Appendix 2 (as supplied by the authors): Study quality assessment

The Newcastle-Ottawa Scale used to grade the quality of each study (maximum=9 stars, higher is better) is as follows:

Study	Selection	Comparability	Outcome	Total
Gillum, et al. 1991 [1]	***	**	***	********
Sandvik et al. 1993[2]	***	**	**	*******
Mensink et al. 1997[3]	**	**	***	*******
Benetos et al. 1999[4]	***	**	**	*******
Greenland et al. 1999[5]	****	**	***	*********
Palatine et al. 1999[6]	**	**	**	******
Kristal-Boneh et al. 2000[7]	***	*	**	******
Reunanen et al. 2000[8]	***	**	**	*******
Nilsson et al. 2001[9]	****	**	***	*********
Seccareccia et al. 2001[10]	**	**	**	******
Cheng et al. 2002[11]	****	**	**	********
Kado et al. 2002[12]	**	**	**	******
Chang et al. 2003[13]	**	**	*	*****
Hozawa et al. 2004[14]	**	**	***	*******
Okamura et al. 2004[15]	****	**	**	********
Fisher et al. 2006[16]	**	*	**	*****
Savonen et al. 2006[17]	***	**	***	********
Theobald et al. 2007[18]	**	**	***	*******
Adabag et al. 2008[19]	****	**	**	********
Hansen et al. 2008[20]	**	**	*	*****
Kizilbash et al. 2008[21]	***	**	***	********
Tverdal et al. 2008[22]	****	**	**	********
Mai et al. 2009[23]	***	**	**	*******
Batty et al. 2010[24]	*	**	**	*****
Cooney et al. 2010[25]	****	**	**	********
Nauman et al. 2010[26]	****	*	**	*******
Jensen et al. 2011[27]	****	**	**	********
Jouven et al. 2011[28]	***	*	**	******
Legeai et al. 2011[29]	**	**	*	*****
Nabi et al. 2011[30]	**	**	*	*****
Nauman et al. 2011[31]	****	**	***	*********
Inoue et l. 2012[32]	***	**	**	*******
Leistner et al. 2012[33]	***	**	*	******
Woodward et al. 2012[34]	***	**	*	******
Jensen et al. 2013[35]	***	**	**	*******
Johansen et al. 2013[36]	***	**	**	*******
Pittaras et al. 2013[37]	***	**	**	*******
Plichart et al. 2013[38]	***	**	*	******
Saxena et al. 2013[39]	****	**	**	********
Aladin et al. 2014[40]	***	**	**	*******

Appendix to: Zhang D, Shen Xl, Qi X. Resting heart rate and all-cause and cardiovascular mortality in the general population: a meta-analysis. *CMAJ* 2015. DOI:10.1503/cmaj.150535.

Floyd et al. 2014[41]	***	**	**	*******
Hisamatsu et al. 2014[42]	***	**	**	*******
Ho et al. 2014[43]	***	**	**	*******
Ó Hartaigh et al. 2014[44]	**	**	**	******
Ryu et al. 2014[45]	***	**	**	*******
Wang et al. 2014[46]	****	**	*	*******

The scales allocate stars, maximum of nine, for quality of selection, comparability, exposure and outcome of study participants.

RHR and risk of all-cause mortality

Every 10 bpm increment: 35 results from 27 studies[3-5, 7-12, 15, 17, 19-20, 22-23, 25, 27, 29, 32, 34-36, 39, 41, 43-44, 46] were used, because 8 studies[3-5, 8-9, 15, 22, 25] reported results by sex.

60-80 bpm: 25 results from 21 studies[1, 4, 7-8, 10, 19, 22, 24, 28-31, 33-35, 37, 39-40, 44-46] were used, because 4 studies[1, 4, 8, 22] reported results by sex.

>80 bpm: 32 results from 27 studies[1, 4, 6-8, 10, 13, 16, 18-19, 22-24, 28-31, 33-35, 37-40, 44-46] were used, because 5 studies[1, 4, 8, 22, 38] reported results by sex.

RHR and risk of cardiovascular mortality

10 bpm: 32 results from 23 studies[2-5, 7-11, 14-15, 17, 20-22, 25, 27, 29, 31-32, 34, 39, 43] were used, because 9 studies[3-5, 8-9, 15, 21-22, 25] reported results by sex.

60-80 bpm: 19 results from 14 studies[1, 4, 7-8, 10, 21-22, 28-29, 33-34, 39, 42, 45] were used, because 5 studies[1, 4, 8, 21-22] reported results by sex.

>80 bpm: 22 results from 16 studies[1, 4, 6-8, 10, 21-22, 26, 28-29, 33-34, 39, 42, 45] were used, because 6 studies[1, 4, 8, 21-22, 26] reported results by sex.

Dose-response analysis with restricted cubic spline functions

For all-cause mortality, data from 13 studies[4, 7-8, 10, 15, 19, 22, 29, 31, 35, 39, 44, 46] were used.

For cardiovascular mortality, data from 10 studies[4, 7-8, 10, 14-15, 21-22, 29, 39] were used.

Appendix to: Zhang D, Shen Xl, Qi X. Resting heart rate and all-cause and cardiovascular mortality in the general population: a meta-analysis. *CMAJ* 2015. DOI:10.1503/cmaj.150535.

References

1. Gillum RF, Makuc DM, Feldman JJ. Pulse rate, coronary heart disease, and death: the NHANES I Epidemiologic Follow-up Study. *Am Heart J* 1991;121:172-177.
2. Sandvik L, Erikssen J, Thaulow E, Erikssen G, Mundal R, Rodahl K. Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *N Engl J Med* 1993;328:533-537.
3. Mensink GB, Hoffmeister H. The relationship between resting heart rate and all-cause, cardiovascular and cancer mortality. *Eur Heart J* 1997;18:1404-1410.
4. Benetos A, Rudnichi A, Thomas F, Safar M, Guize L. Influence of heart rate on mortality in a French population: role of age, gender, and blood pressure. *Hypertension* 1999;33:44-52.
5. Greenland P, Daviglus ML, Dyer AR, Liu K, Huang CF, Goldberger JJ, et al. Resting heart rate is a risk factor for cardiovascular and noncardiovascular mortality: the Chicago Heart Association Detection Project in Industry. *Am J Epidemiol* 1999;149:853-862.
6. Palatini P, Casiglia E, Julius S, Pessina AC. High heart rate: a risk factor for cardiovascular death in elderly men. *Arch Intern Med* 1999;159:585-592.
7. Kristal-Boneh E, Silber H, Harari G, Froom P. The association of resting heart rate with cardiovascular, cancer and all-cause mortality. Eight year follow-up of 3527 male Israeli employees (the CORDIS Study). *Eur Heart J* 2000;21:116-124.
8. Reunanen A, Karjalainen J, Ristola P, Heliovaara M, Knekt P, Aromaa A. Heart rate and mortality. *J Intern Med* 2000;247:231-239.
9. Nilsson PM, Nilsson JA, Hedblad B, Berglund G. Sleep disturbance in association with elevated pulse rate for prediction of mortality--consequences of mental strain? *J Intern Med* 2001;250:521-529.
10. Seccareccia F, Pannozzo F, Dima F, Minoprio A, Menditto A, Lo Noce C, et al. Heart rate as a predictor of mortality: the MATISS project. *Am J Public Health* 2001;91:1258-1263.
11. Cheng YJ, Macera CA, Church TS, Blair SN. Heart rate reserve as a predictor of cardiovascular and all-cause mortality in men. *Med Sci Sports Exerc* 2002;34:1873-1878.
12. Kado DM, Lui LY, Cummings SR. Rapid resting heart rate: a simple and powerful predictor of osteoporotic fractures and mortality in older women. *J Am Geriatr Soc* 2002;50:455-460.
13. Chang M, Havlik RJ, Corti MC, Chaves PH, Fried LP, Guralnik JM. Relation of heart rate at rest and mortality in the Women's Health and Aging Study. *Am J Cardiol* 2003;92:1294-1299.
14. Hozawa A, Ohkubo T, Kikuya M, Ugajin T, Yamaguchi J, Asayama K, et al. Prognostic value of home heart rate for cardiovascular mortality in the general population: the Ohasama study. *Am J Hypertens* 2004;17:1005-1010.
15. Okamura T, Hayakawa T, Kadowaki T, Kita Y, Okayama A, Elliott P, et al. Resting heart rate and cause-specific death in a 16.5-year cohort study of the Japanese general population. *Am Heart J* 2004;147:1024-1032.
16. Fisher AA, Davis MW, Srikusalanukul W, Budge MM. Does heart rate predict

mortality in older, low-level care residents? *Am J Geriatr Cardiol* 2006;15:208-216.
17. Savonen KP, Lakka TA, Laukkanen JA, Halonen PM, Rauramaa TH, Salonen JT, et al. Heart rate response during exercise test and cardiovascular mortality in middle-aged men. *Eur Heart J* 2006;27:582-588.
18. Theobald H, Wandell PE. Effect of heart rate on long-term mortality among men and women. *Acta Cardiol* 2007;62:275-279.
19. Adabag AS, Grandits GA, Prineas RJ, Crow RS, Bloomfield HE, Neaton JD. Relation of heart rate parameters during exercise test to sudden death and all-cause mortality in asymptomatic men. *Am J Cardiol* 2008;101:1437-1443.
20. Hansen TW, Thijs L, Boggia J, Li Y, Kikuya M, Bjorklund-Bodegard K, et al. Prognostic value of ambulatory heart rate revisited in 6928 subjects from 6 populations. *Hypertension* 2008;52:229-235.
21. Kizilbash MA, Daviglus ML, Dyer AR, Garside DB, Hankinson AL, Yan LL, et al. Relation of heart rate with cardiovascular disease in normal-weight individuals: the Chicago Heart Association Detection Project in Industry. *Prev Cardiol* 2008;11:141-147.
22. Tverdal A, Hjellvik V, Selmer R. Heart rate and mortality from cardiovascular causes: a 12 year follow-up study of 379,843 men and women aged 40-45 years. *Eur Heart J* 2008;29:2772-2781.
23. Mai JZ, Zhao LC, Liu XQ, Wu YF, Rao XX, Gao XM, et al. [Association between heart rate and all-cause death and coronary event in the Chinese cohort: 16 years follow up results]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2009;37:750-753.
24. Batty GD, Shipley MJ, Kivimaki M, Marmot M, Davey Smith G. Walking pace, leisure time physical activity, and resting heart rate in relation to disease-specific mortality in London: 40 years follow-up of the original Whitehall study. An update of our work with professor Jerry N. Morris (1910-2009). *Ann Epidemiol* 2010;20:661-669.
25. Cooney MT, Vartiainen E, Laatikainen T, Juolevi A, Dudina A, Graham IM. Elevated resting heart rate is an independent risk factor for cardiovascular disease in healthy men and women. *Am Heart J* 2010;159:612-619 e613.
26. Nauman J, Nilsen TI, Wisloff U, Vatten LJ. Combined effect of resting heart rate and physical activity on ischaemic heart disease: mortality follow-up in a population study (the HUNT study, Norway). *J Epidemiol Community Health* 2010;64:175-181.
27. Jensen MT, Marott JL, Jensen GB. Elevated resting heart rate is associated with greater risk of cardiovascular and all-cause mortality in current and former smokers. *Int J Cardiol* 2011;151:148-154.
28. Jouven X, Escolano S, Celermajer D, Empana JP, Bingham A, Hermine O, et al. Heart rate and risk of cancer death in healthy men. *PLoS One* 2011;6:e21310.
29. Legeai C, Jouven X, Tafflet M, Dartigues JF, Helmer C, Ritchie K, et al. Resting heart rate, mortality and future coronary heart disease in the elderly: the 3C Study. *Eur J Cardiovasc Prev Rehabil* 2011;18:488-497.
30. Nabi H, Kivimaki M, Empana JP, Sabia S, Britton A, Marmot MG, et al. Combined effects of depressive symptoms and resting heart rate on mortality: the Whitehall II prospective cohort study. *J Clin Psychiatry* 2011;72:1199-1206.

31. Nauman J, Janszky I, Vatten LJ, Wisloff U. Temporal changes in resting heart rate and deaths from ischemic heart disease. *JAMA* 2011;306:2579-2587.
32. Inoue R, Ohkubo T, Kikuya M, Metoki H, Asayama K, Kanno A, et al. Predictive value for mortality of the double product at rest obtained by home blood pressure measurement: the Ohasama study. *Am J Hypertens* 2012;25:568-575.
33. Leistner DM, Klotsche J, Palm S, Pieper L, Stalla GK, Lehnert H, et al. Resting heart rate as a tool for risk stratification in primary care: does it provide incremental prognostic information? *Eur J Prev Cardiol* 2012;19:275-284.
34. Woodward M, Webster R, Murakami Y, Barzi F, Lam TH, Fang X, et al. The association between resting heart rate, cardiovascular disease and mortality: evidence from 112,680 men and women in 12 cohorts. *Eur J Prev Cardiol* 2012;21:719-726.
35. Jensen MT, Suadicani P, Hein HO, Gyntelberg F. Elevated resting heart rate, physical fitness and all-cause mortality: a 16-year follow-up in the Copenhagen Male Study. *Heart* 2013;99:882-887.
36. Johansen CD, Olsen RH, Pedersen LR, Kumarathurai P, Mouridsen MR, Binici Z, et al. Resting, night-time, and 24 h heart rate as markers of cardiovascular risk in middle-aged and elderly men and women with no apparent heart disease. *Eur Heart J* 2013;34:1732-1739.
37. Pittaras AM, Faselis C, Doumas M, Myers J, Kheirbek R, Kokkinos JP, et al. Heart rate at rest, exercise capacity, and mortality risk in veterans. *Am J Cardiol* 2013;112:1605-1609.
38. Plichart M, Thomas F, Empana JP, Bean K, Perier MC, Celermajer DS, et al. Gender-specific trends in heart rate in the general population from 1992-2007: a study of 226,288 French adults. *Eur J Prev Cardiol* 2013;20:61-72.
39. Saxena A, Minton D, Lee DC, Sui X, Fayad R, Lavie CJ, et al. Protective role of resting heart rate on all-cause and cardiovascular disease mortality. *Mayo Clin Proc* 2013;88:1420-1426.
40. Aladin AI, Whelton SP, Al-Mallah MH, Blaha MJ, Keteyian SJ, Juraschek SP, et al. Relation of resting heart rate to risk for all-cause mortality by gender after considering exercise capacity (the Henry Ford exercise testing project). *Am J Cardiol* 2014;114:1701-1706.
41. Floyd JS, Sitlani CM, Wiggins KL, Wallace E, Suchy-Dicey A, Abbasi SA, et al. Variation in resting heart rate over 4 years and the risks of myocardial infarction and death among older adults. *Heart* 2014.
42. Hisamatsu T, Miura K, Ohkubo T, Yamamoto T, Fujiyoshi A, Miyagawa N, et al. High long-chain n-3 fatty acid intake attenuates the effect of high resting heart rate on cardiovascular mortality risk: a 24-year follow-up of Japanese general population. *J Cardiol* 2014;64:218-224.
43. Ho JE, Larson MG, Ghorbani A, Cheng S, Coglianese EE, Vasan RS, et al. Long-term cardiovascular risks associated with an elevated heart rate: the Framingham Heart Study. *J Am Heart Assoc* 2014;3:e000668.
44. O. Hartaigh B, Gill TM, Shah I, Hughes AD, Deanfield JE, Kuh D, et al. Association between resting heart rate across the life course and all-cause mortality: longitudinal findings from the Medical Research Council (MRC) National Survey of Health and

Development (NSHD). *J Epidemiol Community Health* 2014;68:883-889.
45. Ryu M, Gombojav B, Nam CM, Lee Y, Han K. Modifying effects of resting heart rate on the association of binge drinking with all-cause and cardiovascular mortality in older Korean men: the Kangwha Cohort Study. *J Epidemiol* 2014;24:274-280.
46. Wang A, Chen S, Wang C, Zhou Y, Wu Y, Xing A, et al. Resting heart rate and risk of cardiovascular diseases and all-cause death: the kailuan study. *PLoS One* 2014;9:e110985.