**Periodontal disease is associated with cardiovascular disease independent of sex: a meta-analysis**

**Supplementary Table S1: Article content checklist**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Section/topic** | | **#** | **Checklist item** | **Reported on page #** |
| **TITLE** | | | |  |
| Title | | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |  |
| Structured summary | | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1 |
| **INTRODUCTION** | | | |  |
| Rationale | | 3 | Describe the rationale for the review in the context of what is already known. | 2 |
| Objectives | | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 2 |
| **METHODS** | | | |  |
| Protocol and registration | | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 3 |
| Eligibility criteria | | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4 |
| Search | | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 4 |
| Study selection | | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 5 |
| Data items | | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 5 |
| Risk of bias in individual studies | | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 |
| Summary measures | | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 6 |
| Synthesis of results | | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 7 |
| Risk of bias across studies | | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 7 |
| Additional analyses | | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7 |
| **RESULTS** | | | |  |
| Study selection | 17 | | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7 |
| Study characteristics | 18 | | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 8 |
| Risk of bias within studies | 19 | | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 9 |
| Results of individual studies | 20 | | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 9 |
| Synthesis of results | 21 | | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 10 |
| Risk of bias across studies | 22 | | Present results of any assessment of risk of bias across studies (see Item 15). | 10 |

**Supplementary Table S2**: **Detailed description of the search strategy**

|  |  |  |
| --- | --- | --- |
| Datebase | Search | Query |
| PubMed database | #1 | (((((((((((("Periodontal Disease"[Mesh]) OR (furcation defects)) OR (gingival diseases)) OR (peri-implantitis)) OR (periapical diseases)) OR (periodontal atrophy)) OR (periodontal cyst)) OR (periodontitis)) OR (tooth migration)) OR (periodontitis)) OR (tooth mobility)) OR (tooth loss)) |
| #2 | (((((((((((((((((((((((("Cardiovascular Diseases"[Mesh]) OR (cardiovascular disease)) OR (cardiovascular diseases)) OR (CVD)) OR (coronary heart disease)) OR (CHD)) OR (coronary artery disease)) OR (CAD)) OR (myocardial infarction)) OR (MI)) OR (coronary arteriosclerosis)) OR (heart attack)) OR (heart failure)) OR (HF)) OR (heart decompensation)) OR (atrial fibrillation)) OR (AF)) OR (sudden cardiac death)) OR (SCD)) OR (arrhythmia)) OR (cardiomyopathy)) OR (hypertrophic cardiomyopathy)) OR (HCM)) OR (dilated cardiomyopathy)) OR (DCM)) |
| #3 | #1 AND #2 |
| Embase database | #1 | ‘Periodontal Disease’/exp |
| #2 | ‘furcation defects’ OR ‘gingival diseases’ OR ‘peri-implantitis’ OR ‘periapical diseases’ OR ‘periodontal atrophy’ OR ‘periodontal cyst’ OR ‘periodontitis’ OR ‘tooth migration’ OR ‘periodontitis’ OR ‘tooth mobility’ OR ‘tooth loss’ |
| #3 | 'Cardiovascular Diseases'/exp |
| #4 | ‘cardiovascular disease’ OR ‘cardiovascular diseases’ OR ‘CVD’ OR ‘coronary heart disease’ OR ‘CHD’ OR ‘coronary artery disease’ OR ‘CAD’ OR ‘myocardial infarction’ OR ‘MI’ OR ‘coronary arteriosclerosis’ OR ‘heart attack’ OR ‘heart failure’ OR ‘HF’ OR ‘heart decompensation’ OR ‘atrial fibrillation’ OR ‘AF’ OR ‘sudden cardiac death’ OR ‘SCD’ OR ‘arrhythmia’ OR ‘cardiomyopathy’ OR ‘hypertrophic cardiomyopathy’ OR ‘HCM’ OR ‘dilated cardiomyopathy’ OR ‘DCM’ |
| #5 | #1 OR #2 |
| #6 | #3 OR #4 |
| #7 | #5 AND #6 |
| Cochrane library | #1 | MeSH descriptor: [Periodontal Disease] explode all trees |
| #2 | (Periodontal Disease):ti,ab,kw |
| #3 | MeSH descriptor: [Cardiovascular Diseases] explode all trees |
| #4 | (Cardiovascular Diseases):ti,ab,kw |
| #5 | #1 OR #2 |
| #6 | #3 OR #4 |
| #7 | #5 AND #6 |

**Embase**

|  |  |
| --- | --- |
| **Search** | **Query** |
| #1 | 'cardiovascular disease':ab,ti OR 'cardiovascular abnormalities':ab,ti OR 'congenital blood vessel malformation':ab,ti OR 'cardiovascular infection':ab,ti OR 'bacterial endocarditis':ab,ti OR 'cardiovascular syphilis':ab,ti OR tuberculosis:ab,ti OR 'heart disease':ab,ti OR 'heart arrhythmia':ab,ti OR 'carcinoid syndrome':ab,ti OR 'heart muscle conduction disturbance':ab,ti OR 'high output heart failure':ab,ti OR 'forward heart failure':ab,ti OR 'heart tamponade':ab,ti OR 'cardiomegaly':ab,ti OR cardiomyopathy:ab,ti OR cardiotoxicity:ab,ti OR endocarditis:ab,ti OR 'heart aneurysm':ab,ti OR 'heart arrest':ab,ti OR 'congenital heart malformation':ab,ti OR 'heart failure':ab,ti OR 'heart tumor':ab,ti OR 'heart rupture':ab,ti OR 'valvular heart disease':ab,ti OR 'heart muscle ischemia':ab,ti OR 'stunned heart muscle':ab,ti OR 'pericardial effusion':ab,ti OR pericarditis:ab,ti OR pneumopericardium:ab,ti OR 'post-cardiac arrest syndrome':ab,ti OR 'postpericardiotomy syndrome':ab,ti OR 'pulmonary heart disease':ab,ti OR 'rheumatic heart disease':ab,ti OR 'ventricular dysfunction':ab,ti OR 'ventricular outflow obstruction':ab,ti OR 'pregnancy complications, cardiovascular':ab,ti OR 'embolism, amniotic fluid':ab,ti OR 'vascular diseases':ab,ti OR aneurysm:ab,ti OR angiodysplasia:ab,ti OR 'angioneurotic edema':ab,ti OR 'angiomatosis +':ab,ti OR 'aortic diseases +':ab,ti OR 'arterial occlusive diseases +':ab,ti OR 'arteriovenous malformations +':ab,ti OR 'capillary leak syndrome':ab,ti OR 'cerebrovascular disease':ab,ti OR 'colitis, ischemic':ab,ti OR 'compartment syndromes':ab,ti OR 'diabetic angiopathy':ab,ti OR (embolism:ab,ti AND thrombosis:ab,ti) OR 'hand-arm vibration syndrome':ab,ti OR hemorrhoid:ab,ti OR 'hemostatic disorders':ab,ti OR 'hepatic veno-occlusive disease':ab,ti OR hyperemia:ab,ti OR hypertension:ab,ti OR hypotension:ab,ti OR 'mesenteric ischemia':ab,ti OR 'myocardial ischemia':ab,ti OR 'optic neuropathy, ischemic':ab,ti OR 'peliosis hepatis':ab,ti OR 'peripheral vascular diseases':ab,ti OR prehypertension:ab,ti OR 'pulmonary veno-occlusive disease':ab,ti OR 'reperfusion injury':ab,ti OR 'retinal vein occlusion':ab,ti OR 'scimitar syndrome':ab,ti OR 'spinal cord vascular diseases':ab,ti OR 'spleen infarction':ab,ti OR 'stenosis, pulmonary vein':ab,ti OR 'superior vena cava syndrome':ab,ti OR telangiectasis:ab,ti OR 'thoracic outlet syndrome':ab,ti OR varicocele:ab,ti OR 'varicose veins':ab,ti OR 'vascular fistula':ab,ti OR 'vascular neoplasms':ab,ti OR 'vascular system injuries':ab,ti OR vasculitis:ab,ti OR vasoplegia:ab,ti OR 'venous insufficiency':ab,ti |
| #2 | 'periodontal disease':ab,ti OR 'furcation defects':ab,ti OR 'gingival diseases':ab,ti OR 'gingival hemorrhage':ab,ti OR 'gingival neoplasms':ab,ti OR 'gingival overgrowth':ab,ti OR gingivitis:ab,ti OR 'granuloma, giant cell':ab,ti OR pericoronitis:ab,ti OR 'peri-implantitis':ab,ti OR 'periapical diseases':ab,ti OR 'radicular cyst':ab,ti OR 'periodontal atrophy':ab,ti OR 'alveolar bone loss':ab,ti OR 'gingival recession':ab,ti OR 'periodontal attachment loss':ab,ti OR 'periodontal cyst':ab,ti OR 'periodontitis':ab,ti OR 'aggressive periodontitis':ab,ti OR 'chronic periodontitis':ab,ti OR 'periapical periodontitis':ab,ti OR 'periodontal abscess':ab,ti OR 'periodontal pocket':ab,ti OR 'tooth loss':ab,ti OR 'tooth migration':ab,ti OR 'mesial movement of teeth':ab,ti OR 'tooth mobility':ab,ti |
| #3 | #1 AND #2 |

**Cochrane**

|  |  |
| --- | --- |
| **Search** | **Query** |
| #1 | (Periodontal Diseases):ti,ab,kw OR (Furcation Defects):ti,ab,kw OR (Gingival Diseases):ti,ab,kw OR (Gingival Hemorrhage):ti,ab,kw OR (Gingival Neoplasms):ti,ab,kw (Word variations have been searched) |
| #2 | (Gingival Overgrowth):ti,ab,kw OR (Gingival Recession):ti,ab,kw OR (Gingivitis):ti,ab,kw OR (Granuloma, Giant Cell):ti,ab,kw OR (Pericoronitis):ti,ab,kw (Word variations have been searched) |
| #3 | (Peri-Implantitis):ti,ab,kw OR (Periapical Diseases):ti,ab,kw OR (Periapical Periodontitis):ti,ab,kw OR ((Radicular Cyst)):ti,ab,kw OR (Periodontal Atrophy):ti,ab,kw (Word variations have been searched) |
| #4 | (Alveolar Bone Loss):ti,ab,kw OR (Gingival Recession):ti,ab,kw OR (Periodontal Attachment Loss):ti,ab,kw OR (Periodontal Cyst):ti,ab,kw OR (Periodontitis):ti,ab,kw (Word variations have been searched) |
| #5 | (Aggressive Periodontitis):ti,ab,kw OR (Chronic Periodontitis):ti,ab,kw OR (Periapical Periodontitis):ti,ab,kw OR (Periodontal Abscess):ti,ab,kw OR (Periodontal Pocket):ti,ab,kw (Word variations have been searched) |
| #6 | (Tooth Loss):ti,ab,kw OR (Tooth Migration):ti,ab,kw OR (Mesial Movement of Teeth):ti,ab,kw OR (Tooth Mobility):ti,ab,kw (Word variations have been searched) |
| #7 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 |
| #8 | (Cardiovascular Diseases):ti,ab,kw OR (Cardiovascular Abnormalities):ti,ab,kw OR (Heart Defects, Congenital):ti,ab,kw OR ((Vascular Malformations):ti,ab,kw OR (Cardiovascular Infections):ti,ab,kw (Word variations have been searched) |
| #9 | (Endocarditis, Bacterial ):ti,ab,kw OR (Syphilis, Cardiovascular):ti,ab,kw OR (Tuberculosis, Cardiovascular ):ti,ab,kw OR (Heart Diseases):ti,ab,kw OR (Arrhythmias, Cardiac):ti,ab,kw (Word variations have been searched) |
| #10 | (Carcinoid Heart Disease ):ti,ab,kw OR (Cardiac Conduction System Disease ):ti,ab,kw OR (Cardiac Output, High ):ti,ab,kw OR (Cardiac Output, Low):ti,ab,kw OR (Cardiac Tamponade):ti,ab,kw (Word variations have been searched) |
| #11 | (Cardiomegaly ):ti,ab,kw OR (Cardiomyopathies ):ti,ab,kw OR (Cardiotoxicity ):ti,ab,kw OR (Endocarditis):ti,ab,kw OR (Heart Aneurysm):ti,ab,kw (Word variations have been searched) |
| #12 | (Heart Arrest ):ti,ab,kw OR (Heart Defects, Congenital ):ti,ab,kw OR (Heart Failure):ti,ab,kw OR (Heart Neoplasms ):ti,ab,kw OR (Heart Rupture):ti,ab,kw (Word variations have been searched) |
| #13 | (Heart Valve Diseases ):ti,ab,kw OR (Myocardial Ischemia ):ti,ab,kw OR (Myocardial Stunning):ti,ab,kw OR (Pericardial Effusion ):ti,ab,kw OR (Pericarditis):ti,ab,kw (Word variations have been searched) |
| #14 | (Pneumopericardium ):ti,ab,kw OR (Post-Cardiac Arrest Syndrome ):ti,ab,kw OR (Postpericardiotomy Syndrome):ti,ab,kw OR (Pulmonary Heart Disease ):ti,ab,kw OR (Rheumatic Heart Disease):ti,ab,kw (Word variations have been searched) |
| #15 | (Ventricular Dysfunction ):ti,ab,kw OR (Ventricular Outflow Obstruction ):ti,ab,kw OR((Pregnancy Complications, Cardiovascular):ti,ab,kw OR (Embolism, Amniotic Fluid ):ti,ab,kw OR (Vascular Diseases):ti,ab,kw (Word variations have been searched) |
| #16 | (Aneurysm):ti,ab,kw OR ((Angiodysplasia ):ti,ab,kw OR ("angioedema-urticaria"):ti,ab,kw OR (Angiomatosis ):ti,ab,kw OR (Aortic Diseases)):ti,ab,kw (Word variations have been searched) |
| #17 | (Arterial Occlusive Diseases):ti,ab,kw OR (Arteriovenous Malformations ):ti,ab,kw OR (Capillary Leak Syndrome):ti,ab,kw OR (Cerebrovascular Disorders):ti,ab,kw OR (Colitis, Ischemic):ti,ab,kw (Word variations have been searched) |
| #18 | (Compartment Syndromes):ti,ab,kw OR (Diabetic Angiopathies):ti,ab,kw OR (Embolism and Thrombosis):ti,ab,kw OR (Hand-Arm Vibration Syndrome):ti,ab,kw OR (Hemorrhoids):ti,ab,kw (Word variations have been searched) |
| #19 | (Hemostatic Disorders):ti,ab,kw OR (Hepatic Veno-Occlusive Disease):ti,ab,kw OR (Hyperemia):ti,ab,kw OR (Hypertension):ti,ab,kw OR (Hypotension):ti,ab,kw (Word variations have been searched) |
| #20 | (Mesenteric Ischemia):ti,ab,kw OR (Myocardial Ischemia):ti,ab,kw OR (Optic Neuropathy, Ischemic):ti,ab,kw OR (Peliosis Hepatis):ti,ab,kw OR (Peripheral Vascular Diseases):ti,ab,kw (Word variations have been searched) |
| #21 | (Prehypertension):ti,ab,kw OR (Pulmonary Veno-Occlusive Disease):ti,ab,kw OR (Reperfusion Injury):ti,ab,kw OR (Retinal Vein Occlusion):ti,ab,kw OR (Scimitar Syndrome):ti,ab,kw (Word variations have been searched) |
| #22 | (Spinal Cord Vascular Diseases):ti,ab,kw OR (Splenic Infarction):ti,ab,kw OR (Stenosis, Pulmonary Vein):ti,ab,kw OR (Superior Vena Cava Syndrome):ti,ab,kw OR (Telangiectasis):ti,ab,kw (Word variations have been searched) |
| #23 | (Thoracic Outlet Syndrome):ti,ab,kw OR (Varicocele):ti,ab,kw OR (Varicose Veins):ti,ab,kw OR (Vascular Fistula):ti,ab,kw OR (Vascular Neoplasms):ti,ab,kw (Word variations have been searched) |
| #24 | (Vascular System Injuries):ti,ab,kw OR (Vasculitis):ti,ab,kw OR (Vasoplegia):ti,ab,kw OR (Venous Insufficiency):ti,ab,kw (Word variations have been searched) |
| #25 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 #14 OR #15 OR #16 OR #17 OR #18 OR #19 #20 OR #21 OR #22 OR #23 OR #24 |
| #26 | #7 AND #25 |

**Supplementary Table S3: Studies excluded (n=55) with reasons**

|  |  |
| --- | --- |
| **Studies excluded** | **Reasons** |
| Gong 20171 | A meta-analysis |
| Grau 20042 | The sample size is insufficient |
| Hada3 | The sample size is insufficient |
| Bal 20154 | The sample size is insufficient |
| Arbes 19995 | Can't extract accurate data |
| Buhlin 20026 | Can't extract accurate data |
| Alade 20187 | A meta-analysis |
| Alim 20207 | The sample size is insufficient |
| Aarabi 20158 | The sample size is insufficient |
| Abou-Raya 20089 | Can't extract accurate data |
| Beck 200010 | The sample size is insufficient |
| Cueto 200511 | The sample size is insufficient |
| Darnaud2015 | Can't extract accurate data |
| Holmlund 201712 | Can't extract accurate data |
| Hujoel 200113 | Unable extract accurate data |
| Hujoel 200214 | Can't extract accurate data |
| Dorn 201015 | Unable extract accurate data |
| Kim 201016 | Can't extract accurate data |
| Kodovazenitis 201417 | Unable extract accurate data |
| Koppolu 201318 | Can't extract accurate data |
| Lee 201919 | Unable extract accurate data |
| Lee 200620 | Unable extract accurate data |
| Loesche 199821 | Can't extract accurate data |
| Pradeep 201022 | Unable extract accurate data |
| Pray 201423 | Unable extract accurate data |
| Pussinen 200424 | The sample size is insufficient |
| Pussinen 200325 | The sample size is insufficient |
| Rastogi 201226 | Unable extract accurate data |
| Renvert 201027 | The sample size is insufficient |
| Ryden 201628 | The sample size is insufficient |
| Sen 201829 | Unable extract accurate data |
| Tu 201730 | The sample size is insufficient |
| Zagaria 201631 | Unable extract accurate data |
| Joshy 201632 | Unable extract accurate data |
| Elter 200433 | The sample size is insufficient |
| Higashi 200934 | Can't extract accurate data |
| Jacobs 200735 | Can't extract accurate data |
| Liljestrand 201536 | Unable extract accurate data |
| Loesche 199637 | Can't extract accurate data |
| Montebugnoli 200538 | Can't extract accurate data |
| Barilli 200639 | Unable extract accurate data |
| Barnett 200940 | Can't extract accurate data |
| Bawankar 202141 | Can't extract accurate data |
| Behle 200642 | The sample size is insufficient |
| Belinga 201843 | The sample size is insufficient |
| Chen 200944 | Unable extract accurate data |
| Choi 201545 | The sample size is insufficient |
| Chou 201546 | Can't extract accurate data |
| Da Venezia 202147 | The sample size is insufficient |
| Dorfer 200448 | The sample size is insufficient |
| Homlund 201149 | Can't extract accurate data |
| Joshipura 200550 | The sample size is insufficient |
| Soory 201051 | Can't extract accurate data |
| Aminzadeh 201352 | The sample size is insufficient |
| Lee 201553 | The type of research is incorrect |
| Lee 201754 | The type of research is incorrect |
| Alhadainy 202155 | Can't extract accurate data |

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**Supplementary Table S4. Quality assessment of the included studies by Newcastle–Ottawa scale.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author  (Publication Year) | Newcastle-Ottawa Scale | | | | | | | | | |
| Selection | | | Comparability | | | Outcome | | | Total |
| a | b | c | d | e | f | g | h | i |
| Yu 2015 | \* | \* |  |  | \* |  | \* | \* | \* | 6 |
| Batty 2018 | \* | \* | \* | \* |  |  | \* | \* | \* | 7 |
| Beck 1996 | \* | \* |  |  |  | \* | \* | \* | \* | 6 |
| Choe 2009 | \* | \* | \* |  | \* | \* | \* | \* | \* | 8 |
| Destefano 1993 | \* | \* |  |  | \* | \* | \* | \* | \* | 7 |
| Dietrich 2008 | \* | \* | \* |  | \* |  | \* | \* | \* | 7 |
| Heitmann 2001 | \* | \* |  |  | \* |  | \* | \* | \* | 6 |
| Hung 2004 | \* | \* |  | \* | \* |  | \* | \* | \* | 7 |
| Hung 2003 | \* | \* | \* | \* | \* |  | \* | \* |  | 7 |
| Jimenez 2009 | \* | \* |  | \* | \* | \* | \* | \* |  | 7 |
| Joshipura 2003 | \* | \* |  |  | \* | \* | \* | \* | \* | 7 |
| Joshipura 1996 | \* | \* | \* |  | \* |  | \* | \* | \* | 7 |
| LaMonte 2017 | \* | \* | \* | \* | \* | \* | \* | \* | \* | 9 |
| Noguchi 2014 | \* | \* | \* | \* | \* |  | \* |  |  | 6 |
| Rivas-Tumanyan 2012 | \* | \* | \* | \* | \* |  | \* | \* |  | 7 |
| Senba 2008 | \* | \* |  |  |  |  | \* | \* | \* | 5 |
| Andriankaja 2007 | \* | \* | \* | \* | \* | \* | \* |  |  | 7 |
| Tuominen 2003 | \* | \* | \* |  | \* |  | \* | \* | \* | 7 |
| Morrison 1999 | \* | \* |  |  | \* | \* |  | \* | \* | 6 |
| Beck 2005 | \* | \* | \* |  | \* | \* |  | \* | \* | 7 |
| Chen 2016 | \* | \* |  | \* | \* | \* | \* | \* | \* | 8 |
| Hansen 2016 | \* | \* | \* |  | \* | \* | \* | \* | \* | 8 |
| Joshy 2016 | \* | \* | \* |  | \* | \* | \* | \* | \* | 8 |
| Howell 2001 | \* | \* |  |  | \* | \* |  | \* | \* | 6 |
| Lee 2013 | \* | \* | \* | \* |  |  | \* | \* | \* | 7 |
| Ahn 2015 | \* | \* | \* |  |  | \* | \* | \* | \* | 7 |

1. Representativeness of the exposed cohort.
2. Selection of the non-exposed cohort.
3. Ascertainment of exposure.
4. Demonstration that outcome of interest was not present at start of study.
5. Comparability of cohorts on the basis of the design or analysis (adjusted for age).
6. Comparability of cohorts on the basis of the design or analysis (adjusted for any other factor).
7. Assessment of outcome.
8. Was follow-up long enough for outcomes to occur.
9. Adequacy of follow-up of cohorts.

**Supplementary Table S5. GRADE evidence profile**

| **Certainty assessment** | | | | | | | **№ of patients** | | **Effect** | | **Certainty** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **periodontal disease patients** | **non-periodontal disease patients** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Risk of CVD (follow-up: range 2 to 34 years; assessed with: ICD 9 or ICD 10)** | | | | | | | | | | | | |
| 20 | observational studies | not serious | serious | serious | not serious | none | 492519/2773424 (17.8%) | 422370/2773424 (15.2%) | **OR 1.25** (1.13 to 1.38) | **31 more per 1,000** (from 16 more to 46 more) | ⨁◯◯◯ Very low | CRITICAL |

**CI: confidence interval; OR: odds ratio**

**Supplementary Figure S1. Forest plot of the prevalence of cardiovascular disease in patients with periodontal disease.**

**(A: CHD; B: Stroke; C: HP; D: HF).**

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# CHD: coronary-heart-disease; HP: hypertension; HF: heart failure

**Supplementary** **Figure S2. Publication bias detected by funnel plot, Egger’s test and Begg’s test for the sex-specific association between periodontal disease and CVD.**

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**Supplementary** **Figure S3. Sensitivity analysis of the association between periodontal disease and CVD.**

**A: Female periodontal disease and CVD; B: Male periodontal disease and CVD**

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