

## 評価対象論文リスト(要因:歯周病、アウトカム:循環器病)

評価判定日:2025/4/25

### ①既存の系統的レビュー・メタ解析・統合解析

1	Beck JD, Offenbacher S. The association between periodontal diseases and cardiovascular diseases: a state-of-the-science review. <i>Ann Periodontol.</i> 2001;6(1):9-15. doi:10.1902/annals.2001.6.1.9
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3	Bahekar AA, Singh S, Saha S, Molnar J, Arora R. The prevalence and incidence of coronary heart disease is significantly increased in periodontitis: A meta-analysis. <i>American Heart Journal.</i> 2007;154(5):830-837. doi:10.1016/j.ahj.2007.06.037
4	Mustapha IZ, Debrey S, Oladubu M, Ugarte R. Markers of systemic bacterial exposure in periodontal disease and cardiovascular disease risk: a systematic review and meta-analysis. <i>Journal of Periodontology.</i> 2007;78(12):2289-2302.
5	Blaizot A, Vergnes JN, Nuwwareh S, Amar J, Sixou M. Periodontal diseases and cardiovascular events: meta-analysis of observational studies. <i>Int Dent J.</i> 2009;59(4):197-209.
6	Sfyroeras GS, Roussas N, Saleptsis VG, Argyriou C, Giannoukas AD. Association between periodontal disease and stroke. <i>Journal of Vascular Surgery.</i> 2012;55(4):1178-1184. doi:10.1016/j.jvs.2011.10.008
7	Khalighinejad N, Aminoshariae MR, Aminoshariae A, Kulild JC, Mickel A, Fouad AF. Association between systemic diseases and apical periodontitis. <i>Journal of Endodontics.</i> 2016;42(10):1427-1434. doi:10.1016/j.joen.2016.07.007
8	Leira Y, Seoane J, Blanco M, et al. Association between periodontitis and ischemic stroke: a systematic review and meta-analysis. <i>Eur J Epidemiol.</i> 2017;32(1):43-53. doi:10.1007/s10654-016-0170-6
9	Berlin-Broner Y, Febbraio M, Levin L. Association between apical periodontitis and cardiovascular diseases: a systematic review of the literature. <i>Int Endodontic J.</i> 2017;50(9):847-859. doi:10.1111/iej.12710
10	Fagundes NCF, Almeida APCPSC, Vilhena KFB, Magno MB, Maia LC, Lima RR. Periodontitis as a risk factor for stroke: a systematic review and meta-analysis. <i>Vasc Health Risk Manag.</i> 2019;15:519-532. doi:10.2147/VHRM.S204097
11	Gao S, Tian J, Li Y, et al. Periodontitis and number of teeth in the risk of coronary heart disease: an updated meta-analysis. <i>Med Sci Monit.</i> 2021;27. doi:10.12659/MSM.930112
12	Joshi C, Bapat R, Anderson W, Dawson D, Cherukara G, Hijazi K. Serum antibody response against periodontal bacteria and coronary heart disease: Systematic review and meta-analysis. <i>J Clin Periodontology.</i> 2021;48(12):1570-1586.
13	Noites R, Teixeira M, Cavero-Redondo I, Alvarez-Bueno C, Ribeiro F. Apical periodontitis and cardiovascular disease in adults: a systematic review with meta-analysis. <i>Rev Cardiovasc Med.</i> 2022;23(3):100. doi:10.31083/j.rcm2303100
14	Dewan M, Pandit AK, Goyal L. Association of periodontitis and gingivitis with stroke: A systematic review and meta-analysis. <i>Dent Med Probl.</i> 2023;61(3):407-415. doi:10.17219/dmp/158793
15	Cannavo A, Babajani N, Saeedian B, et al. Anti- porphyromonas gingivalis antibody levels in patients with stroke and atrial fibrillation: a systematic review and meta-analysis. <i>Clinical &amp; Exp Dental Res.</i> 2024;10(6):e70041. doi:10.1002/cre2.70041

16	Periodontitis and the risk of heart failure:a meta-analysis and mendelian randomisation study. <i>Oral Health and Preventive Dentistry</i> . 2025;23(1):149-164. doi:10.3290/j.ohpd.c 1793
17	Li C, Lv Z, Shi Z, et al. Periodontal therapy for the management of cardiovascular disease in patients with chronic periodontitis. Cochrane Oral Health Group, ed. <i>Cochrane Database of Systematic Reviews</i> . August 2014.
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20	Ye Z, Cao Y, Miao C, et al. Periodontal therapy for primary or secondary prevention of cardiovascular disease in people with periodontitis. Cochrane Oral Health Group, ed. <i>Cochrane Database of Systematic Reviews</i> . 2022;2022(10).

## ②日本人集団の個別疫学研究

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22	Ueno M, Izumi Y, Kawaguchi Y, et al. Prediagnostic plasma antibody levels to periodontopathic bacteria and risk of coronary heart disease. <i>Int Heart J</i> . 2012;53(4):209-214. doi:10.1536/ihj.53.209
23	Noguchi S, Toyokawa S, Miyoshi Y, Suyama Y, Inoue K, Kobayashi Y. Five-year follow-up study of the association between periodontal disease and myocardial infarction among Japanese male workers: MY Health Up Study. <i>J Public Health</i> . October 2014;fdu076. doi:10.1093/pubmed/fdu076
24	Aoyama N, Kobayashi N, Hanatani T, et al. Periodontal condition in Japanese coronary heart disease patients: A comparison between coronary and non-coronary heart diseases. <i>J of Periodontal Research</i> . 2019;54(3):259-265. doi:10.1111/jre.12626

■ 系統的レビュー・メタ解析

Reference			Include study					Design	Category	Relative risk (95% CI or p)	Weight	Magnitude of association								
Author	Title	Year	Ref No.	First author	Year	Study period	Study location	Event (*Definition)												
Bahekar AA, Singh S, Saha S, Molnar J, Arora R.	The prevalence and incidence of coronary heart disease is significantly increased in periodontitis: a meta-analysis	2007	9	DeStefano	1993	14 years	USA	Coronary heart disease	Cohort study	Periodontitis (reference: no)	1.25 (1.06, 1.48)	N/A	↑							
			13	Howell	2001	12.3 years	USA				1.01 (0.89, 1.16)									
			11	Joshiyura	1996	6 years	USA				1.04 (0.86, 1.25)									
			10	Mattila	1995	7.2years	Finland?				1.21 (1.08, 1.36)									
			12	Wu	2000	10years	USA				1.17 (1.04, 1.31)									
			22	Briggs	2006	NA	Northern Ireland				1.14 (1.07, 1.21)									
			21	Buhlin	2005	NA	Sweden?				3.06 (1.02, 9.16)									
			20	Geerts	2004	NA	Belgian				3.80 (1.67, 8.67)									
			19	Malthaner SC	2002	NA	USA				6.50 (1.82, 23.2)									
			23	Spahr	2006	NA	Germany				1.64 (0.47, 5.75)									
										1.67 (1.08, 2.58)										
										Overall	2.23 (1.59, 3.12)		↑ ↑							
Dewan M, Pandit AK, Goyal L.	Association of periodontitis and gingivitis with stroke: A systematic review and meta-analysis	2024	15	Pradeep	2010		India	CVA or stroke	case-control	Periodontitis (reference: no)	2.40 (0.30–17.10)	0.11	↑							
			5	Hashemipour	2013		Iran	ischemic stroke	case-control		2.70 (1.26–6.40)	1.14								
			17	Sen	2013		USA	stroke/TIA	cohort		2.60 (1.20–5.70)	1.47								
			20	Sen	2018		USA	stroke/TIA	cohort		2.20 (1.27–3.81)	4.29								
			22	Mascari	2021		USA	stroke/TIA	cross-sectional		2.60 (1.10–5.80)	1.35								
			13	Grau	2004		Germany	stroke/TIA	case-control		3.38 (1.35–8.40)	0.61								
			11	Loesche	1998		USA	stroke	cross-sectional		1.04 (1.01–1.07)	41.29								
			16	Kim	2010		South Korea	hemorrhagic stroke	case-control		2.53 (1.14–5.61)	1.49								
			21	Beck	2018		USA	stroke	original study		2.39 (1.01–5.64)	1.39								
			19	Leira	2016		Spain	LI	case-control		3.53 (1.07–12.77)	0.22								
			18	Diouf	2015		Senegal	stroke	case-control		1.58 (1.10–3.02)	6.95								
			14	Lee	2006		USA	stroke	cross-sectional		1.03 (0.59–1.79)	14.12								
			12	Elter	2003		USA	stroke/TIA	cross-sectional		1.30 (1.02–1.70)	25.58								
										Overall	1.32 (1.04–1.60)	100.00	↑							
Fagundes NCF, Almeida APCPSC, Vilhena KFB, Magno MB, Maia LC, Lima RR.	Periodontitis As A Risk Factor For Stroke: A Systematic Review And Meta-Analysis	2019	37	Holmlund	2010	12 years	Sweden	CVA	Cohort	Periodontitis (reference: no)	1.40 (0.40, 4.90)	2.4	↑ ↑							
			38	Sen	2018	15 years	USA				2.08 (1.57, 2.76)	46.9								
			36	Wu	2000	18 years	USA				1.73 (1.32, 2.27)	50.7								
														Overall	1.88 (1.55, 2.28)	100.0				
			36	Abolfazli	2011		Iran				1.66 (0.82, 3.36)	14.9								
			44	Diouf	2015		Senegal				1.58 (1.10, 2.27)	18.9								
			39	Dorfer	2004		Germany				2.72 (1.73, 4.28)	17.9								
			42	Ghizoni	2012		Brazil				48.06 (5.96, 387.56)	4.6								
			45	Leira	2016		Spain				4.20 (1.81, 9.75)	13.3								
			43	Palm	2014		Germany				0.69 (0.33, 1.44)	14.5								
			40	Pradeep	2010		India				3.14 (1.70, 5.80)	16.0								
														Overall	2.31 (1.39, 3.84)	100.0	↑ ↑ ↑			
			36	Abolfazli	2011		Iran				1.66 (0.82, 3.36)	18.7								
			39	Dorfer	2004		Germany				2.72 (1.73, 4.28)	43.6								
			45	Leira	2016		Spain				4.20 (1.81, 9.75)	13.3								
40	Pradeep	2010		India	3.14 (1.70, 5.80)	24.5														
										Overall	2.72 (2.00, 3.71)	100.0	↑ ↑ ↑							

■コホート研究

Reference			Study subjects						Category	Number among cases	Relative risk (95%CI or p)	Confounding variables considered	<u>Magnitude of association</u>
Author	Title	Year	Study period	Number of subjects	Source of subjects	Event followed	Number of incident cases or deaths	Participant's race					
Noguchi S, Toyokawa S, Miyoshi Y, Suyama Y, Inoue K, Kobayashi Y.	Five-year follow-up study of the association between periodontal disease and myocardial infarction among Japanese male workers: MY Health Up Study	2014	2004-2009	3,081	MY Health Up Study; Study population is Male	Myocardial infarction incidence	17	Japanese	Periodontal score (0-3, 1 score increase)	17	2.23 (1.37-3.63)	Age, BMI, Current smoking, hypertension, diabetes, dyslipidaemia	
					Employees in Financial Services in Japan.				Periodontitis	17	2.51 (0.95-6.62)	Age	↑ ↑
										17	2.26 (0.84-6.02)	Age, BMI, Current smoking, hypertension, diabetes, dyslipidaemia	↑ ↑

■横断研究

Reference			Study subjects						Category	Number among cases	Relative risk (95%CI or p)	Confounding variables considered	<u>Magnitude of association</u>	
Author	Title	Year	Study period	Number of subjects	Source of subjects	Event followed	Number of incident cases or deaths	Participant's race						
Toshihiko Senba, Yasuki Kobayashi, Kazuo Inoue, Chie Kaneto, Mariko Inoue, Satoshi Toyokawa, Yasuo Suyama, Toshiko Suzuki, Yukie Miyano, Yuji Miyoshi	The Association between Self-reported Periodontitis and Coronary Heart Disease —From MY Health Up Study—	2008	2004-	29,904	MY Health Up Study	Coronary heart disease, myocardial infarction, angina pectoris incidence	Male; CHD=64; MI=25; AP=32; Female; CHD=8; MI=16; AP=61;	Japanese	Periodontitis at present (Ref: no)	Male	64	1.69 (1.02, 2.81)	Age, BMI, Smoking, Freq. tooth brushing, Hypertension at present, Diabetes mellitus at present, Stress score	↑ ↑
									CHD	25	2.34 (1.05, 5.23)		↑ ↑ ↑	
									MI	32	1.17 (0.57, 2.43)		—	
									AP	86	1.62 (1.04, 2.53)		↑ ↑	
									Female	16	1.76 (0.64, 4.88)		↑	
									CHD	61	1.75 (1.04, 2.95)		↑ ↑	

■症例对照研究

Reference			Study subjects				Category	Number among cases	Relative risk (95%CI or p)	P for trend	Confounding variables considered	<b>Magnitude of association</b>
Author	Title	Year	Study period	Type and source	Definition	Number of cases						
Aoyama N, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Takamura C, Yoshikawa S, Matsuo K, Izumi Y, Isobe M.	Periodontal condition in Japanese coronary heart disease patients: A comparison between coronary and non-coronary heart diseases	2019	2012-2015	Subjects were recruited from inpatients admitted to the cardiovascular medicine section in Tokyo Medical and Dental University Hospital	Case; CHD patient; Control; Non CHD patient;	339	558	Periodontal probing pocket depth Average PPD <3 mm Average PPD 3 mm or more Average PPD <3 mm Average PPD 3 mm or more Average PPD <3 mm Average PPD 3 mm or more	1.00 (Reference) 1.78 (1.19-2.64) 1.00 (Reference) 1.69 (1.13-2.52) 1.00 (Reference) 1.31 (0.84-2.05)		Crude age age, sex, smoking status, diabetes mellitus, hypertension, dyslipidemia, C-reactive protein level	—
Ueno M, Izumi Y, Kawaguchi Y, Ikeda A, Iso H, Inoue M, Tsugane S; JPHC Study Group.	Prediagnostic plasma antibody levels to periodontopathic bacteria and risk of coronary heart disease	2012	1990-	JPHC Study	Case; Participants who have been diagnosed with Contro; Participants who did not develop CHD	191	382	Aggregatibacter actinomycetemcomitans, U/mL Antibody Tertiles Low Medium High Porphyromonas gingivalis, U/mL Antibody Tertiles Low Medium High Prevotella intermedia IgG, U/mL Antibody Tertiles Low Medium High	1.00 (Reference) 1.19 (0.71, 1.99) 1.65 (0.98, 2.80) 1.00 (Reference) 1.04 (0.63, 1.71) 1.00 (0.59, 1.70) 1.00 (Reference) 1.39 (0.81, 2.39) 1.89 (1.10, 3.23)	0.061 0.998 0.021	BMI, smoking status, alcohol intake, history of hypertension, history of diabetes mellitus, exercise during leisure time, perceived mental stress	↑ — ↑↑