or placebo O: HbA1c, periodontal attachment level, gingival indices, plaque indices, adverse events, quality of life, cost, diabetic complications T: S: RCTs	35 RCTs	N=2,565 ppts, most of which had T2 diabetes (2 studies among those with T1 diabetes were included)	Non-surgical periodontal therapy	**HbA1c:** Overall, there was a benefit of periodontal therapy compared to no treatment at 3-4 months with a mean percentage reduction in HbA1c of -0.29 (95% confidence interval (CI) -0.48 to -0.10; effect P = 0.003). However, at 6 months there was no benefit for periodontal therapy with mean percentage reduction in HbA1c of -0.02 (95% CI -0.20 to 0.16; effect P = 0.84). **Adverse events:** Twenty-two studies did not report on adverse events. 8 studies reported no adverse events occurred. One study reported adverse events occurred from use of doxycycline. Three studies reported no major adverse occurred. Three studies reported minor adverse events due to treatment in both groups such as diarrhea, headaches, pain, nausea/vomiting, taste change, tooth stain, mouth irritation, swelling, & breathlessness. **Quality of life, cost, diabetic complications**: No studies reported data on any of these outcomes.
D'Isidoro 2019[25]	PubMed, Google Scholar & Scopus. Up to Dec 2018 P: Participants of any age, healthy or affected by CVD I: Periodontal treatment	3 controlled clinical trials examined periodontal treatment exclusively people with periodontal disease + CVD	N=131 people with periodontal disease and CVD (chronic heart disease, refractory hypertension, hyperlipidemia)	Scaling & root planing with or without oral hygiene, non-surgical periodontal treatment	**Chronic heart disease/scaling & root planing/TNF-α, IL-6 and CRP**: A decrease in analyzed markers (TNF-α, IL-6 and CRP) was observed in the test group that received scaling & root planing, and oral hygiene. **Refractory hypertension/non-surgical**

Author Year	Search details Study eligibility criteria	Numbers and designs of included studies applicable to present review; sample sizes	Patient characteristics from included studies applicable to present review	Intervention characteristics from included studies applicable to present review	Overall Results
	C: NR O: Plasma levels of surrogate markers, improvement of periodontal parameters, reduction in mm of carotid intima media thickness (CIMT), possible role of periodontal pathogens. T: NR S: Controlled clinical trials				**periodontal treatment/variety of biomarkers**: CRP, IL-6, and fibrinogen were significantly reduced 6 months after periodontal treatment, as well as other cardiovascular risk markers like left ventricular mass (LVM), arterial stiffness, systolic and diastolic blood pressure Hyperlipidemia/scaling & root planing with or without oral hygiene instructions/LDL and CRP: Non-surgical periodontal therapy improved periodontal health and decreased LDL and CRP levels in hyperlipidemic patients with chronic periodontitis.

DATA ABSTRACTION OF INCLUDED PRIMARY STUDIES

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
Agado 2012[26] RCT N=30 United States	1 month	Adults with COPD and chronic periodontitis (≥1.5 mm MAL) **Mean age:** 64 **%male:** 67% **%white:** 83% **Severity of chronic disease:** NR **Severity of periodontal disease:** Mean plaque index = 1.9; Mean attachment loss (MAL)= 3.9 mm **% comorbidities:** 87% current or former smokers	Periodontal debridgement using magnetostrictive ultrasonic instruments (n=10) vs same treatment with hand instruments (n=10) vs no treatment (n=10)	**KQ1:** No significant pre-post or between-group differences in quality of life in chronic airway disease (SGRQ-A), overall self-assessment of health, or Illness Questionnaire. **KQ2:** NR **KQ3:** Fewer people had a doctor's visit in the 4 weeks after periodontal treatment/no treatment than the 4 weeks before periodontal treatment- but the ratio was similar across groups. **KQ4:** No adverse events occurred during the study period.
Albert 2006[27] Retrospective cohort N=116,306 United States	NR, but maximum of 2 years possible	People with diabetes mellitus, coronary artery disease, and/or cerebrovascular disease with concomitant and continuous medical and dental coverage **Mean age:** 57.2 years (patients with DM), 63.5 years (patients with CAD), 68.5 years (patients with CVD). **%male:** 48% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** Diabetes mellitus (44.33%), Coronary artery disease (64.71%), cerebrovascular diseases (19.05%).	(1) periodontal treatment (periodontitis or gingivitis); (2) regular dental maintenance services (DMS); (3) other dental services; or (4) no dental services	**KQ1:** NR **KQ2:** NR **KQ3:** The DM, CAD and cerebrovascular condition groups who received periodontitis treatment incurred significantly higher PMPM medical costs than enrollees who received gingivitis treatment, DMS, other dental services, or no dental services ($p < .001$). **KQ4:** NR
Blaschke 2020[28]	Years 2-3 after T2	Adults newly diagnosed with T2 diabetes who are continuously insured	Any periodontal treatment (codes	**KQ1:** NR **KQ2:** NR

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
Retrospective claims analysis N=23,771 Germany	diagnosis	**Mean age:** 61 **%male:** 55% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** Charlson comorbidity score= 1.2	on German uniform assessment standard for dental services [BEMA] of P200-P203, 108, and 111) vs no periodontal treatment	**KQ3:** People newly diagnosed with DM who undergo periodontal treatment have 4% lower health care costs compared with those who have no periodontal treatment (ATE = 0.96, 95%CI 0.89; 1.04). Those who undergo periodontal treatment also have lower inpatient costs (-13%; 95%CI 0.69; 1.08), in diabetes-related drug costs (-7%; 95%CI 0.84; 1.03) as well as in other drug costs (-3%; 95%CI 0.89; 1.05). All findings were not statistically significant. **KQ4:** NR
Choi 2020[29] Computer-based simulation model N=10,000 simulated patients United States	NR, but data presented as costs or outcomes per year	Data for model drawn from a nationally representative sample of adults 30-85 years old **Mean age:** NR **%male:** NR **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** NR	Increase of periodontal treatment coverage among ppl with T2 diabetes (from 28% to 88%), which would include an initial treatment of scaling and root planing plus maintenance every 3 months. 100% compliance assumed.	**KQ1:** Expanded coverage expected to avert possible tooth loss by 34.1% (95% CI 239.9, 226.5) and reduce CVD incidence by 7.3% (95% CI 220.3, 20.3) and 5.0% (95% CI 220.8, 3.9) for MI and stroke, respectively. Nephropathy, neuropathy, and retinopathy incidence would be expected to decline by 20.5% (95% CI 231.2, 29.1), 17.7% (95% CI 232.7, 24.7), and 18.4% (95% CI 234.5, 23.5). Expanded periodontal treatment coverage produced an estimated gain of 0.6 discounted QALYs per capita (95% CI 0.5, 0.6) over the life course. **KQ2:** NR **KQ3:** Expanded treatment coverage was cost-saving at a net savings of $5,904 per capita (95% CI 26,039, 25,769) and had an incremental cost-effectiveness ratio (ICER) of $10,542 saved

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
				per QALY gained. People with higher HbA1c (>8%) experienced more QALY gains compared to those with lower HbA1c (<7%). People who were older (65+), and those who were low income and part of racial/ethnic minority groups (black and Mexican Americans) also experienced more QALY gains. **KQ4:** NR
Das 2019[30] RCT N=51 India	3 months	T2DM patients with moderate to severe periodontitis **Mean age:** 45.9 **%male:** 59% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: All had moderate to severe periodontitis **% comorbidities:** All ppts had no evidence of other oral or systemic diseases	Scaling and root planing (SRP) vs SRP with doxycycline (dox) vs no treatment	**KQ1:** NR **KQ2:** SRP with dox reduced HbA1c compared to no treatment (.87%, p>.01) and SRP without dox reduced HbA1c compared to no treatment (.55%, p>.01). SRP with dox reduced fasting plasma glucose (FPG) compared to no treatment (13.23 mg/dL, p>.01) and SRP without dox reduced FPG compared to no treatment (4.99 mg/dL, p>.01). SRP with dox reduced PPG compared to no treatment (22.11 mg/dL, p>.01) and SRP without dox reduced PPG compared to no treatment (13.28 mg/dL, p>.01). **KQ3:** NR **KQ4:** NR
El-Makaky 2020[31] RCT	3 months	T2DM patients with chronic periodontitis **Mean age:** 52 **%male:** 43.2% **%white:** NR **Severity of chronic disease**: None had	Treatment with SRP with antibiotics and oral hygiene instructions vs	**KQ1:** NR **KQ2:** HbA1c decreased in the intervention group and increased in the control group at 3 months (difference in difference of .98%). Difference between groups was significant at 3 months

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
N=88 Egypt		major diabetic complications **Severity of periodontal disease**: All had moderate to severe periodontitis **% comorbidities:** None had any systemic conditions besides hypertension	delayed treatment	(p<.001). **KQ3:** NR **KQ4:** No side effects of periodontal therapy.
Hsu 2019[32] Case-control N=440 Taiwan	NR	T2DM patients with poor and good glycemic control **Mean age:** 56.9 **%male:** 57% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: 24% good or very good oral health, 48% common, 27% poor or very poor **% comorbidities:** 15% were smokers	Non-periodontal disease (NPD), Periodontal treatment (PT), and Non-periodontal treatment (NPT)	**KQ1:** Among those with well-controlled T2DM, there was no significant difference between PT group and non-PT group on OHIP-14T (7.99 vs 8.43). Patients with poorly controlled T2DM in the PT group had a significantly lower OHIP-14T score than did those in the NPT group (6.05 vs 9.02). **KQ2:** NR **KQ3:** NR **KQ4:** NR
Jeffcoat 2014[33] Retrospective observational cohort N=338,891 United States	NR, but maximum of 5 years possible	Patients who had at least 1 pregnancy between 2005-2009 or had a diagnosis of 1 or more specified systemic condition (T2DM, coronary artery disease, cerebrovascular disease, rheumatoid arthritis). **Mean age:** 48.7 **%male:** 55% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** NR	Periodontal treatment vs untreated controls)	**KQ1:** NR **KQ2:** NR **KQ3:** Patients with cerebrovascular, diabetes or CAD who received periodontal tx had significantly lower rates of inpatient admissions than those who did not receive periodontal tx. Patients with CVD, diabetes, or CAD who received periodontal tx had significantly lower annual medical costs. **KQ4:** NR
Kucukcoskun 2013[34]	12 months	Patients with COPD with chronic periodontitis (CP) and a history >1 infective exacerbation in the previous	Periodontal treatment vs no periodontal	**KQ1:** Intervention group had lower frequency of exacerbations (1.95 vs 3.25 exacerbations/patient-year) and lower median number of exacerbations

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
Prospective controlled group trial N=40 Turkey		year **Mean age:** 59.8 **%male:** 87.5% **%white:** NR **Severity of chronic disease**: COPD severity was as follows: 13 moderate and 7 severe to very severe in the test group; 9 moderate and 11 severe to very severe in the control group. **Severity of periodontal disease**: All had chronic periodontitis **% comorbidities:** NR	treatment	(2 vs 3) in follow-up. Intervention had a greater number of pts that had decreased exacerbations (12 vs 6). **KQ2:** NR **KQ3:** NR **KQ4:** NR
Lee 2013[35] Retrospective cohort study N= 719,436 Taiwan	NR, but max length of 10 years	Adult patients (older than 20 years) with periodontal disease (PD) **Mean age:** 87% were <65 years old **%male:** 51.1% **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR**% comorbidities:** Hypertension (24.15%), Diabetes Mellitus (11.25%), Atrial fibrillation (.83%), atherosclerosis (1.5%), chronic kidney diseases (4.1%), dyslipidemia (15.82%)	PD patients who only received dental prophylaxis, PD patients who received intensive periodontal treatments (*ie*, subgingival curettage and root planing, or periodontal flap operation or tooth extraction), and PD patients who received no treatments	**KQ1:** When comparing stroke incident rates (IRs) after being stratified by comorbidity (including hypertension, diabetes, atrial fibrillation and atherosclerosis), the lowest stroke IR of the PD population always appeared in the dental prophylaxis group, followed by intensive treatment or tooth extraction group, and the highest stroke IR appeared in PD without treatment group (P for trend test <0.001 or =0.006). **KQ2:** NR **KQ3:** NR **KQ4:** NR
Lee 2020[36] RCT	3 months	People with periodontal disease (PD) **Mean age:** 72.6	Scaling and root planing (SRP), vs Scaling and root	**KQ1:**NR **KQ2:** No significant differences in HbA1c between intervention and control group at baseline but

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
N=60 Korea		**%male:** 50% male **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **comorbidities:** NR	planing & toothbrushing (SPRT) vs no treatment	there was a difference favoring intervention group at 3 months (difference of .51 to .55 depending on intervention group; p<.05). No significant differences in serum IL-1b levels between intervention and control groups at baseline or 3 months. No significant differences in serum endotoxin between intervention and control group at baseline but there was a difference favoring intervention group at 3 months (difference of 1.27 to 1.43 depending on intervention group; p<.05). **KQ3:** NR **KQ4:** NR
Minassian 2010[37] Self-controlled case series N=1,175 United States	4.25-year observation period on average	Medicaid recipients exposed to invasive dental treatment with a primary hospital discharge diagnosis of ischemic stroke (n=650) or myocardial infarction (n=525) **Mean age:** 55.4% were <65 years old **%male:** 39.8% **%white:** 48.4% **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** Diabetes (41%), hypertension (70.2%) coronary heart disease (40.8%)	Invasive dental treatment (those that may feasibly result in bacteria and induce an inflammatory response, including periodontal therapy and simple or complex tooth extractions). 89% were extractions.	**KQ1:** Rate of vascular events (MI or stroke) significantly increased in the first 4 weeks after invasive dental treatment (incidence ratio, 1.50 [95% CI, 1.09 to 2.06]) compared to baseline and gradually returned to the baseline rate within 6 months. In the entire study population, the rate of myocardial infarction (n =525) was higher in the first 4 weeks after an invasive dental treatment compared with baseline (incidence ratio, 1.56 [CI, 0.98 to 2.47]) and seemed to decrease over 24 weeks. For ischemic stroke (n = 650), a slightly elevated risk was seen during the first 4 weeks after an invasive dental treatment (incidence ratio, 1.39 [CI, 0.89 to 2.15]), although this was less marked and the pattern of resolution was less clear. **KQ2:** NR

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
				KQ3: NR **KQ4:** NR
Mizuno 2017[38] RCT N=40 Japan	6 months	Adults (age 30+) with T2 diabetes and mild to advanced periodontitis **Mean age:** 61 (tx) vs 63 (control) **% male:** 76% male **% white:** NR **Severity of chronic disease:** 38% used insulin **Severity of periodontal disease**: mean PPD 2.4 **Comorbidities:** 19% smokers, 38% drinkers,	Scaling and root planing w/ oral hygiene instruction vs oral hygiene instruction alone	**KQ1:** Intervention and control groups were not significantly different in their total diabetes therapy-related QoL score at 3 months. **KQ2:** No differences between intervention and control in changes in HbA1c at 3 or 6 months. There were improvements in oxidative index (oxidative stress) in intervention vs control at 3 months (-1.19, 95% CI [-2.03 to -0.35]). **KQ3:** NR **KQ4:** No serious study-related adverse events occurred in either group.
Nasseh 2017[39] Retrospective claims analysis N=15,002 United States	Years 3-4 after T2 diagnosis	Adults (age 18-64) newly diagnosed with T2D with continuous medical and dental insurance coverage **Mean age:** 50.9 (PT) vs 50.1 (no PT) **% male:** 58% (PT) vs 53% (no PT) **% white:** NR **Severity of chronic disease:** NR **Severity of periodontal disease**: NR **Comorbidities:** Charlson index = 0.15 (PT) vs 0.14 (no PT)	Any periodontal treatment (PT) visit (codes on dental procedures and nomenclature D4000 through D4999) vs no PT	**KQ1:** NR **KQ2:** NR **KQ3:** Those newly diagnosed with T2D who undergo a periodontal intervention have total health care costs that are $1799 lower on average over years 3 and 4 compared with those who have not had a periodontal intervention. In subgroup analyses, this association was only noted among individuals who did not initiate diabetes prescription drug therapy after diagnosis. Overall, net savings ($1799 savings - $408 periodontal treatment) was $1328 over 2 years. Total medical costs are $1577 less on average for the treatment group. Total diabetes-related healthcare costs are $408 lower on average for the treatment group.

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
				There are not statistically significant differences in total outpatient physician visits, probability of a hospitalization, or the occurrence of an emergency room visit between the treatment and control groups. **KQ4:** NR
Peng 2017[40] Retrospective cohort N= 15,195 Taiwan	NR, but max of 3 years	Patients with type 2 diabetes and periodontal problems. **Mean age:** 53.1 vs 53.0 (unmatched advanced vs non-advanced); 53.1 (matched) **% male:** 60% vs 53.9% (unmatched advanced vs non-advanced); 60% (matched) **% white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** hypertension 54.6-56.2%; chronic liver disease 18.6%-20.3%; COPD 6.9%-8.9%; renal disease 3-3.7%, mental disorder 11-11.3%; cancer 3.1-3.5% depending on group	Periodontal treatment (advanced periodontal treatment group and the non-advanced periodontal treatment group)	**KQ1:** The Cox proportional hazards analysis revealed that although the overall incidence of CVD was not significantly improved (Hazard ratio, HR 0.95; 95% CI 0.90-1.01), advanced periodontal treatment reduced the rates of myocardial infarction (HR 0.92; 95% CI 0.85-0.99) and heart failure (HR 0.60; 95% CI 0.45-0.80). There was no significance difference in the incidence of stroke (HR 0.95; 95% CI 0.85-1.06). **KQ2:** NR **KQ3:** NR **KQ4:** NR
Smits 2020[41] Retrospective claims analysis N=41,598	NR, but 7 years max	Individuals with diabetes **Mean age:** 73.5% <65 years old **%male:** 54.3% **%white:** NR **Severity of chronic disease:** All ppts were taking medication (insulin, metformin, or other DM medication)	Periodontal treatment	KQ1: NR KQ1: NR KQ2: NR KQ3: The median diabetes-related health care costs per patient in 2012 were €38.45 per quarter (IQR €11.52–€263.14), including diagnoses, treatment, medication and hospitalization costs. The fixed

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
Netherlands		**Severity of periodontal disease**: NR **% comorbidities:** NR		effect models showed €12.03 (95% CI −€15.77 to −€8.29) lower diabetes-related health care costs per quarter of a year following periodontal treatment compared with no periodontal treatment. KQ4: NR
Solowiej-Wedderburn 2017[42] Modeling study N= NA UK	NR	Patients with type 2 diabetes **Mean age:** Base case based on a male(female) aged 46 (49), 58 (61), or 69 (72) **%male:** NR **%white:** NR **Severity of chronic disease**: Base case based on those in the 7-7.9%, 8-8.9% and 9-9.9% HbA1c range **Severity of periodontal disease**: NR **% comorbidities:** NR	Periodontal treatment (assumed to be 2 60-minute sessions with a practitioner then regular maintenance therapy every 3 months with a hygienist), repeated every 3 years with 30% compliance	KQ1: NR KQ2: NR KQ3: Cost savings from reduction in HbA1c, and from reductions in tooth loss following periodontal treatment, are modest. After including these savings, total cost in the treatment arm remains higher than the control. Intervention is more cost-effective in patients with higher HbA1c for whom DiabForecaster predicts larger health gains. The intervention is also more cost-effective in older patients for whom lifetime costs of periodontal treatment are lower. KQ4: NR
Wang 2020[43] RCT N=58 China	6 months	Adults (over 40 yrs old) with T2 diabetes with chronic periodontitis **Mean age:** 64 **%male:** 57% **%white:** NR **Severity of chronic disease**: 38% had microvascular complications **Severity of periodontal disease**: NR **% comorbidities:** 12% were smokers, 66% had hypertension, 53% had hyperlipidemia	Non-surgical periodontal treatment (oral health instruction, scaling and root debridement, removal of teeth as needed, reinforcement of oral hygiene & plaque control at 2-3 months) vs oral health instruction & reinforcement only	KQ1: NR KQ2: Periodontal treatment reduced the mean E/e' ratio by 1.66 (95% CI: −2.64 to −0.68, p < .01) compared to controls. Left ventricle mass index (LVMI) was not improved after treatment. There was also no significant improvement in mean HbA1c, hs-CRP, IL-6, or NT-proBNP in intervention compared to control group. KQ3: NR KQ4: NR

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
United Health care 2013[44] Retrospective claims analysis N=130,546 United States	1-4 years, but annual costs reported	Adults (18-65) dual enrolled in medical and dental benefits with 1 of 6 chronic diseases (diabetes, asthma, CAD, congestive heart failure, COPD, chronic kidney/renal disease) **Mean age:** NR **%male:** NR **%white:** NR **Severity of chronic disease**: NR **Severity of periodontal disease**: NR **% comorbidities:** 6.8% of those with diabetes also had CAD; other comorbidities NR	Periodontal treatment (surgical or non-surgical, with or without maintenance) vs cleanings (frequent or infrequent) vs no periodontal treatment (bacteria-removing treatments, other dental claims, no dental claims)	**KQ1:** NR **KQ2:** NR **KQ3:** **Diabetes:** Annual medical costs were $7,838 for diabetics receiving periodontal care. Diabetics receiving other or no dental treatments had medical costs of $9,588, for a medical-only savings of $1,750. **CAD:** Individuals with CAD who visited the dentist for cleanings and/or periodontal treatment had lower medical costs than individuals who received no dental treatment (average annual costs NR). Those received periodontal treatment had lower annual medical costs compared to those who did not receive periodontal treatment (average $15,549-$16,271 in periodontal treatment group vs $20,502-$21,202 in no treatment group depending on compliance with medical care). **Congestive heart failure**: Those with congestive heart failure who received periodontal treatment had lower annual medical costs compared to those who did not receive periodontal treatment (average $35,669-$36,172 vs $47,332-$49,064 depending on medical compliance). **COPD**: Those with COPD who received periodontal treatment had lower annual medical costs compared to no periodontal treatment (average $12,938-$38,450 vs $15,817-$52,484 depending on medical compliance).

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
				KQ4: NR
Vergnes 2018[45] RCT N= 91 France	3 months	Participants with type 1 or 2 diabetes **Mean age (Control vs Treatment):** 53.7 vs 50.9 (Type 1 diabetes) and 63.1 vs 68.3 (type 2 diabetes) **%male:** 57% vs 59% (Type 1 diabetes) and 82% vs 62% (Type 2 diabetes) **%white:** NR **Severity of chronic disease**: HbA1c (baseline 7.83-7.84 T1 diabetes; 7.78-7.96 T2 diabetes) **Severity of periodontal disease**: T1 diabetes (12% generalized/severe, 32% generalized/moderate, 38% localized/severe, 16% localized/moderate periodontal disease); T2 diabetes (25% generalized/severe, 42% generalized/moderate, 33% localized/severe, 0% localized/moderate periodontal disease) **% comorbidities:** Smokers (23-24% T1 diabetes; 0-15% T2 diabetes); receiving drug tx for cardiovascular disease (50-58% T1 diabetes; 30-82% T2 diabetes); receiving drug tx for respiratory tract (0-3% T1 diabetes; 0-8% T2 diabetes)	Periodontal treatment (Non-surgical scaling and root planing, systemic antibiotics, providing supply of if oral hygiene/health products) vs delayed periodontal treatment	**KQ1:** Mean sum of General Oral Health Assessment (GOHAI) increased in the treatment group compared with the control group) when both diabetes types were combined, but there were no differences between treatment and control for T2 diabetes alone. No significant changes any of the 8 domains of the SF-36 for those with either T1 or T2 diabetes. **KQ2:** NR **KQ3:** NR **KQ4:** Fifteen and 18 control and treatment subjects, respectively, experienced oral disorders (p = 0.37). The treatment group experienced more dental hypersensitivity (p = 0.03) but with a tendency towards less diffuse pain (p = 0.07).

Author Year N Setting	Follow-up	Patient Characteristics Mean age %male %white Severity of chronic disease Severity of periodontal disease Comorbidities	Intervention vs comparator	Outcomes KQ1: Patient-reported symptoms & complications of chronic disease KQ2: Indicators of chronic disease mgmt KQ3: Health care utilization & costs KQ4: Harms
Zhou 2014[46] RCT N=60 China	2 years	COPD patients with chronic periodontitis **Mean age:** 63.9 (SRP group), 65.3 (scaling group), 68 (control) **%male:** 80% (SRP), 75% (scaling), 80% control **%white:** NR **Severity of chronic disease**: Gold stage II (60% for all 3 groups); Gold Stage III or IV; 40% for all 3 groups **Severity of periodontal disease**: All had chronic periodontitis **% comorbidities:** Former or current smoker (80% SRP group; 65% scaling group; 70% control group)	Periodontal treatment including scaling and root planing (SRP) treatment, supragingival scaling treatment, or oral hygiene instructions with no periodontal treatment	**KQ1:** The means of forced expiratory volume in the first second/forced vital capacity (FEV1/FVC) and FEV1 were significantly higher in the 2 therapy groups compared with the control group during the follow-up ($p < 0.05$) Frequencies of COPD exacerbation were significantly lower in the 2 therapy groups than in the control group at 2-year follow-up ($p < 0.05$). **KQ2:** NR **KQ3:** NR **KQ4:** NR

Mgmt= Management, RCT= Randomized controlled trial, COPD= Chronic obstructive pulmonary disease, MAL= Mean attachment loss, NR= Not reported, SGRQ-A= American English modified version of the SGRQ, CAD= Coronary Artery Disease, CVD= Cardiovascular disease, DM= Diabetes Mellitus, DMS= Dental Maintenance Services, PMPM= Per member per month, ATE= Average treatment effect, QALYs= Quality-adjusted life years, T2DM= Type 2 Diabetes Mellitus, Ppts= Participants, OHIP-14T= Oral Health Impact Profile, Tx= Treatment, IR= Incidence Rate, QoL= Quality of life, Yrs= Years

QUALITY ASSESSMENT OF PRIORITIZED SYSTEMATIC REVIEWS

Quality Assessment of Prioritized Systematic Reviews

Author Year	Research questions and inclusion criteria included 'PICO'?	Explicit statement that review methods were established prior to conduct of review?	Explained selection of study designs for inclusion?	Comprehensive literature search performed?	Duplicate study selection and data extraction?	List of excluded studies and justification for exclusion provided?	Included studies described in adequate detail?
Ata-Ali 2020[18]	Yes	Partial yes; no registration	Yes	Partial yes; no expert contact and no search in trial registries.	Yes for both.	Yes	Yes
Beza 2020[18]	Yes	Partial yes; no registration	Yes	Partial yes; no extra searching outside of databases.	Yes to study selection; data extraction process not reported.	Yes	Yes
D'Autio 2017[23]	No; PICOs framework not used	No; no discussion of protocol or registration	Yes	Partial yes; no extra searching outside of databases.	Yes to study selection; data extraction process not reported.	No; no list of excluded studies	Yes; Appendix 2
D'Isidoro 2019[25]	Yes	No; no discussion of protocol or registration	Yes; including CCT is reasonable for research question	Partial yes; no extra searching outside of databases.	Yes to data extraction; quality assessment process not reported.	No; no list of excluded studies	Yes; available in table
Garde 2019[20]	Yes	No; no discussion of protocol or registration	Yes	Partial yes; no extra searching outside of databases.	Yes to study selection; data extraction process not reported.	No; no list of excluded studies	Yes
Lima 2019[21]	Yes	Yes	Yes	Partial yes; no expert contact and no search in trial registries	Yes to study selection; data extraction process not reported.	Yes	No; no description of included interventions or comparators.
Liu 2019[22]	Yes	Yes	Yes	Yes	Yes for both.	Yes	Yes
Simpson 2015[24]	Yes	Yes	Yes	Yes	Yes to both.	Yes	Yes

Quality Assessment of Prioritized Systematic Reviews (Continued)

Author Year	Risk of bias of the included studies assessed appropriately?	Reported on sources of funding of studies included in the review?	If meta-analysis performed, appropriate methods for combining results used?	If meta-analysis performed, potential impact of individual studies' ROB on results of meta-analysis assessed?	Accounted for risk of bias in individual studies when interpreting/ discussing results?	Satisfactory explanation for and discussion of hetero-geneity?	Likelihood of publication bias assessed?	Review author conflict of interest stated?	Overall quality (high, moderate, low, critically low)
Ata-Ali 2020[18]	Yes	No; primary studies' funding not reported	Yes	Yes; studies at high risk of bias excluded from meta-analysis.	Yes; studies at high risk of bias excluded from discussion of results.	Yes	Yes	Yes	Moderate
Beza 2020[19]	Yes	No; primary studies' funding not reported	Yes	No; all studies included regardless of ROB.	No; discussed results of all studies regardless of ROB.	Yes	Yes; but small # of studies made visual inspection of funnel plot difficult.	Yes	Moderate
D'Autio 2017[23]	Yes	No; included SRs funding not reported	NA	NA	No; no consistent use of ROB when describing results from studies.	No; heterogeneity between SRs not discussed	No; publication bias not assessed	No; funding info provided but not COI	Critically low
D'Isidoro 2019[25]	Yes; Cochrane ROB tool used	No; no reporting of study funding.	NA	NA	No; discussed all studies regardless of ROB	Yes; studies described individually, no MA conducted because of heterogeneity	No; publication bias not assessed.	Yes	Moderate
Garde 2019[20]	Yes	No; primary studies' funding not reported	Yes	No; all studies included regardless of ROB	No; discussed results of all studies regardless of ROB.	Yes	No; publication bias not assessed.	Yes	Moderate

Lima 2019[21]	No; no assessment of selection or confounding bias.	No; primary studies' funding not reported	NA	NA	Yes; discussed results of all studies because all were deemed high quality	NA	No; publication bias not assessed.	Yes	Low
Liu 2019[22]	Yes	Yes	NA; not enough studies for MA.	NA; not enough studies for MA	Yes; results not reported if study's flaws were too large.	NA	NA; not enough studies for publication bias assessment	Yes	High
Simpson 2015[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High

QUALITY ASSESSMENT OF INCLUDED PRIMARY STUDIES

Quality Assessment of RCTs

Author Year Country	Risk of bias from randomization process	Risk of bias from deviation from intended interventions (assignment)	Risk of bias from deviation from intended interventions (adherence)	Risk of bias from missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Quality Rating (Good, Fair, Poor)
Agado 2012[26]	Some concerns Randomization using random number generator; ppts aware of tx or control group; ultrasonic tx group had worse periodontal disease than hand instrument but not control group at baseline.	Some concerns Ppts & providers aware of tx or control group; unclear if there were any deviations from intended interventions	Low Similar infection control & rinsing/dental suction procedures across tx groups (control group received no tx), no indication of lack of adherence.	Some concerns Unclear if all ppts' completed follow-up assessments.	Low Validated measurements used; ppts completed surveys using confidential code in private location to blind outcome assessment	Some concerns No protocol readily available.	Fair Ppts and providers aware of tx assignment; unclear if all ppts completed follow-up assessments.
Das 2019[30]	Some concerns Block randomization; ppts & providers aware of tx group; unclear if there were differences between groups at baseline as limited data (only age & sex) were presented and differences not statistically evaluated.	Some concerns Ppts & providers aware of tx or control group; unclear if there were any deviations from intended interventions	Some concerns No changes to diabetes diet or medication in either group but no information about dental cointerventions; no indication of lack of adherence	Low All ppts completed follow-up assessments (flowchart 1)	Some concerns Authors do not report how diabetes-related outcomes were measured but presumably this was done using a blood test.	Some concerns Authors state protocol was approved, but no protocol readily available.	Fair Ppts and providers aware of tx assignment, unclear if there were differences between groups at baseline.

Author Year Country	Risk of bias from randomization process	Risk of bias from deviation from intended interventions (assignment)	Risk of bias from deviation from intended interventions (adherence)	Risk of bias from missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Quality Rating (Good, Fair, Poor)
El-Makaky 2019[31]	Some concerns Randomization process not described but "random series" was produced and allocation concealed by using closed envelopes; groups similar at baseline	Some concerns Unclear if ppts blinded but some study staff were; unclear if there were any deviations from intended interventions	Low Unclear if there were differences in cointerventions; no drop-outs.	Low All ppts attended follow-up visit.	Low Appropriate measurement of HbA1c; outcome assessors blinded.	Low No outcomes described in protocol missing from published study.	Fair Ppts presumably aware of intervention status, randomization process not described.
Lee 2020[36]	Some concerns Randomization from rolling dice; unclear if ppts were blinded; no significant differences between groups at baseline	Some concerns Unclear if ppts blinded but some study staff were; unclear if there were any deviations from intended interventions	Some concerns Unclear if there were differences in cointerventions; 15/75 (20%) dropout rate due to "old age and the long intervention period."	Some concerns Since older people dropped out, missing outcome data may be biased	Low Appropriate measurement of outcomes; outcome assessors blinded.	Some concerns Authors refer to protocol but it is not readily available.	Fair Ppts presumably aware of intervention status and high dropouts (20%), some of which were due to old age.

Author Year Country	Risk of bias from randomization process	Risk of bias from deviation from intended interventions (assignment)	Risk of bias from deviation from intended interventions (adherence)	Risk of bias from missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Quality Rating (Good, Fair, Poor)
Mizuno 2020[38]	Some concerns Block randomization based on HbA1c level and # of medications; unclear if ppts blinded; groups similar at baseline but not statistically evaluated	Some concerns Unclear if ppts blinded but study staff were; 3 ppl assigned to intervention group did not complete intervention (could not be contacted)	Some concerns Unclear if there were differences in cointerventions; 30% drop out rate	Some concerns High drop-out but complete data for those who stayed in study	Low Appropriate measurements used; laboratory personnel & PI who conducted analyses blinded	Low No outcomes described in protocol missing from published study.	Fair Ppts presumably aware of tx assignment; high drop-out (30%)
Vergnes 2018[45]	Some concerns Block randomization by center; ppts aware of tx or control group; unclear if there were differences between groups at baseline as this was not analyzed statistically.	Some concerns Ppts & providers aware of tx or control group; unclear if there were any deviations from intended interventions.	Low Unclear if there were differences in cointerventions; low rate of drop-outs in both groups.	Low A few ppts missed V4 visits, but this was similar across groups.	Low Validated measurements used for QoL and OHRQoL; outcome assessors likely knew ppts' group assignment.	Low No outcomes described in protocol missing from published study.	Fair Ppts and providers aware of tx assignment; unclear if groups were different at baseline as this was not statistically assessed.

Author Year Country	Risk of bias from randomization process	Risk of bias from deviation from intended interventions (assignment)	Risk of bias from deviation from intended interventions (adherence)	Risk of bias from missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Quality Rating (Good, Fair, Poor)
Wang 2019[43]	Some concerns Block randomization; unclear if ppts were aware of intervention status; no significant differences between groups at baseline	Some concerns PI blinded but unclear if ppts were; unclear if there were any deviations from intended interventions	Low No changes to diabetes or hypertension medications and no notable lifestyle changes, unclear whether there were dental cointerventions; low rate of drop-outs across groups	Some concerns In addition to drop-outs, 3 people who did not have echo-cardiographic data were excluded from ITT analyses.	Low Appropriate measurements and outcome assessors blinded to allocation	Some concerns Some outcomes from protocol are missing from published study (cholesterol, creatine)	Fair 3 people who did not have echocardiographic data were excluded from ITT analysis; ppts presumably aware of intervention status
Zhou 2014[46]	Low Block randomization using computer-generated list; allocation by programmer not involved in study implementation; individuals involved in study blinded to assignment; baseline characteristics similar between groups	Some concerns Ppts aware of which tx they received but providers masked to COPD status; unclear if there were any deviations from intended interventions	Low Unclear if there were any differences in cointerventions; Low rate of drop-outs across groups	Low Low rates of missing data (Fig 1)	Low Validated, clinical measurements used to assess lung function & COPD exacerbation	Some concerns Authors refer to protocol but it is not readily available.	Fair No readily available protocol

Tx= Treatment, Ppts= participants, Ppl= People, V4= 3 month follow-up visit QOL= Quality of life, OHRQoL= Oral health-related quality of life, ITT= Intention to treat, COPD= Chronic obstructive pulmonary disease

Quality Assessment of Controlled Observational Studies

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
Albert 2006[27]	Low	Low	Unclear	Low	Unclear	Low	Low	Fair
	Selection based on chronic disease status unlikely to be due to intervention; 2-year period for potential periodontal tx for all ppts; no control for selection biases.	Intervention groups well defined; different tx groups defined by medical claims data unlikely to be influenced by knowledge of outcome	Unclear if there were any deviations from intended tx or if there were cointerventions, as groups were defined by whether they received any periodontal therapy.	Costs extracted from medical records (ICD-9 codes that were billed), unlikely to be influenced by knowledge of intervention	Statistical control for differences in disease burden between groups, and only those with medical & dental coverage were included in analyses. Possibility of other confounders (*ie*, whether "no dental tx" group were healthy or had periodontal disease).	No indication of missing data.	Unlikely results due to multiple analyses.	Major limitation of this study is that it is unclear what proportion of people in the "no dental services" group were periodontally healthy vs had periodontal disease and were untreated.
Blaschke 2020[28]	Unclear	Low	Unclear	Low	High	Unclear	Low	Poor
	Selection based on diabetes diagnosis which in some cases was in the same index quarter as periodontal tx, so periodontal therapy could have occurred	Intervention groups well defined; different tx groups defined by dental & medical claims data that are unlikely to be influenced by	Unclear if there were any deviations from intended tx, drop-out, or if there were cointerventions.	Outcomes extracted from claims database and unlikely to be influenced by knowledge of the intervention.	Unclear what proportion of the control group had periodontal disease which may have confounded results.	Some data missing on inpatient costs so this was imputed, limited information on imputation methods.	Unlikely results due to multiple analyses.	Major limitation is that at least some people in the control group probably did not have periodontal disease, which may have confounded the results. Results are also limited to those with

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
	before diabetes diagnosis.	knowledge of outcome.						continuous insurance enrollment, and authors note that groups were different at baseline in terms of visits to dentist and health care costs.
Hsu 2019[32]	Low Selection based on diabetes status & glycemic control in 6 months before periodontal tx; no control for selection biases.	Unclear Intervention groups defined by whether pts said they had ever received treatment for periodontal disease - no information on what the treatment was or when it was received. Tx groups defined after intervention as it was a retrospective	Unclear Limited information on periodontal tx intervention. Cointerventions (periodontal care behaviors) well described.	Unclear Validated tools used to measure outcomes. Outcome assessors not blinded to intervention status.	Unclear Characteristics (age, sex, education, duration of diabetes, etc) of PT group and non-PT group not compared at baseline.	Low No indication of missing data	Low Unlikely results due to multiple analyses.	Fair Major limitation is that it is unclear how similar the PT and non-PT group were at baseline.

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
		study and could have been affected by knowledge of risk of outcome.						
Jeffcoat 2014[33]	Low	High	High	Low	Unclear	High	Low	Poor
	Selection based on chronic disease status unlikely to be due to intervention; 2-year period for potential periodontal tx & outcomes for all ppts; no control for selection biases.	Intervention group well defined, but control group is anyone who completed 1, 2, or 3 tx sessions (not 0 sessions).	High departure from intended tx (most of those with periodontal disease only completed 1, 2, or 3 tx sessions).	Outcomes extracted from insurance claims unlikely to be influenced by knowledge of the intervention.	Some confounders (age, gender, T2D status) controlled for but not others (like education or SES) which could have influenced whether ppts received full tx course.	1 year of cost data missing for those with CVD & CAD due to "technical reasons."	Unlikely results due to multiple analyses.	Major limitation is that control group consisted of those that received 1, 2, or 3 periodontal tx, not 0.
Kucukcoskun 2013[34]	Low	Low	Unclear	Unclear	Unclear	Unclear	Low	Fair
	Selection based on defined criteria before start of intervention; same intervention length for all	Intervention groups clearly defined at the start of prospective study.	Unclear if there were any deviations from intended tx, drop-out, or if there were cointerventions.	Unclear if outcome assessors aware of tx group; possible that outcome could have been	Groups similar at baseline in terms of periodontal disease & patient characteristics; however it's unclear how patients were allocated and if it	Unclear if there were any missing data from either group.	Unlikely results due to multiple analyses.	Major limitation is that it is unclear how pts were assigned to groups and it's possible it was based on patient or provider

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
	ppts; no control for selection biases.			influenced by knowledge of tx.	was by patient or provider choice that could confound results.			choice that could have influenced outcome.
Lee 2013[35]	Low Selection based on first diagnostic code for PD which would presumably occur before PD tx; same 10-year period for tx & outcomes; no control for selection biases.	Low Intervention groups well defined; different tx groups defined by medical record data that are unlikely to be influenced by knowledge of outcome.	Unclear Unclear if there were any deviations from intended tx, drop-out, or if there were cointerventions.	Low Outcomes extracted from medical record data and unlikely to be influenced by knowledge of the intervention.	High PD patients who received intensive dental tx, dental prophylaxis, or no tx likely had differing severity of baseline periodontal disease that could have confounded the results.	Low No indication of missing data.	Low Unlikely results due to multiple analyses.	Poor Major limitation is that PD patients who received intensive dental tx, dental prophylaxis, or no tx likely had differing severity of baseline periodontal disease that could have confounded the results.
Nasseh 2017[39]	Low Selection based on diagnostic code for T2 diabetes, periodontal tx occurred in 2 years following diagnosis; follow-up	Low Intervention groups well defined; different tx groups defined by dental & medical claims data	Unclear Unclear if there were any deviations from intended tx, drop-out, or if there were cointerventions.	Low Outcomes extracted from dental and medical claims database and unlikely to be influenced by knowledge of	High Unclear what proportion of the control group had periodontal disease which may have confounded results.	Low No indication of missing data.	Low Unlikely results due to multiple analyses.	Poor Major limitation is that at least some people in the control group probably did not have periodontal disease, which may have confounded the

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
	period is the same for all ppts; no control for selection biases.	that are unlikely to be influenced by knowledge of outcome.		the intervention.				results. Results are also limited to those with continuous insurance enrollment.
Peng 2017[40]	Low Selection based on ICD-9 PD code which occurred before PD tx. Same 3-year period for tx and outcomes; no control for selection biases.	Unclear Intervention group well-defined but control group is defined as those who received any kind of therapy besides advanced periodontal tx-unclear what this was.	Unclear Excluded ppl who had < 3 periodontal tx codes which likely excluded people who did not adhere to tx. Unclear if there were cointerventions.	Low Outcomes extracted from medical record data and unlikely to be influenced by knowledge of the intervention.	Low Propensity-matching used to control for baseline confounders (age, gender, comorbidities, hypoglycemic agent, statin).	Low No indication of missing data.	Low Unlikely results due to multiple analyses.	Fair Major limitation is lack of clarity of what non-advanced tx the control group received.
United Healthcare 2013[44]	Unclear Selection based on presence of claim related to chronic disease, which may have occurred before	Low Intervention and control groups well-defined; different tx groups defined by dental &	Unclear Authors separate results by dental compliance (whether they received cleanings or	Low Outcomes extracted from dental and medical claims database and unlikely to be influenced by	High Unclear what proportion of the no periodontal tx group had periodontal disease or were periodontally healthy.	Low No indication of missing data.	Low Unlikely results due to multiple analyses.	Poor Major limitation is that at least some people in the control group probably did not have periodontal disease, which may have

Author Year	Selection bias (High, Low, Unclear)	Bias in classification of interventions (High, Low, Unclear)	Bias due to departures from intended interventions (High, Low, Unclear)	Bias due to measurement of outcomes? (High, Low, Unclear)	Bias due to confounding? (High, Low, Unclear)	Bias due to missing data? (High, Low, Unclear)	Bias in the selection of reported results (High, Low, Unclear)	Overall quality (Good, Fair, Poor)
	or after periodontal tx.	medical claims data that are unlikely to be influenced by knowledge of outcome.	periodontal tx). Definition of medical compliance is vague and unclear if other types of co-interventions (brushing, flossing) were adhered to.	knowledge of the intervention.				confounded the results. Participants may also have received chronic disease status designation after periodontal tx.
Smits 2020[41]	Low Selection based on diabetes diagnosis unlikely to be related to intervention; no control for selection biases.	Low Intervention and control groups well defined; claims data unlikely to be affected by knowledge of outcome.	Unclear Unclear adherence to periodontal tx and whether there were any cointerventions	Low Outcomes extracted from claims database and unlikely to be influenced by knowledge of the intervention.	Unclear Those who did and did not receive PD tx were considerably different at baseline in terms of age, sex, comorbidities which was controlled for using a fixed effects model. Possibility of other confounders (those did not receive PD treatment may or may not have had PD).	Low No indication of missing data.	Low Unlikely results due to multiple analyses.	Fair Major limitation of this study is that it is unclear what proportion of people in the "untreated" group were periodontally healthy vs had periodontal disease and were untreated.

Tx= Treatment, Ppts= participants, ICD-9= International Classification of Diseases, 9th Edition, PT= Periodontal treatment, CVD= Cardiovascular disease, CAD= Coronary Artery Disease, PD= Periodontal disease

PEER REVIEW COMMENT TABLE

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	1	Yes	None
2	2	No - This may be a function of the form prescribed by the VA for Evidence Synthesis documents, but I find the document redundant is places, and therefore difficult to read and interpret. A simpler and more streamlined style should be considered.	Thank you for this comment. We have streamlined the "Results" section to make the report more reader-friendly. For each population, we collapsed the separate sections on "systematic reviews" and "primary studies" into a single section. We have also combined the 2 separate tables on systematic review and primary study findings into a single table.
3	3	Yes	None
4	4	Yes	None
Is there any indication of bias in our synthesis of the evidence?			
4	1	No	None
5	2	No	None
6	3	No	None
7	4	Yes - The authors' explanation for excluding relevant studies were not satisfactory. The need to conduct a rapid synthesis does not preclude the authors from considering all available and relevant evidence. Since this approach already skipped some steps by focusing only on gaps that were found in existing systematic reviews and some systematic reviews are a few years old, it seems reasonable to expect the authors to have at least included all the relevant publications that they found.	For the 17 SRs we included but did not prioritize, we have added a brief explanation of our prioritization rationale to the Results section. Most often, these SRs were not prioritized because they were already included in a prioritized review of reviews (Ata-Ali 2020), or their PICOS were covered by a more recent or more relevant review. For transparency, we have also added a table to the Supplementary Materials to provide a list of the 17 non-prioritized SRs along with a specific rationale for why each was not discussed in the report. For primary studies, we included all studies that addressed gaps in evidence from our included SRs (we did not prioritize any primary studies over others – all were discussed). We have added a sentence to the methods section to clarify this.

Comment #	Reviewer #	Comment	Author Response
Are there any published or unpublished studies that we may have overlooked?			
8	1	Yes - A number of economic studies have been conducted by insurers but are not listed. See below:	See responses to comments #9-14.
9	1	Cigna. Improved Health and Lower Medical Costs: Why Good Dental Care is Important. 2010. https://www.cigna.com/assets/docs/life-wall-library/Whygooddentalcareisimportant_whitepaper.pdf. Accessed June 1, 2016.	Excluded- wrong publication type. Though this white paper presents some data on our PICOS of interest, there is not enough information on the methods or results to include this as a study.
10	1	Jeffcoat, M. K., et al. 2009. "Periodontal Treatment and Medical Costs in Diabetes and Cerebrovascular Accident." Paper presented at the 2009 International Association for Dental Research Meeting, Miami, Florida. J	Excluded- wrong publication type. We could not track down the abstract (it is no longer available on the conference website) or FT article for this study.
11	1	Jeffcoat MK, Jeffcoat RL, Gladowski PA, et al. Impact of periodontal therapy on general health: Evidence from insurance data for five systemic conditions. Am J Prev Med. 2014;47(2):166-74.	This study was included in our report.
12	1	Marano, A., et al. 2013. Appropriate Periodontal Therapy Associated with Lower Medical Utilization and Costs. Bloomfield, CT: Cigna	Excluded- wrong publication type. We could not track down the FT for this study. However, based on the abstract, this study does not seem to be focused on people with chronic conditions.
13	1	Nasseh K, Vujicic M, Glick M. The relationship between periodontal interventions and healthcare costs and utilization: Evidence from an integrated dental, medical, and pharmacy commercial claims database. Health Econ. 2017;26:519–527. http://onlinelibrary.wiley.com/doi/10.1002/hec.3316/epdf. Accessed June 1, 2016.	We have added this study to the report.
14	1	United Healthcare. Medical Dental Integration Study 2013. http://www.uhc.com/content/dam/uhcdotcom/en/Private%20Label%20Administrators/100-12683%20Bridge2Health_Study_Dental_Final.pdf.	We have added this study to the report.
15	2	Yes - See the comments below for published papers that were not included	See responses to comments #32-33.
16	3	No	None

Comment #	Reviewer #	Comment	Author Response
17	4	Yes - In addition to re-considering all the relevant studies from the list of excluded studies, a quick pubmed search showed some potentially relevant studies that the authors did not exclude:	See response to comment #7 regarding how we prioritized SRs for discussion, and a brief overview of how we included all relevant studies that addressed gaps in SR evidence. See responses to comments #18-27 regarding your additional suggested articles.
18	4	Cao R, Li Q, Wu Q, Yao M, Chen Y, Zhou H. Effect of non-surgical periodontal therapy on glycemic control of type 2 diabetes mellitus: a systematic review and Bayesian network meta-analysis. BMC Oral Health. 2019 Aug 6;19(1):176. doi: 10.1186/s12903-019-0829-y. PMID: 31387569; PMCID: PMC6685286	This SR was included in our report but de-prioritized because Ata-Ali 2020 covered the same PICOS and was more recent. We have added a table to the Supplementary Materials to provide a list of the de-prioritized SRs and the reasons they were not discussed.
19	4	Al-Hamoudi N. Is antimicrobial photodynamic therapy an effective treatment for chronic periodontitis in diabetes mellitus and cigarette smokers: a systematic review and meta-analysis. Photodiagnosis Photodyn Ther. 2017 Sep;19:375-382. doi: 10.1016/j.pdpdt.2017.05.018. Epub 2017 May 27. PMID: 28559203.	Excluded- wrong comparator. This SR evaluates antimicrobial photodynamic therapy as an adjunct to scaling & root planing- so there is no comparison to "no treatment."
20	4	Abduljabbar T, Javed F, Shah A, Samer MS, Vohra F, Akram Z. Role of lasers as an adjunct to scaling and root planing in patients with type 2 diabetes mellitus: a systematic review. Lasers Med Sci. 2017 Feb;32(2):449-459. doi: 10.1007/s10103-016-2086-5. Epub 2016 Sep 29. PMID: 27686888.	Excluded- wrong comparator. This SR evaluates laser therapy as an adjunct to scaling & root planing- so there is no comparison to "no treatment."
21	4	Teshome A, Yitayeh A. The effect of periodontal therapy on glycemic control and fasting plasma glucose level in type 2 diabetic patients: systematic review and meta-analysis. BMC Oral Health. 2016 Jul 30;17(1):31. doi: 10.1186/s12903-016-0249-1. PMID: 27473177; PMCID: PMC4967318.	This SR was included in our report but de-prioritized because Ata-Ali 2020 covered the same PICOS and was more recent. We have added a table to the Supplementary Materials to provide a list of the de-prioritized SRs and the reasons they were not discussed.

Comment #	Reviewer #	Comment	Author Response
22	4	Pérez-Losada FL, Jané-Salas E, Sabater-Recolons MM, Estrugo-Devesa A, Segura-Egea JJ, López-López J. Correlation between periodontal disease management and metabolic control of type 2 diabetes mellitus. A systematic literature review. Med Oral Patol Oral Cir Bucal. 2016 Jul 1;21(4):e440-6. doi: 10.4317/medoral.21048. PMID: 26827070; PMCID: PMC4920457.	This SR was included in our report but de-prioritized because Ata-Ali 2020 covered the same PICOS and was more recent. We have added a table to the Supplementary Materials to provide a list of the de-prioritized SRs and the reasons they were not discussed.
23	4	Freias CO, Gomes-Filho IS, Naves RC, Nogueira Filho Gda R, Cruz SS, Santos CA, Dunningham L, Miranda LF, Barbosa MD. Influence of periodontal therapy on C-reactive protein level: a systematic review and meta-analysis. J Appl Oral Sci. 2012 Feb;20(1):1-8. doi: 10.1590/s1678-77572012000100002. PMID: 22437670; PMCID: PMC3928764.	Excluded- wrong population. Did not evaluate people with chronic diseases.
24	4	Ioannidou E, Malekzadeh T, Dongari-Bagtzoglou A. Effect of periodontal treatment on serum C-reactive protein levels: a systematic review and meta-analysis. J Periodontol. 2006 Oct;77(10):1635-42. doi: 10.1902/jop.2006.050443. PMID: 17032104.	Excluded- wrong population. Did not evaluate people with chronic diseases.
25	4	Choi SE, Sima C, Pandya A. Impact of Treating Oral Disease on Preventing Vascular Diseases: A Model-Based Cost-effectiveness Analysis of Periodontal Treatment Among Patients With Type 2 Diabetes. Diabetes Care. 2020 Mar;43(3):563-571. doi: 10.2337/dc19-1201. Epub 2019 Dec 27. PMID: 31882408.	We have added this study to the report.
26	4	Blaschke K, Hellmich M, Samel C, Listl S, Schubert I. The impact of periodontal treatment on healthcare costs in newly diagnosed diabetes patients: Evidence from a German claims database. Diabetes Res Clin Pract. 2020 Dec 24;172:108641. doi: 10.1016/j.diabres.2020.108641. Epub ahead of print. PMID: 33359573.	We have added this study to the report.

Comment #	Reviewer #	Comment	Author Response
27	4	Nasseh K, Vujicic M, Glick M. The Relationship between Periodontal Interventions and Healthcare Costs and Utilization. Evidence from an Integrated Dental, Medical, and Pharmacy Commercial Claims Database. Health Econ. 2017 Apr;26(4):519-527. doi: 10.1002/hec.3316. Epub 2016 Jan 22. PMID: 26799518; PMCID: PMC5347922.	We have added this study to the report (see comment #13).
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.			
28	1	Well constructed, well written review.	Thank you
29	1	Key findings p. 5 clear	Thank you
30	1	Note: Conceptually, periodontal health is achieved through dx, initial treatment, and ONGOING periodontal care (every 3-6 months). Therefore, the optimal effect may be missed by included studies. PERIODIC, RECURRING treatment is key to periodontal maintenance, thus studies with beneficial effects for 3-6 months is probably the most we can get unless the treatment is continued long term.	We have added 2 sentences to the “Discussion” section to indicate why changes to chronic disease indicators may only be short term: “This may be due to the fact that periodontal treatment is meant to be a continuous preventive intervention (*ie*, scaling and root planing followed by routine check-ups and addressing subsequent problems that arise). Therefore, a single periodontal treatment session or group of sessions may not be sufficient to improve chronic disease indicators long-term.”
31	2	Thank you for asking me to comment on this Evidence Synthesis document. The literature in is this still-emerging field is not easily summarized, due to the lack of long-term studies and heterogeneity of study design. Nevertheless, the intriguing potential of this body of work, specifically improved health outcomes for patients with certain chronic diseases associated with the provision of preventive dental/periodontal care, makes this an important area of interprofessional research. Here are my comments:	None
32	2	1. Certain statements in the 'Key Findings' are problematic. While the data suggest that preventive care is associated with improved lung function and reduced frequency of exacerbations, it is stated that it is not clear if these improvements translate into reductions in health care utilization and costs. Certainly the first sentence implies reduced health care utilization. As stated in the Summary	We revised the key findings to include the evidence supporting specific statements. Given one of our newly included studies reported those with COPD who receive periodontal treatment have lower medical costs than those who don’t receive treatment, we removed the clause about healthcare utilization and costs. While we agree endothelial function is an important outcome, the

Comment #	Reviewer #	Comment	Author Response
		and Discussion, this phrase appears to be based on one short-term study. a amore specific statement is needed. As for CVD, a report by Tonetti et al (NEJM 2007 PMID 17329698), as well as other literature, has noted improvement in endothelial cell function associated with periodontal treatment. These findings provide additional supporting evidence that are at least as important as the reduction in inflammatory cytokines that are mentioned.	Tonetti study you cite was not conducted in those with chronic diseases, and none of our other included studies report this outcome. One of our newly included studies does measure oxidative stress, so this is now included in the report.
33	2	2. The evidence of an association of diabetes and periodontitis/periodontal treatment is the strongest of the 4 chronic diseases included in this review. One area of investigation that is of interest is research demonstrating reduced health utilization and costs associated with preventive dental care. These studies utilize existing insurance databases and the first of the published studies (Jeffcoat M et al (Am J Prev Med 2014 PMID 24953519; ref #57) examined four chronic diseases, but has been criticized based on methodological concerns (Sheiham A, J Evid Based Dent Pract 2015 PMID 25666581). Other studies on this subject have focused on diabetes, and the Smits study is cited (ref # 52). Further, another study specifically focused on diabetes is not cited (Nasseh K et al 2017 Health Econ PMID 26799518). In general, for all such studies a major problem is the failure to account for confounding variables. This can be due to a variety of reasons, including the use of existing insurance databases that do not contain all relevant variables.	We have added Nasseh 2017 to the report. We previously discussed the limitations of Jeffcoat 2014 (ref #57) – including the fact that their control group consisted of patients who have had 1, 2, or 3 periodontal treatment visits (not 0 visits), which is one of the major criticisms raised by Sheiham 2015. Additionally, in our “Limitations” section, we previously commented that a major limitation of our included non-RCTs is the “high risk that confounders could have influenced results.”
34	2	3. The inability to access the grey literature is mentioned, yet perhaps further elaboration is needed for completeness. There is a significant amount of grey literature ('reports") in the area of preventive dental services and improved health outcomes. These have been prepared by insurance companies as well as in one case by a health care consulting company, funded by a dental service organization. Interesting to note that some insurance companies have decided to offer expanded preventive dental benefits to enrollees with certain chromic	We have reviewed potentially relevant grey literature from insurance care companies suggested by reviewer #1 (see comments #9, #12 & #14) and included studies when they met inclusion criteria.

Comment #	Reviewer #	Comment	Author Response
		diseases (i.e. diabetes, CVD).	
35	2	4. No mention is made in the report of specific periodontal bacteria that have been shown to play a role in these associations. Porphyromonas gingivalis is one bacterium that has been widely implicated in these associations, and presents with a range of virulence factors that should be discussed when mechanisms are reviewed.	We have added *porphyromonas gingivalis* as an example of bacteria that may be involved in the relation between periodontal disease and chronic diseases to the "Background" section.
36	4	General Comments: Overall, I found the study very focused and interesting to read. I believe that the authors were very clear about what they intended to accomplish and laid out their rationale for the study in a succinct manner. They also clearly acknowledged the limitations of the study.	Thank you
37	4	Specific Comments: Key Findings/ Executive Summary: My first impression of the key findings box was that the authors appeared equivocal/ambiguous in their conclusions. The use of words/phrases such as "unclear", "may improve" repeatedly, connotes a lack of confidence about the findings or their conclusions. Could it be that the results are unclear because of the rapid approach to synthesizing the evidence? My fear is that this uncertainty will leave a similar impression on the policy makers who are the intended audience for this report. The review of the evidence should help the readers lean one way or the other, otherwise it does not add much value to the body of knowledge or the decision-making process.	We have removed the ambiguous language when it was used inappropriately (ie, for findings based on moderate or high-quality strength of evidence). However, we left in this language when we made statements based on low or insufficient strength of evidence. It is important that readers have a sense of our level of confidence based on how we frame our results. To that end, we have added information on the underlying studies supporting specific statements so readers can see why we had low levels of certainty.
38	4	Introduction/ Background: I found it sufficient. The purpose, scope, key questions, and eligibility criteria were clearly laid out. Some minor suggestions: Ln 53, Page 2: Please add a reference about who made this hypothesis. Figure 2: KQ4 should include the treatment arm, for those who received treatment for their dental problems	Thank you. Regarding p. 2, line 53- it is difficult to track down who first made this hypothesis, so instead we've rephrased the sentence to say periodontal disease "may contribute to worsening of diseases whose etiology or severity are in part driven by chronic inflammation" and provided 2 references that discuss this possible relationship.

Comment #	Reviewer #	Comment	Author Response
			Regarding figure 2- we have revised the figure so that KQ4 encompasses the treatment arm as well.
39	4	Methods: Ln 9, Page 7: Spell out acronyms in full at first mention. e.g CDSR	Added full name of CDSR (Cochrane Database of Systematic Reviews).
40	4	Ln 20, Page 7: Why did the authors choose to limit the search of primary studies to only address the gaps found with the systematic reviews? Since some of the systematic reviews are at least a few years old, it would have made for a more robust report if all recent primary studies were included in the synthesis. It would have also helped to have a quantitative synthesis/ meta-analysis for the conditions where no systematic reviews were found. i.e. COPD and cerebrovascular disease.	Ultimately, we chose to only search for primary studies that addressed gaps in SR evidence due to 2 factors- 1) there were several moderate and high-quality SRs that addressed several of our PICOs of interest and 2) the review was a rapid product and was to be completed in a short time frame. However, in response to this comment, we have added a search for primary studies on CVD/diabetes & chronic disease indicators from 2019 – 2020. This will ensure we've captured studies published since the end date of our most recent, relevant SRs' searches. To your second point about meta-analysis- we added a statement in the "synthesis of data" section to explain that we did not conduct a meta-analysis specifically among those with COPD or cerebrovascular disease because of variability in study designs, outcome measurements, and timing of outcome timing.
41	4	Ln 44, Page 7: Please provide a detailed description of the "checking" and consensus process throughout the report. Did the second reviewer review a sample of the initial reviewer's list, the entire selection, or just the ones where there were disagreements?	We have clarified that *all* titles, abstract and full text articles were reviewed by one investigator and checked by another.

Comment #	Reviewer #	Comment	Author Response
42	4	Ln 50, Page 7: What was the rationale for prioritizing recent studies? Why did the authors not consider all relevant studies that met their criteria? If the time period was important, then why wasn't it included in the eligibility criteria? What was the time cutoff point used to determine if a study was recent? It isn't clearly stated.	Our prioritization process only applied to SRs. We did not have a strict cut-off point to determine what was a "recent" review. Instead, we started with the most recently published reviews and moved backwards in time to see if older reviews' PICOs were already covered by more recent reviews, or if they offered unique information that should be discussed in the report. We added a sentence to the "results" section to describe the reasons why we did not discuss those 17 non-prioritized SRs, and also added a table to the Supplementary Materials with a specific reason why each SR was not prioritized.
43	4	Results: I strongly feel that the ambiguity of the results are due to the limitations in the approach. An exhaustive search of primary studies for each of these topics, might have yielded more evidence that would have helped to increase the certainty of the authors' conclusions. By focusing on the gaps found with the systematic reviews and not updating the systematic reviews with findings from more recent studies, the authors might have limited their own ability to make more definitive statements.	Given the availability of multiple, moderate or high-quality SRs on the effect of periodontal therapy on chronic disease indicators for those with CVD and diabetes, we believe it was appropriate to focus our report on those SRs' results and only run a search for studies on gaps in evidence. However, in response to this and earlier comments, we have added a search for primary studies on the effect of periodontal therapy on chronic disease outcomes for those with CVD or diabetes published from 2019 – 2020 to ensure we've captured all the most recently published studies on this topic.
44	4	List of Excluded Studies: I recommend reconsidering some of these studies for inclusion in the synthesis. It is unclear what criteria was used to determine "E5", "E7", and "E8". "R" and "E9" are not defined in the legend.	Thank you for pointing this out- the study labeled "R" was an include and was erroneously added in the excluded table. E9 (outdated or ineligible review) has been added to the table. We have also added our full inclusion/exclusion criteria as an additional appendix in the Supplementary Materials for full transparency.

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