

Supplementary Table 1. Literature search strategy in PubMed

1. "resting heart rate"
2. "heart rate"
3. "resting pulse"
4. "coronary heart disease"
5. "heart disease"
6. "ischemic heart disease"
7. "ischaemic heart disease"
8. "coronary artery disease"
9. "myocardial infarction"
10. "angina pectoris"
11. "heart failure"
12. "atrial fibrillation"
13. stroke
14. "ischemic stroke"
15. "haemorrhagic stroke"
16. "cerebrovascular disease"
17. "cardiovascular disease"
18. cancer
19. "total cancer"
20. neoplasm
21. mortality
22. "all-cause mortality"
23. "total mortality"
24. survival
25. death
26. cohort
27. cohorts
28. prospective

29. trial
30. "followed-up"
31. "followed up"
32. "follow up"
33. "hazard ratio"
34. "hazard ratios"
35. "relative risk"
36. RR
37. "Cox proportional hazards"
38. 1 OR 2 OR 3
39. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25
40. 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37
41. 38 AND 39 AND 40

Supplementary Table2. List of excluded studies and reason for exclusion

Exclusion reason	Reference number
Abstract	1-46
Changes in resting heart rate	47
Cross-sectional study	48
Duplicate	49-64
Letter	65,66
News	67
No confidence intervals	68-72
No risk estimates	73-83
Not obtained	84-87
Not relevant data	88-90
Not relevant exposure	91-128
Not relevant outcome	129-143
Patient population	144-223
Review	224-230

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Supplementary Table 3. Resting heart rate and coronary heart disease and sudden cardiac death

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Garcia-Palmieri MR et al, 1988, Puerto Rico	Puerto Rico Heart Health Program	1965-1968 – 1981, 12 years follow-up	7620 men, age 45-64 years: 246 CHD deaths	Heart rate	Per 1 bpm	1.0118 (1.0024-1.0215)	Age, urban/rural status, SBP, cholesterol, cigarettes, abnormal blood glucose, vital capacity, relative weight, physical activity, hematocrit, education, alcohol
Kannel WB et al, 1990, USA	Framingham Heart Study	NA-NA, 28 years follow-up	2011 men and 2534 women, age 35-70 years: 171/80 sudden deaths	Heart rate, men Heart rate, women	Per 10 bpm Per 10 bpm	0.99 (0.86-1.15) 0.84 (0.68-1.05)	Age, BMI, cigarettes, glucose intolerance, hemoglobin, intraventricular block, ECG left ventricular hypertrophy, nonspecific ST.T wave changes, serum cholesterol, SBP, x-ray left ventricular hypertrophy, alcohol, coronary artery disease, congestive heart failure
Gillum RF et al, 1991, USA	National Health and Nutrition Examination Survey 1	1971-1975 – NA, 9.9/10.3 years follow-up (whites/blacks)	5995 men and women, age 45-74 years: 995 CHD cases	Pulse rate, whites, men, CHD incidence Pulse rate, whites, women, CHD incidence Pulse rate, whites, men, CHD mortality Pulse rate, whites, women, CHD mortality	<74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84	1.00 1.19 (0.97-1.47) 1.18 (0.94-1.49) 1.00 1.09 (0.85-1.41) 1.29 (1.01-1.66) 1.00 1.19 (0.85-1.68) 1.29 (0.89-1.86) 1.00 1.01 (0.62-1.63) 1.09 (0.67-1.75)	Age, smoking, SBP, serum total cholesterol, diabetes

Shaper AG et al, 1993, UK	British Regional Heart Study	1978-1980 - NA, 8 years follow-up	7735 men age 40-59 years: 243 major IHD events 89 IHD deaths 44 sudden cardiac deaths	Heart rate, major IHD events Heart rate, IHD mortality Heart rate, sudden cardiac death	<60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90	1.0 1.0 (0.6-1.5) 1.3 (0.8-1.9) 1.1 (0.7-1.8) 1.2 (0.8-1.3) 1.0 1.4 (0.6-3.0) 1.8 (0.8-4.0) 1.7 (0.7-4.1) 3.3 (1.4-7.8) 1.0 1.6 (0.4-5.8) 2.6 (0.7-8.6) 1.9 (0.5-7.4) 5.2 (1.4-18.7)	Age, social class, smoking, heavy drinking, physical activity, SBP, blood cholesterol, blood glucose
Menotti A et al, 1998, Italy	Seven Countries Study on Cardiovascular Diseases – Italy	1960 - 1995, 35 years follow-up	1527 men, age 40-59 years: 319 CHD deaths	Heart rate	Per 10 bpm	0.94 (0.85-1.03)	Age, marital status, FH – heart attack, FH - hypertension, FH – diabetes, physical activity, cigarettes, BMI, skinfold thickness, arm circumference, shoulder-pelvis shape, laterality-linearity index, trunk-height ratio, serum cholesterol, urine glucose, SBP, vital capacity, forced expiratory volume, gerontoxon, xanthelasma
Greenland P et al, 1999, USA	Chicago Heart Association Detection Project	1967-1973 – 1992, 22 years follow-up	18787 men, age 18-74 years and 14994 women, age 18-74 years: 1566 CHD deaths	Resting heart rate, men, age 18-39 years Resting heart rate, men, age 40-59 years Resting heart rate, men, age 60-74 years Resting heart rate, women, age 18-39 years Resting heart rate, women, age 40-59 years Resting heart rate, women, age 60-74 years	Per 12 bpm Per 12 bpm Per 12 bpm Per 12 bpm Per 12 bpm Per 12 bpm	1.20 (1.02-1.42) 1.06 (0.99-1.14) 0.95 (0.85-1.07) NC, too few cases 1.13 (1.01-1.28) 1.01 (0.85-1.19)	Age, education, serum cholesterol, smoking, BMI, BMI ² , major and minor ECG abnormalities, race, diabetes mellitus, SBP
Benetos A et al, 1999, France	Centre d'Investigations Pré-ventives et	1974-1977 – 1994, 18.2 years	19386 men and women, age 40-69 years: 436	Heart rate, men	<60 bpm 60-80 >80-100	1.00 1.20 (0.82-1.75) 1.49 (0.97-2.28)	Age, SBP, DBP, BMI, history of MI, antihypertensive treatment, total cholesterol, physical activity, tobacco

	Cliniques (IPC)	follow-up	CHD deaths	Heart rate, women	>100 <60 bpm 60-80 >80-100 >100	1.90 (1.02-3.94) 1.00 1.09 (0.39-3.04) 0.79 (0.24-2.64) 0.65 (0.11-3.81)	
Reunanen A et al, 2000, Finland	Finnish Mobile Clinic Health Examination Survey	1966-1972 – 1993, 23 years follow-up	5598 men and 5119 women, age 30-59 years: 596/188 CHD deaths	Heart rate, men Heart rate, women Heart rate, men, excluding prevalent CHD Heart rate, women, excluding prevalent CHD	≤60 bpm 61-83 ≥84 ≤66 bpm 67-93 ≥94 ≤60 bpm 61-83 ≥84 ≤66 bpm 67-93 ≥94	1.00 1.06 (0.85-1.33) 0.96 (0.73-1.26) 1.00 1.02 (0.70-1.49) 1.06 (0.67-1.67) 1.00 1.07 (0.85-1.34) 0.91 (0.69-1.20) 1.00 0.96 (0.65-1.41) 0.85 (0.53-1.37)	Age, smoking, blood pressure, cholesterol, diabetes, BMI, perceived health, occupational and leisure time physical activity
Dekker JM et al, 2000, USA	Atherosclerosis Risk in Communities (ARIC) Study	1987-1989 – 1993, ~5 years follow-up	14672 men and women, age 45-65 years: 395 CHD cases	Heart rate	<63 bpm 63-<72 ≥72	1.00 1.03 (0.66-1.61) 1.09 (0.72-1.66)	Age, sex, race, field center, current smoking, cigarette-years, triglycerides, HDL cholesterol, diabetes, hypertension, BMI, waist-to-hip ratio, carotid intima-media thickness
Jouven X et al, 2001, France	Paris Prospective Study 1	1967-1972 – 1994, 23 years follow-up	7079 men, age 42-53 years: 192 fatal MIs 118 sudden deaths	Resting heart rate, MI Resting heart rate, SD	Per 10.2 bpm Per 10.2 bpm	1.05 (0.95-1.16) 1.28 (1.06-1.61)	Age, parental sudden death, parental MI, sport activity, diabetes, tobacco, BMI, SBP, total cholesterol
Kado DM et al, 2002, USA	Study of Osteoporotic Fractures	1986-1988 – 1998, 8.9 years follow-up	9702 women, age ≥65 years: 317 CHD deaths	Resting heart rate	>80 vs. ≤80 bpm Per 10 bpm	1.5 (1.2-2.1) 1.17 (1.05-1.30)	Age, weight, self-reported health, physical activity, hyperthyroidism, hypertension, diabetes mellitus, current smoking
Okamura T et al, 2004, Japan	National Survey on Circulatory Disorders (NIPPONDATA 80 study)	1980-1998, 16.5 years follow-up	8800 men and women, age 30-59 years: 114 CHD deaths	Heart rate, men, age 30-59 years Heart rate, men, age ≥60 years	55 bpm 63 69 82 Per 11 bpm 55 bpm 63	1.00 2.15 (0.55-8.37) 2.49 (0.67-9.24) 3.99 (1.14-14.0) 1.32 (0.95-1.84) 1.00 0.84 (0.43-1.65)	Age, serum albumin, BMI, hypertension, hypercholesterolemia, diabetes mellitus, smoking, drinking

				Heart rate, women, age 30-59 years Heart rate, women, age ≥60 years	69 82 Per 11 bpm 59 bpm 67 73 86 Per 11 bpm 59 bpm 67 73 86 Per 11 bpm	1.05 (0.55-2.02) 1.43 (0.78-2.65) 1.16 (0.93-1.46) 1.00 6.03 (0.64-56.5) 8.40 (0.94-75.1) 9.37 (1.05-83.7) 1.43 (0.99-2.06) 1.00 1.02 (0.58-1.80) 1.04 (0.61-1.77) 0.66 (0.36-1.23) 0.88 (0.71-1.09)	
Jouven X et al, 2005, France	Paris Prospective Study 1	1967-1972 – 1994, 23 years follow-up	5713 men, age 42-53 years: 81 sudden deaths 400 cardiac deaths	Resting heart rate, sudden death from MI Resting heart rate, nonsudden death from M	>75 vs. <60 bpm >75 vs. <60 bpm	3.46 (1.60-7.44) 1.55 (0.90-2.66)	Age, use or nonuse of tobacco, level of physical activity, presence or absence of diabetes, body-mass index, basal SBP, cholesterol level, presence or absence of a parental history of sudden death or myocardial infarction, and exercise duration
Savonen KP et al, 2006, Finland	Kuopio Ischaemic Heart Disease Risk Factor Study	1984-1989 - 1998, 11.4 years follow-up	1378 men, age 42-61 years: 37 CHD deaths	Resting heart rate	Per 13 bpm	1.35 (1.01-1.81)	Age, examination year, alcohol, BMI, cigarette smoking, CVD history, diabetes, serum low-density lipoprotein cholesterol, systolic blood pressure at rest, myocardial ischaemia during exercise
Adabag AS et al, 2008, USA	Multiple Risk Factor Intervention Trial	1973-1976 – 1999, 25 years follow-up	12555 men, age 35-57 years: 1586 CHD deaths 153 sudden deaths 824 fatal/nonfatal MIs	Resting heart rate, CHD death Resting heart rate, sudden death Resting heart rate, fatal/nonfatal MI	<65 bpm 65-71 72-79 ≥80 <65 bpm 65-71 72-79 ≥80 <65 bpm 65-71 72-79 ≥80	1.00 0.94 (0.82-1.09) 0.92 (0.80-1.07) 1.01 (0.88-1.17) 1.00 1.32 (0.81-2.14) 1.22 (0.74-2.01) 1.50 (0.93-2.42) 1.00 1.22 (1.00-1.48) 1.04 (0.84-1.27) 1.11 (0.91-1.37)	Age, cigarettes smoked per day, SBP, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, body mass index, fasting glucose, race, and parental history of CHD

Tverdal A et al, 2008, Norway	Norwegian Health Surveys	1985-1999 – 2005, 12.6 years follow-up	379843 men and women, age 40-45 years: 1057 IHD deaths	Resting heart rate, men Resting heart rate, women	<65 bpm 65-79 80-94 ≥95 Per 10 bpm <65 bpm 65-79 80-94 ≥95 Per 10 bpm	1.00 0.91 (0.74-1.12) 1.05 (0.84-1.31) 1.61 (1.24-2.09) 1.12 (1.06-1.18) 1.00 0.79 (0.42-1.49) 1.11 (0.60-2.07) 1.22 (0.62-2.41) 1.10 (0.98-1.23)	Calendar year, total cholesterol, triglycerides, DBP, smoking, physical activity, family history of CVD
Kikuya M et al, 2008, Japan	Ohasama Study	1987-1995 – 2004, 11.9 years follow-up	2455 men and women, age 35-96 years: 85 cardiac deaths 33 MI deaths	Resting heart rate, cardiac deaths Resting heart rate, MI deaths	Per 7.8 bpm Per 7.8 bpm	1.20 (0.99-1.46) 0.98 (0.69-1.38)	Age, sex, obesity, smoking, drinking, CVD history, diabetes mellitus, hyperlipidemia, treatment with antihypertensive drugs
Hansen TW et al, 2008, Denmark, Sweden, Belgium, Japan, China, Uruguay	The International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes (IDACO)	NA-NA, 9.6 years follow-up	6928 men and women, age ≥18 years: 313 CHD cases 426 cardiac disease cases	Heart rate, CHD cases Heart rate, cardiac disease cases	Per 11.6 bpm Per 11.6 bpm	1.07 (0.94-1.22) 1.06 (0.95-1.19)	Age, systolic blood pressure, cohort, BMI, smoking, alcohol, serum total cholesterol, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs
Cuddy TE et al, 2009, Canada	Manitoba Follow-up Study	1948 - 2005, 58 years follow-up	3983 men, mean age 31 years: 180 sudden unexpected cardiac death 284 controls	Heart rate	≤59 bpm 60-74 ≥75	1.00 2.36 (0.98-5.69) 2.79 (1.02-7.63)	T-wave changes on the examination 5 years prior to death, hypertension, ST-T changes, T-wave changes on the examination prior to death
Hsia J et al, 2009, USA	Women's Health Initiative	1993-1998 – NA, 7.8 years follow-up	129135 women, age 50-79 years: 2281 MI or CHD death	Resting heart rate	≤62 bpm 63-66 67-70 71-76 >76	1.00 1.02 (0.89-1.17) 1.08 (0.95-1.23) 1.02 (0.89-1.16) 1.26 (1.11-1.42)	Age, ethnicity, hypertension, diabetes mellitus, smoking, high cholesterol drugs, depression, nervousness, BMI, physical activity, alcohol, dietary caffeine, saturated fat, hormone use, statin use

Mao Q et al, 2010, China	China National Hypertension Survey Epidemiology Follow-up Study	1991-1999/2000, 8.3 years follow-up	169871 men and women, age ≥40 years: 2961 heart disease cases 2326 CHD cases	Heart rate, heart disease, men Heart rate, heart disease, women Heart rate, CHD, men Heart rate, CHD, women	<60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm	0.99 (0.58-1.68) 1.00 1.18 (1.06-1.32) 1.53 (1.31-1.80) 1.16 (1.11-1.22) 1.51 (0.87-2.64) 1.00 0.97 (0.86-1.10) 1.49 (1.26-1.77) 1.13 (1.07-1.19) 0.67 (0.33-1.35) 1.00 1.12 (0.99-1.26) 1.54 (1.29-1.83) 1.16 (1.10-1.23) 0.90 (0.40-2.03) 1.00 0.97 (0.84-1.12) 1.51 (1.24-1.83) 1.14 (1.07-1.21)	Age, SBP, cigarette smoking, alcohol consumption, BMI, physical activity, education, geographic region and urbanization, time-dependent history of diabetes
Batty GD et al, 2010, United Kingdom	Whitehall study	1967-1970 - 2008, 40 years follow-up	1183 men, age 40-69 years: 307 CHD deaths	Heart rate	≤64 bpm 65-74 ≥75	1.00 0.93 (0.70-1.23) 1.18 (0.89-1.56)	Age, employment grade, SBP, plasma cholesterol, smoking, BMI, glucose intolerance, diabetes, FEV1
Cooney MT et al, 2010, Finland	National FINRISK Study	1982, 1987, 1992, 1997 – 2003, 12 years follow-up	10519 men and 11334 women, age 25-74 years: NA CHD deaths	Heart rate, men, CHD deaths Heart rate, women Heart rate, men, fatal and nonfatal CHD Heart rate, women	≤60 bpm 62-90 >90 Per 15 bpm ≤60 bpm 62-90 >90 Per 15 bpm ≤60 bpm 62-90 >90 Per 15 bpm ≤60 bpm 62-90 >90	1.00 1.49 (0.99-2.25) 2.37 (1.43-3.95) 1.34 (1.17-1.53) 1.00 4.35 (1.06-17.86) 7.59 (1.70-33.92) 1.50 (1.18-1.91) 1.00 1.34 (1.06-1.70) 1.42 (1.01-1.98) 1.06 (0.97-1.17) 1.00 1.45 (0.89-2.36) 1.97 (1.08-3.60)	Age, smoking status, SBP, total cholesterol, diabetes mellitus, BMI, HDL cholesterol, physical activity

Nauman J et al, 2010, Norway	HUNTstudy	1984-1986 – 2004, 18.2 years follow-up	24999 men and 25089 women, age ≥20 years: 1419/718 IHD deaths	Heart rate, women, <70 years Heart rate, women, ≥70 years Heart rate, men, <70 years Heart rate, men, ≥70 years	Per 15 bpm ≤60 bpm 61-72 73-87 88-100 ≥101 Per 10 bpm ≤60 bpm 61-72 73-87 88-100 ≥101 Per 10 bpm ≤60 bpm 61-72 73-87 88-100 ≥101 Per 10 bpm ≤60 bpm 61-72 73-87 88-100 ≥101 Per 10 bpm	1.20 (1.03-1.40) 0.73 (0.43-1.24) 1.00 1.20 (0.91-1.57) 1.60 (1.18-2.17) 2.11 (1.28-3.46) 1.18 (1.08-1.29) 1.28 (0.84-1.95) 1.00 1.04 (0.80-1.34) 1.20 (0.89-1.61) 0.95 (0.55-1.65) 1.04 (0.95-1.14) 1.23 (1.00-1.52) 1.00 1.15 (0.97-1.35) 1.18 (0.97-1.45) 1.67 (1.17-2.38) 1.10 (1.03-1.17) 1.27 (0.95-1.69) 1.00 1.31 (1.05-1.63) 1.27 (0.97-1.66) 1.84 (1.15-2.96) 1.11 (1.02-1.21)	Age, BMI, physical activity, marital status, education, alcohol, smoking status
Legeai C et al, 2011, France	The Three-City Study	1999-2001 – NA, 4.9 years follow-up	6522men and women, age ≥65 years: 228 CHD cases	Resting heart rate	<62 bpm 62-67.5 68-72.5 73-79 >79	1.00 0.83 (0.54-1.29) 0.83 (0.52-1.34) 1.16 (0.75-1.80) 0.99 (0.63-1.54)	Age, sex, study centre, SBP, smoking status, wine, fish, BMI, total cholesterol, HDL cholesterol, diabetes mellitus, previous CVD, living alone, disability status, beta-blocker use, calcium antagonist use
Woodward M et al, 2014, Asia	Asia Pacific Cohort Studies Collaboration (12 cohort studies)	NA-NA, 7.4 years follow-up	112680 men and women, age ≥20 years: 1049 CHD events	Resting heart rate	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.00 1.03 (0.87-1.23) 1.07 (0.90-1.27) 1.11 (0.93-1.31) 1.18 (1.03-1.35)	Age, sex, SBP, cohort
Ho JE et al, 2014, USA	Framingham Heart Study and	1986-1990/ 1987-1991	4058 men and women, mean	Resting heart rate	Per 11 bpm	1.08 (0.96-1.20)	Age, sex, SBP, use of antihypertensive treatment, BMI, diabetes, smoking

	Framingham Offspring Study	– NA, 19 years follow-up	age 55 years: 343 CHD cases				status, physical activity index, valvular heart disease, ECG left ventricular hypertrophy, total/HDL cholesterol ratio, minor cardiovascular diseases, PR interval and QRS duration
Hisamatsu T et al, 2014, Japan	National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged (NIPPON DATA80)	1980-2004, 24 years follow-up	8807 men and women, age 30-95 years: 314 cardiac deaths	Resting heart rate, high n-3 fatty acid intake Resting heart rate, low n-3 fatty acid intake	<70 bpm 70-85 >85 <70 bpm 70-85 >85	1.00 1.24 (0.88-1.74) 0.98 (0.56-1.71) 1.14 (0.81-1.59) 1.32 (0.93-1.87) 1.32 (0.74-2.38)	Age, sex, body mass index, smoking status, drinking habits, SBP, total cholesterol, blood glucose, labor intensity, electrocardiographic findings (left ventricular hypertrophy and suspected coronary heart disease), saturated fatty acids, n-6 polyunsaturated fatty acids, sodium, fiber
Makita S et al, 2014, Japan	Iwate-KENpoku Cohort study	2002-2005 – NA, 5.6 years follow-up	17766 men and women, age 40-79 years: 33 myocardial infarctions	Resting heart rate	<60 bpm 60-69.5 70-79.5 ≥80	2.22 (0.96-5.15) 1.00 1.09 (0.43-2.77) 1.01 (0.32-3.20)	Age
Wang A et al, 2014, China	Kailuan Study	2006-2007 – 2010, 4.0 years follow-up	92562 men and women, age 18-98 years: 399 MI cases	Resting heart rate	<66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm	1.00 1.22 (0.87-1.71) 1.34 (0.94-1.89) 1.34 (0.98-1.83) 1.80 (1.31-2.46) 1.16 (1.06-1.26)	Age, sex, average monthly income of each family member, education, marital status, BMI, waist circumference, smoking status, drinking status, physical activity
Aladin AI et al, 2014, USA	Henry Ford Exercise Testing Project	1991-2009, 11.1 years follow-up	56634 men and women, age ≥18 years: 4463 major adverse cardiac events 1009 myocardial infarctions 1711 coronary revascularizations	Resting heart rate, major adverse cardiac events, men Resting heart rate, major adverse cardiac events, women Resting heart rate,	<60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69	1.00 0.94 (0.86-1.03) 1.03 (0.94-1.14) 1.01 (0.91-1.12) 1.09 (0.97-1.24) 1.00 0.91 (0.80-1.06) 0.93 (0.81-1.07) 0.95 (0.82-1.10) 1.08 (0.92-1.27) 1.00 0.97 (0.80-1.19)	Age, sex, race, SBP, DBP, hypertensive medication use, history of dyslipidemia, lipid lowering medication use, smoking, pulmonary disease medication, diabetes, family history of coronary artery disease, obesity, reason for stress test, atrioventricular-nodal blocking medication, METs in exercise test

				myocardial infarction, men Resting heart rate, myocardial infarction, women Resting heart rate, revascularization, men Resting heart rate, revascularization, women	70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90	0.93 (0.76-1.14) 0.93 (0.74-1.17) 0.93 (0.71-1.21) 1.00 0.89 (0.67-1.17) 0.90 (0.68-1.18) 0.94 (0.40-1.26) 0.93 (0.68-1.28) 1.00 0.83 (0.72-0.96) 0.91 (0.78-1.05) 0.76 (0.64-0.90) 0.87 (0.71-1.06) 1.00 0.96 (0.73-1.27) 0.87 (0.66-1.16) 1.05 (0.78-1.41) 1.09 (0.80-1.50)	
Zhong C et al, 2015, China (Mongolia)	Inner Mongolia	2002-2003 – 2012, 9.2 years follow-up	2530 men and women, age ≥20 years: 75 CHD cases	Heart rate	Per 1 bpm ≥80 vs. <80 bpm	1.01 (1.00-1.03) 1.19 (0.74-1.93)	Age, sex, smoking, drinking, waist circumference, family history of CVD, SBP, DBP, blood glucose, lipids
Floyd JS et al, 2015, USA	Cardiovascular Health Study	1989-1990/1992-1993 – 2010, 12.4 years follow-up	1991 men and women, age 68-96 years: 262 MI cases	Resting heart rate, any MI Resting heart rate, incident MI Resting heart rate, CHD-related death	Per 10 bpm Per 10 bpm Per 10 bpm	0.99 (0.85-1.16) 0.98 (0.63-1.16) 1.24 (0.98-1.57)	Age, sex, race, current smoking, diabetes mellitus, SBP, high-density lipoprotein cholesterol, subclinical cardiovascular disease, marital status, education, self-reported health status, regular moderate or high-intensity exercise, BMI, serum creatinine
Custodis F et al, 2016, Germany	Heinz Nixdorf RECALL study	2000-2003 - NA, 10.5 years follow-up	4091 men and women, age 45-75 years: 159 coronary events	Resting heart rate	≤62 bpm 63-69 70-76 >76	1.00 0.99 (0.62-1.58) 1.10 (0.69-1.77) 1.04 (0.65-1.66)	Age, sex, hypertension, current smoking, diabetes, BMI, known peripheral artery disease, lipid-lowering medication, heart rate lowering medication, LDL-cholesterol, coronary artery calcification

Sharashova E et al, 2016, Norway	The Tromsø Study	1994-1995 - 2012, 18 years follow-up	24006 men and women, age ≥25 years: 996/580 MI cases	Resting heart rate, men	50	0.82 (0.70-0.95)	Age, SBP, total cholesterol, HDL cholesterol, triglycerices, BMI, physical activity, smoking
					60	0.92 (0.86-0.98)	
					70	1.00	
					80	1.06 (1.02-1.12)	
					90	1.12 (1.03-1.22)	
					100	1.16 (1.04-1.30)	
				Resting heart rate, women	50	0.81 (0.71-0.92)	
					60	0.90 (0.85-0.96)	
					70	1.00	
					80	1.11 (1.04-1.18)	
					90	1.23 (1.09-1.40)	
					100	1.37 (1.13-1.66)	

BMI=body mass index, bpm=beats per minute, CHD=coronary heart disease, CVD=cardiovascular disease, DBP=diastolic blood pressure, ECG=echocardiography, FEV1=forced expiratory volume in 1 second, FH=family history, HDL=high-density lipoprotein, IHD=ischemic heart disease, MET=metabolic equivalent task, MI=myocardial infarction, NA=not available, SBP=systolic blood pressure

Supplementary Table 4. Resting heart rate and heart failure

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Mazza A et al, 2005, Italy	CARDiovascular STudy in the ELderly (CASTEL)	NA-NA, 12 years follow-up	3282 men and women, age ≥65 years: 329 congestive heart failure cases	Heart rate	≤71 bpm 72-80 ≥81	1.00 1.02 (0.75-1.39) 1.32 (1.10-1.96)	Age, sex, history of CAD, stroke or transient ischaemic attack, intermittent claudication, chronic obstructive pulmonary disease, hypertension, diabetes, blood lipids, proteinuria, BMI, murmurs at the neck, ECG abnormalities, left ventricular hypertrophy, spirometry
Kalogeropoulos A et al, 2009, USA	The Health, Aging, and Body Composition Study	1997-1998 – NA, 7.1 years follow-up	2934 men and women, age 70-79 years: 258 heart failure cases	Heart rate, whites, all Heart rate, blacks, all	>75 vs. <75 bpm >75 vs. <75 bpm	1.45 (0.94-2.23) 1.97 (1.30-2.99)	SBP, CHD, fasting glucose level, left ventricular hypertrophy, current smoking, GFR, albumin
Woodward M et al, 2012, Asia	Asia Pacific Cohort Studies Collaboration (12 cohort studies)	NA-NA, 7.4 years follow-up	112680 men and women, age ≥20 years: NA heart failure death	Resting heart rate	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.00 0.83 (0.37-1.87) 1.63 (0.83-3.19) 2.08 (1.07-4.06) 1.67 (1.06-2.64)	Age, SBP, cohort
Pfister R et al, 2012, United Kingdom	EPIC-Norfolk Study	1993-1997 – 2009, 12.9 years follow-up	9805 men and 12321 women, age 39-79 years: 1356 heart failure cases	Resting heart rate, all Resting heart rate, men Resting heart rate, women	51-60 bpm 61-70 71-80 81-90 91-100 Per 10 bpm 51-60 bpm 61-70 71-80 81-90 91-100 51-60 bpm 61-70	1.00 1.09 (0.92-1.29) 1.20 (1.00-1.43) 1.44 (1.28-1.76) 1.23 (0.91-1.66) 1.11 (1.05-1.17) 1.00 1.14 (0.93-1.40) 1.33 (1.07-1.66) 1.43 (1.10-1.87) 1.11 (0.70-1.76) 1.00 0.99 (0.74-1.33)	Age, body mass index, SBP, prevalent diabetes, cholesterol concentration, social class, educational level, smoking, physical activity, sex and antihypertensive medication

					71-80 81-90 91-100	1.04 (0.77-1.39) 1.39 (1.00-1.92) 1.23 (0.81-1.87)	
Nanchen D et al, 2013, Netherlands	Rotterdam Study	1990-1993 – 2009, 14.6 years follow-up	4768 men and women, age ≥55 years: 656 HF cases	Heart rate, men Heart rate, baseline Heart rate, time-dependent Heart rate, women Heart rate, baseline Heart rate, time-dependent	<69 bpm 69-78 ≥79 Per 10 bpm Per 10 bpm <69 bpm 69-78 ≥79 Per 10 bpm Per 10 bpm	1.00 1.34 (0.98-1.83) 1.48 (1.09-2.03) 1.14 (1.03-1.27) 1.11 (1.00-1.22) 1.00 0.99 (0.77-1.28) 0.99 (0.77-1.27) 0.94 (0.86-1.03) 0.98 (0.89-1.07)	Age, smoking status, SBP, diabetes mellitus, body mass index, total cholesterol, high-density lipoprotein cholesterol, and antihypertensive treatment, systemic corticoid and antiasthmatic treatment.
Opdahl A et al, 2014, USA	Multi-Ethnic Study of Atherosclerosis	2000-2002 - NA, 7 years follow-up	5000 men and women, age 44-84 years: 176 HF cases	Resting heart rate	<57 bpm 57-62 63-69 >69 Per 1 bpm	1.00 2.62 (1.41-4.87) 2.57 (1.36-4.89) 3.76 (2.00-7.07) 1.04 (1.02-1.06)	Age, ethnicity, sex, alcohol use, intentional exercise, and education level, SBP, DBP, diabetes, BMI, smoking status, total and HDL cholesterol levels, triglyceride levels, and current medications (statins, beta-blockers, and calcium channel blockers), and LV end-diastolic volume, LV mass index, computed tomography coronary calcium score, and baseline ejection fraction.
Ho JE et al, 2014, USA	Framingham Heart Study and Framingham Offspring Study	1986-1990/ 1987-1991 – NA, 19 years follow-up	4058 men and women, mean age 55 years: 303 HF cases	Resting heart rate	Per 11 bpm	1.32 (1.18-1.48)	Age, sex, SBP, use of antihypertensive treatment, BMI, diabetes, smoking status, physical activity index, valvular heart disease, ECG left ventricular hypertrophy, total/HDL cholesterol ratio, minor cardiovascular diseases, PR interval and QRS duration
Khan H et al, 2015, USA, Finland	Health Aging and Body Composition (Health ABC) study, the Cardiovascular Health Study	1997-1998-NA, 13.1 years follow-up 1989-1990/ 1992-1993 – NA, 13.1	7073 men and women, age 70-79/ 65-100 and 42-61 years: 1189 HF cases	Resting heart rate Resting heart rate, men Resting heart rate, women	<57 bpm 58-63 64-71 ≥72 Per 10 bpm Per 10 bpm	1.00 0.83 (0.70-0.99) 1.12 (0.96-1.32) 1.30 (1.10-1.53) 1.16 (1.03-1.29) 1.14 (1.06-1.22)	Age, sex, BMI, history of diabetes, history of hypertension, smoking status, serum creatinine, left ventricular hypertrophy

	(CHS), the Kuopio Ischemic Heart Disease (KIHD) Study	years follow-up 1984-1989 – NA, 13.1 years follow-up					
Parikh KS et al, 2016, USA	Jackson Heart Study	2000-2011 - 2015, 8.9 years follow-up	5156 African American men and women, median age 55.8 years: 329 heart failure hospitalization	Resting heart rate	30-55 56-60 61-66 67-72 72-118 Per 5 bpm	1.00 1.22 (0.83-1.79) 1.34 (0.92-1.96) 1.19 (0.80-1.76) 1.79 (1.25-2.58) 1.10 (1.05-1.16)	Age, sex, prior MI, heart failure, hypertension, stroke, diabetes, lung disease, current smoking, prior smoking, alcohol, physical activity, caffeine intake, BMI, neck circumference, SBP, sodium, estimated glomerular filtration rate, hemoglobin, ejection fraction, left ventricular hypertrophy, left ventricular dimension, left bundle-branch block, right bundle-branch block, QRS interval duration, use of angiotensin-converting enzyme inhibitor or angiotensin 2 receptor blocker, antiarrhythmic agent, antiplatelet agent, beta-blocker, calcium channel blocker, digoxin, diuretic, statin

BMI=body mass index, bpm=beats per minute, CAD=coronary artery disease, CHD=coronary heart disease, DBP=diastolic blood pressure, ECG=echocardiography, glomerular filtration rate, HDL=high-density lipoprotein, LV=left ventricular, NA=not available, SBP=systolic blood pressure

Supplementary Table 5. Resting heart rate and atrial fibrillation

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Wilhelmsen L et al, 2001, Sweden	The Multifactor Primary Prevention Study	1970-1973 – 1996, 27 years follow-up	7495 men, age 55-79 years: 754 atrial fibrillation hospitalizations	Heart rate	≤65 bpm 66-80 ≥81	1.00 0.85 (0.72-1.02) 0.89 (0.73-1.09)	Age
Thelle DS et al, 2013, Norway	Norwegian Health Surveys	1985-1999 (recruitment) – 2005-2009, 5 years follow-up	162078 women and 147462 men, age 40-45 years: 575/288 atrial fibrillation cases	Resting heart rate, men Resting heart rate, women	Per 10 bpm decrease Per 10 bpm decrease	1.26 (1.17-1.35) 1.15 (1.05-1.27)	Age, year of screening, education, BMI, height, daily smoking, self-reported cardiovascular disease at screening, dispensed cardiovascular drug in 2004
Grundvold I et al, 2013, Norway	Cardiovascular Health Survey	1972-1975 – 2008, 30 years follow-up	2014 men, age 40-59 years: 270 atrial fibrillation cases	Resting heart rate	<50 bpm ≥50	1.10 (0.69-1.66) 1.00	Age, SBP, physical fitness
Alonso A et al, 2013, USA	Framingham Heart Study Offspring cohort	1995-1998 - 2005, NA years of follow-up	2838 men and women, mean age 60 years: 143 atrial fibrillation cases	Heart rate	Per 10 bpm	0.99 (0.84-1.16)	Age, sex
Alonso A et al, 2013, USA	Atherosclerosis Risk in Communities Cohort	1996-1998, -2005, NA years of follow-up	10675 men and women, age 45-64 years: 419 atrial fibrillation cases	Heart rate, whites Heart rate, African Americans	Per 10 bpm Per 10 bpm	1.12 (1.00-1.24) 0.99 (0.80-1.23)	Age, sex
Alonso A et al, 2013, Island	Age, Gene/ Environment Susceptibility Reykjavik Study	2002-2006 - 2011, NA years of follow-up	4469 men and women, mean age 76 years: 408 atrial	Heart rate	Per 10 bpm	0.97 (0.89-1.06)	Age, sex

			fibrillation cases				
Alonso A et al, 2013, Netherlands	Rotterdam Study	1997-2005, NA years of follow-up	3203 men and women, age ≥55 years: 177 atrial fibrillation cases	Heart rate	Per 10 bpm	0.92 (0.80-1.06)	Age, sex
O'Neal WT et al, 2015, USA	Cardiovascular Health Study	1999 – 2008, 12.7 years follow-up	5226 men and women, age ≥65 years: 532 atrial fibrillation cases	Heart rate	≤60 bpm >60-90 >90 Per 5 bpm decrease Per 5 bpm decrease Per 5 bpm decrease	1.3 (1.1-1.5) 1.0 1.1 (0.52-2.3) 1.06 (1.01-1.10) 1.05 (0.99-1.10) 1.06 (0.99-1.10)	Age, sex, race, education, income, baseline CVD, smoking, SBP, diabetes, BMI, total cholesterol, HDL cholesterol, aspirin, statins, antihypertensive and antiarrhythmic medications, high sensitive C-reactive protein
Sharashova E et al, 2016, Norway	The Tromsø Study	1994-1995 - 2012, 18 years follow-up	24291 men and women, age ≥25 years: 863/649 atrial fibrillation cases	Resting heart rate, men	50 60 70 80 90 100	0.88 (0.79-0.98) 0.94 (0.89-0.99) 1.00 1.07 (1.01-1.13) 1.14 (1.02-1.27) 1.21 (1.03-1.43)	Age, SBP, total cholesterol, HDL cholesterol, triglycerides, BMI, physical activity, smoking
				Resting heart rate, women	50 60 70 80 90 100	0.90 (0.79-1.02) 0.95 (0.89-1.01) 1.00 1.06 (0.99-1.12) 1.11 (0.98-1.26) 1.18 (0.97-1.42)	
Skov MW et al, 2016, Denmark	The Copenhagen Electrocardiographic Study	2001-2011 - 2013, 8.4 years follow-up	281451 men and women, age 42-67 years: 15666 AF cases	Resting heart rate	30-51 52-59 60-65 66-72 73-80 81-94 95-120	1.16 (1.06-1.27) 1.04 (0.98-1.10) 1.05 (1.00-1.11) 1.00 1.08 (1.02-1.13) 1.15 (1.10-1.21) 1.36 (1.26-1.46)	Age, sex, hypertension, heart failure, myocardial infarction, valvular heart disease, diabetes, hyperthyroidism, ECG criteria of left ventricular hypertrophy, treatment with heart-rate lowering medication at the date of index ECG

BMI=body mass index, bpm=beats per minute, CVD=cardiovascular disease, HDL=high-density lipoprotein, SBP=systolic blood pressure

Supplementary Table 6. Resting heart rate and stroke

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Menotti A et al, 1998, Italy	Seven Countries Study on Cardiovascular Diseases – Italy	1960 - 1995, 35 years follow-up	1527 men, age 40-59 years: 146 stroke deaths	Heart rate	Per 10 bpm	0.89	Age, marital status, FH – heart attack, FH - hypertension, FH – diabetes, physical activity, cigarettes, BMI, skinfold thickness, arm circumference, shoulder-pelvis shape, laterality-linearity index, trunk-height ratio, serum cholesterol, urine glucose, SBP, vital capacity, forced expiratory volume, gerontoxon, xanthelasma
Benetos A et al, 1999, France	Centre d'Investigations Préventives et Cliniques (IPC)	1974-1977 – 1994, 18.2 years follow-up	19386 men and women, age 40-69 years: 188 stroke deaths	Heart rate, men Heart rate, women	<60 bpm 60-80 >80-100 >100 <60 bpm 60-80 >80-100 >100	1.00 1.29 (0.68-2.42) 1.18 (0.55-2.49) 1.23 (0.40-3.77) 1.00 1.03 (0.31-3.34) 1.54 (0.43-5.47) 3.23 (0.72-13.4)	Age, SBP, DBP, BMI, history of MI, antihypertensive treatment, total cholesterol, physical activity, tobacco
Reunanen A et al, 2000, Finland	Finnish Mobile Clinic Health Examination Survey	1966-1972 – 1993, 23 years follow-up	5598 men and 5119 women, age 30-59 years: 146/104 stroke deaths	Heart rate, men Heart rate, women	≤60 bpm 61-83 ≥84 ≤66 bpm 67-93 ≥94	1.00 1.63 (0.98-2.70) 1.39 (0.76-2.52) 1.00 1.16 (0.69-1.93) 0.98 (0.52-1.86)	Age, smoking, blood pressure, cholesterol, diabetes, BMI, perceived health, occupational and leisure time physical activity
Kado DM et al, 2002, USA	Study of Osteoporotic Fractures	1986-1988 – 1998, 8.9 years follow-up	9702 women, age ≥65 years: 203 stroke deaths	Resting heart rate	>80 vs. 80 bpm Per 10 bpm	1.3 (0.90-1.50) 1.02 (0.89-1.17)	Age, weight, self-reported health, physical activity, hyperthyroidism, hypertension, diabetes mellitus, current smoking
Kikuya M et al, 2008, Japan	Ohasama Study	1987-1995 – 2004, 11.9 years follow-up	2455 men and women, age 35-96 years: 83 stroke deaths	Resting heart rate, stroke deaths Resting heart rate, cerebral infarction deaths	Per 7.8 bpm Per 7.8 bpm	1.27 (1.06-1.53) 1.14 (0.90-1.45)	Age, sex, obesity, smoking, drinking, CVD history, diabetes mellitus, hyperlipidemia, treatment with antihypertensive drugs

			51 cerebral infarction deaths				
Tverdal A et al, 2008, Norway	Norwegian Health Surveys	1985-1999 – 2005, 12.6 years follow-up	379843 men and women, age 40-45 years: 342 stroke deaths	Resting heart rate, men Resting heart rate, women	<65 bpm 65-79 80-94 ≥95 Per 10 bpm <65 bpm 65-79 80-94 ≥95 Per 10 bpm	1.00 0.84 (0.53-1.46) 0.88 (0.53-1.45) 1.32 (0.73-2.40) 1.06 (0.94-1.20) 1.00 0.63 (0.38-1.05) 0.52 (0.30-0.87) 0.50 (0.27-0.93) 0.87 (0.77-0.99)	Calendar year, total cholesterol, triglycerides, DBP, smoking, physical activity, family history of CVD
Hansen TW et al, 2008, Denmark, Sweden, Belgium, Japan, China, Uruguay	The International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes (IDACO)	NA-NA, 9.6 years follow-up	6928 men and women, age ≥18 years: 269 stroke cases	Heart rate	Per 11.6 bpm	0.94 (0.81-1.09)	Age, systolic blood pressure, cohort, BMI, smoking, alcohol, serum total cholesterol, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs
Hsia J et al, 2009, USA	Women's Health Initiative	1993-1998 – NA, 7.8 years follow-up	129135 women, age 50-79 years: 1877 stroke cases	Resting heart rate	≤62 bpm 63-66 67-70 71-76 >76	1.00 1.04 (0.90-1.20) 0.96 (0.83-1.11) 1.07 (0.94-1.23) 1.01 (0.87-1.16)	Age, ethnicity, hypertension, diabetes mellitus, smoking, high cholesterol drugs, depression, nervousness, BMI, physical activity, alcohol, dietary caffeine, saturated fat, hormone use, statin use
Mao Q et al, 2010, China	China National Hypertension Survey Epidemiology Follow-up Study	1991-1999/2000, 8.3 years follow-up	169871 men and women, age ≥40 years: 3876 stroke cases 523 ischemic stroke cases 1286 hemorrhagic stroke cases	Heart rate, total stroke, men Heart rate, total stroke, women	<60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm	1.18 (0.78-1.79) 1.00 1.08 (0.98-1.18) 1.17 (1.01-1.35) 1.04 (1.00-1.08) 1.23 (0.71-2.14) 1.00 1.06 (0.95-1.18) 1.01 (0.84-1.20) 1.03 (0.98-1.08) 1.96 (0.79-4.86)	Age, SBP, cigarette smoking, alcohol consumption, BMI, physical activity, education, geographic region and urbanization, time-dependent history of diabetes

				Heart rate, ischemic stroke, men Heart rate, ischemic stroke, women Heart rate, hemorrhagic stroke, men Heart rate, hemorrhagic stroke, women	60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm	1.00 1.25 (0.97-1.61) 1.19 (0.79-1.78) 0.99 (0.88-1.11) 1.09 (0.26-4.55) 1.00 0.87 (0.65-1.16) 0.84 (0.53-1.34) 0.96 (0.84-1.11) 1.09 (0.51-2.33) 1.00 1.08 (0.92-1.26) 1.39 (1.10-1.76) 1.08 (1.01-1.16) 0.28 (0.04-1.97) 1.00 1.01 (0.84-1.22) 0.88 (0.65-1.20) 1.02 (0.94-1.12)	
Batty GD et al, 2010, United Kingdom	Whitehall study	1967-1970 - 2008, 40 years follow-up	1183 men, age 40-69 years: 90 stroke deaths	Heart rate	≤64 bpm 65-74 ≥75	1.00 1.15 (0.71-1.87) 0.74 (0.42-1.30)	Age, employment grade, SBP, plasma cholesterol, smoking, BMI, glucose intolerance, diabetes, FEV1
Xu T et al, 2013, China	Inner Mongolia	2003-2012, 9.2 years follow-up	2530 men and women, age ≥20 years: 76 ischemic stroke cases	Resting heart rate, nonsmokers Resting heart rate, smokers	<80 bpm ≥80 <80 bpm ≥80	1.00 1.42 (0.62-3.28) 2.11 (1.06-4.23) 2.86 (1.33-6.14)	Age, sex, body mass index, drinking status, family history of cardiovascular disease, blood glucose, SBP, DBP, lipids
Woodward M et al, 2014, Asia	Asia Pacific Cohort Studies Collaboration (12 cohort studies)	NA-NA, 7.4 years follow-up	112680 men and women, age ≥20 years: 1114 total stroke events 389 Hemorrhagic strokes 432 Ischemic strokes 293 Unclassified	Resting heart rate, total stroke Resting heart rate, hemorrhagic stroke Resting heart rate,	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm <65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm <65 bpm	1.00 1.16 (0.95-1.42) 1.29 (1.07-1.55) 1.46 (1.22-1.75) 1.32 (1.17-1.48) 1.00 1.22 (0.85-1.76) 1.38 (0.99-1.91) 1.43 (1.04-1.97) 1.29 (1.07-1.57) 1.00	Age, sex, SBP, cohort

			strokes	ischemic stroke	65-71.9 72-79.9 ≥80 Per 10 bpm <65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.08 (0.76-1.53) 1.38 (1.03-1.86) 1.40 (1.04-1.87) 1.28 (1.06-1.56) 1.00 1.15 (0.82-1.61) 1.02 (0.73-1.44) 1.70 (1.24-2.32) 1.44 (1.16-1.78)	
Hisamatsu T et al, 2014, Japan	National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged (NIPPON DATA80)	1980-2004, 24 years follow-up	8807 men and women, age 30-95 years: 285 stroke deaths	Resting heart rate, high n-3 fatty acid intake Resting heart rate, low n-3 fatty acid intake	<70 bpm 70-85 >85 <70 bpm 70-85 >85	1.00 0.80 (0.56-1.16) 0.89 (0.49-1.61) 0.92 (0.65-1.29) 0.90 (0.61-1.32) 2.05 (1.24-3.37)	Age, sex, body mass index, smokingstatus, drinking habits, SBP, total cholesterol, blood glucose, labor intensity, electrocardiographicfindings (left ventricular hypertrophy and suspected coronary heart disease), saturated fatty acids, n-6 polyunsaturated fatty acids, sodium, fiber
Makita S et al, 2014, Japan	Iwate-KENpoku Cohort study	2002-2005 – NA, 5.6 years follow-up	17766 men and women, age 40-79 years: 101 cerebral infarctions 49 intracerebral hemorrhages	Resting heart rate, cerebral infarction Resting heart rate, intracerebral hemorrhage	<60 bpm 60-69.5 70-79.5 ≥80 <60 bpm 60-69.5 70-79.5 ≥80	1.60 (0.93-2.73) 1.00 1.24 (0.73-2.11) 2.15 (1.25-3.70) 1.29 (0.55-3.01) 1.00 1.37 (0.63-2.95) 2.67 (1.25-5.67)	Age

Wang A et al, 2014, China	Kailuan Study	2006-2007 – 2010, 4.0 years follow-up	92562 men and women, age 18-98 years: 1519 stroke cases 1122 ischemic stroke cases 397 hemorrhagic stroke cases	Resting heart rate, total stroke Resting heart rate, ischemic stroke Resting heart rate, hemorrhagic stroke	<66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm <66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm <66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm	1.00 1.18 (1.00-1.40) 1.24 (1.04-1.47) 1.24 (1.06-1.45) 1.29 (1.10-1.53) 1.09 (1.04-1.14) 1.00 1.17 (0.97-1.43) 1.33 (1.09-1.62) 1.30 (1.08-1.56) 1.31 (1.08-1.59) 1.10 (1.04-1.16) 1.00 1.21 (0.89-1.65) 1.00 (0.70-1.41) 1.09 (0.80-1.48) 1.24 (0.91-1.71) 1.05 (0.96-1.15)	Age, sex, average monthly income of each family member, education, marital status, BMI, waist circumference, smoking status, drinking status, physical activity
Ho JE et al, 2014, USA	Framingham Heart Study and Framingham Offspring Study	1986-1990/1987-1991 – NA, 19 years follow-up	4058 men and women, mean age 55 years: 216 stroke cases	Resting heart rate	Per 11 bpm	1.10 (0.96-1.26)	Age, sex, SBP, use of antihypertensive treatment, BMI, diabetes, smoking status, physical activity index, valvular heart disease, ECG left ventricular hypertrophy, total/HDL cholesterol ratio, minor cardiovascular diseases, PR interval and QRS duration
O'Neal WT et al, 2015, USA	Reasons for Geographic And Racial Differences in Stroke (REGARDS) study	2003-2007 – NA, 7.6 years follow-up	24730 men and women, mean age 64 years: 646 ischemic stroke cases	Resting heart rate Resting heart rate, men Resting heart rate, women	<61 bpm 61-70 >70 Per 10 bpm Per 10 bpm Per 10 bpm	1.00 1.29 (1.06-1.57) 1.37 (1.12-1.67) 1.10 (1.02-1.18) 1.12 (1.02-1.24) 1.07 (0.97-1.19)	Age, sex, race, education, income, region of residence, SBP, smoking, diabetes, left ventricular hypertrophy, antihypertensive medications, antiarrhythmic agents, statins, aspirin, warfarin, coronary heart disease
Zhong C et al, 2015, China (Mongolia)	Inner Mongolia	2002-2003 – 2012, 9.2 years follow-up	2530 men and women, age ≥20 years: 120 stroke cases	Heart rate	Per 1 bpm ≥80 vs. <80 bpm	1.01 (1.00-1.02) 1.05 (0.71-1.55)	Age, sex, smoking, drinking, waist circumference, family history of CVD, SBP,DBP, blood glucose, lipids

Sharashova E et al, 2016, Norway	The Tromsø Study	1994-1995 - 2012, 18 years follow-up	24347 men and women, age ≥25 years: 549/417 ischemic stroke cases	Resting heart rate, men	50	0.81 (0.65-1.02)	Age, SBP, total cholesterol, HDL cholesterol, triglycerices, BMI, physical activity, smoking
					60	0.91 (0.83-1.01)	
					70	1.00	
					80	1.04 (0.96-1.12)	
					90	0.98 (0.84-1.16)	
					100	0.83 (0.60-1.15)	
				Resting heart rate, women	50	1.31 (0.90-1.90)	
					60	1.01 (0.91-1.12)	
					70	1.00	
					80	1.08 (0.99-1.17)	
					90	1.19 (1.01-1.41)	
					100	1.32 (1.04-1.69)	

BMI=body mass index, bpm=beats per minute, CVD=cardiovascular disease, DBP=diastolic blood pressure, ECG=echocardiography, FEV1=forced expiratory volume in 1 second, FH=family history, HDL=high-density lipoprotein, MI=myocardial infarction, NA=not available, SBP=systolic blood pressure

Supplementary Table 7. Resting heart rate and cardiovascular disease

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Gillum RF et al, 1991, USA	National Health and Nutrition Examination Survey 1	1971-1975 – NA, 9.9/10.3 years follow-up (whites/ blacks)	5995 men and women, age 45-74 years: 638 CVD deaths	Pulse rate, whites, men Pulse rate, whites, women Pulse rate, blacks, men Pulse rate, blacks, women	<74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84	1.00 1.23 (0.93-1.61) 1.44 (1.08-1.92) 1.00 1.02 (0.72-1.45) 1.26 (0.89-1.76) 1.00 1.00 (0.56-1.77) 1.52 (0.86-2.70) 1.00 1.52 (0.71-3.27) 3.03 (1.46-6.28)	Age, smoking, SBP, serum total cholesterol, diabetes
Sandvik L et al, 1993, Norway	Rikshospitalet, Norway	1972-1975 - 1989, 16 years follow-up	1960 men, age 40-59 years: 53 CVD deaths	Resting heart rate	Per 18 bpm	1.2 (0.8-1.8)	Age, smoking status, cigarettes per day, fitness, K value, systolic blood pressure, cholesterol, vital capacity, triglycerides, BMI, physical activity
Mensink GBM et al, 1997, Germany	The Spandau Health Test	1984 – 1991 – 1994, 12 years follow-up	1827 men and 2929 women, age 40-80 years: 153 CVD deaths	Resting heart rate, men Resting heart rate, women	Per 20 bpm Per 20 bpm	1.7 (1.4-2.2) 1.4 (1.1-1.8)	Age, serum cholesterol, BMI, SBP, smoking, diabetes mellitus
Menotti A et al, 1998, Italy	Seven Countries Study on Cardiovascular Diseases – Italy	1960 - 1995, 35 years follow-up	1527 men, age 40-59 years: 505 CVD deaths	Heart rate	Per 10 bpm	0.94 (0.85-1.03)	Age, marital status, FH – heart attack, FH - hypertension, FH – diabetes, physical activity, cigarettes, BMI, skinfold thickness, arm circumference, shoulder-pelvis shape, laterality-linearity index, trunk-height ratio, serum cholesterol, urine glucose, SBP, vital capacity, forced expiratory volume, gerontoxon, xanthelasma
Benetos A et al,	Centre	1974-1977	19386 men and	Heart rate, men	<60 bpm	1.00	Age, SBP, DBP, BMI, history of MI,

1999, France	d'Investigations Pre'ventives et Cliniques (IPC)	– 1994, 18.2 years follow-up	women, age 40- 69 years: 844 CVD deaths	Heart rate, women	60-80 >80-100 >100 <60 bpm 60-80 >80-100 >100	1.35 (1.01-1.80) 1.44 (1.04-2.00) 2.18 (1.37-3.47) 1.00 0.93 (0.50-1.73) 0.99 (0.49-1.99) 1.06 (0.42-2.68)	antihypertensive treatment, total cholesterol, physical activity, tobacco
Dekker JM et al, 2000, USA	Atherosclerosis Risk in Communities (ARIC) Study	1987-1989 – 1993, ~5 years follow-up	14672 men and women, age 45- 65 years: 140 CVD deaths	Heart rate	<63 bpm 63-<72 ≥72	1.00 1.06 (0.52-2.17) 1.84 (0.94-3.59)	Age, sex, race, field center, current smoking, cigarette-years, triglycerides, HDL cholesterol, diabetes, hypertension, BMI, waist-to-hip ratio, carotid intima- media thickness
Reunanen A et al, 2000, Finland	Finnish Mobile Clinic Health Examination Survey	1966-1972 – 1993, 23 years follow-up	5598 men and 5119 women, age 30-59 years: 1033/426 CVD deaths	Heart rate, men Heart rate, women	≤60 bpm 61-83 ≥84 ≤66 bpm 67-93 ≥94	1.00 1.17 (0.97-1.42) 1.05 (0.83-1.32) 1.00 1.11 (0.84-1.48) 1.22 (0.87-1.70)	Age, smoking, blood pressure, cholesterol, diabetes, BMI, perceived health, occupational and leisure time physical activity
Kristal-Boneh E et al, 2000, Israel	CORDIS Study	1985-1987 - 1994, 8 years follow-up	3527 men, mean age 43 years: 57 CVD deaths	Resting heart rate	<70 bpm 70-79 80-89 ≥90	1.00 0.54 (0.2-1.2) 0.83 (0.4-1.9) 2.02 (1.1-4.0)	Age, education, smoking, BMI, cholesterol, sport, hemoglobin
Seccareccia F et al, 2001, Italy	Malattie Cardiovascolari Aterosclerotiche , Istituto Superiore di Sanità (MATISS) Project	1984-1993 – 1997, 9.7 years follow-up	2533 men, age 40-69 years: 133 CVD deaths	Heart rate, CVD	<60 bpm 60-69 70-79 80-89 ≥90	1.00 1.38 (0.85-2.24) 1.87 (1.11-3.16) 1.78 (0.95-3.34) 2.54 (1.25-5.16)	Age, SBP, serum cholesterol, cigarettes, BMI, arm circumference, FEV, diabetes mellitus, preexisting CVD
Nilsson PM et al, 2001, Sweden	Malmö Preventive Project	1974-1992 - 1997, 17/12 years follow-up (men/ women)	13466 men and 9467 women, age NA: 727/85 CVD deaths	Heart rate, men Heart rate, women	Per 20 bpm Per 20 bpm	1.30 (1.14-1.49) 1.33 (0.85-2.08)	Age, serum cholesterol, BMI, systolic blood pressure, smoking, problematic alcohol drinking habits

Okamura T et al, 2004, Japan	National Survey on Circulatory Disorders (NIPPONDATA 80 study)	1980-1998, 16.5 years follow-up	8800 men and women, age ≥30 years: 577 CVD deaths	Heart rate, men, age 30-59 years Heart rate, men, age ≥60 years Heart rate, women, age 30-59 years Heart rate, women, age ≥60 years	55 bpm 63 69 82 Per 11 bpm 55 bpm 63 69 82 Per 11 bpm 59 bpm 67 73 86 Per 11 bpm 59 bpm 67 73 86 Per 11 bpm	1.00 1.61 (0.73-3.53) 1.79 (0.84-3.82) 2.55 (1.22-5.31) 1.27 (1.02-1.58) 1.00 0.86 (0.59-1.26) 0.93 (0.63-1.37) 1.01 (0.70-1.48) 1.00 (0.87-1.15) 1.00 2.12 (0.73-6.11) 3.61 (1.34-9.72) 2.72 (0.97-7.61) 1.16 (0.90-1.49) 1.00 0.85 (0.58-1.25) 0.90 (0.63-1.28) 0.85 (0.58-1.24) 0.95 (0.82-1.09)	Age, serum albumin, BMI, hypertension, hypercholesterolemia, diabetes mellitus, smoking, drinking
Savonen KP et al, 2006, Finland	Kuopio Ischaemic Heart Disease Risk Factor Study	1984-1989 - 1998, 11.4 years follow-up	1378 men, age 42-61 years: 56 CVD deaths	Resting heart rate	Per 13 bpm	1.21 (0.94-1.55)	Age, examination year, alcohol, BMI, cigarette smoking, CVD history, diabetes, serum low-density lipoprotein cholesterol, systolic blood pressure at rest, myocardial ischaemia during exercise
Tverdal A et al, 2008, Norway	Norwegian Health Surveys	1985-1999 – 2005, 12.6 years follow-up	379843 men and women, age 40-45 years: 1743 CVD deaths	Resting heart rate, men Resting heart rate, women	<65 bpm 65-79 80-94 ≥95 Per 10 bpm <65 bpm 65-79 80-94 ≥95 Per 10 bpm	1.00 0.94 (0.79-1.11) 1.01 (0.84-1.22) 1.51 (1.21-1.87) 1.10 (1.05-1.15) 1.00 0.67 (0.48-0.94) 0.70 (0.50-0.99) 0.78 (0.53-1.15) 1.00 (0.93-1.07)	Calendar year, total cholesterol, triglycerides, DBP, smoking, physical activity, family history of CVD
Kizilbash MA et al, 2008, USA	Chicago Heart Association Detection	1967-1973 – 2002, 32 years	3724/1959 men and 4929/3735 women, age 18-	Heart rate, age 18-39 years, men	<75 bpm 75-84 ≥85	0.58 (0.34-0.84) 0.78 (0.50-1.21) 1.00	Age, race, education, SBP, cigarette smoking, diabetes mellitus, total cholesterol

	Project in Industry	follow-up	39/40-59 years: 126/370/60/467 CVD deaths	Heart rate, age 18-39 years, women Heart rate, age 40-59 years, men Heart rate, age 40-59 years, women Heart rate, age 18-39 years, men, converted Heart rate, age 18-39 years, women, converted Heart rate, age 40-59 years, men, converted Heart rate, age 40-59 years, women, converted	Per 12.2 bpm lower <75 bpm 75-84 ≥85 Per 12.2 bpm lower <75 bpm 75-84 ≥85 Per 12.3 bpm lower <75 bpm 75-84 ≥85 Per 11.7 bpm lower <75 bpm 75-84 ≥85 Per 12.2 bpm <75 bpm 75-84 ≥85 Per 12.2 bpm <75 bpm 75-84 ≥85 Per 12.3 bpm <75 bpm 75-84 ≥85 Per 11.7 bpm	0.79 (0.66-0.94) 1.04 (0.54-1.98) 0.84 (0.44-1.60) 1.00 0.98 (0.70-1.37) 0.73 (0.56-0.95) 0.71 (0.53-0.94) 1.00 0.86 (0.77-0.96) 0.77 (0.61-0.98) 0.88 (0.69-1.12) 1.00 0.93 (0.85-1.02) 1.00 1.34 (0.71-2.53) 1.72 (1.10-2.71) 1.27 (1.06-1.51) 1.00 1.24 (0.50-3.09) 0.96 (0.50-1.84) 1.02 (0.73-1.43) 1.00 0.97 (0.66-1.44) 1.37 (1.05-1.78) 1.16 (1.04-1.30) 1.00 1.14 (0.81-1.60) 1.30 (1.02-1.65) 1.08 (0.98-1.18)	
Hozawa A et al, 2008, Japan	Ohasama study	1988-1994 – 2004, 12 years follow-up	1444 men and women, age ≥40 years: 101 CVD deaths	Daytime heart rate, CVD deaths	<68.2 bpm 68.3-73.5 73.6-78.7 ≥78.8 Per 10 bpm	1.00 1.25 (0.76-2.04) 0.77 (0.41-1.48) 0.81 (0.43-1.52) 0.95 (0.65-1.40)	Age, sex, antihypertensive medication, smoking, diabetes mellitus, hyperlipidemia, SBP
Kikuya M et al, 2008, Japan	Ohasama Study	1987-1995 – 2004, 11.9 years follow-up	2455 men and women, age 35-96 years: 168 CVD deaths	Resting heart rate	Per 7.8 bpm	1.24 (1.08-1.42)	Age, sex, obesity, smoking, drinking, CVD history, diabetes mellitus, hyperlipidemia, treatment with antihypertensive drugs

Hansen TW et al, 2008, Denmark, Sweden, Belgium, Japan, China, Uruguay	The International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes (IDACO)	NA-NA, 9.6 years follow-up	6928 men and women, age ≥18 years: 325 CVD deaths 693 CVD cases	Heart rate, CVD deaths Heart rate, CVD cases	Per 11.6 bpm Per 11.6 bpm	1.14 (0.99-1.32) 1.03 (0.94-1.12)	Age, systolic blood pressure, cohort, BMI, smoking, alcohol, serum total cholesterol, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs
Cooney MT et al, 2010, Finland	National FINRISK Study	1982, 1987, 1992, 1997 – 2003, 12 years follow-up	10519 men and 11334 women, age 25-74 years: 372/140 CVD deaths	Heart rate, men Heart rate, women	≤60 bpm 62-90 >90 Per 15 bpm ≤60 bpm 62-90 >90 Per 15 bpm	1.00 1.34 (0.97-1.86) 1.93 (1.26-2.95) 1.24 (1.11-1.40) 1.00 2.61 (1.14-5.99) 3.05 (1.18-7.89) 1.32 (1.08-1.60)	Age, smoking status, SBP, total cholesterol, diabetes mellitus, BMI, HDL cholesterol, physical activity
Mao Q et al, 2010, China	China National Hypertension Survey Epidemiology Follow-up Study	1991-1999/2000, 8.3 years follow-up	169871 men and women, age ≥40 years: 6837 CVD cases	Heart rate, men Heart rate, women	<60 bpm 60-74 75-89 ≥90 Per 10 bpm <60 bpm 60-74 75-89 ≥90 Per 10 bpm	1.10 (0.80-1.54) 1.00 1.12 (1.04-1.20) 1.32 (1.18-1.47) 1.09 (1.06-1.13) 1.35 (0.91-2.00) 1.00 1.02 (0.94-1.11) 1.23 (1.09-1.38) 1.07 (1.03-1.11)	Age, SBP, cigarette smoking, alcohol consumption, BMI, physical activity, education, geographic region and urbanization, time-dependent history of diabetes
Legeai C et al, 2011, France	The Three-City Study	1999-2001 – NA, 4.9 years follow-up	7147 men and women, age ≥65 years: 110 CVD deaths	Resting heart rate	<62 bpm 62-67.5 68-72.5 73-79 >79	1.00 1.19 (0.62-2.28) 1.04 (0.51-2.16) 1.32 (0.64-2.73) 1.87 (0.98-3.58)	Age, sex, study centre, SBP, smoking status, wine, fish, BMI, total cholesterol, HDL cholesterol, diabetes mellitus, previous CVD, living alone, disability status, beta-blocker use, calcium antagonist use
Jensen MT et al, 2011, Denmark	Copenhagen City Heart Study	1976-1978 – 2009, 21.2 years follow-up	16516 men and women, age ≥20 years: 3821 CVD deaths	Resting heart rate, never smokers Resting heart rate, former smokers Resting heart rate,	Per 10 bpm Per 10 bpm Per 10 bpm	1.06 (0.99-1.13) 1.11 (1.07-1.17) 1.15 (1.09-1.21)	Age, leisure time physical activity, BMI, SBP, pulmonary function, alcohol, triglycerides

				moderate smokers Resting heart rate, heavy smokers	Per 10 bpm	1.13 (1.08-1.18)	
Jouven X et al, 2011, France	Paris Prospective Study	1967-1972 - 1994, 25 years follow-up	6101 men, age 42-53 years: 435 CVD deaths	Resting heart rate, CVD mortality	<60 bpm 60-67 68-73 ≥74	1.0 1.4 (1.0-1.8) 1.6 (1.2-2.1) 2.0 (1.5-2.7)	Age, smoking
Leistner DM et al, 2012, Germany	Diabetes Cardiovascular Risk Evaluation Targets and Essential Data for Commitment of Treatment (DETECT) cohort study	2003-2008, 5 years follow-up	5320 men and women, mean age 55.9 years: 258 CVD events	Resting heart rate, CVD events Resting heart rate, CVD mortality Resting heart rate, major CVD events	35-66 bpm 67-72 73-80 81-120 35-66 bpm 67-72 73-80 81-120 35-66 bpm 67-72 73-80 81-120	1.00 0.78 (0.43-1.40) 1.12 (0.63-1.96) 0.94 (0.46-1.90) 1.00 0.36 (0.11-1.22) 0.47 (0.14-1.60) 0.84 (0.22-3.31) 1.00 0.69 (0.41-1.18) 1.01 (0.61-1.67) 0.93 (0.49-1.75)	Age, sex, atrial fibrillation, rate control medication, diabetes mellitus, hypertension, smoking status, family history of coronary artery disease, hyperlipidemia, BMI
Johansen CD et al, 2013, Denmark	Copenhagen Holter Study	1998-2000 – NA, 6.3 years follow-up	653 men and women, age 55, 60, 65, 70, 75 years: 22 CVD deaths	Resting heart rate	Per 5 bpm	1.12 (1.00-1.26)	Age, SBP, age, sex, smoking, diabetes, and total cholesterol, high-sensitive C-reactive protein and NT-proBNP, use of beta-blockers, use of ACE-inhibitors/angiotensin II receptor blockers, diuretics, and calcium channel blockers
Saxena A et al, 2013, USA	Aerobics Center Longitudinal Study	1974-2002 – 2003, 15 years follow-up	53322 men and women, age ≥20 years: 1081 CVD deaths	Resting heart rate	<60 bpm 60-69 70-79 ≥80	1.00 0.93 (0.86-1.02) 0.99 (0.90-1.10) 1.38 (1.21-1.58)	Age, sex, examination year, body mass index, smoking status, heavy alcohol drinking, physical activity, parental cardiovascular disease, abnormal electrocardiographic findings, diabetes, measured high blood pressure (>140/90 mm Hg), hypertension, hypercholesterolemia
Woodward M et al, 2014, Asia	Asia Pacific Cohort Studies Collaboration (12 cohort studies)	NA-NA, 7.4 years follow-up	112680 men and women, age ≥20 years: 2726 CVD events	Resting heart rate, CVD death	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.00 1.03 (0.90-1.18) 1.13 (0.99-1.28) 1.45 (1.28-1.64) 1.42 (1.30-1.55)	Age, sex, SBP, cohort

				Resting heart rate, CVD incidence	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.00 1.08 (0.96-1.22) 1.19 (1.06-1.33) 1.44 (1.29-1.60) 1.36 (1.26-1.47)	
Hisamatsu T et al, 2014, Japan	National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged (NIPPON DATA80)	1980-2004, 24 years follow-up	8807 men and women, age 30-95 years: 617 CVD deaths	Resting heart rate, high n-3 fatty acid intake Resting heart rate, low n-3 fatty acid intake	<70 bpm 70-85 >85 <70 bpm 70-85 >85	1.00 1.01 (0.79-1.30) 0.92 (0.61-1.38) 1.04 (0.82-1.32) 1.13 (0.88-1.45) 1.67 (1.15-2.43)	Age, sex, body mass index, smoking status, drinking habits, SBP, total cholesterol, blood glucose, labor intensity, electrocardiographic findings (left ventricular hypertrophy and suspected coronary heart disease), saturated fatty acids, n-6 polyunsaturated fatty acids, sodium, fiber
Makita S et al, 2014, Japan	Iwate-KENpoku Cohort study	2002-2005 – NA, 5.6 years follow-up	17766 men and women, age 40-79 years: 430 CVD cases	Resting heart rate, men Resting heart rate, women	<60 bpm 60-69.5 70-79.5 ≥80 <60 bpm 60-69.5 70-79.5 ≥80	1.55 (1.05-2.27) 1.00 1.06 (0.71-1.56) 1.72 (1.16-2.57) 0.73 (0.37-1.44) 1.00 1.24 (0.86-1.78) 1.10 (0.73-1.64)	Age
Sadeghi M et al, 2014, Iran	Isfahan Cohort Study	2001-NA, 6.8 years follow-up	Nested case-control study: 432 CVD cases 401 controls Age ≥35 years	Heart rate	57.3 bpm 67.1 73.4 80.4 93.5 Per 1 bpm	1.00 0.93 (0.55-1.56) 1.92 (1.11-3.32) 2.01 (1.14-3.54) 2.45 (1.42-4.24) 1.02 (1.01-1.03)	Age, sex, heart-rate lowering drugs, hypertension, diabetes, high LDL-cholesterol, central obesity, smoking
Wang A et al, 2014, China	Kailuan Study	2006-2007 – 2010, 4.0 years follow-up	92562 men and women, age 18-98 years: 1903 CVD cases	Resting heart rate	<66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm	1.00 1.20 (1.03-1.39) 1.25 (1.07-1.46) 1.26 (1.10-1.45) 1.39 (1.20-1.61) 1.10 (1.05-1.14)	Age, sex, average monthly income of each family member, education, marital status, BMI, waist circumference, smoking status, drinking status, physical activity
Ho JE et al, 2014, USA	Framingham Heart Study and Framingham	1986-1990/ 1987-1991 – NA, 19	4058 men and women, mean age 55 years:	Resting heart rate, incidence Resting heart rate,	Per 11 bpm Per 11 bpm	1.15 (1.07-1.24) 1.18 (1.04-1.33)	Age, sex, SBP, use of antihypertensive treatment, BMI, diabetes, smoking status, physical activity index, valvular

	Offspring Study	years follow-up	708 CVD cases 252 CVD deaths	mortality			heart disease, ECG left ventricular hypertrophy, total/HDL cholesterol ratio, minor cardiovascular diseases, PR interval and QRS duration
Zhong C et al, 2015, China (Mongolia)	Inner Mongolia	2002-2003 – 2012, 9.2 years follow-up	2530 men and women, age ≥20 years: 195 CVD cases	Heart rate	Per 1 bpm ≥80 vs. <80 bpm	1.01 (1.00-1.02) 1.35 (1.01-1.82)	Age, sex, smoking, drinking, waist circumference, family history of CVD, SBP, DBP, blood glucose, lipids
Ganna A et al, 2015, United Kingdom	UK Biobank Study	2007-2010 – 2014, 4.9 years follow-up	498103 men and women, age 37-73 years: 1352/442 circulatory disease deaths	Resting heart rate, men Resting heart rate, women	30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0 30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0	1.0 1.0 (0.8-1.2) 0.9 (0.7-1.1) 1.3 (1.1-1.6) 1.9 (1.6-2.2) 0.7 (0.6-0.8) 0.8 (0.7-0.9) 0.9 (0.8-1.0) 1.0 1.4 (1.3-1.6)	Age
Sharashova E et al, 2016, Norway	The Tromsø Study	1994-1995 - 2012, 18 years follow-up	24489 men and women, age ≥25 years: 634/585 CVD deaths	Resting heart rate, men Resting heart rate, women	50 60 70 80 90 100 50 60 70 80 90 100	0.68 (0.61-0.76) 0.83 (0.78-0.87) 1.00 1.21 (1.14-1.28) 1.46 (1.31-1.64) 1.77 (1.49-2.10) 1.17 (0.84-1.64) 0.94 (0.85-1.03) 1.00 1.17 (1.09-1.25) 1.38 (1.21-1.59) 1.63 (1.33-2.00)	Age, SBP, total cholesterol, HDL cholesterol, triglycerides, BMI, physical activity, smoking
Ryu M et al, 2016, Korea	Kangwha Cohort Study	1985 – 2005, 20.8 years follow-up	6100 men and women, age 55-99 years: 340/417 CVD deaths	Resting heart rate, men Resting heart rate, women	≤60 bpm 61-79 ≥80 ≤60 bpm 61-79 ≥80	1.00 (0.83-1.21) 1.00 1.15 (1.02-1.25) 1.04 (0.88-1.22) 1.00 1.11 (1.03-1.28)	Age, education, smoking, alcohol, BMI, occupation, chronic disease, blood pressure

Zhang M et al, 2016, China	Xin'an County	2007-2008 - 2014, 5.88 years follow-up	17151 men and women, age ≥18 years: 479 CVD deaths	Resting heart rate, hypertensive participants	<60 60-69 70-79 80-89 ≥90	1.23 (0.77-1.95) 1.00 1.22 (0.89-1.68) 1.55 (1.09-2.19) 1.72 (1.15-2.56)	Age, education, income, alcohol, waist circumference, pulse pressure, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, fasting glucose, history of disease - dyslipidemia, diabetes, MI, heart failure, stroke
				Resting heart rate, normotensive participants	<60 60-69 70-79 80-89 ≥90	1.04 (0.52-2.10) 1.00 1.10 (0.72-1.67) 1.47 (0.94-2.29) 2.41 (1.38-4.19)	
Li K et al, 2016, China	China National Hypertension Survey	1991 - 1999, 8.3 years follow-up	6209 men and women, age ≥40 years: 676 CVD cases	Resting heart rate, <60 years	<72 72-75 76-83 ≥84	1.00 1.02 (0.64-1.63) 1.15 (0.76-1.76) 1.17 (0.75-1.80)	Age, sex, systolic blood pressure, BMI, smoking, alcohol
				Resting heart rate, ≥60 years	<72 72-75 76-83 ≥84	1.00 1.03 (0.78-1.37) 1.17 (0.91-1.51) 1.34 (1.04-1.71)	

ACE=angiotensin-converting enzyme, BMI=body mass index, bpm=beats per minute, CVD=cardiovascular disease, DBP=diastolic blood pressure, FH=family history, HDL=high-density lipoprotein, LDL=low-density lipoprotein, MI=myocardial infarction, NA=not available, NT-proBNP=N-terminal prohormone of brain natriuretic peptide, SBP=systolic blood pressure

Supplementary Table 8. Resting heart rate and total cancer

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants , gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Wannamethee G et al, 1993, UK	British Regional Heart Study	1978-1980 – 1989, 9.5 years follow-up	7496 men, age 40-59 years: 217 cancer deaths	Heart rate	<60 bpm 60-69 70-79 80-89 ≥90	1.00 1.50 (0.92-2.41) 1.67 (1.02-2.66) 2.08 (1.23-3.49) 1.65 (0.88-3.03)	Age, social class, smoking, BMI, heavy alcohol drinking, SBP, cholesterol, preexisting IHD, physical activity, forced expiratory volume
Mensink GBM et al, 1997, Germany	The Spandau Health Test	1984 – 1991 – 1994, 12 years follow-up	1827 men and 2929 women, age 40-80 years: 126 cancer deaths	Resting heart rate, men Resting heart rate, women	Per 20 bpm Per 20 bpm	1.5 (1.0-2.5) 1.1 (0.7-1.7)	Age, serum cholesterol, BMI, SBP, smoking, diabetes mellitus
Cerhan JR et al, 1999, USA	Iowa 65+ Rural Health Study	1981-1982 – 1993, 8.5 years follow-up	2819 men and women, age 65-102 years: 471 cancer cases	Resting pulse, men Resting pulse, women	<63 bpm 63-68 69-74 75-82 >83 <65 bpm 65-70 71-74 75-80 >80	1.00 1.68 (1.06-2.66) 1.54 (0.95-2.49) 1.62 (1.03-2.55) 1.66 (1.03-2.65) 1.00 1.06 (0.71-1.57) 0.84 (0.55-1.30) 1.03 (0.70-1.50) 1.15 (0.77-1.73)	Age, BMI, pack-years of smoking, and physical activity.
Greenland P et al, 1999, USA	Chicago Heart Association Detection Project	1967-1973 – 1992, 22 years follow-up	18787 men and 14994 women, age 18-74 years: 1810 cancer deaths	Resting heart rate, men, age 18-39 years Resting heart rate, men, age 40-59 years Resting heart rate, men, age 60-74 years Resting heart rate,	Per 12 bpm Per 12 bpm Per 12 bpm Per 12 bpm	1.09 (0.92-1.29) 1.17 (1.09-1.26) 1.04 (0.91-1.19) 0.99 (0.78-1.25)	Age, education, serum cholesterol, smoking, BMI, BMI ² , major and minor ECG abnormalities, race, diabetes mellitus, SBP

				women, age 18-39 years Resting heart rate, women, age 40-59 years Resting heart rate, women, age 60-74 years	Per 12 bpm Per 12 bpm	1.13 (1.03-1.24) 0.94 (0.78-1.11)	
Kristal-Boneh E et al, 2000, Israel	CORDIS Study	1985-1987 - 1994, 8 years follow-up	3527 men, mean age 43 years: 43 cancer deaths	Resting heart rate	<70 bpm 70-79 80-89 ≥90	1.00 0.86 (0.3-2.0) 1.55 (0.7-3.5) 1.13 (0.4-3.0)	Age, education, smoking, sport, hemoglobin
Dekker JM et al, 2000, USA	Atherosclerosis Risk in Communities (ARIC) Study	1987-1989 – 1993, ~5 years follow-up	14672 men and women, age 45-65 years: 173 cancer deaths	Heart rate	<63 bpm 63-<72 ≥72	1.00 1.04 (0.62-1.76) 1.39 (0.86-2.25)	Age, sex, race, field center, current smoking, cigarette-years, triglycerides, HDL cholesterol, diabetes, hypertension, BMI, waist-to-hip ratio, carotid intima- media thickness
Reunanen A et al, 2000, Finland	Finnish Mobile Clinic Health Examination Survey	1966-1972 – 1993, 23 years follow-up	5598 men and 5119 women, age 30-59 years: 364/215 cancer deaths	Heart rate, men Heart rate, women	60 bpm 61-83 ≥84 66 bpm 67-93 ≥94	1.00 0.90 (0.69-1.18) 0.89 (0.64-1.24) 1.00 0.88 (0.63-1.24) 1.06 (0.70-1.60)	Age, smoking, blood pressure, cholesterol, diabetes, BMI, perceived health, occupational and leisure time physical activity
Nilsson PM et al, 2001, Sweden	Malmö Preventive Project	1974-1992 - 1997, 17/12 years follow-up (men/ women)	13466 men and 9467 women, age NA: 629/215 cancer deaths	Heart rate, men Heart rate, women	Per 20 bpm Per 20 bpm	1.12 (0.95-1.31) 0.91 (0.66-1.24)	Age, serum cholesterol, BMI, systolic blood pressure, smoking, problematic alcohol drinking habits
Kado DM et al, 2002, USA	Study of Osteoporotic Fractures	1986-1988 – 1998, 8.9 years follow-up	9702 women, age ≥65 years: 580 cancer deaths	Resting heart rate	>80 vs. <80 bpm Per 10 bpm	1.20 (0.90-1.50) 1.13 (1.04-1.22)	Age, weight, self-reported health, physical activity, hyperthyroidism, hypertension, diabetes mellitus, current smoking
Batty GD et al, 2010, United Kingdom	Whitehall study	1967-1970 - 2008, 40 years follow-up	1183 men, age 40-69 years: 244 cancer deaths	Heart rate	≤64 bpm 65-74 ≥75	1.00 1.10 (0.81-1.49) 1.08 (0.79-1.49)	Age, employment grade, SBP, plasma cholesterol, smoking, BMI, glucose intolerance, diabetes, FEV1

Jouven X et al, 2011, France	Paris Prospective Study	1967-1972 - 1994, 25 years follow-up	6101 men, age 42-53 years: 758 cancer deaths	Resting heart rate	<60 bpm 60-67 68-73 ≥74	1.0 1.6 (1.2-2.0) 1.6 (1.3-2.0) 2.4 (1.9-2.9)	Age, smoking
Ganna A et al, 2015, United Kingdom	UK Biobank Study	2007-2010 – 2014, 4.9 years follow-up	498103 men and women, age 37-73 years: 2795/2288 cancer deaths	Resting heart rate, men Resting heart rate, women	30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0 30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0	1.0 1.2 (1.1-1.4) 1.4 (1.2-1.6) 1.6 (1.4-1.8) 2.2 (2.0-2.5) 0.7 (0.6-0.8) 0.8 (0.7-0.9) 0.9 (0.8-1.0) 1.0 1.4 (1.3-1.6)	Age

BMI=body mass index, bpm=beats per minute, ECG=echocardiography, FEV1=forced expiratory volume in 1 second, HDL=high-density lipoprotein, IHD=ischemic heart disease, SBP=systolic blood pressure

Supplementary Table 9. Resting heart rate and mortality

Author, publication year, country	Study name	Study period, duration of follow-up	Number of participants, gender, age, number of cases/deaths	Exposure and subgroup	Heart rate level	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Gillum RF et al, 1991, USA	National Health and Nutrition Examination Survey 1	1971-1975 – NA, 9.9/10.3 years follow-up (whites/blacks)	5995 men and women, age 45-74 years: 1320 deaths	Pulse rate, whites, men Pulse rate, whites, women Pulse rate, blacks, men Pulse rate, blacks, women	<74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84 <74 bpm 74-84 >84	1.00 1.13 (0.93-1.37) 1.67 (1.37-2.03) 1.00 1.00 (0.79-1.26) 1.13 (0.89-1.42) 1.00 1.33 (0.90-1.97) 1.71 (1.14-2.56) 1.00 1.52 (0.93-2.50) 1.95 (1.16-3.27)	Age, smoking, SBP, serum total cholesterol, diabetes
Hoes AW et al, 1993, Netherlands	Zoetermeer	1975-1978 – 1987, 9-12 years follow-up	6057 men and women, age ≥20 years: 307/270 deaths	Pulse rate, men Pulse rate, women	Per 10 bpm Per 10 bpm	1.10 (1.01-1.20) 1.02 (0.93-1.13)	Age, BMI, SBP, serum uric acid, serum creatinine, current cigarette use, antihypertensive drugs, diabetes mellitus, myocardial infarction, stroke
Mensink GBM et al, 1997, Germany	The Spandau Health Test	1984 – 1991 – 1994, 12 years follow-up	1827 men and 2929 women, age 40-80 years: 412 deaths	Resting heart rate, men Resting heart rate, women	Per 20 bpm Per 20 bpm	1.7 (1.4-2.2) 1.4 (1.1-1.8)	Age, serum cholesterol, BMI, SBP, smoking, diabetes mellitus
Greenland P et al, 1999, USA	Chicago Heart Association Detection Project	1967-1973 – 1992, 22 years follow-up	18787 men and 14994 women, age 18-74 years: 4977 deaths	Resting heart rate, men, age 18-39 years Resting heart rate, men, age 40-59 years Resting heart rate, men, age 60-74 years Resting heart rate,	Per 12 bpm Per 12 bpm Per 12 bpm Per 12 bpm	1.04 (0.95-1.14) 1.11 (1.06-1.15) 1.03 (0.96-1.11) 0.97 (0.82-1.14)	Age, education, serum cholesterol, smoking, BMI, BMI ² , major and minor ECG abnormalities, race, diabetes mellitus, SBP

				women, age 18-39 years Resting heart rate, women, age 40-59 years Resting heart rate, women, age 60-74 years	Per 12 bpm Per 12 bpm	1.15 (1.08-1.22) 0.97 (0.88-1.07)	
Benetos A et al, 1999, France	Centre d'Investigation s Pre'ventives et Cliniques (IPC)	1974-1977 – 1994, 18.2 years follow- up	19386 men and women, age 40-69 years: 2036/610 deaths	Heart rate, men Heart rate, women	<60 bpm 60-80 >80-100 >100 <60 bpm 60-80 >80-100 >100	1.00 1.18 (1.00-1.37) 1.54 (1.29-1.84) 1.97 (1.50-2.58) 1.00 1.55 (1.05-2.30) 1.60 (1.04-2.44) 1.90 (1.09-3.31)	Age, SBP, DBP, BMI, history of MI, antihypertensive treatment, total cholesterol, physical activity, tobacco
Dekker JM et al, 2000, USA	Atherosclerosi s Risk in Communities (ARIC) Study	1987-1989 – 1993, ~5 years follow-up	14672 men and women, age 45-65 years: 443 deaths	Heart rate	<63 bpm 63-<72 ≥72	1.00 1.02 (0.66-1.58) 1.71 (1.14-2.55)	Age, sex, race, field center, current smoking, cigarette-years, triglycerides, HDL cholesterol, diabetes, hypertension, BMI, waist-to-hip ratio, carotid intima- media thickness
Kristal-Boneh E et al, 2000, Israel	CORDIS Study	1985-1987 - 1994, 8 years follow-up	3527 men, mean age 43 years: 135 deaths	Resting heart rate	<70 bpm 70-79 80-89 ≥90	1.00 0.95 (0.6-1.6) 1.45 (0.9-2.4) 2.23 (1.4-3.6)	Age, education, smoking, BMI, cholesterol, sport, hemoglobin
Reunanen A et al, 2000, Finland	Finnish Mobile Clinic Health Examination Survey	1966-1972 – 1993, 23 years follow-up	5598 men and 5119 women, age 30-59 years: 1848/840 deaths	Heart rate, men Heart rate, women	≤60 bpm 61-83 ≥84 ≤66 bpm 67-93 ≥94	1.00 1.11 (0.96-1.27) 1.10 (0.93-1.30) 1.00 1.03 (0.85-1.26) 1.23 (0.97-1.55)	Age, smoking, blood pressure, cholesterol, diabetes, BMI, perceived health, occupational and leisure time physical activity
Nilsson PM et al, 2001, Sweden	Malmö Preventive Project	1974-1992 - 1997, 17/12 years follow- up (men/ women)	13466 men and 9467 women, age NA: 1902/397 deaths	Heart rate, men Heart rate, women	Per 20 bpm Per 20 bpm	1.38 (1.26-1.50) 1.05 (0.84-1.31)	Age, serum cholesterol, BMI, systolic blood pressure, smoking, problematic alcohol drinking habits
Seccareccia F et al, 2001, Italy	Malattie Cardiovascolari Aterosclerotiche, Istituto	1984-1993 – 1997, 9.7 years follow- up	2533 men, age 40-69 years: 393 deaths	Heart rate	<60 bpm 60-69 70-79 80-89 ≥90	1.00 1.16 (0.87-1.55) 1.61 (1.18-2.20) 1.38 (0.93-2.06) 2.67 (1.76-4.04)	Age, SBP, serum cholesterol, cigarettes, BMI, arm circumference, FEV, diabetes mellitus, preexisting CVD

	Superiore di Sanità (MATISS) Project						
Fujiura Y et al, 2001, Japan	Tanushimaru Survey	1977-1994, 18 years follow-up	573 men, age 40-64 years: 82 deaths	Resting heart rate	<60 bpm 60-69 70-79 80-89 ≥90	1.20 (0.59-2.43) 1.00 1.41 (0.72-2.78) 2.13 (0.91-4.97) 3.71 (1.35-10.22)	Age, DBP, serum cholesterol, uric acid, antihypertensive medication status
Kado DM et al, 2002, USA	Study of Osteoporotic Fractures	1986-1988 – 1998, 8.9 years follow-up	9702 women, age ≥65 years: 1947 deaths	Resting heart rate	>80 vs. 80 bpm Per 10 bpm	1.40 (1.20-1.50) 1.12 (1.07-1.17)	Age, weight, self-reported health, physical activity, hyperthyroidism, hypertension, diabetes mellitus, current smoking
Chang M et al, 2003, USA	The Women's Health and Aging Study	NA-NA, 3 years follow-up	942 women, age ≥65 years: NA deaths	Heart rate	≥90 vs. <60 bpm	2.0 (1.2-3.3)	Age, disease status, cardiovascular risk factors, physical activity, and physical and pulmonary function
Perk G et al, 2003, Israel	The Jerusalem 70-year-old Longitudinal Study	1990-1991 – NA, 6 years follow-up	422 men and women, age 69-71 years: 68 deaths	Heart rate, women, standing Heart rate, women, sitting Heart rate, women, ECG Heart rate, men, standing Heart rate, men, sitting Heart rate, men, ECG	>77 vs. ≤77 bpm >77 vs. ≤77 bpm >77 vs. ≤77 bpm >77 vs. ≤77 bpm >77 vs. ≤77 bpm >77 vs. ≤77 bpm	3.37 (0.96-11.8) 3.20 (1.01-13.2) 3.71 (1.41-9.80) 1.2 (0.5-3.2) 1.1 (0.51-5.2) 1.3 (0.81-5.8)	IADLs, cognitive problems, anemia, CHD, cerebrovascular disease, CHF, cancer, hypertension, renal disease, diabetes mellitus, respiratory diagnosis, BMI, smoking status, social status, physical activity
Okamura T et al, 2004, Japan	National Survey on Circulatory Disorders (NIPPON-DATA 80 study)	1980-1998, 16.5 years follow-up	8800 men and women, age ≥30 years: 875/731 deaths	Heart rate, men, age 30-59 years Heart rate, men, age ≥60 years Heart rate, women, age 30-59 years	55 bpm 63 69 82 Per 11 bpm 55 bpm 63 69 82 Per 11 bpm 59 bpm 67 73 86 Per 11 bpm	1.00 0.86 (0.69-1.22) 1.18 (0.85-1.63) 1.45 (1.06-2.00) 1.21 (1.08-1.36) 1.00 1.03 (0.82-1.30) 0.97 (0.76-1.24) 1.14 (0.90-1.43) 1.05 (0.97-1.15) 1.00 1.20 (0.75-1.91) 1.83 (1.19-2.80) 1.94 (1.26-3.01) 1.19 (1.04-1.35)	Age, serum albumin, BMI, hypertension, hypercholesterolemia, diabetes mellitus, smoking, drinking

				Heart rate, women, age ≥60 years	59 bpm 67 73 86 Per 11 bpm	1.00 0.78 (0.61-1.01) 0.92 (0.73-1.16) 0.93 (0.73-1.19) 0.99 (0.91-1.08)	
Tice JA et al, 2006, USA	The Breast and Bone Follow-up Study of the Fracture Intervention Trial (B-FIT)	1990-1992 – 2001, 9 years follow-up	17748 post- menopausal women, age 55-80 years: 1886 deaths	Heart rate	≤63 bpm 64-68 69-72 73-78 >78	1.0 1.0 (0.8-1.1) 1.0 (0.9-1.2) 1.1 (1.0-1.3) 1.3 (1.1-1.4)	Age, hypertension, diabetes mellitus, heart disease, stroke, breast cancer, hormone replacement therapy, weight loss, self-reported health status, smoking history, alcohol, physical function scale, waist-to-hip ratio, SBP, BMI, timed up and go test, grip strength
Fisher AA et al, 2006, Australia	Canberra, Australia	1999 - 2004, 4.7 years follow-up	179 men and women, age 65 years: 97 deaths	Resting heart rate	≤60 bpm 61-89 ≥90	1.00 1.46 (0.71-2.99) 1.19 (0.45-3.18)	Age, sex
Savonen KP et al, 2006, Finland	Kuopio Ischaemic Heart Disease Risk Factor Study	1984-1989 - 1998, 11.4 years follow- up	1378 men, age 42-61 years: 146 deaths	Resting heart rate	Per 13 bpm	1.08 (0.92-1.27)	Age, examination year, alcohol, BMI, cigarette smoking, CVD history, diabetes, serum low-density lipoprotein cholesterol, systolic blood pressure at rest, myocardial ischaemia during exercise
Theobald H et al, 2007, Sweden	Stockholm County	1969-1970 – 1996, 26 years follow-up	2445 men and women, age 18-64 years: 337/238 deaths	Heart rate, men Heart rate, women	>75 vs. ≤75 bpm >75 vs. ≤75 bpm	1.57 (1.05-2.35) 0.82 (0.48-1.41)	Age, exercise test, hypertension, smoking, BMI, care need
Cacciatore F et al, 2007, Italy	Osservatorio Geriatrico Regione Campania	1991 – 2003, 12 years follow-up	1163 men and women, mean age 74.2 years: 668 deaths	Heart rate	High vs. Low	0.69 (0.27-1.73)	Age, sex, diabetes, neurological disease, SBP, DBP, CAD, HF, comorbidity, ACE inhibitors, nitrates, digoxin, amiodaron, calcium channels blockers, physical activity, BMI, smoking, alcohol
Hansen TW et al, 2008, Denmark, Sweden, Belgium, Japan, China, Uruguay	The International Database on Ambulatory Blood	NA-NA, 9.6 years follow- up	6928 men and women, age ≥18 years: 852 deaths	Heart rate	Per 11.6 bpm	1.14 (1.04-1.25)	Age, systolic blood pressure, cohort, BMI, smoking, alcohol, serum total cholesterol, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs

	Pressure Monitoring in Relation to Cardiovascular Outcomes (IDACO)						
Adabag AS et al, 2008, USA	Multiple Risk Factor Intervention Trial	1973-1976 – 1999, 25 years follow-up	12555 men, age 35-57 years: 4642 deaths	Resting heart rate	<65 bpm 65-71 72-79 ≥80	1.00 1.02 (0.94-1.11) 1.02 (0.94-1.11) 1.17 (1.07-1.27)	Age, cigarettes smoked per day, SBP, low-density lipoproteincholesterol, high-density lipoproteincholesterol, triglycerides, body mass index, fasting glucose, race, and parental history of CHD
Kuzuya M et al, 2008, Japan	Nagoya Longitudinal Study of the Frail Elderly (NLS-FE)	NA-NA, 3 years follow-up	932 men and women, mean age 80.4 years: NA	Resting pulse rate	61.5 bpm 70.8 77.6 88.1	1.56 (1.07-2.28) 1.00 1.58 (1.08-2.32) 2.53 (1.53-3.21)	Age, sex, ADL score, SBP, DBP, presence of chronic disease
Hozawa A et al, 2008, Japan	Ohasama study	1988-1994 – 2004, 12 years follow-up	1444 men and women, age ≥40 years: 296 deaths	Daytime heart rate	<68.2 bpm 68.3-73.5 73.6-78.7 ≥78.8	1.00 1.11 (0.81-1.52) 1.13 (0.80-1.60) 1.09 (0.78-1.54)	Age, sex, antihypertensive medication, smoking, diabetes mellitus, hyperlipidemia, SBP
Kikuya M et al, 2008, Japan	Ohasama Study	1987-1995 – 2004, 11.9 years follow-up	2455 men and women, age 35-96 years: 462 deaths	Resting heart rate	Per 7.8 bpm	1.21 (1.11-1.31)	Age, sex, obesity, smoking, drinking, CVD history, diabetes mellitus, hyperlipidemia, treatment with antihypertensive drugs
Tverdal A et al, 2008, Norway	Norwegian Health Surveys	1985-1999 – 2005, 12.6 years follow-up	180353 men and 199490 women, age 40-45 years: 8951 deaths	Heart rate, men Heart rate, women	<65 bpm 65-79 80-94 ≥95 Per 10 bpm <65 bpm 65-79 80-94 ≥95 Per 10 bpm	1.00 1.05 (0.97-1.13) 1.21 (1.11-1.33) 1.82 (1.62-2.04) 1.14 (1.11-1.17) 1.00 1.06 (0.94-1.19) 1.28 (1.13-1.44) 1.37 (1.19-1.59) 1.09 (1.06-1.12)	Age, calendar year, total cholesterol, triglycerides, DBP, smoking, physical activity, family history of CVD
Cooney MT et al,	National	1982, 1987,	10519 men	Heart rate, men	≤60 bpm	1.00	Age, smoking status, SBP, total

2010, Finland	FINRISK Study	1992, 1997, 2002 – 2003, 12 years follow-up	and 11334 women, age 25-74 years: NA	Heart rate, women	62-90 >90 Per 15 bpm ≤60 bpm 62-90 >90 Per 15 bpm	1.23 (1.03-1.46) 1.76 (1.38-2.25) 1.19 (1.11-1.28) 1.00 1.30 (0.98-1.73) 1.71 (1.17-2.48) 1.21 (1.09-1.34)	cholesterol, diabetes mellitus, BMI, HDL cholesterol, physical activity
Batty GD et al, 2010, United Kingdom	Whitehall study	1967-1970 - 2008, 40 years follow-up	1183 men, age 40-69 years: 940 deaths	Heart rate	≤64 bpm 65-74 ≥75	1.00 1.11 (0.95-1.30) 1.17 (0.99-1.37)	Age, employment grade, SBP, plasma cholesterol, smoking, BMI, glucose intolerance, diabetes, FEV1
Legeai C et al, 2011, France	The Three-City Study	1999-2001 – NA, 4.9 years follow-up	7147 men and women, age ≥65 years: 615 deaths	Resting heart rate	<62 bpm 62-67.5 68-72.5 73-79 >79	1.00 0.92 (0.69-1.23) 1.35 (1.02-1.79) 1.05 (0.77-1.43) 1.74 (1.32-2.29)	Age, sex, study centre, SBP, smoking status, wine, fish, BMI, total cholesterol, HDL cholesterol, diabetes mellitus, previous CVD, living alone, disability status, beta-blocker use, calcium antagonist use
Jensen MT et al, 2011, Denmark	Copenhagen City Heart Study	1976-1978 – 2009, 21.2 years follow-up	16516 men and women, age ≥20 years: 8709 deaths	Resting heart rate, never smokers Resting heart rate, former smokers Resting heart rate, moderate smokers Resting heart rate, heavy smokers	Per 10 bpm Per 10 bpm Per 10 bpm Per 10 bpm	1.06 (1.01-1.10) 1.11 (1.07-1.15) 1.13 (1.09-1.16) 1.13 (1.10-1.16)	Age, leisure time physical activity, BMI, SBP, pulmonary function, alcohol, triglycerides
Nabi H et al, 2011, United Kingdom	Whitehall II Prospective Cohort Study	1985 – 2009, 5.6 years follow-up	5936 men, age 35-55 years: 170 deaths	Resting heart rate	<60 bpm 60-80 >80	0.75 (0.49-1.15) 1.00 1.67 (1.14-2.45)	Age, sex, ethnicity, SES, BMI, alcohol, smoking status, exercise, hypertension, antihypertensive drugs, total cholesterol, diabetes, CVD medication, antidepressant medication, lipid lowering medication, history of CHD, depression
Puddu PE et al, 2011, Europe	Seven Countries Study	1960-NA, 25-40 years follow-up	6554 men, age 40-59 years: 5590 deaths	Heart rate	Per 12.51 bpm	1.07 (1.04-1.10)	Age, study, father status, mother status, SES, physical activity, cigarettes per day, BMI, arm circumference, mean blood pressure, serum cholesterol, FEV, ECG abnormalities
Jouven X et al, 2011, France	Paris Prospective	1967-1972 - 1994, 25 years	6101 men, age 42-53	Resting heart rate	<60 bpm 60-67	1.0 1.3 (1.2-1.6)	Age, smoking

	Study	follow-up	years: 1635 deaths		68-73 ≥74	1.5 (1.3-1.8) 2.1 (1.8-2.4)	
Leistner DM et al, 2012, Germany	Diabetes Cardiovascular Risk Evaluation Targets and Essential Data for Commitment of Treatment (DETECT) cohort study	2003-2008, 5 years follow-up	5320 men and women, mean age 55.9 years: 137 deaths	Resting heart rate	35-66 bpm 67-72 73-80 81-120	1.00 1.11 (0.66-1.86) 1.44 (0.85-2.44) 1.58 (0.86-2.92)	Age, sex, atrial fibrillation, rate control medication, diabetes mellitus, hypertension, smoking status, family history of coronary artery disease, hyperlipidemia, BMI
Pittaras AM et al, 2013, USA	Veterans Affairs Medical Centers	1986-2011, 10 years follow-up	18462 men, mean age 58 years: 5100 deaths	Resting heart rate	<60 beats/min 60-69 70-79 80-89 90-99 ≥100 Per 1 beat/min	1.00 1.04 (0.94-1.14) 1.14 (1.04-1.25) 1.21 (1.09-1.33) 1.45 (1.29-1.63) 1.49 (1.29-1.73) 1.009 (1.006-1.011)	Age, blood pressure, BMI, hypertension, diabetes mellitus, smoking, dyslipidemia, atrial fibrillation or flutter, CVD, cardiac medications, alcohol or drug abuse, ethnicity, lipid-lowering agents, hypoglycemic agents, sleep apnea, muscle-wasting disease, METs
Jensen MT et al, 2013, Denmark	Copenhagen Male Study	1985-1986 - 2001, 16 years follow-up	2798 men and women, age 53-75 years: 1082 deaths	Heart rate	≤50 bpm 51-60 61-70 71-80 81-90 >90	1.00 1.40 (1.06-1.85) 1.46 (1.10-1.93) 1.51 (1.11-2.06) 2.04 (1.43-2.92) 3.06 (1.97-4.75)	Age, VO ₂ Max, leisure-time physical activity, tobacco, alcohol, BMI, SBP, DBP, serum triglycerides, serum total cholesterol, social class
Johansen CD et al, 2013, Denmark	Copenhagen Holter Study	1998-2000 – NA, 6.3 years follow-up	653 men and women, age 55, 60, 65, 70, 75 years: 80 deaths	Resting heart rate	Per 5 bpm	1.11 (1.01-1.22)	Age, SBP, age, sex, smoking, diabetes, and total cholesterol, high-sensitive C-reactive protein and NT-proBNP, use of b-blockers, use of ACE-inhibitors/angiotensin II receptor blockers, diuretics, and calcium channel blockers
Saxena A et al, 2013, USA	Aerobics Center Longitudinal Study	1974-2002 – 2003, 15 years follow-up	53322 men and women, age ≥20 years: 3125 deaths	Resting heart rate	<60 bpm 60-69 70-79 ≥80	1.00 0.93 (0.86-1.02) 0.99 (0.90-1.10) 1.38 (1.21-1.58)	Age, sex, examination year, BMI, smoking status, heavy alcohol drinking, physical activity, parental cardiovascular disease, abnormal ECG findings, diabetes, high blood pressure, hypertension, hypercholesterolemia

Stessman J et al, 2013, Israel	Jerusalem Longitudinal Cohort Study	1990, 1998, 2005-2010, NA	2353 men and women, age 70, 78, 85 years: 635 deaths	Resting pulse rate, age 70-77 Resting pulse rate, age 78-84 Resting pulse rate, age 85-90	Per 10 bpm Per 10 bpm Per 10 bpm	1.13 (0.87-1.47) 1.35 (1.11-1.65) 1.17 (1.01-1.37)	Sex, education, diabetes mellitus, IHD, CHF, hypertension, renal disease, anemia, self-rated health, BMI, dementia, physical activity, beta-blocker use, beta-blocker x resting pulse interaction term
Woodward M et al, 2014, Asia	Asia Pacific Cohort Studies Collaboration (12 cohort studies)	NA-NA, 7.4 years follow-up	112680 men and women, age ≥20 years: 6086 deaths	Resting heart rate	<65 bpm 65-71.9 72-79.9 ≥80 Per 10 bpm	1.00 1.10 (1.02-1.19) 1.24 (1.15-1.34) 1.54 (1.43-1.66) 1.40 (1.33-1.48)	Age, sex, SBP, cohort
O'Hartaigh BO et al, 2014, USA	Cardiovascular Health Study	1989-1993 – NA, 7.9 years follow-up	5691 men and women, age ≥65 years: 974 deaths	Resting heart rate	65 bpm 75 85 95 105 115 125 Per 10 bpm	1.00 1.30 (1.23-1.37) 1.69 (1.52-1.87) 2.19 (1.87-2.55) 2.84 (2.30-3.49) 3.68 (2.83-4.77) 4.78 (3.49-6.52) 1.33 (1.26-1.40)	Age, sex, smoking, exercise intensity, education, BMI, type 2 diabetes mellitus, C-reactive protein, interleukin-6, CHD, CHF, ACE-inhibitors, aspirin
O'Hartaigh B et al, 2014, United Kingdom	National Survey of Health and Development	1971-2012, 40 years follow-up	4638 men and women, age 43: 246 deaths	Resting heart rate at age 43 years	≤63 bpm 64-68 69-72 73-80 ≥81 Per 10 bpm	1.00 1.13 (0.71-1.80) 1.68 (1.06-2.64) 1.36 (0.87-2.13) 2.17 (1.40-3.36) 1.27 (1.13-1.44)	Sex, blood pressure, BMI, own occupational class, leisure-time physical activity, smoking and antihypertensive treatment
Ho JE et al, 2014, USA	Framingham Heart Study and Framingham Offspring Study	1986-1990/ 1987-1991 – NA, 19 years follow-up	4058 men and women, mean age 55 years: 1186 deaths	Resting heart rate	Per 11 bpm	1.17 (1.11-1.24)	Age, sex, SBP, use of antihypertensive treatment, BMI, diabetes, smoking status, physical activity index, valvular heart disease, ECG left ventricular hypertrophy, total/HDL cholesterol ratio, minor cardiovascular diseases, PR interval and QRS duration
Aladin AI et al, 2014, USA	Henry Ford Exercise Testing Project	1991-2009, 11.1 years follow-up	56634 men and women, age ≥18 years: 6255 deaths	Resting heart rate, all Resting heart rate, men	<60 bpm 60-69 70-79 80-89 ≥90 <60 bpm 60-69	1.00 0.97 (0.89-1.05) 1.03 (0.94-1.12) 1.10 (0.99-1.20) 1.22 (1.10-1.35) 1.00 0.99 (0.89-1.10)	Age, sex, race, SBP, DBP, hypertensive medication use, history of dyslipidemia, lipid lowering medication use, smoking, pulmonary disease medication, diabetes, family history of coronary artery disease, obesity, reason for stress test, atrioventricular-nodal blocking

				Resting heart rate, women	70-79 80-89 ≥90 <60 bpm 60-69 70-79 80-89 ≥90	1.08 (0.97-1.21) 1.18 (1.04-1.32) 1.29 (1.12-1.47) 1.00 0.93 (0.81-1.07) 0.92 (0.80-1.07) 0.97 (0.84-1.13) 1.10 (0.93-1.29)	medication, METs in exercise test
Wang A et al, 2014, China	Kailuan Study	2006-2007 – 2010, 4.0 years follow-up	92562 men and women, age 18-98 years: 1589 deaths	Resting heart rate	<66 bpm 67-70 71-74 75-80 ≥81 Per 10 bpm	1.00 1.15 (0.97-1.36) 1.23 (1.03-1.47) 1.49 (1.28-1.73) 1.70 (1.45-1.99) 1.22 (1.17-1.27)	Age, sex, average monthly income of each family member, education, marital status, BMI, waist circumference, smoking status, drinking status, physical activity
Korshoj M et al, 2015, Belgium	Belgian Physical Fitness Study	1976-1978 - NA, 16.5 years follow-up	439 men, age 40-55 years: 48 deaths	Resting heart rate	58.1 bpm 68.5 82.1 Per 1 bpm Per 10 bpm	1.00 1.09 (0.45-2.65) 1.94 (0.78-4.84) 1.03 (1.00-1.06) 1.34 (0.98-1.83)	Age, education, BMI, leisure-time physical activity, smoking, SBP, total cholesterol, occupational physical activity, cardiorespiratory fitness
Ganna A et al, 2015, United Kingdom	UK Biobank Study	2007-2010 – 2014, 4.9 years follow-up	498103 men and women, age 37-73 years: 5224/3308 deaths	Resting heart rate, men Resting heart rate, women	30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0 30.5-60.0 bpm 60.0-66.0 66.0-71.5 71.5-79.0 79.0-174.0	1.0 1.2 (1.1-1.3) 1.3 (1.2-1.4) 1.5 (1.4-1.7) 2.3 (2.1-2.5) 0.7 (0.6-0.8) 0.8 (0.7-0.9) 0.8 (0.7-0.9) 1.0 1.5 (1.4-1.7)	Age
Custodis F et al, 2016, Germany	Heinz Nixdorf RECALL study	2000-2003 - NA, 10.5 years follow-up	4091 men and women, age 45-75 years: 398 deaths	Resting heart rate	≤62 bpm 63-69 70-76 >76	1.00 0.94 (0.67-1.30) 1.31 (0.96-1.79) 1.64 (1.22-2.22)	Age, sex, hypertension, current smoking, diabetes, BMI, known peripheral artery disease, lipid-lowering medication, heart rate lowering medication, LDL-cholesterol, coronary artery calcification

Sharashova E et al, 2016, Norway	The Tromsø Study	1994-1995 - 2012, 18 years follow-up	24489 men and women, age ≥25 years: 1918/1796 deaths	Resting heart rate, men Resting heart rate, women	50 60 70 80 90 100 50 60 70 80 90 100	0.64 (0.58-0.72) 0.80 (0.76-0.84) 1.00 1.24 (1.20-1.30) 1.50 (1.40-1.62) 1.72 (1.52-1.94) 0.75 (0.69-0.80) 0.86 (0.83-0.90) 1.00 1.16 (1.12-1.20) 1.34 (1.25-1.44) 1.55 (1.39-1.73)	Age, SBP, total cholesterol, HDL cholesterol, triglycerides, BMI, physical activity, smoking
Ryu M et al, 2016, Korea	Kangwha Cohort Study	1985 – 2005, 20.8 years follow-up	6100 men and women, age 55-99 years: 1990/2075 deaths	Resting heart rate, men Resting heart rate, women	≤60 bpm 61-79 ≥80 ≤60 bpm 61-79 ≥80	1.08 (0.92-1.27) 1.00 1.10 (1.00-1.21) 1.09 (0.94-1.27) 1.00 1.20 (1.07-1.33)	Age, education, smoking, alcohol, BMI, occupation, chronic disease, blood pressure
Skov MW et al, 2016, Denmark	The Copenhagen Electrocardiographic Study	2001-2011 - 2013, 8.4 years follow-up	281451 men and women, age 42-67 years: 37793 deaths	Resting heart rate	30-51 52-59 60-65 66-72 73-80 81-94 95-120	0.69 (0.64-0.74) 0.75 (0.72-0.79) 0.87 (0.84-0.90) 1.00 1.19 (1.15-1.23) 1.51 (1.46-1.56) 2.14 (2.06-2.23)	Age, sex, hypertension, heart failure, myocardial infarction, valvular heart disease, diabetes, hyperthyroidism, ECG criteria of left ventricular hypertrophy, treatment with heart-rate lowering medication at the date of index ECG
Parikh KS et al, 2016, USA	Jackson Heart Study	2000-2011 - 2015, 8.9 years follow-up	5261 African American men and women, median age 55.8 years: 510 deaths	Resting heart rate	30-55 56-60 61-66 67-72 72-118 Per 5 bpm	1.00 1.29 (0.95-1.76) 1.50 (1.10-2.04) 1.42 (1.03-1.95) 2.38 (1.78-3.19) 1.14 (1.10-1.19)	Age, sex, prior MI, heart failure, hypertension, stroke, diabetes, lung disease, current smoking, prior smoking, alcohol, physical activity, caffeine intake, BMI, neck circumference, SBP, sodium, estimated glomerular filtration rate, hemoglobin, ejection fraction, left ventricular hypertrophy, left ventricular dimension, left bundle-branch block, right bundle-branch block, QRS interval duration, use of angiotensin-converting enzyme inhibitor or angiotensin 2 receptor blocker, antiarrhythmic agent, antiplatelet agent, beta-blocker, calcium

							channel blocker, digoxin, diuretic, statin
Li K et al, 2016, China	China National Hypertension Survey	1991 - 1999,	6209 men and women, age ≥40 years: 840 deaths	Resting heart rate, <60 years Resting heart rate, ≥60 years	<72 72-75 76-83 ≥84 <72 72-75 76-83 ≥84	1.00 1.48 (0.92-2.37) 1.16 (0.73-1.85) 1.23 (0.76-1.97) 1.00 1.26 (0.99-1.62) 1.34 (1.07-1.68) 1.61 (1.29-2.01)	Age, sex, systolic blood pressure, BMI, smoking, alcohol
Alhalabi L et al, 2017, USA	National Health and Nutrition Examination Survey 3	1988-1994 - 2006, 13.9 years follow-up	6743 men and women, mean age 58.7 years: 2212 deaths	Resting heart rate	Per 10 bpm	1.20 (1.16-1.24)	Age, sex, race, hypertension, diabetes, obesity, dyslipidemia, previous CVD, smoking, cancer, chronic obstructive pulmonary disease, thyroid disease, serum creatinine

ACE=angiotensin-converting enzyme, ADL=activities of daily living, BMI=body mass index, bpm=beats per minute, CAD=coronary artery disease, CHD=coronary heart disease, CHF=congestive heart failure, CVD=cardiovascular disease, DBP=diastolic blood pressure, ECG=echocardiography, FEV=forced expiratory volume, FEV1=forced expiratory volume in 1 second, HDL=high-density lipoprotein, HF=heart failure, IADLs=instrumental activities of daily living, IHD=ischemic heart disease, MET=metabolic equivalent task, MI=myocardial infarction, NA=not available, NT-proBNP=N-terminal prohormone of brain natriuretic peptide, VO₂-max=maximal volume of oxygen uptake, SBP=systolic blood pressure, SES=socio-economic status, WHR=waist-to-hip ratio

Supplementary Table 10: Table of relative risks from the nonlinear dose-response analysis

Outcome bpm	Coronary heart disease	Sudden cardiac death	Heart failure	Atrial fibrillation	Stroke	Cardiovascular disease	Total cancer	All-cause mortality
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
40	0.92 (0.91-0.92)	-	0.97 (0.95-0.99)	1.04 (1.02-1.05)	0.88 (0.83-0.92)	0.89 (0.88-0.90)	0.92 (0.91-0.93)	0.85 (0.81-0.90)
50	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
60	1.10 (1.09-1.10)	1.60 (0.93-2.74)	1.06 (1.04-1.07)	0.98 (0.97-0.99)	1.10 (1.07-1.13)	1.13 (1.12-1.14)	1.09 (1.08-1.09)	1.19 (1.14-1.26)
70	1.20 (1.19-1.21)	2.21 (1.06-4.64)	1.14 (1.11-1.17)	0.98 (0.96-1.00)	1.17 (1.14-1.21)	1.28 (1.26-1.29)	1.19 (1.18-1.20)	1.44 (1.30-1.59)
80	1.31 (1.30-1.32)	2.63 (1.27-5.46)	1.26 (1.21-1.31)	1.02 (1.00-1.05)	1.24 (1.20-1.28)	1.44 (1.41-1.46)	1.29 (1.26-1.32)	1.75 (1.50-2.03)
90	1.43 (1.41-1.46)	2.89 (1.47-5.66)	1.43 (1.35-1.53)	1.11 (1.08-1.14)	1.29 (1.26-1.32)	1.62 (1.58-1.66)	1.40 (1.34-1.47)	2.13 (1.74-2.61)
100	1.56 (1.53-1.60)	3.03 (1.57-5.86)	1.57 (1.44-1.71)	1.26 (1.22-1.31)	1.33 (1.31-1.36)	1.81 (1.75-1.88)	1.52 (1.41-1.64)	2.61 (2.03-3.37)
110	1.70 (1.65-1.76)	3.10 (1.51-6.36)	-	1.39 (1.33-1.44)	1.37 (1.36-1.39)	2.03 (1.94-2.13)	1.60 (1.45-1.77)	2.82 (2.15-3.72)
P _{nonlinearity}	<0.0001	0.30	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Sudden cardiac death min: 52.1, Heart failure max: 95.38, Total cancer max: 106.87, All-cause mortality max: 103.87

Supplementary Table 11: Subgroup analyses of resting heart rate and coronary heart disease, heart failure and stroke, per 10 bpm

	Coronary heart disease					Heart failure					Stroke				
	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²
All studies	31	1.07 (1.05-1.10)	61.9	<0.0001		8	1.18 (1.10-1.27)	74.5	<0.0001		16	1.06 (1.02-1.10)	59.5	0.001	
Duration of follow-up															
<10 yrs follow-up	12	1.11 (1.08-1.14)	25.0	0.20	0.02	3	1.37 (1.17-1.60)	36.5	0.21	0.08	7	1.09 (1.02-1.15)	76.1	<0.0001	0.42
≥10 yrs follow-up	19	1.06 (1.03-1.08)	61.9	<0.0001		5	1.13 (1.06-1.21)	73.5	0.004		9	1.04 (0.99-1.09)	27.5	0.20	
Outcome type															
Coronary heart disease	26	1.07 (1.05-1.10)	63.8	<0.0001	0.33	-				-	-				
Myocardial infarction	8	1.04 (0.99-1.10)	73.6	<0.0001		-					-				
Ischemic stroke	-					-					7	1.08 (1.02-1.14)	51.7	0.05	0.75
Hemorrhagic stroke	-					-					4	1.11 (1.01-1.21)	54.8	0.09	
Gender															
Men	18	1.06 (1.04-1.09)	63.6	<0.0001	0.16/	3	1.16 (1.06-1.28)	25.4	0.26	0.34/	6	1.04 (1.00-1.08)	0	0.89	0.09/

[illegible]

0-3		0				0.24	0				NC	0				0.009
4-6		1	1.18 (1.03-1.35)				0					1	1.32 (1.17-1.48)			
7-9		30	1.07 (1.05-1.09)	62.2	<0.0001		8	1.18 (1.10-1.27)	74.5	<0.0001		15	1.05 (1.02-1.08)	37.5	0.07	
Adjustment for confounding factors																
Age	Yes	31	1.07 (1.05-1.10)	61.9	<0.0001	NC	8	1.18 (1.10-1.27)	74.5	<0.0001	NC	16	1.06 (1.02-1.10)	59.5	0.001	0.11
	No	0					0					0				
Education	Yes	6	1.10 (1.06-1.15)	64.3	0.02	0.10	2	1.26 (0.95-1.67)	87.5	0.005	0.70	2	1.06 (1.01-1.11)	69.4	0.07	0.95
	No	25	1.06 (1.04-1.09)	53.9	0.001		6	1.17 (1.07-1.28)	74.4	0.002		14	1.07 (1.01-1.12)	61.4	0.001	
Fasting glucose	Yes	6	1.05 (1.01-1.08)	0	0.43	0.44	0				NC	3	1.06 (0.98-1.16)	16.4	0.30	0.80
	No	25	1.08 (1.05-1.10)	66.8	<0.0001		8	1.18 (1.10-1.27)	74.5	<0.0001		13	1.07 (1.02-1.11)	65.2	0.001	
Diabetes	Yes	18	1.08 (1.04-1.11)	65.0	<0.0001	0.96	7	1.17 (1.09-1.26)	75.7	<0.0001	0.23	8	1.03 (0.99-1.07)	24.7	0.23	0.21
	No	13	1.07 (1.05-1.10)	52.3	0.01		1	1.67 (1.06-2.64)				8	1.10 (1.03-1.17)	67.3	0.003	
Cardiovascular disease or ECG abnormality	Yes	9	1.06 (1.03-1.09)	0	0.71	0.70	3	1.25 (1.16-1.34)	0	0.63	0.51	5	1.07 (0.99-1.17)	48.7	0.10	0.84
	No	22	1.08 (1.05-1.10)	71.2	<0.0001		5	1.15 (1.05-1.26)	78.5	0.001		11	1.06 (1.01-1.11)	65.5	0.001	
BMI	Yes	25	1.07 (1.05-1.10)	67.0	<0.0001	0.72	7	1.17 (1.09-1.26)	75.7	<0.0001	0.23	12	1.05 (1.02-1.08)	23.1	0.22	0.19

	No	6	1.08 (1.04-1.12)	13.4	0.33		1	1.67 (1.06-2.64)				4	1.14 (0.98-1.33)	85.0	<0.0001	
Physical activity	Yes	17	1.08 (1.05-1.10)	75.2	<0.0001	0.74	4	1.25 (1.11-1.40)	77.4	0.004	0.29	9	1.04 (1.02-1.07)	12.6	0.33	0.14
	No	14	1.06 (1.03-1.09)	3.2	0.42		4	1.12 (1.01-1.24)	70.8	0.02		7	1.12 (1.01-1.25)	72.9	0.001	
Alcohol	Yes	10	1.11 (1.08-1.14)	21.5	0.25	0.02	2	1.34 (1.12-1.59)	53.9	0.14	0.18	5	1.05 (1.01-1.09)	47.2	0.11	0.47
	No	21	1.06 (1.03-1.08)	57.8	0.001		6	1.14 (1.07-1.23)	72.3	0.003		11	1.08 (1.01-1.16)	65.0	0.001	
Smoking	Yes	29	1.07 (1.05-1.10)	62.5	<0.0001	0.50	6	1.17 (1.09-1.27)	79.6	<0.0001	0.63	14	1.04 (1.01-1.07)	31.1	0.13	0.00 ²
	No	2	1.00 (0.66-1.52)	69.3	0.07		2	1.31 (0.95-1.80)	51.1	0.15		2	1.31 (1.18-1.45)	0	0.73	
Systolic blood pressure	Yes	22	1.06 (1.04-1.09)	66.4	<0.0001	0.05	6	1.21 (1.09-1.34)	81.6	<0.0001	0.69	10	1.07 (1.01-1.12)	58.6	0.01	0.98
	No	9	1.11 (1.08-1.14)	0	0.54		2	1.15 (1.09-1.21)	0	0.78		6	1.07 (0.99-1.15)	66.9	0.01	
Hypertension	Yes	10	1.07 (1.03-1.12)	39.2	0.10	0.96	6	1.14 (1.07-1.22)	70.6	0.004	0.05	6	1.05 (0.98-1.12)	44.4	0.11	0.78
	No	21	1.07 (1.05-1.10)	61.1	<0.0001		2	1.51 (1.26-1.80)	0	0.63		10	1.07 (1.02-1.12)	67.5	0.001	
Triglycerides	Yes	4	1.07 (1.03-1.11)	55.9	0.08	0.71	1	1.48 (1.22-1.79)			0.12	1	0.96 (0.88-1.05)			0.22
	No	27	1.08 (1.05-1.10)	62.5	<0.0001		7	1.15 (1.08-1.23)	69.9	0.003		15	1.07 (1.03-1.11)	57.3	0.003	
Total cholesterol	Yes	22	1.06 (1.04-1.09)	51.2	0.003	0.11	5	1.15 (1.06-1.25)	75.7	0.002	0.28	11	1.04 (0.99-1.08)	32.1	0.14	0.17
	No	9	1.10 (1.05-1.15)	63.0	0.006		3	1.34 (1.06-1.69)	76.5	0.01		5	1.12 (1.03-1.20)	80.3	<0.0001	

n denotes the number of studies.
¹ P for heterogeneity within each subgroup,
² P for heterogeneity between subgroups with meta-regression analysis,

³ P for heterogeneity between men and women (studies with genders mixed were excluded)

Supplementary Table 12: Subgroup analyses of resting heart rate and cardiovascular disease, total cancer and all-cause mortality, per 10 bpm

	Cardiovascular disease					Total cancer					All-cause mortality				
	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²	<i>n</i>	RR (95% CI)	<i>I</i> ² (%)	<i>P</i> _h ¹	<i>P</i> _h ²
All studies	35	1.15 (1.11-1.18)	84.3	<0.0001		12	1.14 (1.06-1.23)	90.2	<0.0001		48	1.17 (1.14-1.19)	94.0	<0.0001	
Duration of follow-up															
<10 yrs follow-up	17	1.19 (1.13-1.25)	83.0	<0.0001	0.05	6	1.17 (1.07-1.28)	77.1	0.001	0.53	20	1.22 (1.19-1.25)	70.0	<0.0001	0.001
≥10 yrs follow-up	18	1.12 (1.08-1.16)	85.2	<0.0001		6	1.12 (1.01-1.23)	90.5	<0.0001		28	1.13 (1.10-1.15)	91.5	<0.0001	
Gender															
Men	20	1.15 (1.10-1.19)	85.6	<0.0001	0.72/ 0.06	10	1.16 (1.06-1.27)	88.7	<0.0001	0.44/ 0.28	25	1.15 (1.12-1.19)	91.9	<0.0001	0.14/ 0.03
Women	14	1.07 (1.03-1.11)	62.8	0.001		7	1.09 (0.99-1.19)	83.1	<0.0001		15	1.08 (1.05-1.11)	60.5	0.001	
Men and women	15	1.17 (1.12-1.22)	68.5	<0.0001		1	1.21 (0.93-1.58)				21	1.21 (1.17-1.25)	90.8	<0.0001	
Outcome type															
Incidence	9	1.14 (1.08-1.20)	80.9	<0.0001	0.81	1	1.07 (0.97-1.18)			0.58	-				NC
Mortality	28	1.15 (1.11-1.19)	84.7	<0.0001		11	1.15 (1.06-1.24)	90.9	<0.0001		48	1.17 (1.14-1.19)	94.0	<0.0001	

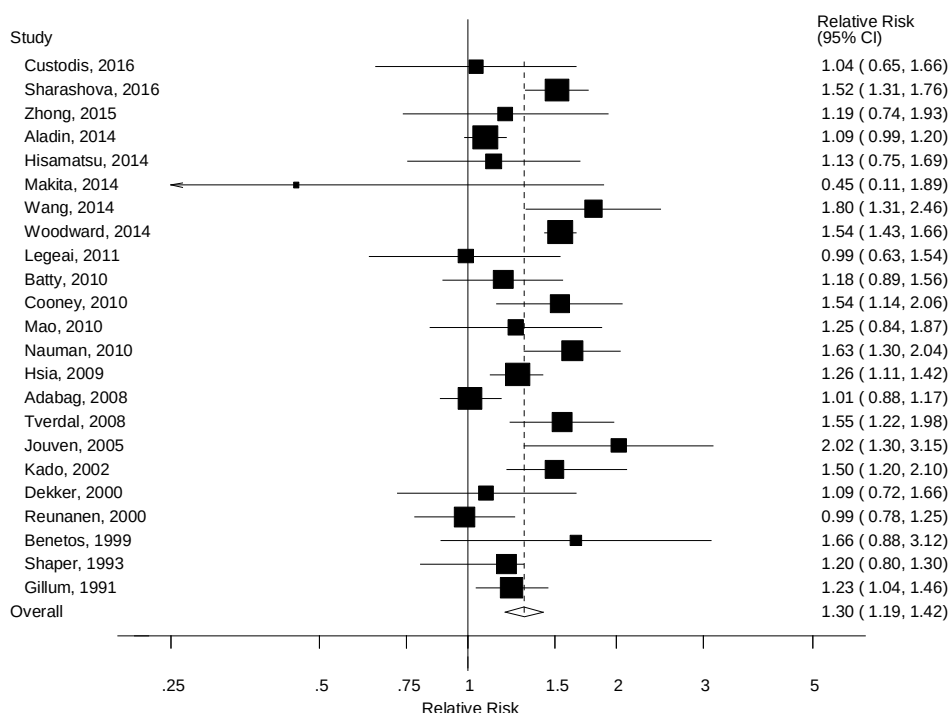
Geographic location																
Europe	17	1.15 (1.10-1.21)	88.2	<0.0001	0.89	7	1.15 (1.03-1.30)	94.0	<0.0001	0.69	24	1.17 (1.13-1.21)	95.4	<0.0001	0.86	
America	5	1.12 (1.09-1.17)	12.7	0.33		4	1.10 (1.06-1.13)	0	0.72		12	1.15 (1.11-1.20)	91.7	<0.0001		
Asia	12	1.15 (1.10-1.21)	82.7	<0.0001		1	1.16 (0.86-1.56)				10	1.19 (1.12-1.26)	88.2	<0.0001		
Australia	0					0					1	1.04 (0.88-1.23)				
International	1	1.03 (0.95-1.10)				0					1	1.12 (1.03-1.21)				
Number of cases																
Cases <500	15	1.22 (1.18-1.26)	0	0.53	0.09	6	1.10 (1.04-1.16)	0	0.90	0.47	14	1.25 (1.20-1.30)	31.7	0.12	0.006	
Cases 500-<1000	10	1.10 (1.05-1.14)	72.8	<0.0001		4	1.14 (0.97-1.35)	94.4	<0.0001		8	1.18 (1.11-1.24)	70.8	0.001		
Cases ≥1000	10	1.14 (1.08-1.20)	93.5	<0.0001		2	1.19 (1.00-1.42)	97.4	<0.0001		24	1.14 (1.11-1.17)	96.7	<0.0001		
Study quality score																
0-3	0				0.89	0				NC	0				0.97	
4-6	2	1.16 (0.84-1.59)	97.1	<0.0001		0					4	1.16 (1.06-1.28)	97.0	<0.0001		
7-9	33	1.14 (1.11-1.18)	82.3	<0.0001		12	1.14 (1.06-1.23)	90.2	<0.0001		44	1.16 (1.14-1.19)	91.1	<0.0001		
Adjusment for confounding factors																
Age	Yes	35	1.15 (1.11-1.18)	84.3	<0.0001	NC	12	1.14 (1.06-1.23)	90.2	<0.0001	NC	46	1.16 (1.14-1.19)	94.2	<0.0001	0.35

	No	0					0					2	1.24 (1.14-1.34)	0	0.60	
Education	Yes	6	1.10 (1.06-1.15)	72.0	0.003	0.46	2	1.09 (1.05-1.14)	0	0.70	0.74	7	1.19 (1.10-1.30)	94.2	<0.0001	0.59
	No	29	1.15 (1.11-1.20)	84.2	<0.0001		10	1.15 (1.05-1.25)	91.4	<0.0001		41	1.16 (1.13-1.19)	93.9	<0.0001	
Fasting glucose	Yes	3	1.13 (1.02-1.25)	72.1	0.03	0.72	1	1.08 (1.00-1.17)			0.63	1	1.08 (1.00-1.17)			0.37
	No	32	1.15 (1.11-1.18)	85.2	<0.0001		11	1.15 (1.06-1.24)	90.9	<0.0001		47	1.17 (1.14-1.19)	94.1	<0.0001	
Diabetes	Yes	18	1.14 (1.10-1.19)	75.2	<0.0001	0.86	6	1.07 (1.02-1.13)	61.1	0.03	0.10	29	1.16 (1.12-1.21)	94.4	<0.0001	0.76
	No	17	1.14 (1.10-1.19)	88.2	<0.0001		6	1.20 (1.09-1.33)	84.6	<0.0001		19	1.17 (1.13-1.20)	93.0	<0.0001	
Cardiovascular disease or ECG abnormality	Yes	11	1.12 (1.08-1.17)	51.9	0.02	0.63	2	1.10 (1.06-1.14)	0	0.41	0.79	21	1.16 (1.12-1.21)	95.1	<0.0001	0.82
	No	24	1.15 (1.11-1.19)	88.2	<0.0001		10	1.15 (1.04-1.26)	91.4	<0.0001		27	1.17 (1.13-1.20)	92.0	<0.0001	
BMI	Yes	24	1.12 (1.08-1.15)	81.0	<0.0001	0.02	9	1.08 (1.04-1.12)	44.3	0.07	<0.0001	38	1.15 (1.12-1.17)	89.8	<0.0001	0.03
	No	11	1.21 (1.13-1.28)	85.9	<0.0001		3	1.34 (1.23-1.47)	61.4	0.08		10	1.23 (1.16-1.30)	94.8	<0.0001	
Physical activity	Yes	13	1.10 (1.06-1.14)	85.8	<0.0001	0.02	5	1.08 (1.00-1.16)	64.5	0.02	0.23	21	1.14 (1.11-1.17)	92.6	<0.0001	0.23
	No	22	1.19 (1.13-1.24)	81.8	<0.0001		7	1.18 (1.07-1.30)	91.0	<0.0001		27	1.18 (1.14-1.23)	92.1	<0.0001	
Alcohol	Yes	13	1.11 (1.08-1.15)	62.3	0.001	0.33	2	1.11 (1.01-1.21)	0	0.36	0.71	16	1.14 (1.11-1.17)	82.5	<0.0001	0.26
	No	22	1.16 (1.11-1.21)	87.4	<0.0001		10	1.15 (1.06-1.25)	91.9	<0.0001		32	1.18 (1.14-1.22)	95.2	<0.0001	
Smoking	Yes	31	1.12 (1.10-1.15)	78.9	<0.0001	0.00	11	1.12 (1.05-1.20)	81.8	<0.0001	0.17	41	1.15 (1.13-1.18)	90.5	<0.0001	0.10

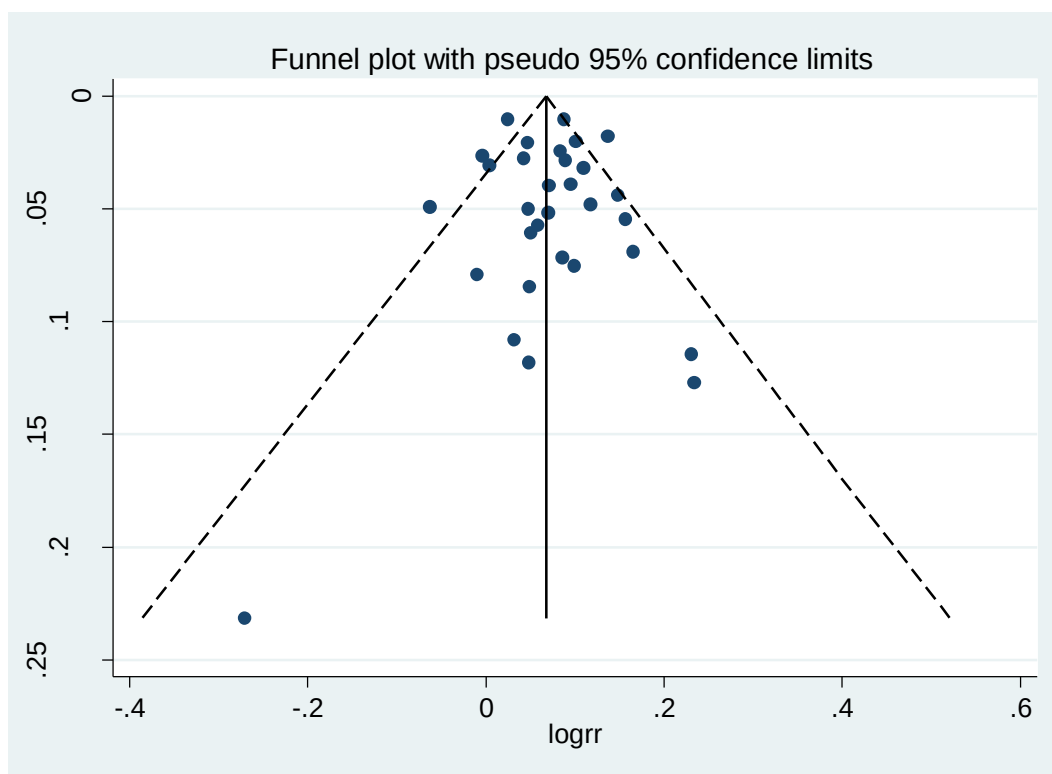
	No	4	1.28 (1.20-1.36)	58.4	0.07	4	1	1.30 (1.25-1.35)				7	1.24 (1.20-1.28)	51.3	0.06	
Systolic blood pressure	Yes	23	1.13 (1.09-1.16)	84.6	<0.0001	0.10	6	1.07 (1.02-1.12)	56.1	0.04	0.04	28	1.13 (1.10-1.16)	90.4	<0.0001	0.003
	No	12	1.20 (1.13-1.27)	83.2	<0.0001		6	1.22 (1.11-1.35)	83.6	<0.0001		20	1.22 (1.17-1.27)	93.1	<0.0001	
Hypertension	Yes	10	1.13 (1.08-1.18)	48.1	0.04	0.93	2	1.14 (1.05-1.23)	0	0.63	0.90	23	1.17 (1.13-1.21)	93.6	<0.0001	0.90
	No	25	1.15 (1.11-1.19)	87.9	<0.0001		10	1.14 (1.05-1.24)	92.0	<0.0001		25	1.16 (1.13-1.20)	93.6	<0.0001	
Triglycerides	Yes	5	1.16 (1.09-1.23)	83.7	<0.0001	0.72	1	1.21 (0.93-1.58)			0.73	5	1.14 (1.10-1.19)	92.4	<0.0001	0.76
	No	30	1.14 (1.10-1.18)	83.6	<0.0001		11	1.14 (1.05-1.23)	91.1	<0.0001		43	1.17 (1.14-1.20)	94.2	<0.0001	
Total cholesterol	Yes	24	1.12 (1.09-1.16)	78.8	<0.0001	0.09	6	1.07 (1.02-1.12)	56.1	0.04	0.04	30	1.13 (1.11-1.16)	88.8	<0.0001	0.03
	No	11	1.20 (1.12-1.27)	90.7	<0.0001		6	1.22 (1.11-1.35)	83.6	<0.0001		18	1.20 (1.16-1.25)	91.4	<0.0001	

*n*denotes the number of studies.
¹ P for heterogeneity within each subgroup,
² P for heterogeneity between subgroups with meta-regression analysis,
³ P for heterogeneity between men and women (studies with genders mixed were excluded)

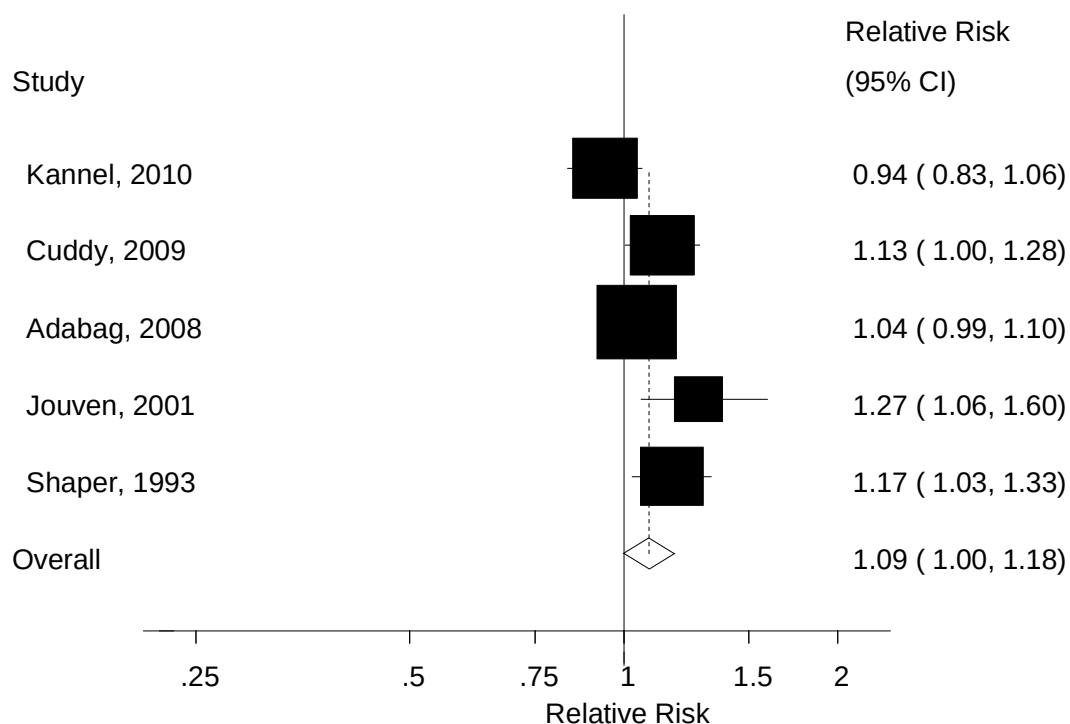
Supplementary Figure 1. Resting heart rate and coronary heart disease, high vs. low analysis



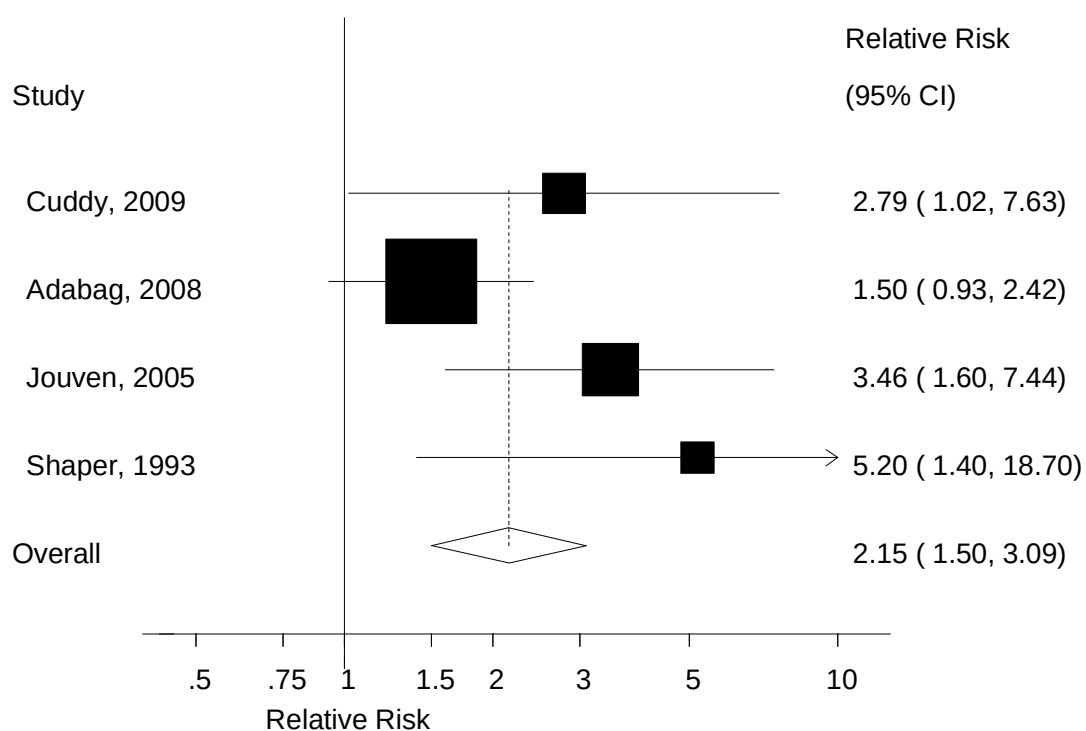
Supplementary Figure 2. Funnel plot of resting heart rate and coronary heart disease



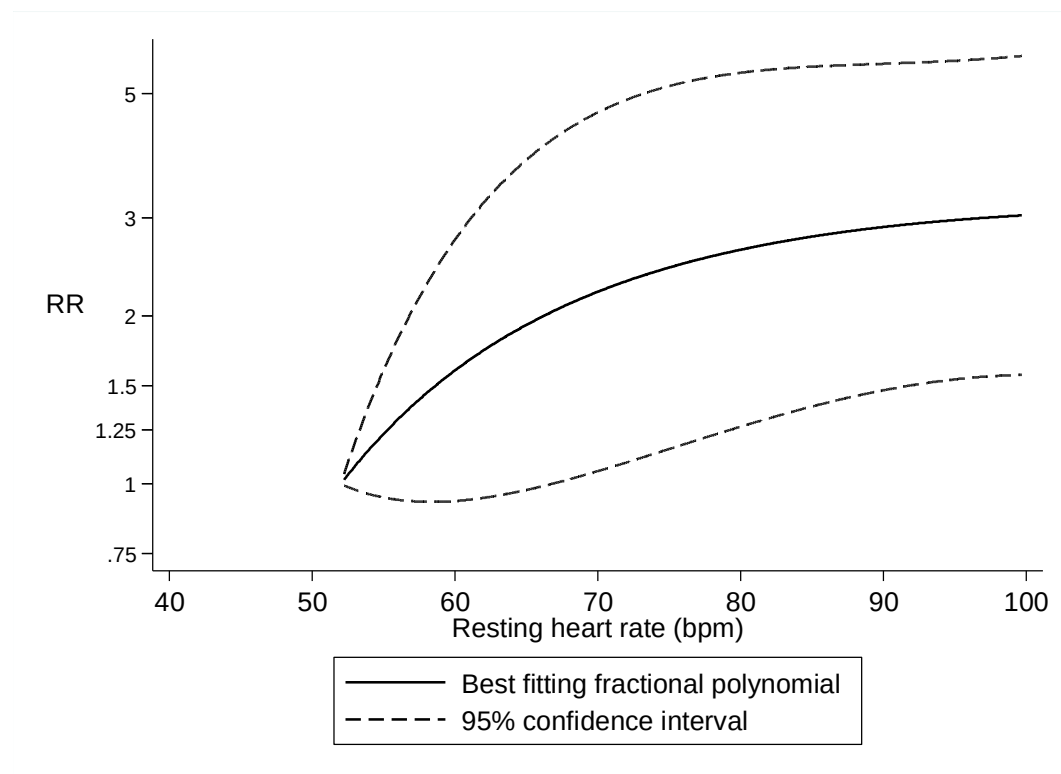
Supplementary Figure 3. Resting heart rate and sudden cardiac death, dose-response analysis



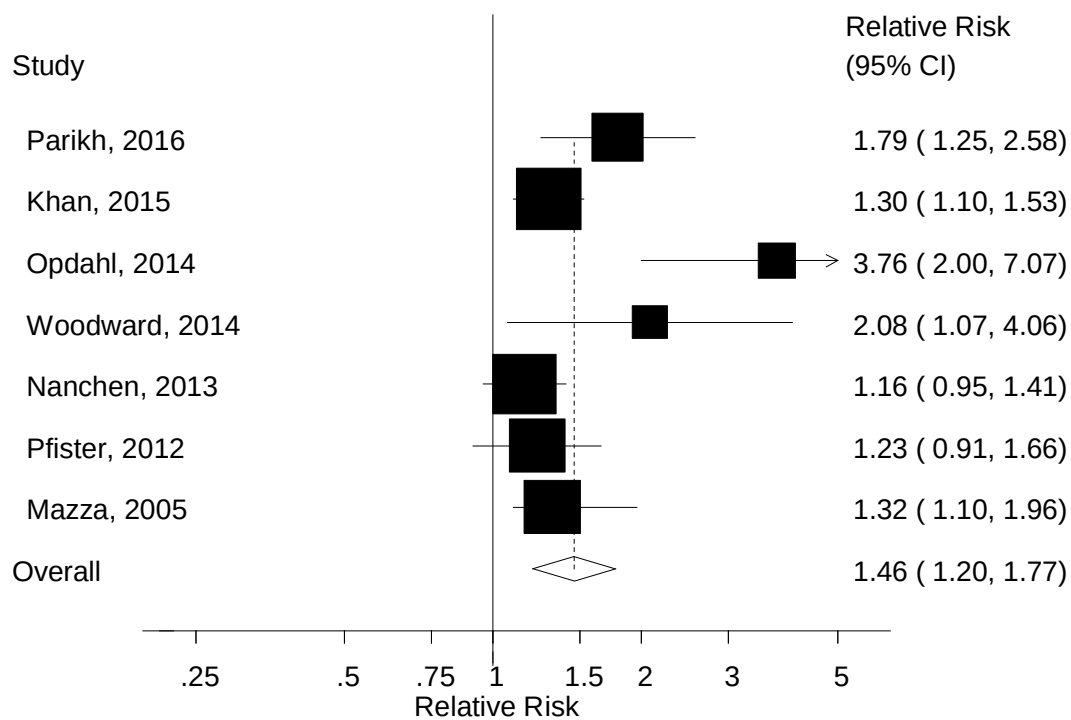
Supplementary Figure 4. Resting heart rate and sudden cardiac death, high vs. low analysis



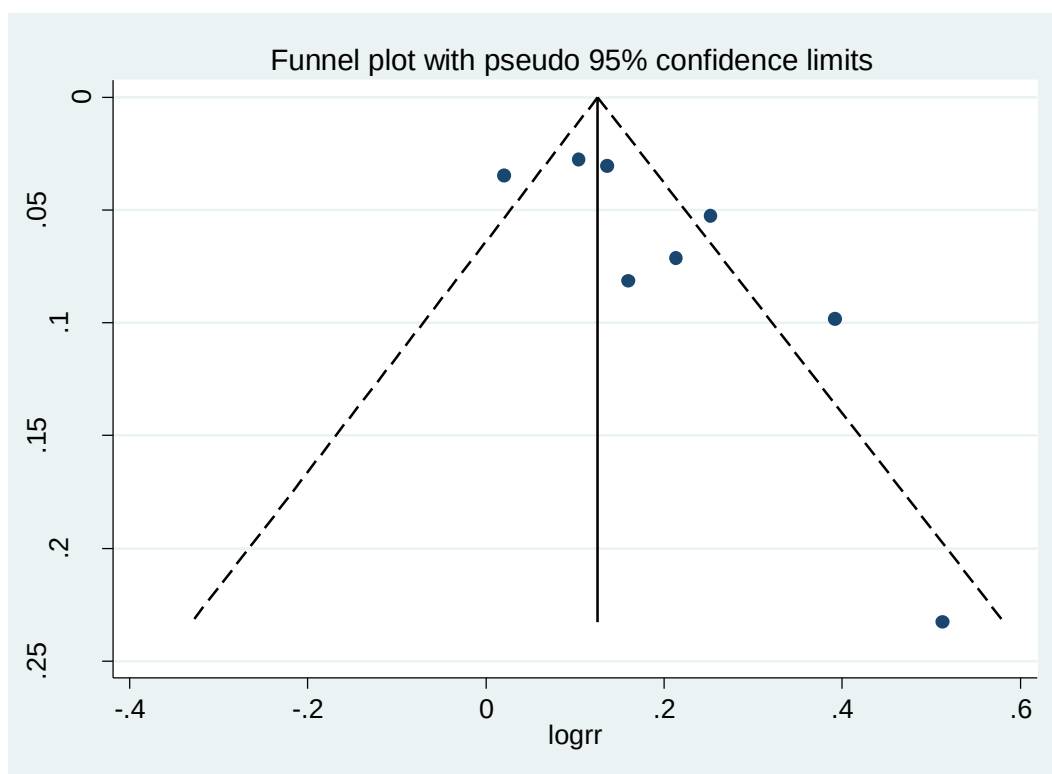
Supplementary Figure 5. Resting heart rate and sudden cardiac death, nonlinear dose-response analysis



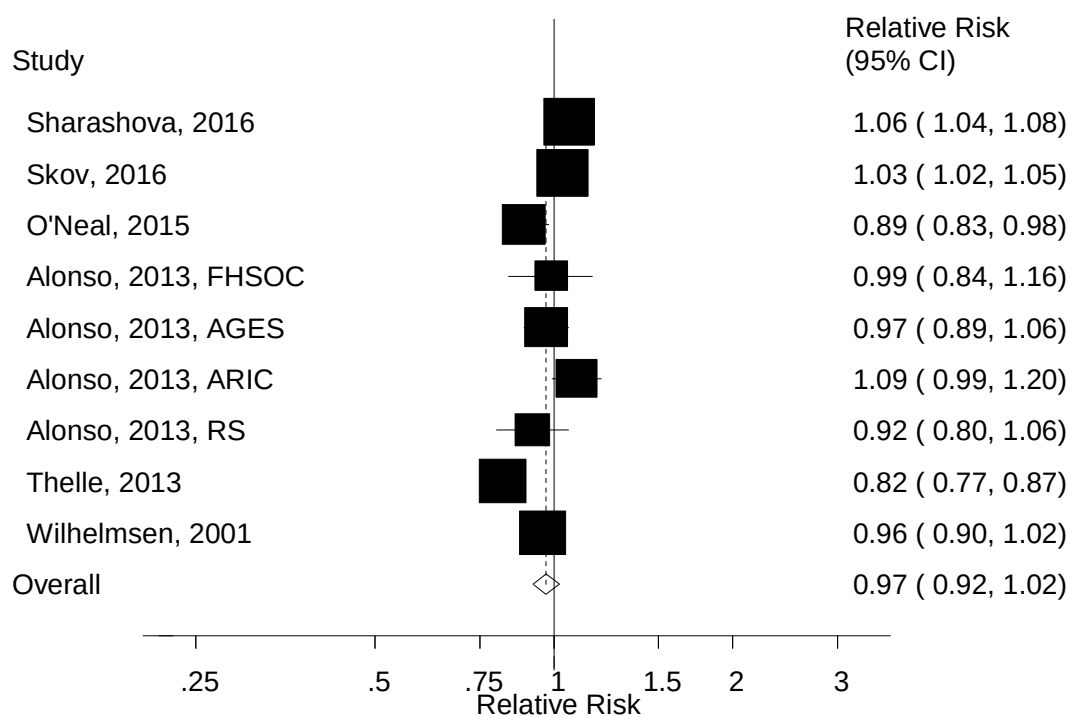
Supplementary Figure 6. Resting heart rate and heart failure, high vs. low analysis



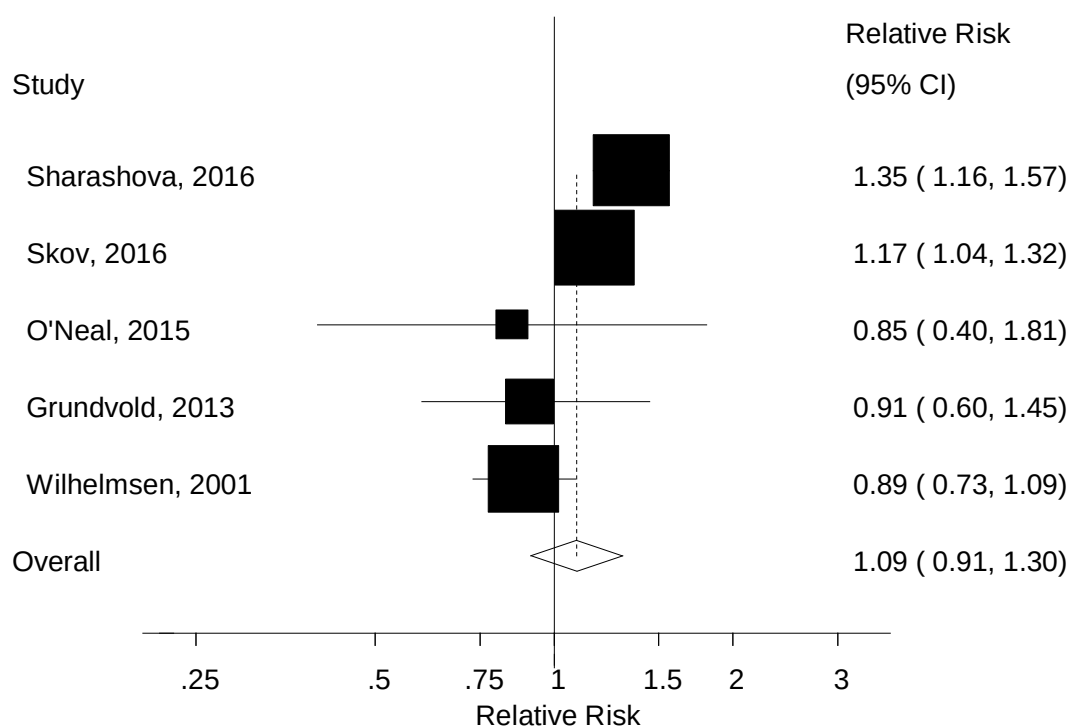
Supplementary Figure 7. Funnel plot of resting heart rate and heart failure



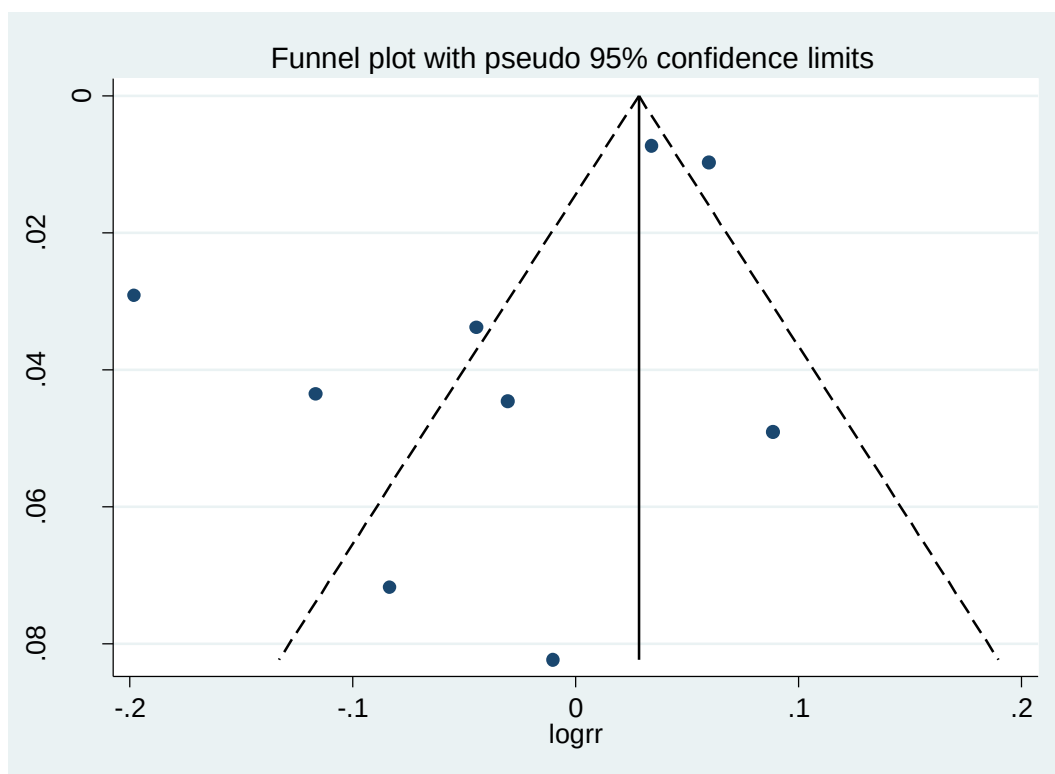
Supplementary Figure 8. Resting heart rate and atrial fibrillation, dose-response analysis



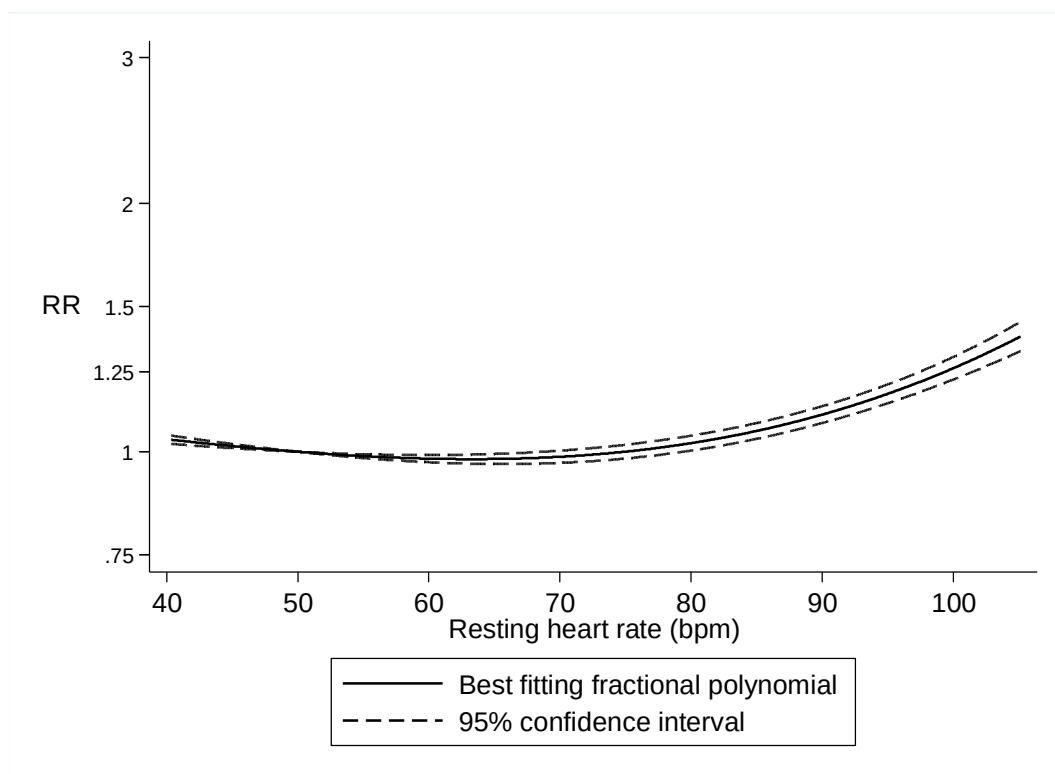
Supplementary Figure 9. Resting heart rate and atrial fibrillation, high vs. low analysis



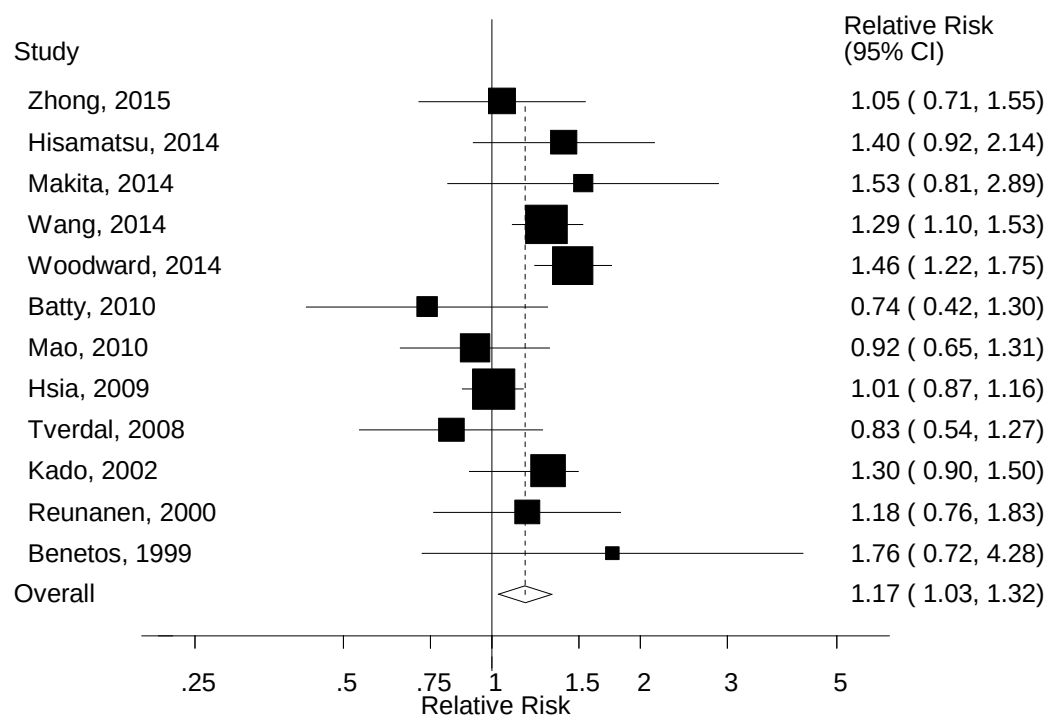
Supplementary Figure 10. Funnel plot of resting heart rate and atrial fibrillation



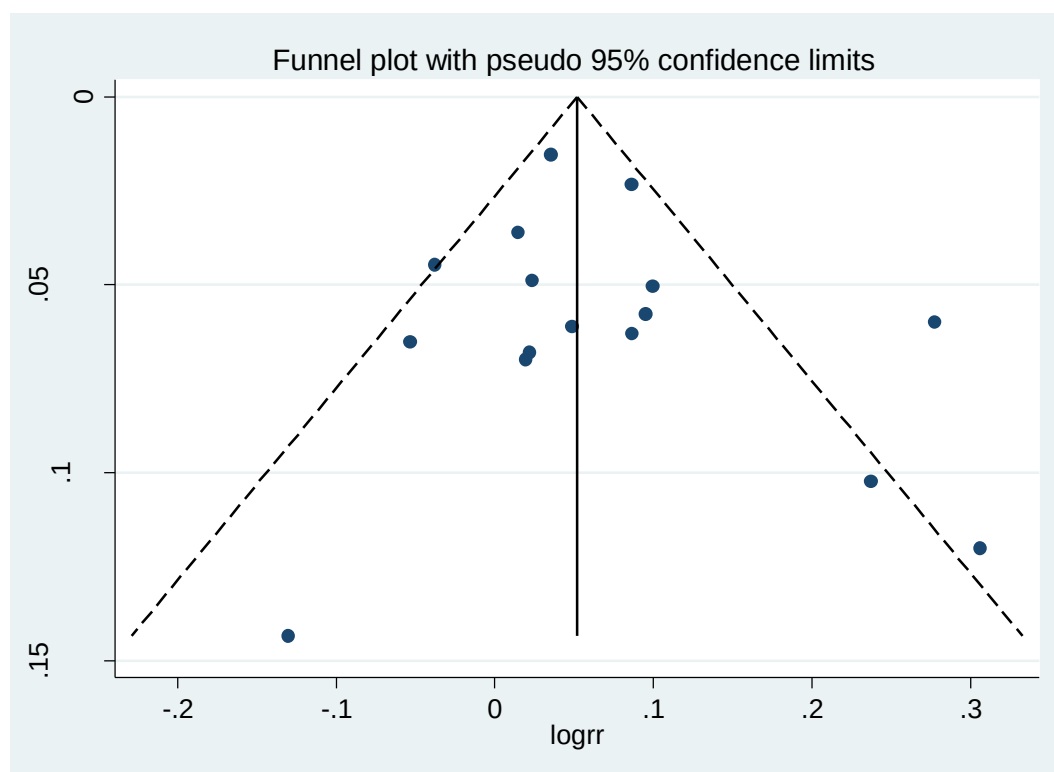
Supplementary Figure 11. Resting heart rate and atrial fibrillation, nonlinear dose-response analysis



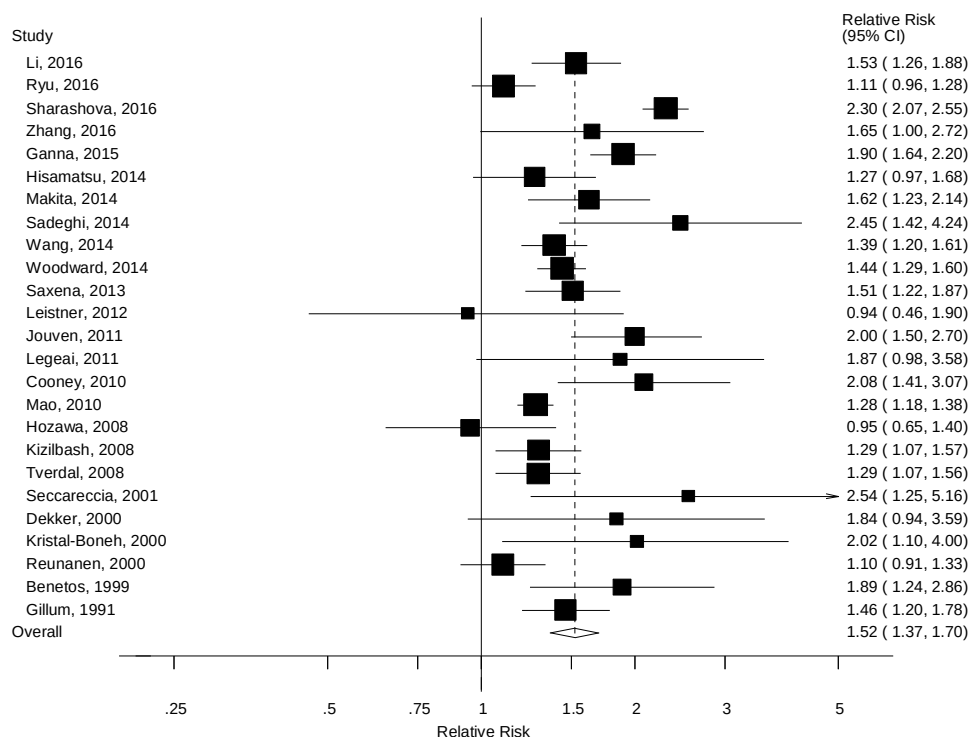
Supplementary Figure 12. Resting heart rate and total stroke, high vs. low analysis



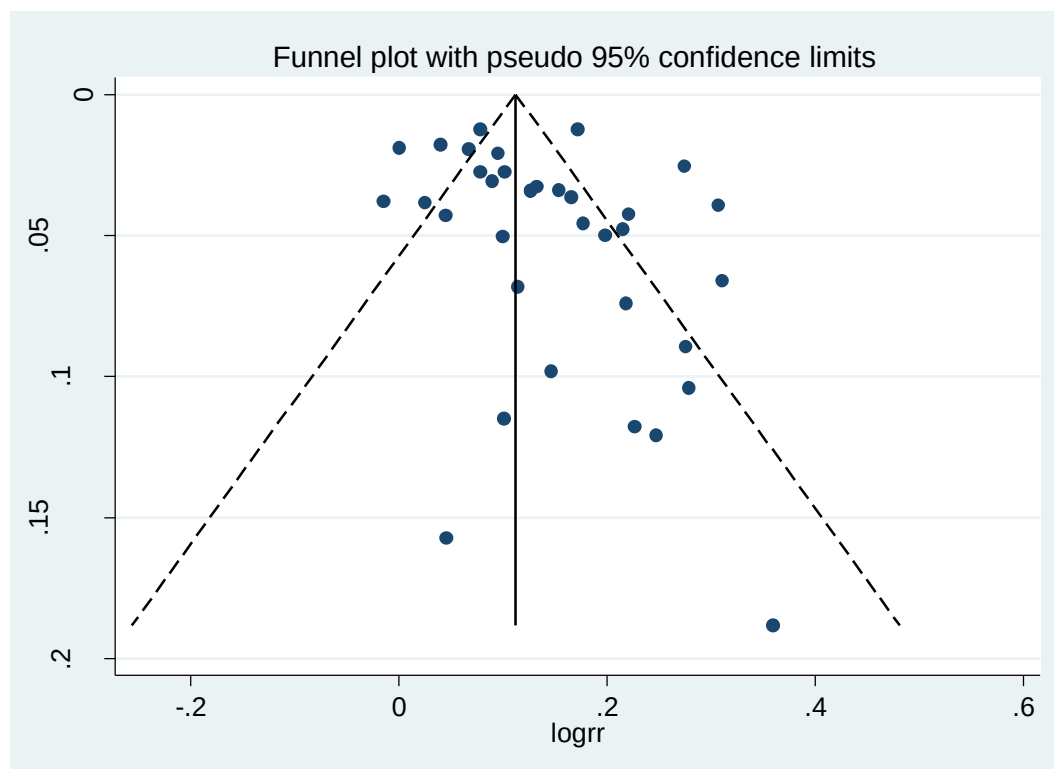
Supplementary Figure 13. Funnel plot of resting heart rate and total stroke



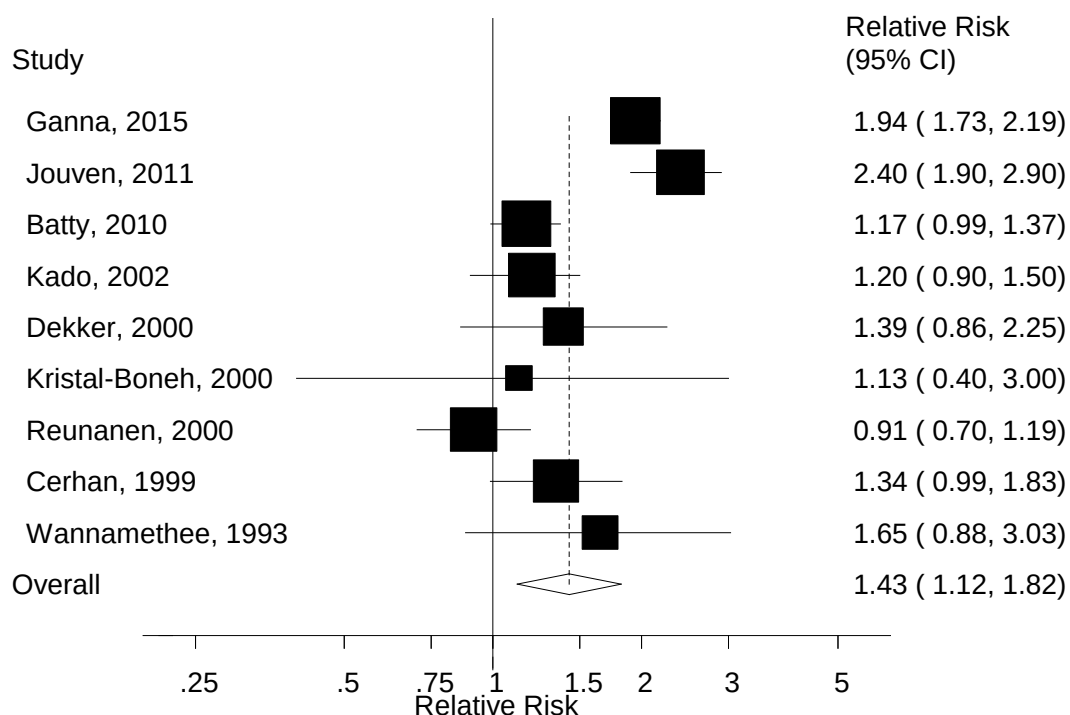
Supplementary Figure 14. Resting heart rate and cardiovascular disease, high vs. low analysis



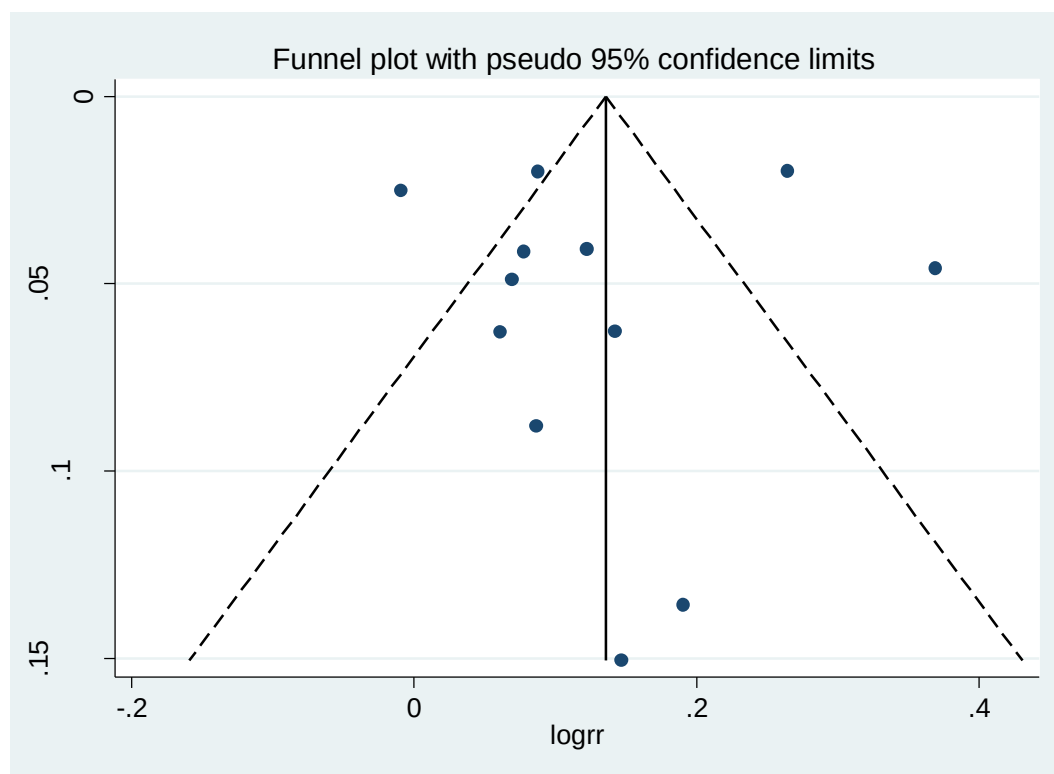
Supplementary Figure 15. Funnel plot of resting heart rate and cardiovascular disease



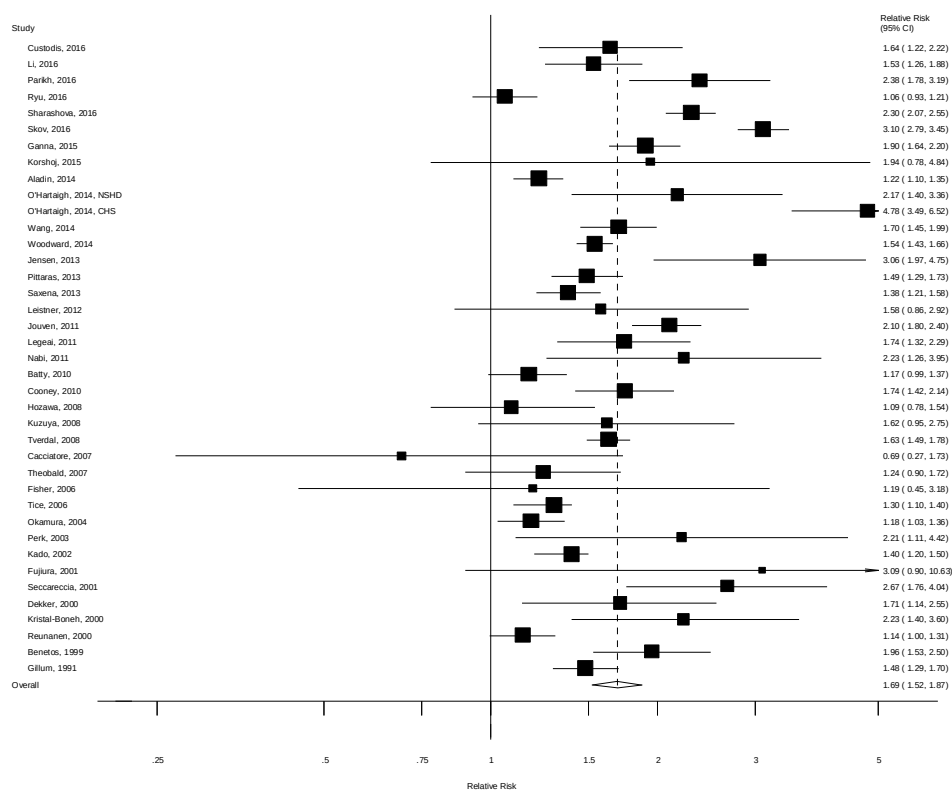
Supplementary Figure 16. Resting heart rate and total cancer, high vs. low analysis



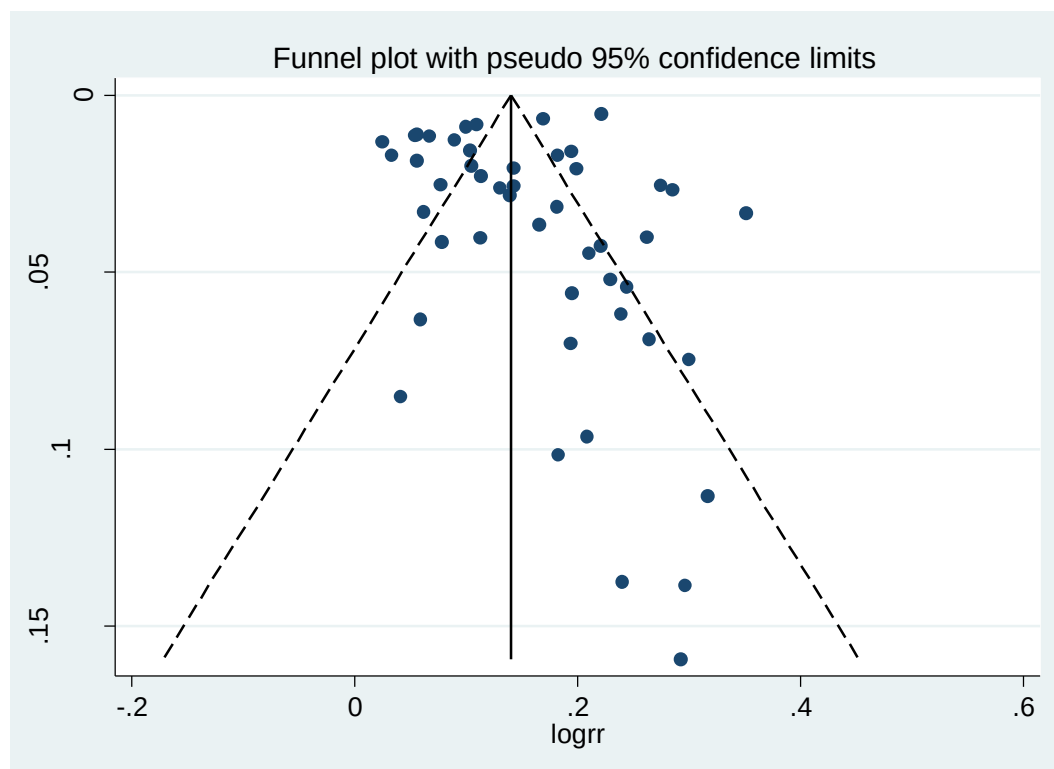
Supplementary Figure 17. Funnel plot of resting heart rate and total cancer



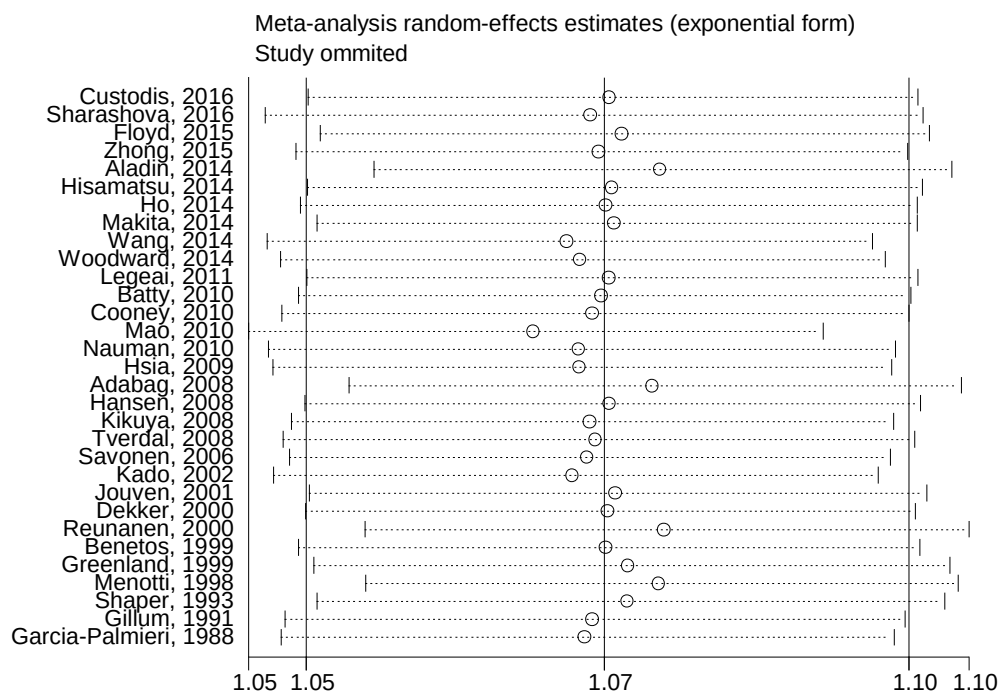
Supplementary Figure 18. Resting heart rate and mortality, high vs. low analysis



Supplementary Figure 19. Funnel plot of resting heart rate and mortality

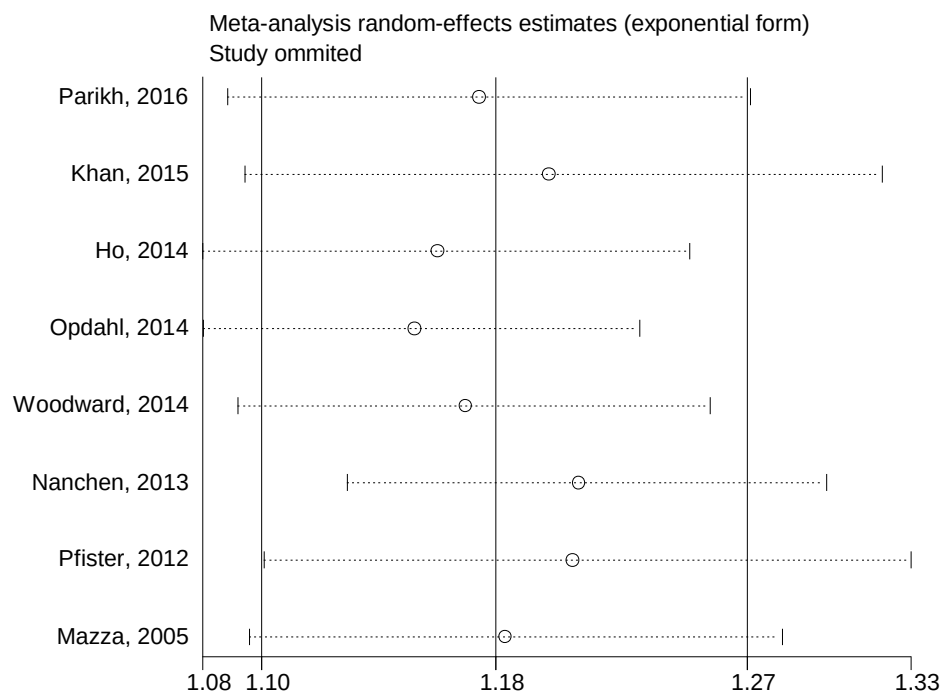


Supplementary Figure 20. Resting heart rate and coronary heart disease, influence analysis



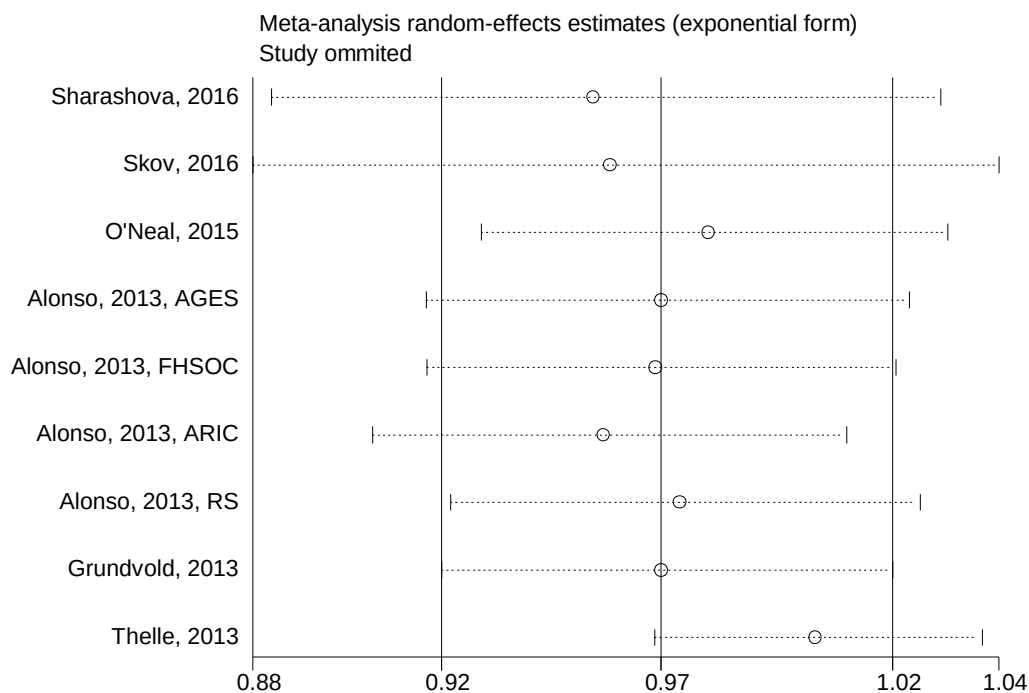
Study omitted	Estimate	[95% Conf. Interval]
Custodis, 2016	1.0749551	1.0531332 1.0972291
Sharashova, 2016	1.0735598	1.0500149 1.0976326
Floyd, 2015	1.0758278	1.0540202 1.0980867
Zhong, 2015	1.0741384	1.052247 1.0964851
Aladin, 2014	1.0785898	1.0579003 1.0996839
Hisamatsu, 2014	1.0751054	1.0530962 1.0975746
Ho, 2014	1.074665	1.0525742 1.0972193
Makita, 2014	1.0752611	1.0537753 1.0971849
Wang, 2014	1.0718442	1.050171 1.0939648
Woodward, 2014	1.0727923	1.051138 1.0948926
Legeai, 2011	1.0749079	1.05302 1.0972509
Batty, 2010	1.0743501	1.0524209 1.0967363
Cooney, 2010	1.0736791	1.0512557 1.0965807
Mao, 2010	1.0694065	1.0488033 1.0904145
Nauman, 2010	1.0727044	1.0502378 1.0956516
Hsia, 2009	1.0727519	1.050602 1.0953686
Adabag, 2008	1.078028	1.0560974 1.1004139
Hansen, 2008	1.0749491	1.0529083 1.0974513
Kikuya, 2008	1.0734996	1.0519419 1.095499
Tverdal, 2008	1.0739261	1.0513315 1.0970063
Savonen, 2006	1.0732961	1.0517683 1.0952646
Kado, 2002	1.0722713	1.0506159 1.0943732
Jouven, 2001	1.0753417	1.0532376 1.0979097
Dekker, 2000	1.0747766	1.0529639 1.0970411
Reunanen, 2000	1.0788817	1.0572486 1.1009576
Benetos, 1999	1.0746714	1.0524194 1.0973939
Greenland, 1999	1.0763005	1.0535439 1.0995487
Menotti, 1998	1.0785128	1.057281 1.1001711
Shaper, 1993	1.0762293	1.0537583 1.0991795
Gillum, 1991	1.0736659	1.0514873 1.096312
Garcia-Palmieri, 1988	1.0731403	1.051182 1.0955572
Combined	1.0745741	1.0529805 1.0966104

Supplementary Figure 21. Resting heart rate and heart failure, influence analysis



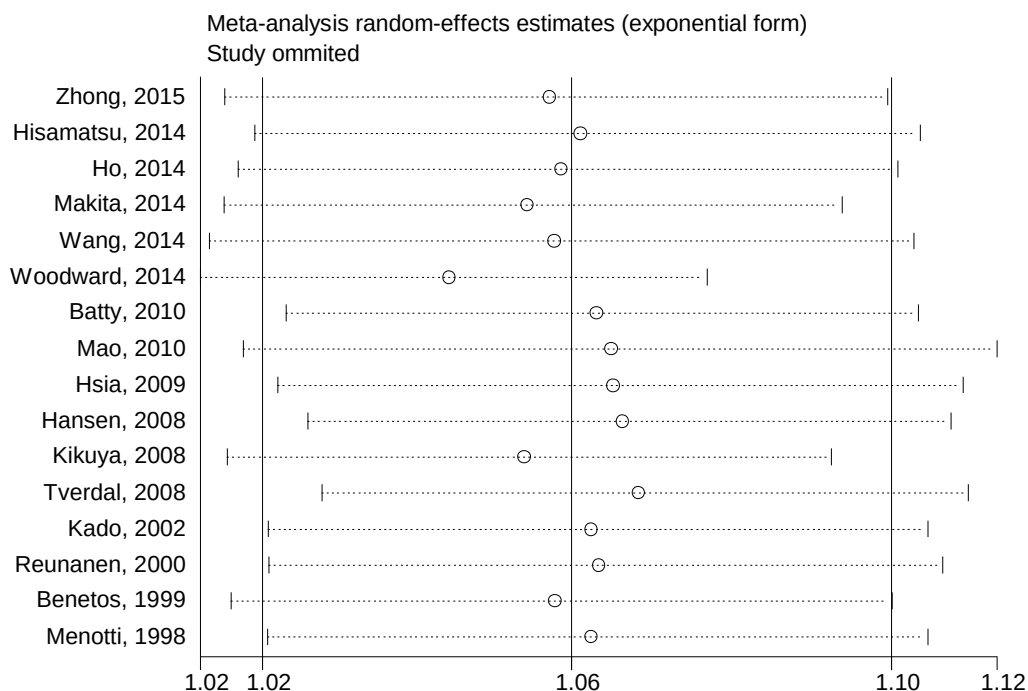
Study omitted	Estimate	[95% Conf. Interval]	
Parikh, 2016	1.1769367	1.0888687	1.2721276
Khan, 2015	1.2014649	1.0949779	1.3183079
Ho, 2014	1.1623948	1.080227	1.2508125
Opdahl, 2014	1.1543285	1.0803931	1.2333236
Woodward, 2014	1.1723635	1.0925711	1.2579832
Nanchen, 2013	1.2119061	1.130796	1.298834
Pfister, 2012	1.2097875	1.1017765	1.3283871
Mazza, 2005	1.1861808	1.0964495	1.2832557
Combined	1.1828371	1.1008256	1.2709584

Supplementary Figure 22. Resting heart rate and atrial fibrillation, influence analysis



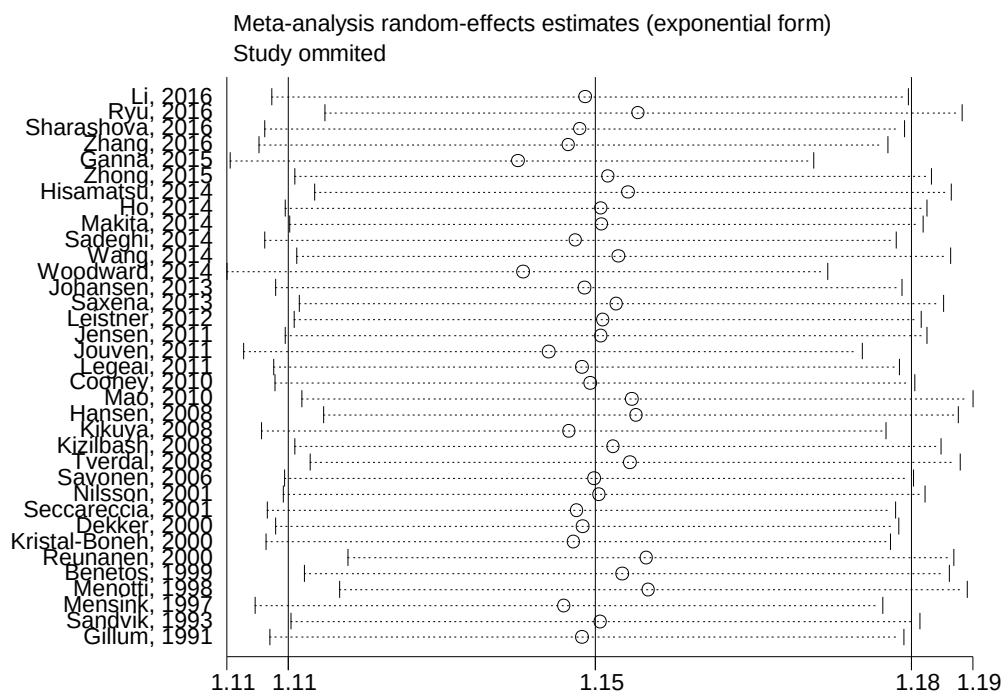
Study omitted	Estimate	[95% Conf. Interval]	
Sharashova (2016)	0.95505804	0.88390845	1.0319347
Skov (2016)	0.95872784	0.87975442	1.0447905
O'Neal (2015)	0.98055828	0.93031919	1.0335103
Alonso (2013)	0.97004414	0.91811168	1.024914
Alonso (2013)	0.96877337	0.9183054	1.0220149
Alonso (2013)	0.95727903	0.90628374	1.0111437
Alonso (2013)	0.97410387	0.92353433	1.0274425
Grundvold (2013)	0.97013146	0.92150736	1.0213213
Thelle (2013)	1.0042315	0.96865362	1.041116
Combined	0.97013147	0.92150739	1.0213212

Supplementary Figure 23. Resting heart rate and total stroke, influence analysis



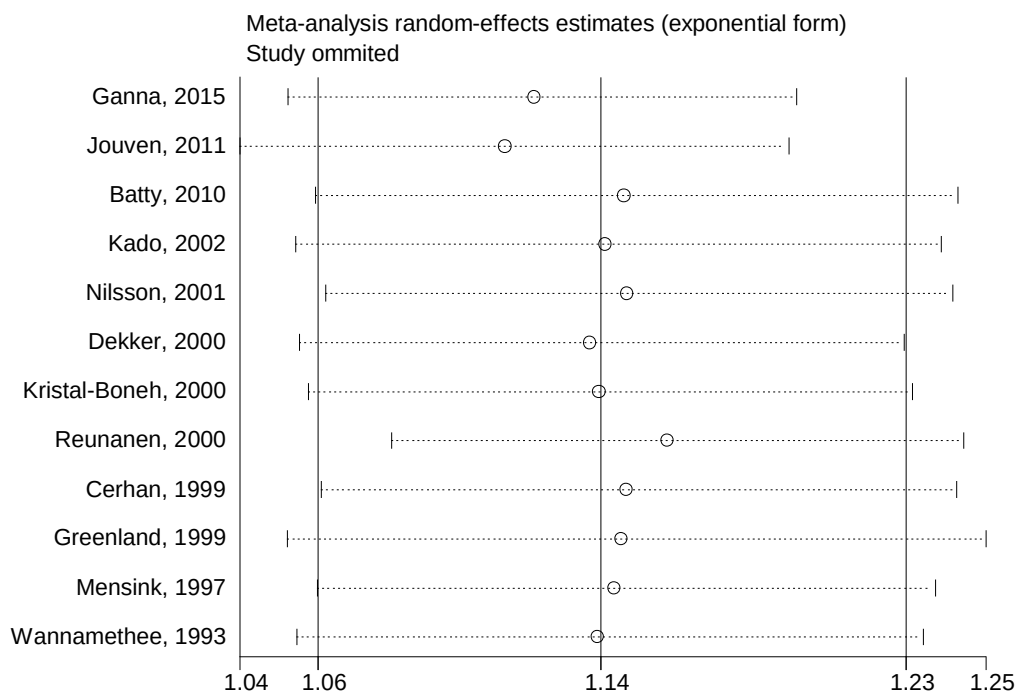
Study omitted	Estimate	[95% Conf. Interval]	
Zhong (2015)	1.0606205	1.0188466	1.1041073
Hisamatsu (2014)	1.0646139	1.0227003	1.1082455
Ho (2014)	1.0621086	1.0205265	1.1053849
Makita (2014)	1.0577598	1.018774	1.0982375
Wang (2014)	1.0612109	1.0168676	1.1074877
Woodward (2014)	1.0477567	1.0156648	1.0808625
Batty (2010)	1.0666277	1.0267357	1.1080699
Mao (2010)	1.0685807	1.0211923	1.1181682
Hsia (2009)	1.0688221	1.0256867	1.1137717
Hansen (2008)	1.0700598	1.0295105	1.1122063
Kikuya (2008)	1.0573075	1.0191716	1.0968703
Tverdal (2008)	1.0720655	1.0313147	1.1144265
Kado (2002)	1.0660021	1.0244397	1.1092508
Reunanen (2000)	1.066954	1.0245296	1.111135
Benetos (1999)	1.0613209	1.0197001	1.1046407
Menotti (1998)	1.0659665	1.0243412	1.1092832
Combined	1.0633988	1.0237117	1.1046245

Supplementary Figure 24. Resting heart rate and cardiovascular disease, influence analysis



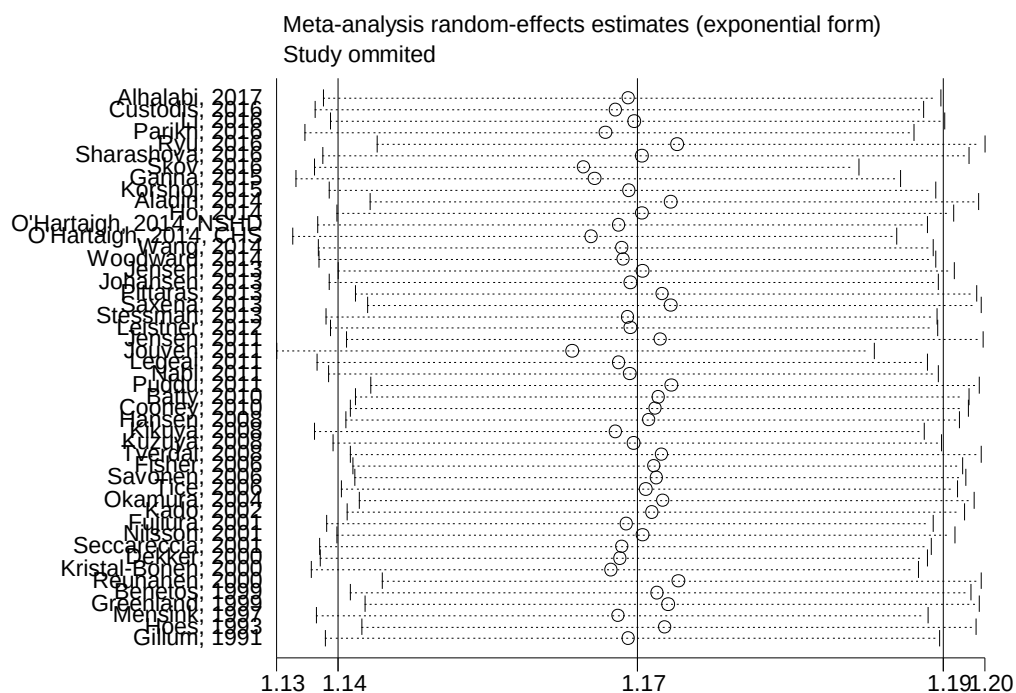
Study omitted	Estimate	[95% Conf. Interval]	
Li (2016)	1.1442122	1.1110075	1.1784095
Ryu (2016)	1.1498345	1.116621	1.184036
Sharashova (2016)	1.143622	1.1102949	1.1779493
Zhang (2016)	1.1424527	1.1096598	1.1762149
Ganna (2015)	1.137069	1.1066302	1.168345
Zhong (2015)	1.1466329	1.1134369	1.1808186
Hisamatsu (2014)	1.1487125	1.1155176	1.1828951
Ho (2014)	1.145884	1.1124408	1.1803325
Makita (2014)	1.1459283	1.1129169	1.1799189
Sadeghi (2014)	1.1431873	1.1102831	1.1770667
Wang (2014)	1.1477287	1.1136689	1.1828301
Woodward (2014)	1.1376085	1.1062628	1.1698422
Johansen (2013)	1.1440991	1.1114354	1.1777228
Saxena (2013)	1.1475145	1.1139539	1.182086
Leistner (2012)	1.14608	1.1133873	1.1797326
Jensen (2011)	1.145884	1.1124408	1.1803325
Jouven (2011)	1.1403096	1.108065	1.1734927
Legeai (2011)	1.1438631	1.1112347	1.1774495
Cooney (2010)	1.1447057	1.111385	1.1790253
Mao (2010)	1.1491588	1.1141942	1.1852208
Hansen (2008)	1.1495751	1.1164635	1.1836686
Kikuya (2008)	1.1425205	1.1099619	1.1760343
Kizilbash (2008)	1.1471454	1.1134545	1.1818557
Tverdal (2008)	1.1489375	1.1150616	1.1838423
Savonen (2006)	1.1451564	1.1123409	1.1789399
Nilsson (2001)	1.1456891	1.1122258	1.1801593
Seccareccia (2001)	1.1432854	1.1105322	1.1770045
Dekker (2000)	1.1438864	1.1113955	1.1773274
Kristal-Boneh (2000)	1.1429734	1.110409	1.1764928
Reunanen (2000)	1.1506861	1.11909	1.1831744
Benetos (1999)	1.148101	1.1144787	1.1827375
Menotti (1998)	1.1509106	1.1181897	1.1845891
Mensink (1997)	1.1419827	1.1092603	1.1756703
Sandvik (1993)	1.1458149	1.1130306	1.1795648
Gillum (1991)	1.143851	1.1108086	1.1778765
Combined	1.1452794	1.1127961	1.1787109

Supplementary Figure 25. Resting heart rate and total cancer, influence analysis



Study omitted	Estimate	[95% Conf. Interval]	
Ganna (2015)	1.1219496	1.0514694	1.197154
Jouven (2011)	1.1135545	1.0376651	1.1949941
Batty (2010)	1.1476986	1.0593396	1.2434276
Kado (2002)	1.142437	1.0536778	1.238673
Nilsson (2001)	1.148549	1.0622337	1.2418783
Dekker (2000)	1.1380464	1.0547472	1.2279241
Kristal-Boneh (2000)	1.1405009	1.057245	1.2303129
Reunanen (2000)	1.160148	1.0810596	1.2450225
Cerhan (1999)	1.1483994	1.0610089	1.2429876
Greenland (1999)	1.1470532	1.0513269	1.2514957
Mensink (1997)	1.1449881	1.0598614	1.2369519
Wannamethee (1993)	1.1401851	1.0539844	1.2334358
Combined	1.1411795	1.0600269	1.228545

Supplementary Figure 26. Resting heart rate and mortality, influence analysis



Study omitted	Estimate	[95% Conf. Interval]	
Alhalabi (2017)	1.1643665	1.1373497	1.1920249
Custodis (2016)	1.1632663	1.1366528	1.1905029
Li (2016)	1.1648673	1.1380281	1.1923393
Parikh (2016)	1.1623689	1.135741	1.1896212
Ryu (2016)	1.168713	1.1421206	1.1959245
Sharashova (2016)	1.1655821	1.1373359	1.1945298
Skov (2016)	1.1604114	1.1365672	1.1847558
Ganna (2015)	1.1613595	1.1349155	1.1884197
Korshoj (2015)	1.1644127	1.1378802	1.191564
Aladin (2014)	1.1681224	1.1414953	1.1953706
Ho (2014)	1.1655477	1.1385888	1.193145
O'Hartaigh (2014)	1.1635486	1.1368939	1.1908283
O'Hartaigh (2014)	1.1610761	1.134675	1.1880914
Wang (2014)	1.1638002	1.1369253	1.1913105
Woodward (2014)	1.1639528	1.1369888	1.1915562
Jensen (2013)	1.1656259	1.1386948	1.1931939
Johansen (2013)	1.1645274	1.1379128	1.1917647
Pittaras (2013)	1.1673815	1.1402245	1.1951854
Saxena (2013)	1.1681311	1.1412998	1.1955932
Stessman (2013)	1.164323	1.137604	1.1916696
Leistner (2012)	1.1645662	1.138007	1.1917452
Jensen (2011)	1.1672194	1.1393964	1.1957216
Jouven (2011)	1.1594014	1.1332643	1.1861414
Legeai (2011)	1.1635191	1.1368318	1.190833
Nabi (2011)	1.1644934	1.1378161	1.1917963
Puddu (2011)	1.1681643	1.1415545	1.1953944
Batty (2010)	1.1670206	1.1401892	1.1944833
Cooney (2010)	1.1667639	1.1397302	1.1944388
Hansen (2008)	1.1661897	1.1393446	1.1936673
Kikuya (2008)	1.1632459	1.136585	1.1905321
Kuzuya (2008)	1.1648495	1.1382322	1.1920892
Tverdal (2008)	1.1673458	1.139765	1.195594
Fisher (2006)	1.1666431	1.1399689	1.1939416
Savonen (2006)	1.1668695	1.1401303	1.1942358
Tice (2006)	1.1659019	1.1389438	1.1934981
Okamura (2004)	1.1674311	1.1405194	1.1949778
Kado (2002)	1.1664512	1.1394511	1.1940911
Fujiura (2001)	1.1641906	1.1376522	1.1913483
Nilsson (2001)	1.1656047	1.1385647	1.1932869
Seccareccia (2001)	1.1637992	1.1370628	1.1911643
Dekker (2000)	1.1636487	1.1371106	1.1908062
Kristal-Boneh (2000)	1.1628525	1.1362858	1.1900405
Reunanen (2000)	1.1687751	1.1425946	1.1955554
Benetos (1999)	1.1669046	1.1397648	1.1946905
Greenland (1999)	1.1679219	1.1410465	1.1954304
Mensink (1997)	1.1635025	1.1367779	1.1908553
Hoes (1993)	1.1676335	1.1407824	1.1951166
Gillum (1991)	1.1643952	1.137548	1.1918762
Combined	1.1651527	1.1386673	1.1922541

Online Methods. Search and inclusion criteria and statistical methods

For one publication the data was available through a website which was linked in the publication.¹ In case of duplicate publications from the same study, the study with the largest number of cases was used, but if the overlapping publication provided additional data for subgroups by gender or other study characteristics or categorical data when the main publication only contained continuous data, the overlapping publication was used in subgroup analyses or in nonlinear dose-response analyses (which requires ≥ 3 categories of resting heart rate), but each study was only included once in each analysis. When studies reported results separately by gender or other subgroups, but no overall result, the data were combined using a fixed effects model before inclusion in the overall meta-analysis.

Reference List

- (1) Ganna A, Ingelsson E. 5 year mortality predictors in 498,103 UK Biobank participants: a prospective population-based study. *Lancet*. 2015;386:533-540.