

Supplementary material 1: PRISMA (Preference Reporting Requirements for Systematic Review and Meta-Analysis) guidelines checklist

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	27-28
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	93
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1-17
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	449-454
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input checked="" type="checkbox"/>	<input type="checkbox"/>	133-134
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	443-446
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	81-84
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	98-101
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	98-106; 122-124
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	104-106

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	106-109
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	110-111
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	111-125
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	118-120;124-125
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	98-103;106-109;126-128
111-113 Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	98-103
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	137-144
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	148-183
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	152-183
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	171-183
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	186-193

Supplementary material 2: Inclusion criteria following the PECO strategy [17].

Inclusion Criteria	
P (participants)	Humans at any age.
E (exposition)	Exposition to periodontitis
C (comparison)	Absence of periodontitis
O (outcome)	Primary outcome: The risk of different types of cerebrovascular damages and their correlation or association with periodontitis. Secondary outcome: Correlation or association of age, gender, previous history of vascular disease, heart disease, smoking, hypertension, diabetes, physical inactivity, cholesterol, alcohol, drugs and hormonal rate in patients with periodontitis and the prevalence of cerebrovascular damage.
S (type of studies included)	Observational studies

Supplementary material 3: Database and Search Strategy

Database	Search Strategy
Pubmed	<p>#1</p> <p>(((((Cerebrovascular Circulation[Title/Abstract]) OR Flows, Cerebral Blood[Title/Abstract]) OR Cerebral Circulation[Title/Abstract]) OR Cerebral Circulations[Title/Abstract]) OR Circulation, Cerebral[Title/Abstract]) OR Circulations, Cerebral[Title/Abstract]) OR Circulation, Cerebrovascular[Title/Abstract]) OR Cerebral Blood Flow[Title/Abstract]) OR Blood Flow, Cerebral[Title/Abstract]) OR Blood Flows, Cerebral[Title/Abstract]) OR Cerebral Blood Flows[Title/Abstract]) OR Flow, Cerebral Blood[Title/Abstract]) OR Central nervous system[MeSH Terms]) OR Central nervous system[Title/Abstract]) OR Systems, Central Nervous[Title/Abstract]) OR Central Nervous Systems[Title/Abstract]) OR Nervous System, Central[Title/Abstract]) OR Nervous Systems, Central[Title/Abstract]) OR System, Central Nervous[Title/Abstract]) OR Brain[MeSH Terms]) OR Brain[Title/Abstract]) OR encephalons[Title/Abstract]) OR Brains[Title/Abstract]) OR Encephalon[Title/Abstract]) OR Blood-Brain Barrier[MeSH Terms]) OR Blood-Brain Barrier[Title/Abstract]) OR Brain-Blood Barriers[Title/Abstract]) OR Barrier, Blood-Brain[Title/Abstract]) OR Barriers, Blood-Brain[Title/Abstract]) OR Blood Brain Barrier[Title/Abstract]) OR Blood-Brain Barriers[Title/Abstract]) OR Hemato-Encephalic Barrier[Title/Abstract]) OR Barrier, Hemato-Encephalic[Title/Abstract]) OR Barriers, Hemato-Encephalic[Title/Abstract]) OR Hemato Encephalic Barrier[Title/Abstract]) OR Hemato-Encephalic Barriers[Title/Abstract]) OR Brain-Blood Barrier[Title/Abstract]) OR Barrier, Brain-Blood[Title/Abstract]) OR Barriers, Brain-Blood[Title/Abstract]) OR Brain Blood Barrier[Title/Abstract]) OR Stroke[MeSH Terms]) OR Stroke[Title/Abstract]) OR Cerebral Strokes[Title/Abstract]) OR Strokes[Title/Abstract]) OR Cerebrovascular Accident[Title/Abstract]) OR Cerebrovascular Accidents[Title/Abstract]) OR CVA AND (Cerebrovascular Accident) AND Title/Abstract) OR CVAs AND (Cerebrovascular Accident) AND Title/Abstract) OR Cerebrovascular Apoplexy[Title/Abstract]) OR Apoplexy, Cerebrovascular[Title/Abstract]) OR Vascular Accident, Brain[Title/Abstract]) OR Brain Vascular Accident[Title/Abstract]) OR Brain Vascular Accidents[Title/Abstract]) OR Vascular Accidents, Brain[Title/Abstract]) OR Cerebrovascular Stroke[Title/Abstract]) OR Cerebrovascular Strokes[Title/Abstract]) OR Stroke, Cerebrovascular[Title/Abstract]) OR Strokes, Cerebrovascular[Title/Abstract]) OR Apoplexy[Title/Abstract]) OR Cerebral Stroke[Title/Abstract]) OR Cerebrovascular Accidents, Acute[Title/Abstract]) OR Stroke, Cerebral[Title/Abstract]) OR Strokes, Cerebral[Title/Abstract]) OR Stroke, Acute[Title/Abstract]) OR Acute Stroke[Title/Abstract]) OR Acute Strokes[Title/Abstract]) OR Strokes, Acute[Title/Abstract]) OR Cerebrovascular Accident, Acute[Title/Abstract]) OR Acute Cerebrovascular Accident[Title/Abstract]) OR Acute Cerebrovascular Accidents[Title/Abstract]) OR Brain Ischemia[MeSH Terms]) OR Brain Ischemia[Title/Abstract]) OR Ischemia, Cerebral[Title/Abstract]) OR Brain Ischemias[Title/Abstract]) OR Ischemia, Brain[Title/Abstract]) OR Ischemic Encephalopathy[Title/Abstract]) OR Encephalopathy, Ischemic[Title/Abstract]) OR Ischemic Encephalopathies[Title/Abstract]) OR Cerebral Ischemia[Title/Abstract]) OR Cerebral Ischemias[Title/Abstract]) OR Ischemias, Cerebral[Title/Abstract]) OR Ischemic stroke[Title/Abstract]) OR Stroke, Lacunar[MeSH Terms]) OR Stroke, Lacunar[Title/Abstract]) OR Lacunar Infarcts[Title/Abstract]) OR Lacunar Stroke[Title/Abstract]) OR Lacunar Strokes[Title/Abstract]) OR Strokes, Lacunar[Title/Abstract]) OR Lacunar Syndrome[Title/Abstract]) OR Lacunar Syndromes[Title/Abstract]) OR Syndrome, Lacunar[Title/Abstract]) OR Syndromes, Lacunar[Title/Abstract]) OR Infarction, Lacunar[Title/Abstract]) OR Infarctions, Lacunar[Title/Abstract]) OR Lacunar Infarction[Title/Abstract]) OR Lacunar Infarctions[Title/Abstract]) OR Infarct, Lacunar[Title/Abstract]) OR Infarcts, Lacunar[Title/Abstract]) OR Lacunar Infarct[Title/Abstract]) OR Cerebrovascular Circulation[MeSH Terms]))</p> <p>#2</p> <p>(((((Periodontal Diseases[MeSH Terms]) OR Periodontal Diseases[Title/Abstract]) OR Pyorrhea Alveolaris[Title/Abstract]) OR</p>

Disease, Periodontal[Title/Abstract]) OR Diseases, Periodontal[Title/Abstract]) OR Periodontal Disease[Title/Abstract]) OR Parodontosis[Title/Abstract]) OR Parodontoses[Title/Abstract]) OR Periodontal Atrophy[MeSH Terms]) OR Periodontal Atrophy[Title/Abstract]) OR Gingivo-Osseous Atrophies[Title/Abstract]) OR Periodontal Atrophies[Title/Abstract]) OR Atrophy of Periodontium[Title/Abstract]) OR Periodontium Atrophies[Title/Abstract]) OR Periodontium Atrophy[Title/Abstract]) OR Gingivo-Osseous Atrophy[Title/Abstract]) OR Gingivo Osseous Atrophy[Title/Abstract]) OR periodontitis[MeSH Terms]) OR periodontitis[Title/Abstract]) OR Periodontitides[Title/Abstract]) OR chronic periodontitis[MeSH Terms]) OR Aggressive Periodontitis[MeSH Terms]) OR Periapical Periodontitis[MeSH Terms]) OR Alveolar Bone Loss[MeSH Terms]) OR Alveolar Bone Loss[Title/Abstract]) OR Bone Loss, Alveolar[Title/Abstract]) OR Alveolar Bone Losses[Title/Abstract]) OR Alveolar Process Atrophy[Title/Abstract]) OR Alveolar Process Atrophies[Title/Abstract]) OR Alveolar Resorption[Title/Abstract]) OR Alveolar Resorptions[Title/Abstract]) OR Resorption, Alveolar[Title/Abstract]) OR Resorptions, Alveolar[Title/Abstract]) OR Bone Loss, Periodontal[Title/Abstract]) OR Bone Losses, Periodontal[Title/Abstract]) OR Periodontal Bone Losses[Title/Abstract]) OR Periodontal Bone Loss[Title/Abstract]) OR Periodontal Resorption[Title/Abstract]) OR Periodontal Resorptions[Title/Abstract]) OR Resorption, Periodontal[Title/Abstract]) OR Alveolar Bone Atrophy[Title/Abstract]) OR Alveolar Bone Atrophies[Title/Abstract]) OR Bone Atrophies, Alveolar[Title/Abstract]) OR Bone Atrophy, Alveolar[Title/Abstract])

Final search: #1 AND #2

Scopus

((TITLE-ABS-KEY (periodontitis) OR TITLE-ABS-KEY ("chronic periodontitis") OR TITLE-ABS-KEY ("Aggressive Periodontitis") OR TITLE-ABS-KEY ("Periapical Periodontitis") OR TITLE-ABS-KEY ("Periodontal Disease") OR TITLE-ABS-KEY (parodontosis) OR TITLE-ABS-KEY (parodontoses) OR TITLE-ABS-KEY ("Pyorrhoea Alveolaris") OR TITLE-ABS-KEY ("Periodontal Atrophy") OR TITLE-ABS-KEY ("Atrophy of Periodontium") OR TITLE-ABS-KEY ("Periodontium Atrophy") OR TITLE-ABS-KEY ("Gingivo-Osseous Atrophy") OR TITLE-ABS-KEY ("Gingivo Osseous Atrophy") OR TITLE-ABS-KEY ("Alveolar Bone Loss") OR TITLE-ABS-KEY ("Alveolar Process Atrophy") OR TITLE-ABS-KEY ("Alveolar Resorption") OR TITLE-ABS-KEY ("Periodontal Bone Loss") OR TITLE-ABS-KEY ("Periodontal Resorption") OR TITLE-ABS-KEY ("Alveolar Bone Atrophy") OR TITLE-ABS-KEY ("Alveolar Bone Atrophies") OR TITLE-ABS-KEY ("Periodontal Resorptions") OR TITLE-ABS-KEY ("Periodontal Bone Losses") OR TITLE-ABS-KEY ("Alveolar Process Atrophies") OR TITLE-ABS-KEY ("Alveolar Bone Losses") OR TITLE-ABS-KEY ("Gingivo Osseous Atrophies") OR TITLE-ABS-KEY ("Gingivo-Osseous Atrophies") OR TITLE-ABS-KEY ("Periodontal Atrophies") OR TITLE-ABS-KEY ("Periodontium Atrophies") OR TITLE-ABS-KEY (periodontitides))) AND ((TITLE-ABS-KEY ("Cerebrovascular Circulation") OR TITLE-ABS-KEY ("Cerebrovascular Circulations") OR TITLE-ABS-KEY ("Cerebral Blood Flow") OR TITLE-ABS-KEY ("Cerebral Blood Flows") OR TITLE-ABS-KEY ("Central nervous system") OR TITLE-ABS-KEY ("Central nervous systems") OR TITLE-ABS-KEY (brain) OR TITLE-ABS-KEY (brains) OR TITLE-ABS-KEY (encephalon) OR TITLE-ABS-KEY (encephalons) OR TITLE-ABS-KEY ("Blood-Brain Barrier") OR TITLE-ABS-KEY ("Blood-Brain Barriers") OR TITLE-ABS-KEY ("Blood Brain Barrier") OR TITLE-ABS-KEY ("Blood Brain Barriers") OR TITLE-ABS-KEY ("Hemato-Encephalic Barrier") OR TITLE-ABS-KEY ("Hemato-Encephalic Barriers") OR TITLE-ABS-KEY ("Brain-Blood Barrier") OR TITLE-ABS-KEY ("Brain-Blood Barriers") OR TITLE-ABS-KEY ("Brain Blood Barrier") OR TITLE-ABS-KEY ("Brain Blood Barriers") OR TITLE-ABS-KEY (stroke) OR TITLE-ABS-KEY (strokes) OR TITLE-ABS-KEY ("Cerebrovascular Accident") OR TITLE-ABS-KEY ("Cerebrovascular Accidents") OR TITLE-ABS-KEY ("Cerebrovascular Apoplexy") OR TITLE-ABS-KEY ("Brain Vascular Accident") OR TITLE-ABS-KEY ("Brain Vascular Accidents") OR TITLE-ABS-KEY ("Cerebrovascular Stroke") OR TITLE-ABS-KEY ("Cerebrovascular Strokes") OR TITLE-ABS-KEY ("Cerebrovascular Stroke") OR TITLE-ABS-KEY ("Cerebral Stroke") OR TITLE-ABS-KEY ("Cerebral Strokes") OR TITLE-ABS-KEY ("Acute Stroke") OR

TITLE-ABS-KEY ("Acute Strokes") OR TITLE-ABS-KEY ("Acute Cerebrovascular Accident") OR TITLE-ABS-KEY ("Acute Cerebrovascular Accidents") OR TITLE-ABS-KEY ("Brain Ischemia") OR TITLE-ABS-KEY ("Brain Ischemias") OR TITLE-ABS-KEY ("Ischemic Encephalopathy") OR TITLE-ABS-KEY ("Ischemic Encephalopathies") OR TITLE-ABS-KEY ("Cerebral Ischemia") OR TITLE-ABS-KEY ("Cerebral Ischemias") OR TITLE-ABS-KEY ("Ischemic stroke") OR TITLE-ABS-KEY ("Lacunar Stroke") OR TITLE-ABS-KEY ("Lacunar Strokes") OR TITLE-ABS-KEY ("Lacunar Syndrome") OR TITLE-ABS-KEY ("Lacunar Syndromes") OR TITLE-ABS-KEY ("Lacunar Infarction") OR TITLE-ABS-KEY ("Lacunar Infarctions") OR TITLE-ABS-KEY ("Lacunar Infarct") OR TITLE-ABS-KEY ("Lacunar Infarcts"))

Web of
Science

#1- TOPIC: ("Cerebrovascular Circulation") OR TOPIC: ("Cerebral Circulation") OR TOPIC: ("Cerebral Circulations") OR TOPIC: ("Cerebral Blood Flow") OR TOPIC: ("Cerebral Blood Flows") OR TOPIC: ("Central nervous system") OR TOPIC: ("Central nervous systems") OR TOPIC: (Brain) OR TOPIC: (Brains) OR TOPIC: (Encephalon) OR TOPIC: (Encephalons) OR TOPIC: ("Blood-Brain Barrier") OR TOPIC: ("Blood-Brain Barriers") OR TOPIC: ("Blood Brain Barrier") OR TOPIC: ("Blood Brain Barriers") OR TOPIC: ("Hemato-Encephalic Barrier") OR TOPIC: ("Hemato-Encephalic Barriers") OR TOPIC: ("Hemato Encephalic Barrier") OR TOPIC: ("Hemato Encephalic Barriers") OR TOPIC: ("Brain-Blood Barrier") OR TOPIC: ("Brain-Blood Barriers") OR TOPIC: ("Brain Blood Barrier") OR TOPIC: ("Brain Blood Barriers") OR TOPIC: (Stroke) OR TOPIC: (Strokes) OR TOPIC: ("Cerebrovascular Accident") OR TOPIC: ("Cerebrovascular Accidents") OR TOPIC: ("Cerebrovascular Apoplexy") OR TOPIC: ("Brain Vascular Accident") OR TOPIC: ("Brain Vascular Accidents") OR TOPIC: ("Cerebrovascular Stroke") OR TOPIC: ("Cerebrovascular Strokes") OR TOPIC: (Apoplexy) OR TOPIC: ("Cerebral Stroke") OR TOPIC: ("Cerebral Strokes") OR TOPIC: ("Acute Stroke") OR TOPIC: ("Acute Strokes") OR TOPIC: ("Acute Cerebrovascular Accident") OR TOPIC: ("Acute Cerebrovascular Accidents") OR TOPIC: ("Brain Ischemia") OR TOPIC: ("Brain Ischemias") OR TOPIC: ("Ischemic Encephalopathy") OR TOPIC: ("Ischemic Encephalopathies") OR TOPIC: ("Cerebral Ischemia") OR TOPIC: ("Cerebral Ischemias") OR TOPIC: ("Ischemic stroke") OR TOPIC: ("Lacunar Stroke") OR TOPIC: ("Lacunar Strokes") OR TOPIC: ("Lacunar Syndrome") OR TOPIC: ("Lacunar Syndromes") OR TOPIC: ("Lacunar Syndrome") OR TOPIC: ("Lacunar Syndromes") OR TOPIC: ("Lacunar Infarction") OR TOPIC: ("Lacunar Infarctions") OR TOPIC: ("Lacunar Infarction") OR TOPIC: ("Lacunar Infarctions")

#2- TOPIC: (periodontitis) OR TOPIC: (Periodontitides) OR TOPIC: ("chronic periodontitis") OR TOPIC: ("Aggressive Periodontitis") OR TOPIC: ("Periapical Periodontitis") OR TOPIC: ("Periodontal Diseases") OR TOPIC: ("Periodontal Disease") OR TOPIC: (Parodontosis) OR TOPIC: (Parodontoses) OR TOPIC: ("Pyorrhea Alveolaris") OR TOPIC: ("Periodontal Atrophy") OR TOPIC: ("Periodontal Atrophies") OR TOPIC: ("Atrophy of Periodontium") OR TOPIC: ("Periodontium Atrophies") OR TOPIC: ("Periodontium Atrophy") OR TOPIC: ("Gingivo-Osseous Atrophy") OR TOPIC: ("Gingivo Osseous Atrophy") OR TOPIC: ("Gingivo Osseous Atrophies") OR TOPIC: ("Gingivo-Osseous Atrophies") OR TOPIC: ("Alveolar Bone Loss") OR TOPIC: ("Alveolar Bone Losses") OR TOPIC: ("Alveolar Process Atrophy") OR TOPIC: ("Alveolar Process Atrophies") OR TOPIC: ("Alveolar Resorption") OR TOPIC: ("Alveolar Resorptions") OR TOPIC: ("Periodontal Bone Losses") OR TOPIC: ("Periodontal Bone Loss") OR TOPIC: ("Periodontal Resorption") OR TOPIC: ("Periodontal Resorptions") OR TOPIC: ("Alveolar Bone Atrophy") OR TOPIC: ("Alveolar Bone Atrophies")

Final search: #1 AND #2

The
Cochrane
Library

#1 "Central nervous system" or "Central Nervous Systems" or "Nervous System, Central" or "Nervous Systems, Central" or "System, Central Nervous" or "Systems, Central Nervous" or "Cerebrovascular Circulation" or "Circulation, Cerebrovascular" or brain or brains or encephalon or encephalons or "Blood-Brain Barrier" or "Barrier, Blood-Brain" or "Barriers, Blood-Brain" or "Blood Brain Barrier" or "Blood-Brain Barriers" or "Hemato-Encephalic Barrier" or "Barrier, Hemato-Encephalic" or "Barriers, Hemato-Encephalic" or "Hemato Encephalic Barrier" or "Hemato-Encephalic Barriers" or "Brain-Blood Barrier" or "Barrier, Brain-Blood" or "Barriers, Brain-Blood" or "Brain

Blood Barrier" or "Brain Blood Barrier" or Stroke* or "Cerebrovascular Accident*" or CVA* or "Cerebrovascular Apoplexy" or "Apoplexy, Cerebrovascular" or "Vascular Accident*, Brain" or "Brain Vascular Accident*" or "Cerebrovascular Stroke*" or "Stroke*, Cerebrovascular" or Apoplexy or "Cerebral Stroke*" or "Stroke*, Cerebral" or "Stroke*, Acute" or "Acute Stroke*" or "Cerebrovascular Accident*, Acute" or "Acute Cerebrovascular Accident*" or "Brain Ischemia*" or "Ischemia, Brain" or "Ischemic Encephalopath*" or "Encephalopathy, Ischemic" or "Cerebral Ischemia*" or "Ischemia*, Cerebral" or "Ischemic stroke" or "Lacunar Stroke" OR "Lacunar Strokes" OR "Lacunar Syndrome" OR "Lacunar Syndromes" OR "Lacunar Syndrome" OR "Lacunar Syndromes" OR "Lacunar Infarction" OR "Lacunar Infarctions" OR "Lacunar Infarction" OR "Lacunar Infarctions"

#2 "periodontitis" OR "Periodontitides" OR "chronic periodontitis" OR "Aggressive Periodontitis" OR "Periapical Periodontitis" OR "Periodontal Diseases" OR "Disease, Periodontal" OR "Diseases, Periodontal" OR "Periodontal Disease" OR "Parodontosis" OR "Parodontoses" OR "Pyorrhea Alveolaris" OR "Periodontal Atrophy" OR "Periodontal Atrophies" OR "Atrophy of Periodontium" OR "Periodontium Atrophies" OR "Periodontium Atrophy" OR "Gingivo-Osseous Atrophy" OR "Gingivo Osseous Atrophy" OR "Gingivo-Osseous Atrophies" OR "Alveolar Bone Loss" OR "Alveolar Bone Losses" OR "Alveolar Process Atrophy" OR "Alveolar Process Atrophies" OR "Alveolar Resorption" OR "Alveolar Resorptions" OR "Resorption, Alveolar" OR "Resorptions, Alveolar" OR "Bone Loss, Periodontal" OR "Bone Losses, Periodontal" OR "Periodontal Bone Losses" OR "Periodontal Bone Loss" OR "Periodontal Resorption" OR "Periodontal Resorptions" OR "Resorption, Periodontal" OR "Alveolar Bone Atrophy" OR "Alveolar Bone Atrophies" OR "Bone Atrophies, Alveolar" OR "Bone Atrophy, Alveolar" OR "Bone Loss, Alveolar"

Final search: #1 AND #2

LILACS

(tw:(Cerebrovascular Circulation) OR (Circulation, Cerebrovascular) OR (Central nervous system\$) OR (Nervous System\$, Central) OR (System\$, Central Nervous) OR (Brain\$) OR (Encephalon\$) OR (Blood-Brain Barrier\$) OR (Barrier\$, Blood-Brain) OR (Blood Brain Barrier) OR (Blood-Brain Barriers) OR (Hemato-Encephalic Barrier\$) OR (Barrier\$, Hemato-Encephalic) OR (Hemato Encephalic Barrier) OR (Brain-Blood Barrier\$) OR (Barrier\$, Brain-Blood) OR (Brain Blood Barrier) OR (Stroke\$) OR (Cerebrovascular Accident\$) OR (Cerebrovascular Apoplexy) OR (Apoplexy, Cerebrovascular) OR (Vascular Accident\$, Brain) OR (Brain Vascular Accident\$) OR (Cerebrovascular Stroke\$) OR (Stroke\$, Cerebrovascular) OR (Apoplexy) OR (Cerebral Stroke\$) OR (Stroke\$, Cerebral) OR (Stroke\$, Acute) OR (Acute Stroke) OR (Cerebrovascular Accident\$, Acute) OR (Acute Cerebrovascular Accident\$) OR (Brain Ischemia\$) OR (Ischemia, Brain) OR (Ischemic Encephalopath\$) OR (Encephalopathy, Ischemic) OR (Cerebral Ischemia\$) OR (Ischemia\$, Cerebral) OR (Ischemic stroke) OR (Lacunar Stroke) OR (Lacunar Strokes) OR (Lacunar Syndrome) OR (Lacunar Syndromes) OR (Lacunar Infarction) OR (Lacunar Infarct) OR (Lacunar Infarctions) OR (Lacunar Infarcts))) AND (tw:(periodontitis) OR (Periodontitides) OR (chronic periodontitis) OR (Aggressive Periodontitis) OR (Periapical Periodontitis) OR (Periodontal Disease\$) OR (Disease\$, Periodontal) OR (Parodontos\$) OR (Pyorrhea Alveolaris) OR (Periodontal Atroph\$) OR (Atrophy of Periodontium) OR (Periodontium Atroph\$) OR (Gingivo-Osseous Atroph\$) OR (Alveolar Bone Loss\$) OR (Alveolar Process Atroph\$) OR (Alveolar Resorption\$) OR (Resorption\$, Alveolar) OR (Bone Loss\$, Periodontal) OR (Periodontal Bone Loss\$) OR (Periodontal Resorption\$) OR (Resorption, Periodontal) OR (Alveolar Bone Atroph\$) OR (Bone Atroph\$, Alveolar) OR (Bone Loss, Alveolar)))

OpenGrey

"Central nervous system" or Stroke and "periodontitis"

Google Scholar

"Central nervous system" + Stroke - "periodontitis" - review - animal - in vitro - book - systematic review - case control - letter to editor

Supplementary material 4: Domains and Risk of Bias considered in Risk of Bias evaluation according to Fowkes and Fulton [18].

Guideline	Checklist	Description
Study design appropriate to objectives?	objective common design prevalence Cross-sectional Prognosis Cohort Treatment Controlled trial Cause Cohort, case-control, cross-sectional	The type of study was marked in the appropriate type of study. If the type of study was appropriate according to the study design, it was marked as "0", and as "++" if it was not appropriate.
	Source of sample	The domain was considered (0) in cases of detailed origin, (+) to specified origin of only one group and (++) in cases of absence of specification of the origin of the groups
	Sampling method	The item was assigned (0) for full description of sampling method, (+) for poor or no description of sample method, with no problem in matching between groups, and (++) for poor or no description of sample method, interfering in matching of the groups.
Study sample representative?	Sample size	A minor problem (+) was considered when the sample was not representative or did not report a sample calculation. To a major problem, (++) was considered when no sample calculation was provided and the number of participants was less than 50 participants, (0) was considered in absence of the above factors.
	Entry criteria/exclusion	A minor problem (+) was attributed when the control and case group reported a current use of antibiotics or anti-inflammatories, diabetes, smoking or pregnancy. In the case of presence of more than two previously mentioned items, it was considered as a major problem (++).
	Non-respondents	The (0) was attributed when there was no refusal to participation in the study, (+) was assigned when there was refusal, but did not compromise the sample, and (++) when there was refusal and impairment of the sample size.
Control group acceptable?	Definition of controls	It was attributed (0) when all characteristics of control group were described, (+) when any information was pendent as the origin of control group, the selection criterions and a different origin between case and control groups and (++) when two or more items described in previously items.
	Source of controls	It was considered (0) when control group was referred, (+) when the origin of groups was different, but with reasons and (++) when the groups presented different origins without reasons.
	Matching/randomization	In this item, (0) was assigned to cases of randomized/matched groups, (+) to cases of no description of randomization, but with matching of groups and (++) to no description of randomization or matching.
	Comparable characteristics	It was attributed (0) to matched groups or not matched by the impossibility of being subsequently adjusted and (++) presence of unpaired variables that were not paired or adjusted.
Quality of measurements and outcomes?	Validity	It was considered (0) when the evaluation method applied is appropriate; (+) when using a single method, but with appropriate sensitivity with good specificity; (++) when using a single method, without an adequate specificity or good sensitivity.
	Reproducibility	It was considered (0) whether the evaluation methods were well described; (+) when a lack description of any step of the method was presented, for example, the identification of the patients of the groups studied in laboratory samples, evaluations at different times or application of different methods between groups of certain pathology; (++) when two or more of the previous items are present.
	Blindness	The condition of the study participants was considered to be "Blind", in this case being assigned the signal (0), in cases of "not blind" the signal (++) was attributed.

	Quality control	it was considered a problem when the examiner was not qualified, a partial periodontal exam was performed (not in all teeth or not in all the 6 periodontal sites/teeth), the measurement of periodontitis was only radiographic or the absence of the number of evaluated teeth sites. A Minor problem (+) was considered when 2 of these characteristics were present, and a major problem (++) if more than 2 of these characteristics were present.
	Compliance	It was assigned (0) for a sample size that remains the same from the beginning to the end or decreases without compromising the power of the test; (+) for differences in sample size at the end of the study, compromising the power of the test, but with reasons and adjusts; (++) for difference in sample size at the end of the study, compromising the power of the test, without reasons.
Completeness	Drop outs	The (0) was scored when there is no loss during the study, (+) when there is withdrawal that involves the inclusion criteria, such as age, sex, (++) when there is withdrawal and it compromises more than one criterion.
	Deaths	This item was scored as Not Applicable (NA), due the type of PECO strategy.
	Missing data	In this item, (0) was assigned to cases of randomized/matched groups, (+) to cases of no description of randomization, but with matching of groups and (++) to no description of randomization or matching.
	Extraneous treatments	In this item, (0) was considered when there were no external influences; (+) when there are external influences, but that does not interfere in the results; (++) when there are external influences and interferes with the results.
	Contamination	This item was scored as Not Applicable (NA), due the type of PECO strategy.
Distorting influences?	Changes over time	In this item, (0) was attributed to data collected in the same time period; (+) to data collected from the control group and the study group at different times that may cause distortions; (++) when the previous item was associated with data from studies already published.
	Confounding factors	A problem was assigned when the data analysis involved smokers, diabetics, hypertension, coronary heart disease and/or peripheral arterial disease. A minor problem (+) was assigned when 1 or 2 of these characteristics were present and a major problem (++) if there were 3 or more.
	Distortion reduced by analysis Bias: Are the results erroneously biased in certain direction?	It was considered (0) when it cites the adjustments of the covariates that present distortions; (+) when the article report adjustment, but does not say the criteria; (++) when a distortions was identified, without adjustment.
Summary questions	Confounding: Are there any serious confusing or other distorting influences?	YES or "NO" answers were assigned for each question. If the answer is NO at the three questions, the article is considered reliable, with low risk of bias.
	Chance: Is it likely that the results occurred by chance?	

Supplementary material 5: Articles excluded after reading in full and reasons for exclusions

Reference	Reason for exclusion
1. Grau Armin J., Becher Heiko, Ziegler Christoph M., Lichy Christoph, Buggle Florian, Kaiser Claudia, Lutz Rainer, Bültmann Stefan, Preusch Michael and Dörfer Christof E.. Periodontal Disease as a Risk Factor for Ischemic Stroke. <i>Stroke</i> . 2004;35:496-501	Absence of control group
2. Hashemipour Maryam Alsadat, Afshar Afsaneh Jahanshahi, Borna Roya, Seddighi Behnas, and Motamedi Amin. Gingivitis and periodontitis as a risk factor for stroke: A case control study in the Iranian population <i>Dent Res J (Isfahan)</i> . 2013 SepOct; 10(5): 613–619.	Absence of control group
3. Jimenez Monik, Krall Elizabeth A., Garcia Raul I., Vokonas Pantel S., and Dietrich Thomas. Periodontitis and Incidence of Cerebrovascular Disease in Men. <i>Ann Neurol</i> 2009;66:505–512	Absence of control group
4. Kim Hyun-Duck, Sim Seon-Ju, Moon Ja-Young, Hong Yoon-Chul, and Han Dong-Hun. Association Between Periodontitis and Hemorrhagic Stroke Among Koreans: A Case-Control Study. <i>J Periodontol</i> . Volume 81 • Number 5. May 2010.	Absence of control group
5. Sim Seon-Ju, Kim Hyun-Duck, Moon Ja-Young, Zavras Athanasio I., Zdanowicz John, Jang Sun-Ja, Jin Bo-Hyoung, Bae Kwang-Hak, Paik Dai-Il, and Douglass Chester W. Periodontitis and the Risk for Non-Fatal Stroke in Korean Adults. <i>J Periodontol</i> . Volume 79. Number 9. September 2008	Absence of control group
6. Lafon Arnaud, Tala Stéphane, Ahoosi Victorin, Perrin Daniel, Giroud Maurice & Béjot Yannick (2014) Association between periodontal disease and non-fatal ischemic stroke: a case-control study, <i>Acta Odontologica Scandinavica</i> , 72:8, 687-693, DOI:10.3109/00016357.2014.898089	Absence of control group
7. Joshipura Kaumudi J., Hung Hsin-Chia, Rimm Eric B., Willett Walter C. and Ascherio Alberto. Periodontal Disease, Tooth Loss, and Incidence of Ischemic Stroke. <i>Stroke</i> . 2003;34:47-52; originally published online December 12, 2002; doi: 10.1161/01.STR.0000052974.79428.0C	Absence of control group
8. Lee Hyo-Jung, Garcia Raul I., Janket Sok-Ja, Jones Judith A., Mascarenhas Ana Karina, Scott Thayer E., and Nunn Martha E. The Association Between Cumulative Periodontal Disease and Stroke History in Older Adults <i>J Periodontol</i> . Volume 77; Number 10; October, 2006.	Absence of control group
9. Beck JD, Moss KL, Morelli T, Offenbacher S. Periodontal profile class is associated with prevalent diabetes, coronary heart disease, stroke, and systemic markers of C-reactive protein and interleukin-6. <i>J Periodontol</i> . 2018;89:157–165. https://doi.org/10.1002/JPER.17-0426	Absence of control group

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10. Elter J.R., Offenbacher S., Toole J.F., and Beck J.D. Relationship of Periodontal Disease and Edentulism to Stroke/TIA. *J Dent Res* 82(12):998-1001, 2003 Absence of control group

 11. Holmlund, A., Lampa, E., and Lind, L. (2017). Oral health and cardiovascular disease risk in a cohort of periodontitis patients. *Atherosclerosis* 262, 101-106. Absence of control group
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