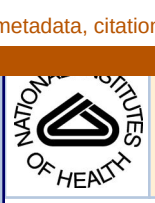

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Association between resting heart rate across the life course and all-cause mortality: longitudinal findings from the Medical Research Council (MRC) National Survey of Health and Development (NSHD)

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Abstract

Background—Resting heart rate (RHR) is an independent risk factor for mortality. Nevertheless, it is unclear whether elevations in childhood and mid-adulthood RHR, including changes over time, are associated with mortality later in life. We sought to evaluate the association between RHR across the life course, along with its changes and all-cause mortality.

Methods—We studied 4638 men and women from the Medical Research Council (MRC) National Survey of Health and Development (NSHD) cohort born during 1 week in 1946. RHR was obtained during childhood at ages 6, 7 and 11, and in mid-adulthood at ages 36 and 43. Using multivariable Cox regression, we calculated the HR for incident mortality according to RHR measured at each time point, along with changes in mid-adulthood RHR.

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Contributors BÓH, RH, DK, TMG and IS made substantial contributions towards the study's conception and design, acquisition of data or analysis and interpretation of data. BH and RH were responsible for the initial drafting of the manuscript. All authors were involved in critically revising the manuscript for important intellectual content. All authors approved the final version.

Ethics approval The appropriate Ethics Committees approved this study, with the latest assessment at ages 60–64 approved by the Central Manchester Research Ethics Committee for the data collection that took place in England and Wales, and by the Scotland A Research Ethics Committee for the data collection that took place in Scotland. All of the study participants provided informed consent.

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Results—At age 11, those in the top fifth of the RHR distribution (≥97 bpm) had an increased adjusted hazard of 1.42 (95% CI 1.04 to 1.93) for all-cause mortality. A higher adjusted risk (HR, 95% CI 2.17, 1.40 to 3.36) of death was also observed for those in the highest fifth (≥81 bpm) at age 43. For a > 25 bpm increased change in the RHR over the course of 7 years (age 36–43), the adjusted hazard was elevated more than threefold (HR, 95% CI 3.26, 1.54 to 6.90). After adjustment, RHR at ages 6, 7 and 36 were not associated with all-cause mortality.

Conclusions—Elevated RHR during childhood and midlife, along with greater changes in mid-adulthood RHR, are associated with an increased risk of all-cause mortality.

INTRODUCTION

Experimental and clinical evidence indicate that elevations in resting heart rate (RHR) contribute to an unfavourable cardiovascular profile, with an increased risk of cardiovascular morbidity and mortality among healthy individuals,[1–3] as well as in subgroups of patients at elevated risk for cardiovascular diseases (CVD).[4–9]

To date, few studies have evaluated longitudinal changes in RHR in relation to all-cause mortality, [3 10] and the available studies have used age-heterogeneous samples whose mean age was approximately 50 years at first measurement of RHR. Studies reporting the relationship between RHR and mortality at different phases of the life course, particularly in earlier adulthood, are sparse, and to our knowledge, studies investigating whether childhood and adolescent RHR is associated with adult all-cause mortality have not been completed.[11] Determining whether an increase in RHR over time heightens the risk of death would enhance our understanding of the importance of this modifiable and easily assessed measure.

In the current study, we investigated the association between RHR measured during childhood, from age 6, and during early midlife, from age 36, with subsequent mortality in a cohort of British men and women who were followed until the age of 66.

METHODS

Study participants

The Medical Research Council (MRC) National Survey of Health and Development (NSHD) is a birth cohort study sampled from 16 695 birth registrations in one week of March 1946 in mainland Britain. Of these births, a socially stratified sample of 5362 (2547 male and 2815 female) individuals were selected for follow-up: all births from females with husbands in non-manual and agricultural employment, and a random selection of one in four births to females with husbands in manual employment.[12] Study members were flagged for death notification on the National Health Service Central Register (NHSCR) in 1971. Hence, notification of death, including date and cause, has been automatically received by the NSHD since this date. At that time, 288 had already died, 400 had emigrated prior to age 26, 9 were unconfirmed deaths and 27 were not flagged. Thus, a sample of 4638 (2410 men and 2228 women) who were alive and living in Britain in 1971 and flagged on the NHSCR were eligible for analysis.

Resting heart rate

Physicians collected RHR in childhood at ages 6, 7 and 11 during medical examinations that occurred in school. RHR was measured in the seated position and recorded as beats per min using the radial artery at the beginning and end of the medical examinations. For the current study, we used the second measurement obtained during childhood, which was on average the lower of the two measures. In mid-adulthood (at ages 36 and 43), RHR was recorded once by trained research nurses during home assessments. At these visits, RHR was determined as beats per min using the radial artery following 3 min of rest in the seated position before blood pressure measurements were taken.

Assessments during childhood and mid-adulthood

During the childhood medical examinations, height and weight were measured at the same ages at which RHR was determined, and body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Childhood socioeconomic position at age 11 was based on the father's occupation and classified as professional, intermediate, skilled non-manual, skilled manual or partly skilled and unskilled according to the Registrar General's classification. In mid-adulthood, potential confounders that were available at both 36 and 43 years included socioeconomic position, smoking habits, leisure time physical activity, BMI, blood pressure and antihypertensive treatment. Socioeconomic position was based on the participant's occupation using the same classification as reported during childhood. Smoking status was defined as current, ex-smoker or never, and physical activity categories were defined as inactive, moderately active and active.[13] Height and weight were measured according to a standard protocol and BMI was calculated. Systolic and diastolic blood pressure (mm Hg) was measured twice using the Hawksley random zero sphygmomanometer. The second of the two measures was used unless the second was missing or invalid.[14] Participants were also asked to report whether they were currently being treated for hypertension.

From birth, all hospital admissions have been recorded. For all self-reported hospital admissions at age 36 and 43 years, hospital records were requested and International Classification of Diseases (ICD) codes obtained. Confirmed admissions for coronary heart disease (CHD) or cerebrovascular disease before age 43 years were defined using ICD9 codes 401–414 and ICD10 codes I20–I25 for CHD and ICD9 codes 430–438 and ICD10 codes I60–I69 for cerebrovascular disease. Physician diagnoses of diabetes, date of diagnosis and antidiabetic medication use were self-reported during interviews at age 36 and 43 and on postal questionnaires at age 31. The age at onset of diabetes and the history of reported medication for each individual reporting diabetes were subsequently reviewed by a general practitioner to define cases of type 2 diabetes mellitus.[15]

Statistical methods

Baseline characteristics—Both childhood and mid-adulthood variables were summarised according to quintiles of RHR, reporting means and SDs, or counts and proportions.

Childhood and mid-adulthood RHR and all-cause mortality—Cox proportional hazard regression models reporting HRs with 95% CIs were used to investigate the

relationship between childhood, and separately, adult RHR with all-cause mortality. For the evaluation of childhood RHR, follow-up time was from January 1971 (ie, when the cohort were flagged for death notification) until the first date of death, emigration or the end of March 2012 (the cohort's 66th birthday). For the non-decedents, follow-up was treated as censored. To investigate adult RHR, follow-up for mortality was from the cohort's 43rd birthday (March 1989) until the end of March 2012, given that our main interest was in the change in RHR from age 36 to 43. For the main analysis of adult RHR, only those free from CHD, cerebrovascular disease and type 2 diabetes at the start of follow-up were included in the analyses.

We investigated how continuous RHR (10 bpm increments) at ages 6, 7 and 11, and separately, at ages 36 and 43 was associated with all-cause mortality. Further, we categorised RHR at each time point using quintiles and tested for deviation from a linear trend by comparing the model with RHR fitted as a categorical variable with RHR fitted as a linear trend across the five categories. The proportional hazards assumption in all models was checked by visual inspection of the plots and by testing of time-dependent covariates. We tested for sex by childhood and adult RHR interactions and found no evidence of a sex difference in the associations; thus, models including men and women adjusted for sex but without the interaction term were used. All models were subsequently adjusted for potential confounders.

Change in mid-adulthood RHR and all-cause mortality—Subsequently, we examined the association between change in RHR from age 36 to 43 and all-cause mortality. First, we fitted a model including RHR at both ages 36 and at 43 so that the HR for RHR at age 43 represented the association with conditional change in RHR. We then used the following categories of change in RHR following the approach of Nauman *et al*,[10] (a) a decrease of greater than 25 bpm; (b) a decrease between 15 and 25 bpm; (c) a decrease between 5 and 15 bpm; (d) a change from −5 to 5 bpm (reference); (e) an increase between 5 and 15 bpm; (f) an increase between 15 and 25 bpm and (g) an increase of greater than 25 bpm. Sex–adjusted and then fully adjusted models were fitted.

Multiple imputation procedures—In order to maintain the sample size and minimise bias introduced by missing data in fully adjusted analyses, we employed a multiple imputation procedure to impute missing childhood and mid-adulthood covariates.[16] For models with childhood RHR, 453 (11.3%) had imputed values for BMI or father's social class at age 6, 555 (14.2%) at age 7 and 161 (4.2%) at age 11. For adult RHR change models, 462 (16.1%) had imputed values for systolic and diastolic blood pressure, occupational social class, physical activity, smoking or antihypertensive medication (see online supplementary table S1 for details). A total of 20 imputed datasets were obtained using chained equations implemented using ice in STATAV.12 (StataCorp, Texas, USA), which is able to handle both categorical and continuous covariates.[16] The estimates and SDs were calculated for each and then combined using Rubin's rule. The imputation models included all variables in each fully adjusted analytic model as well as the event indicator (death) and the estimate of the cumulative baseline hazard and additional variables (ie, cognitive test scores in childhood, birth weight, BMI measured at other ages in childhood,

maternal and paternal education and father's occupational social class at other ages in childhood, and for adult RHR models only, early adult measures of BMI, cigarette smoking and own social class) that helped predict the missing covariates. [17] Complete case analyses were carried out for comparison.

Sensitivity analyses—For analysis of RHR in adulthood, we conducted a number of sensitivity checks. First, we omitted participants who died within the first 3 years of follow-up (n=238) to reduce the effect of subclinical and undetected pre-existing illnesses that could influence the initial findings. Second, we removed those who reported the use of antihypertensive medications (n=233) as such treatments may alter the RHR.

All statistical calculations were computed using STATA V.12 (StataCorp). All analyses were considered significant at a two-tailed p value < 0.05.

RESULTS

Starting at age 26, of the 4638 participants flagged, 533 died over the next 40 years (incidence=3.09 deaths per 1000 person-years). During childhood assessments, there was little variation in the pattern of covariates according to quintiles of RHR (table 1). During mid-adulthood assessments, however, participants in the uppermost fifth of RHR tended to have higher blood pressure and were more likely to be inactive, current smokers and unemployed compared with those in the lowest fifth (table 1).

Higher RHR at age 11, but not at ages 6 or 7, was associated with a modest increase in mortality rate from 26 to 66 years (table 2, model 1); each 10 bpm increment in RHR was associated with a hazard of 1.09 (95% CI 1.01 to 1.17). There was little attenuation in this association after adjusting for sex, childhood BMI, height or father's social class (table 2, model 2). Further investigation of this relationship showed that those in the top fifth of the RHR distribution at age 11 (≥97 bpm) had a significant 1.42 (95% CI 1.04 to 1.93) increase in the adjusted hazard for adult mortality compared with those in the lowest fifth (≤76 bpm).

Higher RHR at ages 36 and 43 was associated with an increase in mortality rate (table 3, model 1). Both associations were attenuated after adjustment for sex, blood pressure, BMI, own occupational class, leisure-time physical activity, smoking and antihypertensive treatment, although each 10 bpm increment in RHR at age 43 was still associated with a 1.27 (95% CI 1.13 to 1.44) increase in the adjusted hazard for all-cause mortality (table 3, model 2). In the categorical analysis, the risk (adjusted HR, 95% CI 2.17, 1.40 to 3.36) of death was greater among those in the highest (≥81 bpm) compared with the lowest (≤63 bpm) fifth at age 43 (table 3, model 2).

RHR at age 43 remained associated with a higher mortality rate even after adjusting for prior RHR at age 36 (adjusted HR per 10 bpm increment, 95% CI 1.35, 1.19 to 1.53), indicating that a greater increase in RHR between 36 and 43 years was a risk factor for mortality. The attenuation after adjusting for covariates was only modest (table 3, model 2). In figure 1, compared with a minimal change of 5 bpm, an increase between 16 and 25 bpm as well as more than a 25 bpm increase in the RHR from age 36 to 43 was associated with a 1.75 (95%

CI 1.11 to 2.75) and 3.26 (95% CI 1.54 to 6.90) adjusted hazard for all-cause mortality, respectively.

The findings in this study did not change appreciably when deaths during the first 3 years of follow-up were excluded (adjusted HR per 10 bpm increment, 95% CI 1.39, 1.24 to 1.56) or when those on antihypertensive medication were omitted from analyses (adjusted HR per 10 bpm increment, 95% CI 1.44, 1.28 to 1.62) at age 43. The results from complete case analyses were very similar to the main analyses. The unadjusted associations in the reduced complete case sample were generally slightly weaker than those in the full sample, although the effects of further covariate adjustment were virtually the same (see online supplementary tables S2 and S3).

DISCUSSION

In the present study, we observed a modest significant relationship between elevated RHR measured at age 11 and a higher rate of all-cause mortality. While the positive relationship between elevated RHR and the risk of dying has been well documented in adults,[18–22] the role of RHR as a distinct marker of health status in childhood remains relatively unclear. Modifiable risk factors including BMI and blood pressure have been reported to track into adulthood and have been shown to act independently in children towards influencing cardiovascular risk later in life.[23 24] A higher RHR found during childhood may be an additional risk factor to consider. Though further studies are needed to test whether these findings are replicated.

During early mid-life at age 43, elevated RHR was also found to be associated with subsequent all-cause mortality independently of other risk factors. Moreover, in spite of the small group size, an increased change of more than 25 bpm in RHR between the ages of 36 and 43 raised the risk of death by more than threefold. Our findings are in line with the few prior studies that evaluated the association between changes in RHR and mortality. In a prospective study of 29 325 patients without known cardiovascular disease,[10] a greater increase in RHR over 10 years was associated with a greater risk of death due to ischaemic heart disease (IHD). The adjusted risk of dying was almost twofold higher among subjects whose RHR was below 70 bpm at the first measurement but greater than 85 bpm at the second.[10] In 5139 asymptomatic working men, Jouven and coworkers[3] evaluated the prognostic implications of RHR measured 5 years apart with the risk of total mortality. In that study, individuals with an increase of more than 3 bpm in RHR had a 19% greater risk of death.[3] Collectively, these data highlight the importance of a high RHR and its changes over the life course for heightening the risk of death.

Dysfunctional autonomic nervous activity likely plays a central role in the pathogenesis of numerous adverse health conditions. For instance, predominant sympathetic overactivity is considered a crucial feature in atherosclerotic plaque development via initiation of several hemodynamic (ie, tachycardia, hypertension) alterations.[25] Thus, it may seem that RHR is merely a marker of autonomic nervous system dysregulation rather than a risk factor per se. Despite this, however, ample evidence supports the notion that a high RHR may intervene along a chain of events, thereby promoting CVD.[26 27] These mechanisms include, but are

unlikely restricted to, disturbed haemodynamics and mechanical stress, oxidative stress, vascular remodelling, endothelial dysfunction and inflammation.[25 26] Moreover, elevated RHR may induce myocardial ischaemia by amplifying myocardial oxygen demand as well as limiting coronary blood supply.[26 28] These actions, in part, influenced by RHR may increase plaque vulnerability as well as erosion and rupture.[26]

Based on the findings from this study, slowing the RHR in early midlife may prove a useful adjunct for interrupting the unhealthy processes found later in life. Notably, in the general population, physical exercise may exert beneficial health effects by augmenting parasympathetic outflow while diminishing sympathetic overactivity in the human heart.[29] Reducing the RHR through physical activity could therefore improve a host of adverse risk factors, including obesity, type 2 diabetes, hypertension and increased inflammatory activity.[30–35] Further examination of the potential role of exercise training towards slowing the RHR in apparently healthy adults is warranted.

The current investigation had limitations. This study lacked some measurements that could have confounded or mediated the relationship between RHR and mortality. During childhood, the main aim of the NSHD was to investigate how the environment at home and at school affected physical and mental development and educational attainment. Thus, some measures (eg, blood pressure) were not of primary concern. In addition, during adulthood, measures that reflect autonomic nervous system dysregulation or inflammatory activity, as well as the reported use of specific cardiovascular medications (eg, β blockers), or medical devices (eg, cardiac pacemakers) were lacking.[30 36–38] The numbers of events in some subgroups according to changes in the RHR from ages 36 to 43 were small. Thus, caution should be taken when drawing firm conclusions from these estimates. We evaluated the association between RHR and mortality using 10 bpm increments as well as quintiles; additional studies may wish to include other heart rate metrics. Nevertheless, strengths of the present study include the analysis of a nationally representative cohort living in Britain, as well as repeat information on RHR obtained early in life through mid-adulthood, which afforded a unique opportunity to study the relationship between RHR measured across life with the risk of death from all causes.

In conclusion, elevations in the RHR during childhood, as well as greater changes in early midlife, were associated with all-cause mortality from young adulthood to early old age. Though the relationship between high RHR and all-cause mortality is well defined in adult populations, the deleterious role of RHR during childhood remains unsettled. As such, forthcoming studies are encouraged to explore the potential role of childhood RHR for later mortality risk and the disease processes through which it operates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known on this subject

- Prior epidemiological studies have documented a strong and independent relationship between fast resting heart rate and all-cause mortality, especially among older adults.
- Studies have yet to determine the association between resting heart rate and risk of mortality at different phases of the life course.

What this study adds

- Elevations in the resting heart rate found during childhood and greater changes in midlife increased the likelihood of dying from any cause.
- As a distinct marker of health status, a high resting heart rate found earlier in life may track into late-adulthood and act independently towards influencing cardiovascular risk later in life.

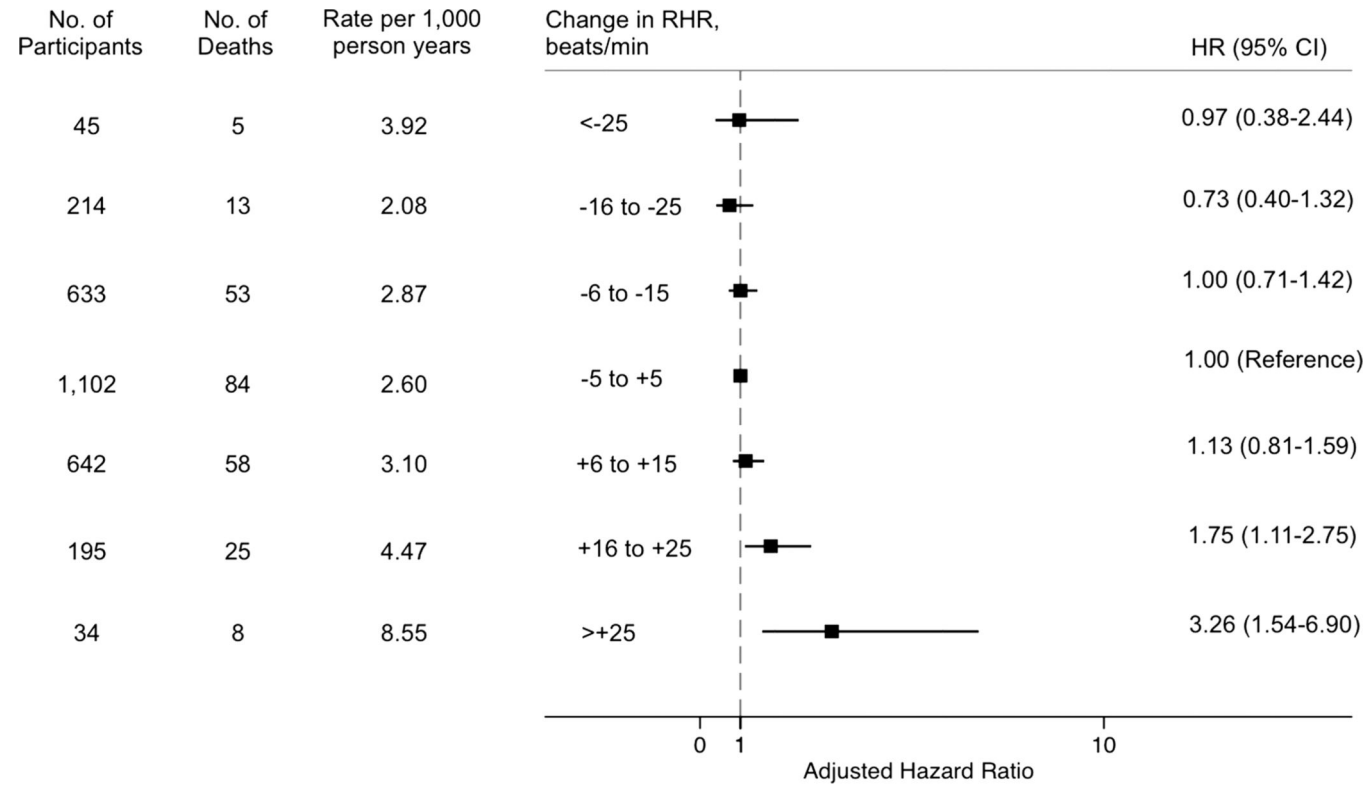

Figure 1.

Death from all causes according to changes in the resting heart rate categories from age 36 to 43 years. Model included cases free from coronary heart disease, cerebrovascular disease, and type 2 diabetes mellitus at baseline (age 43 years). Model adjusted as reported in table 3. Multiple imputation used to impute missing covariates (20 imputations used).

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Table 1

Participant characteristics according to quintiles of resting heart rate at different ages

			Resting heart rate quintiles				
Variable	**n**	**Total**	**1st**	**2nd**	**3rd**	**4th**	**5th**
6 years							
Sex (% female)	3993	1924(48.2)	424(43.7)	437(45.0)	232(49.4)	451(51.0)	380(54.7)
Resting heart rate(beats per min)	3993	91(13)	76(4)	86(2)	91(1)	98(2)	111(8)
Body mass index (kg/m^2)	3614	15.8(1.4)	15.9(1.4)	15.8(1.3)	15.9(1.4)	15.8(1.4)	15.7(1.3)
Height(cm)	3766	114.0(5.3)	114.3(5.3)	114.0(5.3)	114.1(5.1)	113.8(5.3)	114.0(5.5)
7 years							
Sex (% female)	3912	1906(48.7)	337(42.7)	458(47.5)	329(47.1)	348(51.3)	434(55.4)
Resting heart rate(beats per min)	3912	89(12)	74(4)	82(2)	88(1)	95(2)	107(8)
Body mass index (kg/m^2)	3686	15.8(1.5)	16.0(1.6)	15.8(1.4)	15.8(1.4)	15.8(1.5)	15.7(1.5)
Height(cm)	3838	119.9(5.7)	120.2(5.8)	120.1(5.8)	119.8(5.5)	119.9(5.6)	119.6(5.5)
11 years							
Sex (% female)	3789	1829(48.3)	380(42.0)	324(46.5)	448(45.6)	336(52.4)	341(60.6)
Resting heart rate(beats per min)	3789	85(12)	72(4)	80(1)	85(2)	92(3)	106(8)
Body mass index (kg/m^2)	3680	17.4(2.4)	17.3(2.3)	17.4(2.5)	17.3(2.3)	17.4(2.5)	17.5(2.7)
Height(cm)	3738	140.8(6.9)	140.8(6.9)	140.7(6.8)	140.8(6.8)	140.8(7.0)	140.8(7.4)
Father's occupational social class(%)	3737						
Professional		214(5.7)	55(6.2)	43(6.3)	57(5.9)	35(5.5)	24(4.3)
Intermediate		715(19.1)	183(20.5)	125(18.3)	166(17.1)	132(20.8)	109(19.7)
Skilled non-manual		577(15.4)	134(15.0)	109(15.9)	154(15.8)	92(14.5)	88(15.9)
Skilled manual		1253(33.5)	291(32.6)	219(32.0)	340(35.0)	203(32.0)	200(36.2)
Partly skilled		736(19.7)	159(17.8)	141(20.6)	206(21.2)	130(20.5)	100(18.1)
Unskilled		242(6.5)	71(8.0)	48(7.0)	49(5.0)	42(6.6)	32(5.8)
36 years							
Sex (% female)	2911	1468(50.4)	359(43.0)	183(46.3)	324(53.4)	347(55.6)	255(56.7)
Resting heart rate(beats per min)	2911	72(10)	61(4)	67(1)	72(1)	78(2)	88(6)
Systolic blood pressure(mm Hg)	2893	120(15)	118(15)	119(15)	119(14)	121(15)	123(15)
Diastolic blood pressure(mm Hg)	2890	77(12)	76(12)	76(12)	76(12)	77(12)	79(12)

			Resting heart rate quintiles				
Variable	**n**	**Total**	**1st**	**2nd**	**3rd**	**4th**	**5th**
Body mass index (kg/m^2)	2885	24.2(3.7)	24.0(3.4)	24.0(3.5)	23.8(3.5)	24.4(3.7)	24.8(4.6)
Occupational social class (%)	2541						
Professional		202(8.0)	73(9.5)	30(8.8)	36(6.9)	41(7.7)	22(5.8)
Intermediate		789(31.1)	240(31.3)	121(35.5)	161(30.7)	159(30.0)	108(28.7)
Skilled non-manual		542(21.3)	161(21.0)	63(18.5)	114(21.7)	116(21.9)	88(23.3)
Skilled manual		544(21.4)	157(20.4)	70(20.5)	123(23.4)	112(21.1)	82(21.8)
Partly skilled		379(14.9)	112(14.6)	46(13.5)	74(14.1)	84(15.9)	63(16.7)
Unskilled		85(3.4)	25(3.3)	11(3.2)	17(3.2)	18(3.4)	14(3.7)
Physical activity	2903						
Inactive		1054(36.3)	245(29.3)	129(32.7)	221(36.5)	247(39.8)	212(47.2)
Less active		735(25.3)	190(22.8)	98(24.9)	168(27.8)	169(27.3)	110(24.5)
Most active		1114(38.4)	400(47.9)	167(42.4)	216(35.7)	204(32.9)	127(28.3)
Smoking	290 9						
Never		873(30.0)	286(34.2)	128(32.4)	168(27.7)	183(29.4)	104(24.1)
Ex		1106(38.0)	385(46.1)	153(38.7)	234(38.6)	207(33.2)	175(28.3)
Current		930(32.0)	164(19.6)	114(28.9)	205(33.8)	233(37.4)	214(47.7)
Antihypertensive medication (%)	2911	42(1.4)	12(1.4)	7(1.8)	6(1.0)	8(1.3)	9(2.0)
43 years							
Sex (% female)	2911	1468(50.4)	237(40.2)	343(49.7)	248(51.2)	392(57.7)	248(53.0)
Resting heart rate(beats per min)	2911	72(10)	59(4)	66(2)	71(1)	78(2)	88(6)
Systolic blood pressure(mm Hg)	2686	123(16)	121(15)	121(15)	123(15)	124(17)	128(18)
Diastolic blood pressure(mm Hg)	2686	80(13)	78(12)	79(11)	80(12)	80(13)	82(14)
Body mass index (kg/m^2)	2894	25.5(4.2)	24.7(3.3)	25.3(4.0)	25.5(4.2)	25.7(4.5)	26.3(5.0)
Occupational social class (%)	2902						
Professional		179(6.2)	60(10.2)	36(5.2)	20(4.2)	36(5.3)	27(5.8)
Intermediate		1049(36.2)	235(40.0)	255(37.0)	178(37.0)	238(35.3)	143(30.6)
Skilled non-manual		617(21.3)	110(18.7)	149(21.6)	109(22.7)	139(20.6)	110(23.5)
Skilled manual		485(16.7)	87(14.8)	118(17.1)	84(17.5)	114(16.9)	82(17.5)
Partly skilled		304(10.5)	62(10.5)	80(11.6)	48(10.0)	66(9.8)	48(10.3)
Unskilled		94(3.2)	12(2.0)	20(2.9)	12(2.5)	33(4.9)	17(3.6)

Variable	n	Total	Resting heart rate quintiles				
			1st	2nd	3rd	4th	5th
Unemployed since 1982		174(6.0)	22(3.7)	32(4.6)	30(6.2)	49(7.3)	41(8.8)
Physical activity	2911						
Inactive		1516(52.1)	231(39.2)	343(49.7)	267(55.2)	388(57.1)	287(61.3)
Less active		670(23.0)	141(23.9)	152(22.0)	120(24.8)	152(22.4)	105(22.4)
Most active		725(24.9)	218(37.0)	195(28.3)	97(20.4)	139(20.5)	76(16.2)
Smoking	2907						
Never		883(30.4)	232(39.3)	216(31.4)	131(27.2)	179(26.4)	125(26.8)
Ex		1174(40.4)	254(43.1)	307(44.6)	201(41.6)	252(36.5)	160(34.3)
Current		850(29.2)	104(17.6)	166(24.1)	151(31.3)	248(36.5)	181(38.8)
Antihypertensive medication (%)	2911	99(3.5)	31(5.4)	18(2.6)	9(1.2)	18(2.7)	23(5.0)
Coronary heart disease (%)	2911	24(0.8)	9(1.5)	2(0.3)	3(0.6)	8(1.2)	2(0.4)
Cerebrovascular disease (%)	2911	3(0.1)	1(0.2)	1(0.1)	0(0)	1(0.2)	0(0)
Type 2 diabetes mellitus (%)	2911	20(0.7)	4(0.7)	1(0.1)	1(0.2)	6(0.9)	8(1.7)

Values reported as mean±SD or counts with proportions.

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Table 2

Risk of all-cause mortality according to resting heart rate in childhood

Resting heart rate	n	Deaths	Rate per 1000 person-years	Model 1 hazard ratio(95% CI)*	Model 2 hazard ratio(95% CI)†
Age 6 years	3993	453	3.05		
10 bpm increment				0.99(0.92 to 1.07)	0.99(0.92 to 1.07)
Quintiles					
1st ≤80	971	102	2.82	1(reference)	1(reference)
2nd 81–88	972	134	3.74	1.33(1.03 to 1.73)	1.33(1.03 to 1.72)
3rd 89–92	470	56	3.17	1.15(0.83 to 1.59)	1.17(0.84 to 1.62)
4th 93–100	885	88	2.67	0.96(0.72 to 1.28)	0.96(0.73 to 1.28)
5th ≥101	695	73	2.79	1.02(0.75 to 1.37)	1.02(0.75 to 1.37)
P_{trend}				0.4	0.4
Age 7 years	3912	443	3.04		
10 bpm increment				1.05(0.97 to 1.13)	1.05(0.97 to 1.13)
Quintiles					
1st ≤78	789	77	2.59	1(reference)	1(reference)
2nd 79–84	964	125	3.51	1.38(1.04 to 1.83)	1.40(1.06 to 1.87)
3rd 85–90	698	68	2.62	1.03(0.74 to 1.42)	1.03(0.74 to 1.43)
4th 91–99	678	78	3.09	1.22(0.89 to 1.67)	1.24(0.90 to 1.70)
5th ≥100	783	95	3.26	1.31(0.97 to 1.77)	1.32(0.97 to 1.78)
P_{trend}				0.3	0.3
Age 11 years	3789	440	3.12		
10 bpm increment				1.09(1.01 to 1.17)	1.08(1.00 to 1.17)
Quintiles					
1st ≤76	905	92	2.71	1(reference)	1(reference)
2nd 77–80	697	86	3.31	1.24(0.92 to 1.66)	1.22(0.91 to 1.64)
3rd 81–88	983	120	3.26	1.22(0.93 to 1.59)	1.21(0.92 to 1.59)
4th 89–96	641	67	2.82	1.08(0.79 to 1.48)	1.07(0.78 to 1.47)
5th ≥97	563	75	3.61	1.43(1.05 to 1.94)	1.42(1.04 to 1.93)
P_{trend}				0.09	0.1

Multiple imputation was carried out to impute missing covariates(20 imputations).

* Model adjusted for sex only.

† Model also adjusted for body mass index, height at same age as resting heart rate and father's occupational social class.

Table 3

Hazard ratios for all-cause mortality according to resting heart rate in midlife

Resting heart rate	n	Deaths	Rate per 1000 person-years	Model 1 hazard ratio(95% CI)*,†	Model 2 hazard ratio(95% CI)*,‡
Age 36 years	2865	246	2.94		
10 bpm increment				1.23(1.09 to 1.39)	1.08(0.95 to 1.22)
Quintiles					
1st ≤ 64	824	61	2.53	1(reference)	1(reference)
2nd 65–68	390	35	3.09	1.24(0.82 to 1.88)	1.12(0.74 to 1.71)
3rd 69–74	599	46	2.62	1.08(0.74 to 1.59)	0.91(0.62 to 1.35)
4th 75–80	613	50	2.80	1.17(0.80 to 1.70)	0.93(0.64 to 1.36)
5th ≥81	439	54	4.24	1.79(1.24 to 2.59)	1.22(0.83 to 1.79)
P_{trend}				0.01	0.6
Age 43 years	2865	246	2.94		
10 bpm increment				1.40(1.24 to 1.57)	1.27(1.13 to 1.44)
Quintiles					
1st ≤ 63	577	32	1.89	1(reference)	1(reference)
2nd 64–68	686	43	2.13	1.17(0.74 to 1.85)	1.13(0.71 to 1.80)
3rd 69–72	480	48	3.42	1.90(1.21 to 2.97)	1.68(1.06 to 2.64)
4th 73–80	664	57	2.94	1.68(1.09 to 2.59)	1.36(0.87 to 2.13)
5th ≥81	458	66	5.03	2.83(1.86 to 4.33)	2.17(1.40 to 3.36)
P_{trend}				<0.001	<0.001
Change from 36 to 43 years	2865	246	2.94		
Age 36, 10 bpm increment				1.10(0.96 to 1.25)	0.97(0.85 to 1.11)
Age 43, 10 bpm increment				1.35(1.19 to 1.53)	1.29(1.13 to 1.47)

Multiple imputation was used to impute missing covariates(20 imputations used).

*Models included cases free from coronary heart disease, cerebrovascular disease and type 2 diabetes mellitus at baseline(age 43 years).

†Model adjusted for sex only.

‡Model also adjusted for blood pressure, body mass index, own occupational class, leisure-time physical activity, smoking and antihypertensive treatment.