Appendix 6 (as supplied by the authors): P values for non-linearity ($P_{for\ non\text{-}linearity}$) in the dose-response analysis restricted cubic spline functions

Coronary heart disease		Stroke		All other diseases		All Cancer		Total other diseases		Sudden death	
Study	P	Study	P	Study	P	Study	P	Study	P	Study	P
Overall	0.05		1.00		0.23		0.87		0.36		0.62
Woodward et al. 2014[1]	0.99	O'Neal et al. 2015[2]	0.23	Legeai et al. 2011[3]	0.28	Jouven et al. 2011[4]	0.40	Okamura(M) et al. 2004[5]	0.16	Adabag et al. 2008[6]	1.00
Wang et al. 2014[7]	0.80	Woodward et al. 2014[1]	0.81	Jouven et al. 2011[4]	0.12	Batty et al. 2010[8]	0.66	Okamura(W) et al. 2004[5]	0.09	Shaper et al. 1993[9]	0.92
Aladin(M) et al. 2014[10]	0.72	Wang et al. 2014[7]	0.12	Tverdal(M) et al. 2008[11]	0.00	Thomas et al. 2001[12]	0.78	Reunanen(M) et al. 2000[13]	0.93	Tverdal(M) et al. 2008[11]	0.84
Aladin(W) et al. 2014[10]	0.38	Hisamatsu et al. 2014[14]	0.18	Tverdal(W) et al. 2008[11]	0.89	Reunanen(M) et al. 2000[13]	0.94	Reunanen(W) et al. 2000[13]	0.98	Tverdal(W) et al. 2008[11]	0.21
Nauman et al. 2011[15]	0.19	Mao(M) et al. 2010[16]	0.36	Hozawa et al. 2008[17]	0.22	Reunanen(W) et al. 2000[13]	0.12	Wannamethee et al. 1993[18]	0.42	---	--
Legeai et al. 2011[3]	0.76	Mao(W) et al. 2010[16]	0.80	Seccareccia et al. 2001[19]	0.33	Kristal-Boneh et al. 2000[20]	0.68	---	--	---	--
Nauman(W) et al. 2010[21]	0.77	Batty et al. 2010[8]	0.18	Benetos(M) et al. 1999[22]	0.08	Wannamethee et al. 1993[18]	0.19	---	--	---	--
Nauman(M) et al. 2010[21]	0.01	Hsia et al. 2009[23]	0.73	Benetos(W) et al. 1999[22]	0.04	---	--	---	--	---	--
Mao(M) et al. 2010[16]	0.42	Tverdal(M) et al. 2008[11]	0.22	Wannamethee et al. 1993[18]	0.14	---	--	---	--	---	--
Mao(W) et al. 2010[16]	0.03	Tverdal(W) et al. 2008[11]	0.30	Gillum(M) et al. 1991[24]	0.62	---	--	---	--	---	--

Batty et al. 2010[8]	0.20	Reunanen(M) et al. 2000[13]	0.13	Gillum(W) et al. 1991[24]	0.53	---	--	---	--	---	--
Hsia et al. 2009[23]	0.07	Reunanen(W) et al. 2000[13]	0.53	---	--	---	--	---	--	---	--
Tverdal(M) et al. 2008[11]	0.01	Benetos(M) et al. 1999[22]	0.45	---	--	---	--	---	--	---	--
Tverdal(W) et al. 2008[11]	0.35	Benetos(W) et al. 1999[22]	0.41	---	--	---	--	---	--	---	--
Adabag et al. 2008[6]	0.13	---	--	---	--	---	--	---	--	---	--
Reunanen(M) et al. 2000[13]	0.25	---	--	---	--	---	--	---	--	---	--
Reunanen(W) et al. 2000[13]	0.76	---	--	---	--	---	--	---	--	---	--
Benetos(M) et al. 1999[22]	0.86	---	--	---	--	---	--	---	--	---	--
Benetos(W) et al. 1999[22]	0.55	---	--	---	--	---	--	---	--	---	--
Shaper et al. 1993[9]	0.95	---	--	---	--	---	--	---	--	---	--
Gillum(M) et al. 1991[24]	0.30	---	--	---	--	---	--	---	--	---	--
Gillum(W) et al. 1991[24]	0.70	---	--	---	--	---	--	---	--	---	--

RHR levels at the 25th, 50th and 75th percentiles were 65, 73 and 85 bpm for CHD analysis, 65, 72 and 84 in stroke analysis, 65, 75 and 87 bpm in all other diseases, 64, 72 and 85 in cancer analysis, 55, 69 and 82 in total other diseases analysis, and 65, 75 and 87 in sudden death analysis. In CHD analysis, there was marginal between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=21%) and second (I2=16%) spline transformations of RHR levels.

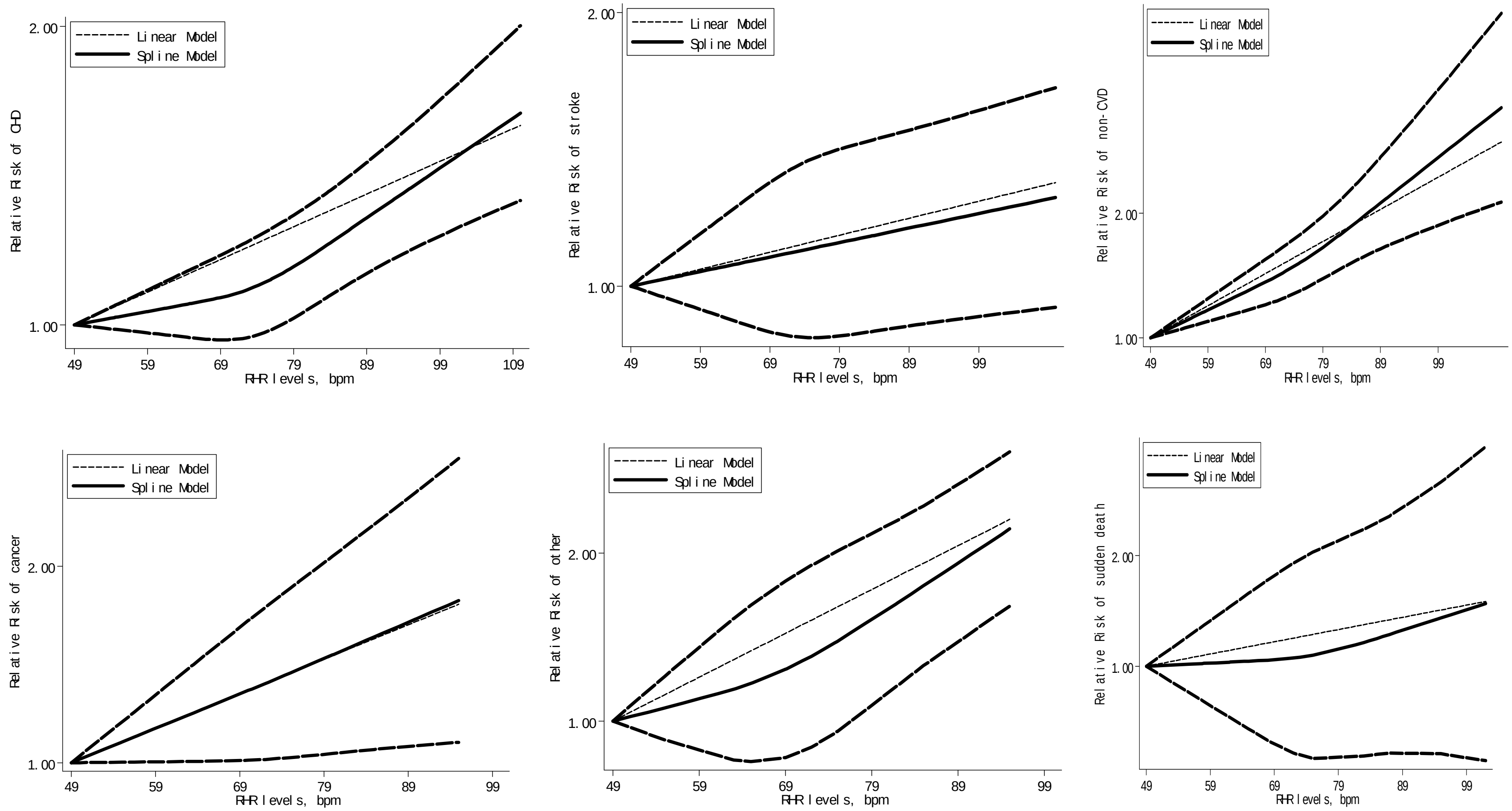
In stroke analysis, there was marginal between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=35%) and second (I2=14%) spline transformations of RHR levels.

In all other diseases analysis, there was moderate between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=40%) and second (I2=48%) spline transformations of RHR levels.

In all cancer analysis, there was marginal between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=30%) and second (I2=0%) spline transformations of RHR levels.

In total other diseases (all other diseases after excluding cancer) analysis, there was marginal between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=19%) and second (I2=20%) spline transformations of RHR levels.

In sudden death analysis, there was no between-study heterogeneity among study-specific trends, defined by the coefficients of the first (I2=0.00%) and second (I2=0.00%) spline transformations of RHR levels.



The dose–response analysis of resting heart rate (RHR) with risk of coronary heart disease (CHD), stroke, all other diseases [non-cardiovascular diseases (CVD)], all cancer, total other diseases and sudden death. The solid and long dash lines represent the estimated relative risks (RRs) and 95% confidence intervals. The short dash lines represent the linear relation. The vertical axis is on a log scale. To be consistent with the analysis (compared with the lowest category of RHR) in table 1, we used the lowest value in the included studies (49 beats/minute) as the reference level.

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