

## SUPPLEMENTAL DIGITAL CONTENT

**Table.** Summary of primary human and animal research, review articles and meta-analyses on associations between candidate pathogens and pathogen burden, and cardiovascular disease related outcomes

Exposure	Presence in Human Atherosclerotic Plaque	Atherosclerotic Lesions in Animal Models	Cardiovascular Mortality	Cardiovascular Diseases		Adverse Intermediate Cardiovascular Phenotype
				Myocardial Infarction	Ischaemic Stroke	
<i>C. pneumoniae</i>	+ <sup>(1)</sup>	+ <sup>(2)</sup>	+ <sup>(3)</sup>	+ <sup>(3)</sup>	+ <sup>(4)</sup>	+/- <sup>(5,6)</sup>
<i>H. pylori</i>	+ <sup>(7)</sup>	+/- <sup>(8)</sup>	+/- <sup>(3,9)</sup>	+/- <sup>(3,9)</sup>	+ <sup>(10)</sup>	+/- <sup>(5,6)</sup>
HIV	+ <sup>(11)</sup>			+ <sup>(12)</sup>	+ <sup>(12)</sup>	+ <sup>(13)</sup>
Hepatitis C virus	+ <sup>(14)</sup>		+ <sup>(15)</sup>	+ <sup>(15)</sup>		+ <sup>(16)</sup>
Cytomegalovirus	+ <sup>(17)</sup>	+ <sup>(2, 18)</sup>	+ <sup>(19,20)</sup>	+ <sup>(20)</sup>		
Periodontal Bacteria	+ <sup>(21)</sup>	+ <sup>(22)</sup>	+ <sup>(23)</sup>	+ <sup>(24)</sup>	+ <sup>(24)</sup>	+ <sup>(25)</sup>
Total Pathogen Burden	N/A	N/A	+ <sup>(26)</sup>	+ <sup>(20)</sup>	+ <sup>(27)</sup>	+/- <sup>(26,6)</sup>

+ Evidence for positive association  
+/- Conflicting evidence for association

### Supplemental References

- Shor A, Kuo CC, Patton DL. Detection of Chlamydia pneumoniae in coronary arterial fatty streaks and atheromatous plaques. *S Afr Med J* 1992;**82**(3):158-61.
- Burnett MS, Gaydos CA, Madico GE, Glad SM, Paigen B, Quinn TC, Epstein SE. Atherosclerosis in apoE knockout mice infected with multiple pathogens. *J Infect Dis* 2001;**183**(2):226-231.
- Danesh J, Appleby P. Persistent infection and vascular disease: a systematic review. *Expert Opin Investig Drugs* 1998;**7**(5):691-713.
- Su X, Chen H-L. Chlamydia pneumoniae infection and cerebral infarction risk: a meta-analysis. *International Journal of Stroke* 2014;**9**(3):356-364.
- Player MS, Mainous AG, Everett CJ, Diaz VA, Knoll ME, Wright RU. Chlamydia pneumoniae and progression of subclinical atherosclerosis. *European Journal of Preventive Cardiology* 2014;**21**(5):559-565.
- Laek B, Szklo M, McClelland RL, Ding J, Tsai M, Bluemke DA, Tracy R, Matsushita K. The prospective association of Chlamydia pneumoniae and four other pathogens with development of coronary artery calcium: the Multi-Ethnic Study of Atherosclerosis (MESA). *Atherosclerosis* 2013;**230**(2):10.1016/j.atherosclerosis.2013.07.053.
- Ameriso SF, Fridman EA, Leiguarda RC, Sevlever GE. Detection of Helicobacter pylori in human carotid atherosclerotic plaques. *Stroke* 2001;**32**(2):385-91.
- Mach F, Sukhova GK, Michetti M, Libby P, Michetti P. Influence of Helicobacter pylori infection during atherogenesis in vivo in mice. *Circ Res* 2002;**90**(1):E1-4.
- Schöttker B, Adamu MA, Weck MN, Müller H, Brenner H. Helicobacter pylori infection, chronic atrophic gastritis and major cardiovascular events: A population-based cohort study. *Atherosclerosis* 2012;**220**(2):569-574.

10. Cremonini F, Gabrielli M, Gasbarrini G, Pola P, Gasbarrini A. The relationship between chronic *H. pylori* infection, CagA seropositivity and stroke: meta-analysis. *Atherosclerosis* 2004;**173**(2):253-9.
11. Eugenin EA, Morgello S, Klotman ME, Mosoian A, Lento PA, Berman JW, Schecter AD. Human immunodeficiency virus (HIV) infects human arterial smooth muscle cells in vivo and in vitro: implications for the pathogenesis of HIV-mediated vascular disease. *Am J Pathol* 2008;**172**(4):1100-11.
12. Islam FM, Wu J, Jansson J, Wilson DP. Relative risk of cardiovascular disease among people living with HIV: a systematic review and meta-analysis. *HIV Medicine* 2012;**13**(8):453-468.
13. Post WS, Budoff M, Kingsley L, Palella FJ, Witt MD, Li X, George RT, Brown T, Jacobson LP. Associations between HIV Infection and Subclinical Coronary Atherosclerosis: The Multicenter AIDS Cohort Study (MACS). *Annals of internal medicine* 2014;**160**(7):458-467.
14. Boddi M, Abbate R, Chellini B, Giusti B, Giannini C, Pratesi G, Rossi L, Pratesi C, Gensini GF, Paperetti L, Zignego AL. Hepatitis C virus RNA localization in human carotid plaques. *J Clin Virol* 2010;**47**(1):72-5.
15. Roed T, Lebech A-M, Kjaer A, Weis N. Hepatitis C virus infection and risk of coronary artery disease: a systematic review of the literature. *Clinical Physiology and Functional Imaging* 2012;**32**(6):421-430.
16. Alyan O, Kacmaz F, Ozdemir O, Deveci B, Astan R, Celebi AS, Ilkay E. Hepatitis C Infection is Associated With Increased Coronary Artery Atherosclerosis Defined by Modified Reardon Severity Score System. *Circulation Journal* 2008;**72**(12):1960-1965.
17. Liu R, Moroi M, Yamamoto M, Kubota T, Ono T, Funatsu A, Komatsu H, Tsuji T, Hara H, Nakamura M, Hirai H, Yamaguchi T. Presence and severity of *Chlamydia pneumoniae* and Cytomegalovirus infection in coronary plaques are associated with acute coronary syndromes. *Int Heart J* 2006;**47**(4):511-9.
18. Rosenfeld ME, Campbell LA. Pathogens and atherosclerosis: Update on the potential contribution of multiple infectious organisms to the pathogenesis of atherosclerosis. *Thromb Haemost* 2011;**106**(5):858-867.
19. Roberts BW, Cech I. Association of type 2 diabetes mellitus and seroprevalence for cytomegalovirus. *South Med J* 2005;**98**(7):686-92.
20. Zhu J, Nieto FJ, Horne BD, Anderson JL, Muhlestein JB, Epstein SE. Prospective study of pathogen burden and risk of myocardial infarction or death. *Circulation* 2001;**103**(1):45-51.
21. Haraszthy VI, Zambon JJ, Trevisan M, Zeid M, Genco RJ. Identification of periodontal pathogens in atheromatous plaques. *J Periodontol* 2000;**71**(10):1554-60.
22. Ford PJ, Gemmell E, Timms P, Chan A, Preston FM, Seymour GJ. Anti-P. gingivalis response correlates with atherosclerosis. *J Dent Res* 2007;**86**(1):35-40.
23. Schwahn C, Polzer I, Haring R, Dörr M, Wallaschofski H, Kocher T, Mundt T, Holtfreter B, Samietz S, Völzke H, Biffar R. Missing, unreplaced teeth and risk of all-cause and cardiovascular mortality. *International Journal of Cardiology* 2013;**167**(4):1430-1437.
24. Lockhart PB, Bolger AF, Papapanou PN, Osinbowale O, Trevisan M, Levison ME, Taubert KA, Newburger JW, Gornik HL, Gewitz MH, Wilson WR, Smith SC, Jr., Baddour LM, American Heart Association Rheumatic Fever E, Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young CoE, Prevention CoPVD, Council on Clinical C. Periodontal disease and atherosclerotic vascular disease: does the evidence support an independent association?: a scientific statement from the American Heart Association. *Circulation* 2012;**125**(20):2520-44.
25. Orlandi M, Suvan J, Petrie A, Donos N, Masi S, Hingorani A, Deanfield J, D'Aiuto F. 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.
26. Espinola-Klein C, Rupprecht HJ, Blankenberg S, Bickel C, Kopp H, Rippin G, Victor A, Hafner G, Schlumberger W, Meyer J. Impact of infectious burden on extent and long-term prognosis of atherosclerosis. *Circulation* 2002;**105**(1):15-21.
27. Elkind MV, Ramakrishnan P, Moon YP, et al. Infectious burden and risk of stroke: The northern manhattan study. *Archives of Neurology* 2010;**67**(1):33-38.