

SUPPLEMENTAL DATA

Long-term exposure to elevated systolic blood pressure in predicting incident cardiovascular disease: evidence from large-scale routine electronic health records

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Data S1

Estimating 'usual' systolic blood pressure values

To understand the relationship between a risk factor and disease in the population, it is a common practice to measure the risk factor at a single point in time (at 'baseline' period) and prospectively follow the population for the occurrence of a health outcome, such as cardiovascular disease. However, risk factors, such as blood pressure (as well as many other biological markers of disease) are measured imprecisely and fluctuates over time, so blood pressure measured singly may not reflect the 'true' exposure to, or 'usual' levels of, the risk factor. This imprecision tend to attenuate associations between risk factor and the disease, a statistical phenomenon commonly referred to as *regression dilution bias*. Thus, risk estimates associated with baseline blood pressure tend to be smaller in magnitude than when based on 'usual' blood pressure.¹⁻³ The impact of regression dilution also varies with time, so the longer the time between baseline and the disease outcome, the greater the effect of regression dilution bias on risk estimates. Regression dilution bias may be 'statistically' corrected to obtain an estimate of the 'usual' level of blood pressure using methods that typically require repeated measurements of blood pressure (for all, or a subset of, participants) from which a correction factor (also referred to as the *regression dilution ratio*) is derived. We used Rosner's regression method⁴ and employed the *geeglm* function of the GEEPACK package in R to obtain the correction factor. We also used other correction factor values from published data as part of our sensitivity analyses.^{1, 2}

Table S1. The ICD-10 and Read codes used to define coronary heart disease and stroke/transient ischemic attack.

| Outcome | Code |
|---|--|
| <u>Coronary heart disease</u> | |
| ICD-10 | I20, I20.0, I20.8, I20.9, I21, I21.0, I21.1, I22.2, I21.3, I21.4, I21.9, I22, I22.0, I22.1, I22.8, I22.9, I23.7, I25, I25.0, I25.1, I25.2, I25.3, I25.4, I25.5, I25.6, I25.7, I25.8, I25.9 |
| Read | 7320, 22383, 1676, 52517, 36523, 4656, 39655, 1431, 19655, 7347, 17307, 54251, 39449, 9276, 66388, 11983, 34328, 18118, 8568, 32450, 45960, 1430, 20095, 18125, 29902, 25842, 54535, 7696, 1414, 9555, 26863, 12804, 28554, 24540, 39546, 737, 18249, 8312, 8679, 7634, 7442, 11610, 7137, 51515, 9414, 7134, 44561, 10209, 42708, 7609, 32651, 57241, 19402, 36011, 33461, 67554, 37682, 28837, 33718, 48822, 44723, 22647, 56990, 96804, 24888, 55598, 34963, 3159, 33471, 31571, 2901, 5703, 18670, 33735, 42462, 86071, 41547, 732, 22828, 19046, 8942, 42304, 93618, 22020, 43939, 60067, 87849, 85947, 92927, 96537, 61208, 733, 38813, 70185, 86773, 20903, 64923, 66921, 737, 18249, 8312, 8679, 7634, 7442, 11610, 7137, 51515, 9414, 7134, 44561, 19413, 10209, 42708, 61310, 7609, 31556, 32651, 70111, 57241, 45886, 45370, 59423, 48767, 19402, 36011, 92419, 66664, 66236, 67761, 19193, 37682, 28837, 33718, 31519, 51507, 22647, 68123, 68139, 37719, 56990, 96804, 62608, 67591, 60753, 72780, 5744, 55598, 55092, 93828, 70755, 34963, 3159, 33471, 69776, 12734, 1021, 1628, 19827, 5233, 8246, 26973, 35287, 42104, 26965, 46230, 26967, 58135, 33461, 67554, 48822, 44723, 24888, 31571, 18913, 18643, 5030, 5674, 6980, 33650, 6182, 31679, 5904, 51702, 41757, 34965, 43446, 56905, 61248, 33620, 10603, 6183, 240, 24783, 20416, 1792, 27951, 9413, 27977, 28138, 5413, 1655, 1344, 3999, 5254, 6331, 27484, 2155, 67087, 59193, 41677, 36609, 7320, 23078, 15754, 18889, 13566, 1204, 17689, 17133, 23579, 4017, 16408, 18842, 45809, 38609, 72562, 46166, 15661, 36423, 24126, 23708, 37657, 59189, 59940, 69474, 29553, 35119, 12229, 10562, 7783, 26975, 26972, 55401, 52705, 59032, 61670, 241, 2491, 30421, 1677, 13571, 12139, 5387, 40429, 17872, 14897, 8935, 29643, 23892, 14898, 63467, 3704, 9507, 1678, 30330, 32854, 29758, 34803, 28736, 62626, 41221, 46017, 14658, 68357, 32272, 46112, 46276, 41835, 68748, 96838, 61072, 21844, 29421 |
| <u>Stroke (including transient ischemic attack)</u> | |
| ICD-10 | I60, I60.0, I60.1, I60.2, I60.3, I60.4, I60.5, I60.6, I60.7, I60.8, I60.9, I61, I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.7, I61.8, I61.9, I62.0, I63, I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9, I67, I67.0, I67.1, I67.2, I67.3, I67.4, I67.5, I67.6, I68, I68.0, I68.1, I68.2, I69, I69.0, I69.1, I69.2, I69.3, G45*, G45.0*, G45.1*, G45.2*, G45.3*, G45.8*, G45.9* |
| Read | 56007, 19412, 17326, 65745, 1786, 42331, 9696, 41910, 60692, 23580, 44740, 5051, 6960, 18604, 31595, 40338, 46316, 13564, 7912, 30045, 30202, 57315, 31060, 28314, 19201, 3535, 53810, 96630, 48149, 43451, 62342, 5363, 6155, 40053, 40758, 33543, 91627, 53745, 90572, 92036, 94482, 39403, 23671, 24446, 8837, 569, 16517, 36717, 15019, 34758, 27975, 3149, 15252, 5602, 25615, 9985, 10504, 26424, 55247, 16507, 93459, 47642, 5185, 1469, 1298, 6253, 6116, 8443, 17322, 33499, 51767, 7780, 12833, 47607, 56279, 55351, 56458, 6228, 52246, 18687, 57183, 95347, 70536, 42248, 18689, 19280, 19260, 63746*, 504*, 1433*, 19354*, 1895*, 15788* |

ICD-10 - World Health Organization's International Classification of Diseases, Tenth Revision. *Codes for

transient ischemic attack.

Table S2. Baseline characteristics of participants aged 50 years at study entry who were randomly assigned to derivation and validation cohorts.

| Characteristics | Derivation cohort (N=64,772) | Validation cohort (N=16,192) |
|---|---|---|
| Women, % (n) | 70.1 (45,420) | 70.1 (11,343) |
| Men, % (n) | 29.9 (19,352) | 29.9 (4849) |
| Current systolic blood pressure (mmHg), mean (SD) | 130.7 (17.0) | 130.4 (16.9) |
| Deprivation index* | | |
| Recorded, % (n) | 99.7 (64,549) | 99.6 (16,128) |
| Mean (SD) | 3.6 (1.3) | 3.6 (1.3) |
| Smoking status, % (n) | | |
| Recorded | 64.4 (41,744) | 64.6 (10,462) |
| Smoker | 24.9 (10,409) | 24.2 (2531) |
| Ex-smoker | 20.9 (8,729) | 21.8 (2277) |
| Non-smoker | 54.2 (22,606) | 54.0 (5654) |
| With diabetes, % (n) | 2.8 (1821) | 2.9 (472) |
| Body mass index (kg/m ²) | | |
| Recorded, % (n) | 56.5 (36,570) | 57.0 (9237) |
| Mean (SD) | 27.4 (5.6) | 27.5 (5.7) |
| Total cholesterol (mmol/L) | | |
| Recorded, % (n) | 33.1 (21,450) | 32.9 (5333) |
| Mean (SD) | 5.59 (1.01) | 5.57 (1.03) |
| LDL-cholesterol (mmol/L) | | |
| Recorded, % (n) | 21.4 (13,829) | 21.0 (3408) |
| Mean (SD) | 3.45 (0.91) | 3.42 (0.90) |
| HDL-cholesterol (mmol/L) | | |
| Recorded, % (n) | 25.4 (16,424) | 25.3 (4089) |
| Mean (SD) | 1.48 (0.42) | 1.48 (0.43) |

LDL - low-density lipoprotein; HDL - high-density lipoprotein; Denominators to calculate percentages only included all those with information on the relevant variable; *Based on Index of Multiple Deprivation 2015.⁵

Table S3 (data to Figures 2 and 3). Discrimination (concordance) and calibration of incident cardiovascular disease risk prediction models at age 50 years.

| | Derivation cohort | Validation cohort |
|--|------------------------------------|------------------------------------|
| 1. Discrimination | | |
| | <i>C statistic (95% CrI)</i> | <i>C statistic (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.682 (0.666 to 0.698) | 0.689 (0.688 to 0.689) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.747 (0.722 to 0.811) | 0.750 (0.716 to 0.810) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.747 (0.722 to 0.811) | 0.750 (0.716 to 0.810) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.747 (0.722 to 0.811) | 0.750 (0.716 to 0.810) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.750 (0.727 to 0.811) | 0.755 (0.723 to 0.812) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.750 (0.726 to 0.811) | 0.755 (0.722 to 0.812) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.748 (0.723 to 0.811) | 0.753 (0.719 to 0.813) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.751 (0.725 to 0.811) | 0.757 (0.725 to 0.815) |
| 2. Calibration | | |
| | <i>Calibration slope (95% CrI)</i> | <i>Calibration slope (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.991 (0.856 to 1.100) | 1.076 (1.045 to 1.109) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.989 (0.845 to 1.139) | 0.918 (0.821 to 0.981) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.989 (0.845 to 1.139) | 0.918 (0.821 to 0.981) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.989 (0.845 to 1.139) | 0.918 (0.821 to 0.981) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.986 (0.808 to 1.133) | 0.939 (0.837 to 1.005) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.986 (0.817 to 1.129) | 0.935 (0.839 to 1.000) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.990 (0.850 to 1.137) | 0.924 (0.827 to 0.991) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.987 (0.821 to 1.127) | 0.939 (0.842 to 1.007) |

SBP – systolic blood pressure; CrI - credible interval; LDL - low-density lipoprotein; HDL - high-density lipoprotein; SBP_{PRD} - current SBP corrected using published correction factor; SBP_{HRD} – current SBP corrected using past blood pressure readings; Risk predictions based on Cox regression models and reflect the average of estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement; All models included a parameter for calendar year at study entry.

Table S4. Risk of incident cardiovascular disease associated with past, current and usual systolic blood pressure (SBP), by landmark age cohort.

| Systolic blood pressure (mmHg) | Age 40 years | Age 50 years | Age 60 years |
|--|-----------------------------------|-----------------------------------|-----------------------------------|
| | N=64,356 | N=80,964 | N=67,458 |
| | <u>HR (95% credible interval)</u> | <u>HR (95% credible interval)</u> | <u>HR (95% credible interval)</u> |
| <u>Exposure: SBP measures in separate models</u> | | | |
| Model: Current SBP | 1.18 (1.08 to 1.26) | 1.22 (1.18 to 1.30) | 1.22 (1.19 to 1.24) |
| Model: Usual SBP_{pRD} | 1.31 (1.14 to 1.46) | 1.40 (1.33 to 1.55) | 1.38 (1.13 to 1.44) |
| Model: Usual SBP_{hRD} | 1.37 (1.16 to 1.56) | 1.45 (1.36 to 1.62) | 1.48 (1.43 to 1.55) |
| Model: Mean of past SBP | 1.40 (1.27 to 1.55) | 1.44 (1.35 to 1.51) | 1.35 (1.31 to 1.39) |
| Model: Time-weighted mean of past SBP | 1.41 (1.30 to 1.57) | 1.39 (1.31 to 1.46) | 1.32 (1.28 to 1.14) |
| Model: Variability of past SBP | 1.12 (1.08 to 1.15) | 1.11 (1.10 to 1.14) | 1.10 (1.09 to 1.12) |
| <u>Exposure: Current and past SBP in the same model</u> | | | |
| Model: Current SBP | 1.02 (0.94 to 1.08) | 1.03 (0.97 to 1.10) | 1.08 (1.05 to 1.11) |
| Past SBP mean | 1.37 (1.20 to 1.51) | 1.40 (1.27 to 1.52) | 1.26 (1.22 to 1.31) |
| Model: Current SBP | 1.03 (0.94 to 1.09) | 1.08 (1.03 to 1.14) | 1.11 (1.08 to 1.13) |
| Past SBP time-weighted mean | 1.38 (1.22 to 1.53) | 1.32 (1.22 to 1.41) | 1.22 (1.17 to 1.26) |
| Model: Current SBP | 1.15 (1.07 to 1.14) | 1.08 (1.07 to 1.11) | 1.19 (1.17 to 1.22) |
| Past SBP variability | 1.11 (1.07 to 1.14) | 1.20 (1.16 to 1.28) | 1.07 (1.06 to 1.09) |

HR - hazard ratio; HR reflect the average of risk estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement using data from the derivation cohort; Risks were estimated per 20-mmHg higher baseline, usual or mean of past SBP or per 5-mmHg higher past SBP variability; Usual SBP - current SBP corrected for regression dilution using published correction factor (SBP_{pRD}=0.7) or correction factor calculated from past blood pressure recording (SBP_{hRD}=0.5); All models also adjusted for calendar year of study entry, sex and other baseline characteristics (smoking, deprivation index, diabetes, body mass index, total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol).

Table S5. Discrimination (concordance) and calibration of incident cardiovascular disease risk prediction models at age 40 years.

| | Derivation cohort | Validation cohort |
|--|------------------------------------|------------------------------------|
| 1. Discrimination | | |
| | <i>C statistic (95% CrI)</i> | <i>C statistic (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.707 (0.684 to 0.739) | 0.725 (0.721 to 0.728) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.712 (0.687 to 0.746) | 0.739 (0.730 to 0.746) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.712 (0.687 to 0.746) | 0.739 (0.730 to 0.742) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.712 (0.687 to 0.746) | 0.739 (0.730 to 0.746) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.713 (0.686 to 0.749) | 0.736 (0.727 to 0.744) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.714 (0.687 to 0.750) | 0.736 (0.727 to 0.744) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.712 (0.688 to 0.743) | 0.739 (0.729 to 0.746) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.714 (0.689 to 0.747) | 0.737 (0.728 to 0.744) |
| 2. Calibration | | |
| | <i>Calibration slope (95% CrI)</i> | <i>Calibration slope (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.988 (0.833 to 1.157) | 1.034 (0.996 to 1.082) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.981 (0.841 to 1.132) | 0.918 (0.652 to 1.081) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.981 (0.841 to 1.132) | 0.918 (0.652 to 1.081) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.981 (0.841 to 1.132) | 0.918 (0.652 to 1.081) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.981 (0.839 to 1.142) | 0.877 (0.619 to 1.072) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.982 (0.842 to 1.148) | 0.871 (0.615 to 1.072) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.979 (0.845 to 1.131) | 0.914 (0.656 to 1.073) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.980 (0.838 to 1.144) | 0.873 (0.621 to 1.065) |

SBP – systolic blood pressure; CrI - credible interval; LDL - low-density lipoprotein; HDL - high-density lipoprotein; SBP_{PRD} - current SBP corrected using published correction factor; SBP_{HRD} – current SBP corrected using past blood pressure readings; Risk predictions based on Cox regression models and reflect the average of estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement; All models included a parameter for calendar year at study entry.

Table S6. Discrimination (concordance) and calibration for incident cardiovascular disease risk prediction models at age 60 years.

| | Derivation cohort | Validation cohort |
|--|------------------------------------|------------------------------------|
| 1. Discrimination | | |
| | <i>C statistic (95% CrI)</i> | <i>C statistic (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.656 (0.637 to 0.671) | 0.637 (0.636 to 0.638) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.662 (0.636 to 0.678) | 0.647 (0.642 to 0.658) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.662 (0.636 to 0.678) | 0.647 (0.642 to 0.658) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.662 (0.636 to 0.678) | 0.647 (0.642 to 0.658) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.665 (0.641 to 0.681) | 0.653 (0.648 to 0.664) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.665 (0.640 to 0.680) | 0.653 (0.647 to 0.664) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.663 (0.637 to 0.678) | 0.650 (0.644 to 0.660) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.665 (0.640 to 0.680) | 0.654 (0.649 to 0.665) |
| 2. Calibration | | |
| | <i>Calibration slope (95% CrI)</i> | <i>Calibration slope (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Sex, smoking, deprivation, diabetes and baseline SBP | 0.982 (0.829 to 1.111) | 0.832 (0.797 to 0.858) |
| Model 2: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.978 (0.836 to 1.099) | 0.854 (0.810 to 0.889) |
| Model 3: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.978 (0.836 to 1.099) | 0.854 (0.810 to 0.889) |
| Model 4: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.978 (0.836 to 1.099) | 0.854 (0.810 to 0.889) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.980 (0.825 to 1.106) | 0.865 (0.821 to 0.900) |
| Model 6: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.979 (0.825 to 1.105) | 0.870 (0.827 to 0.905) |
| Model 7: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.977 (0.831 to 1.095) | 0.874 (0.831 to 0.907) |
| Model 8: Sex, smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.978 (0.821 to 1.103) | 0.887 (0.844 to 0.920) |

SBP – systolic blood pressure; CrI - credible interval; LDL - low-density lipoprotein; HDL - high-density lipoprotein; SBP_{PRD} - current SBP corrected using published correction factor; SBP_{HRD} – current SBP corrected using past blood pressure readings; Risk predictions based on Cox regression models and reflect the average of estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement; All models included a parameter for calendar year at study entry.

Table S7. Risk of incident cardiovascular disease associated with past, current and usual systolic blood pressure (SBP) at age 50 years.

| Systolic blood pressure (mmHg) | Men | Women |
|--|-----------------------------------|-----------------------------------|
| | <u>HR (95% credible interval)</u> | <u>HR (95% credible interval)</u> |
| <u>Exposure: SBP measures in separate models</u> | | |
| Model: Current SBP | 1.17 (1.11 to 1.22) | 1.28 (1.15 to 1.37) |
| Model: Usual SBP_{pRD} | 1.29 (1.20 to 1.39) | 1.52 (1.26 to 1.69) |
| Model: Usual SBP_{hRD} | 1.35 (1.23 to 1.46) | 1.60 (1.30 to 1.81) |
| Model: Mean of past SBP | 1.31 (1.23 to 1.42) | 1.55 (1.39 to 1.69) |
| Model: Time-weighted mean of past SBP | 1.27 (1.19 to 1.35) | 1.49 (1.35 to 1.62) |
| Model: Variability of past SBP | 1.08 (1.04 to 1.11) | 1.15 (1.11 to 1.18) |
| <u>Exposure: Current and past SBP in the same model</u> | | |
| Model: Current SBP | 1.03 (0.98 to 1.10) | 1.06 (0.93 to 1.14) |
| Past SBP mean | 1.28 (1.13 to 1.41) | 1.48 (1.33 to 1.63) |
| Model: Current SBP | 1.07 (1.02 to 1.13) | 1.11 (0.99 to 1.19) |
| Past SBP time-weighted mean | 1.20 (1.08 to 1.32) | 1.38 (1.29 to 1.52) |
| Model: Current SBP | 1.15 (1.10 to 1.20) | 1.24 (1.11 to 1.33) |
| Past SBP variability | 1.06 (1.02 to 1.09) | 1.11 (1.08 to 1.14) |

HR – hazard ratio; HR reflect the average of risk estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement using data from the derivation cohort; Risks were estimated per 20-mmHg higher current, usual or mean of past SBP or per 5-mmHg higher past SBP variability; Usual SBP - current SBP corrected for regression dilution using published correction factor (SBP_{pRD}=0.70) or correction factor calculated from past blood pressure recording (SBP_{hRD}=0.50); All models also adjusted for calendar year of study entry and other baseline characteristics (smoking, deprivation index, diabetes, body mass index, total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol).

Table S8. Discrimination (concordance) and calibration of incident cardiovascular disease risk prediction models in men at age 50 years.

| | Derivation cohort | Validation cohort |
|---|------------------------------------|------------------------------------|
| 1. Discrimination | <i>C statistic (95% CI)</i> | <i>C statistic (95% CI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Smoking, deprivation, diabetes and baseline SBP | 0.603 (0.573 to 0.626) | 0.631 (0.629 to 0.634) |
| Model 2: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.670 (0.610 to 0.743) | 0.687 (0.637 to 0.748) |
| Model 3: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.670 (0.610 to 0.743) | 0.687 (0.637 to 0.748) |
| Model 4: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.670 (0.610 to 0.743) | 0.687 (0.637 to 0.748) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.671 (0.613 to 0.736) | 0.689 (0.641 to 0.749) |
| Model 6: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.671 (0.613 to 0.736) | 0.688 (0.639 to 0.748) |
| Model 7: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.670 (0.611 to 0.734) | 0.694 (0.645 to 0.754) |
| Model 8: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and previous SBP variability | 0.670 (0.612 to 0.732) | 0.694 (0.646 to 0.754) |
| 2. Calibration | <i>Calibration slope (95% CrI)</i> | <i>Calibration slope (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Smoking, deprivation, diabetes and baseline SBP | 0.958 (0.658 to 1.231) | 1.243 (1.158 to 1.333) |
| Model 2: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 1.002 (0.662 to 1.266) | 1.196 (1.005 to 1.464) |
| Model 3: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 1.002 (0.662 to 1.266) | 1.196 (1.005 to 1.464) |
| Model 4: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 1.002 (0.662 to 1.266) | 1.196 (1.005 to 1.464) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 1.015 (0.639 to 1.271) | 1.197 (1.001 to 1.483) |
| Model 6: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 1.010 (0.643 to 1.292) | 1.189 (0.993 to 1.475) |
| Model 7: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.997 (0.666 to 1.243) | 1.200 (1.015 to 1.455) |
| Model 8: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 1.004 (0.647 to 1.268) | 1.187 (0.997 to 1.460) |

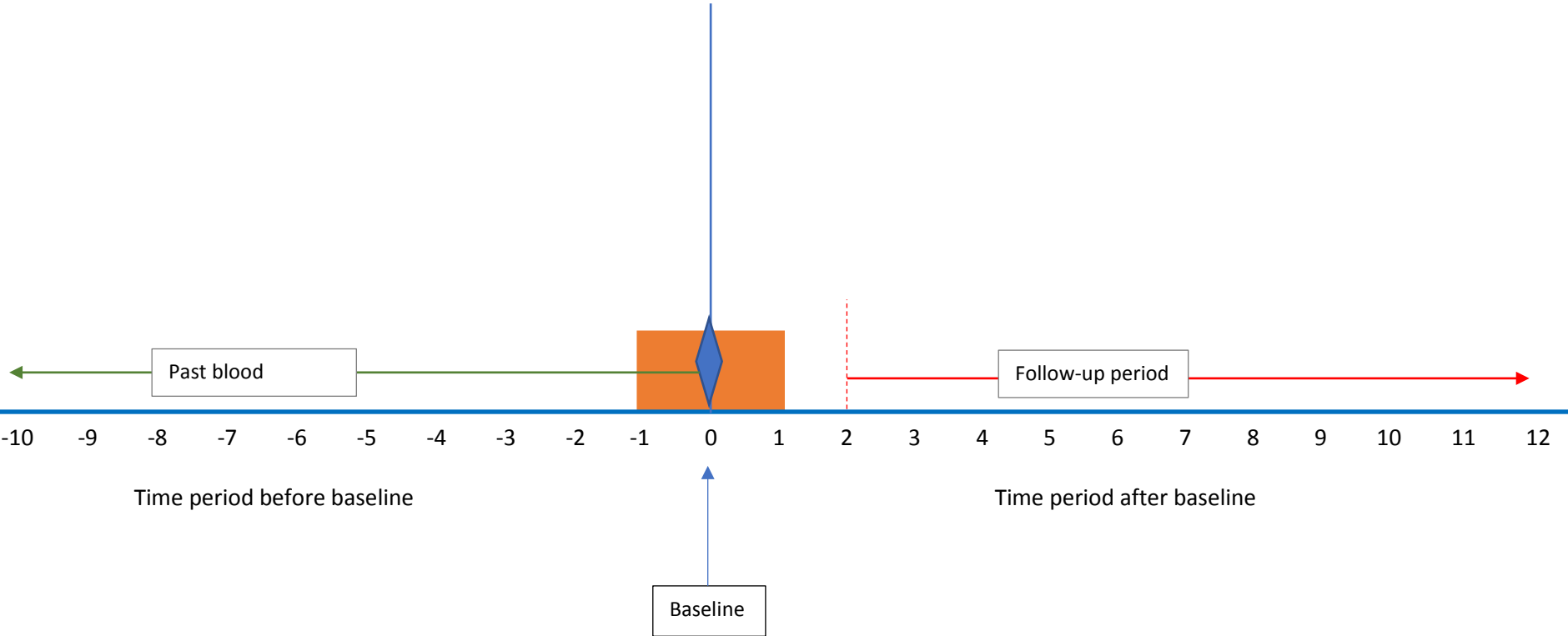
SBP – systolic blood pressure; CrI - credible interval; LDL - low-density lipoprotein; HDL - high-density lipoprotein; SBP_{PRD} - current SBP corrected using published correction factor; SBP_{HRD} – current SBP corrected using past blood pressure readings; Risk predictions based on Cox regression models and reflect the average of estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement; All models included a parameter for calendar year at study entry.


Table S9. Discrimination (concordance) and calibration of incident cardiovascular disease risk prediction models in women at age 50 years.

| | Derivation cohort | Validation cohort |
|---|------------------------------------|------------------------------------|
| 1. Discrimination | | |
| | <i>C statistic (95% CrI)</i> | <i>C statistic (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Smoking, deprivation, diabetes and baseline SBP | 0.646 (0.613 to 0.680) | 0.625 (0.623 to 0.626) |
| Model 2: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.681 (0.625 to 0.742) | 0.659 (0.629 to 0.710) |
| Model 3: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.681 (0.625 to 0.742) | 0.659 (0.629 to 0.710) |
| Model 4: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.681 (0.615 to 0.747) | 0.659 (0.629 to 0.710) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.688 (0.635 to 0.749) | 0.673 (0.643 to 0.723) |
| Model 6: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.685 (0.631 to 0.748) | 0.673 (0.643 to 0.724) |
| Model 7: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.684 (0.633 to 0.744) | 0.661 (0.631 to 0.710) |
| Model 8: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.687 (0.637 to 0.750) | 0.673 (0.644 to 0.723) |
| 2. Calibration | | |
| | <i>Calibration slope (95% CrI)</i> | <i>Calibration slope (95% CrI)</i> |
| <u>Current and usual SBP in separate models</u> | | |
| Model 1: Smoking, deprivation, diabetes and baseline SBP | 0.978 (0.747 to 1.227) | 0.879 (0.825 to 0.937) |
| Model 2: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and baseline SBP | 0.954 (0.741 to 1.200) | 0.887 (0.838 to 0.980) |
| Model 3: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{PRD} | 0.954 (0.741 to 1.200) | 0.887 (0.838 to 0.980) |
| Model 4: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol and usual SBP _{HRD} | 0.954 (0.741 to 1.200) | 0.887 (0.838 to 0.980) |
| <u>Current with past SBP in combined models</u> | | |
| Model 5: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP mean | 0.952 (0.743 to 1.211) | 0.886 (0.839 to 0.982) |
| Model 6: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP time-weighted mean | 0.952 (0.725 to 1.225) | 0.893 (0.838 to 0.998) |
| Model 7: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP and past SBP variability | 0.952 (0.738 to 1.177) | 0.879 (0.831 to 0.965) |
| Model 8: Smoking, deprivation, diabetes, total cholesterol, LDL-cholesterol, HDL-cholesterol, current SBP, past SBP time-weighted mean and past SBP variability | 0.950 (0.725 to 1.217) | 0.890 (0.837 to 0.989) |

SBP – systolic blood pressure; CrI - credible interval; LDL - low-density lipoprotein; HDL - high-density lipoprotein; SBP_{PRD} - current SBP corrected using published correction factor; SBP_{HRD} – current SBP corrected using past blood pressure readings; Risk predictions based on Cox regression models and reflect the average of estimates obtained from Monte-Carlo cross-validation using 50 random resamples without replacement; All models included a parameter for calendar year at study entry.

Figure S1. Schematic diagram showing landmark approach for each age cohort analysed.



Landmark age timepoint (age 40, 50 or 60 years at study entry): 


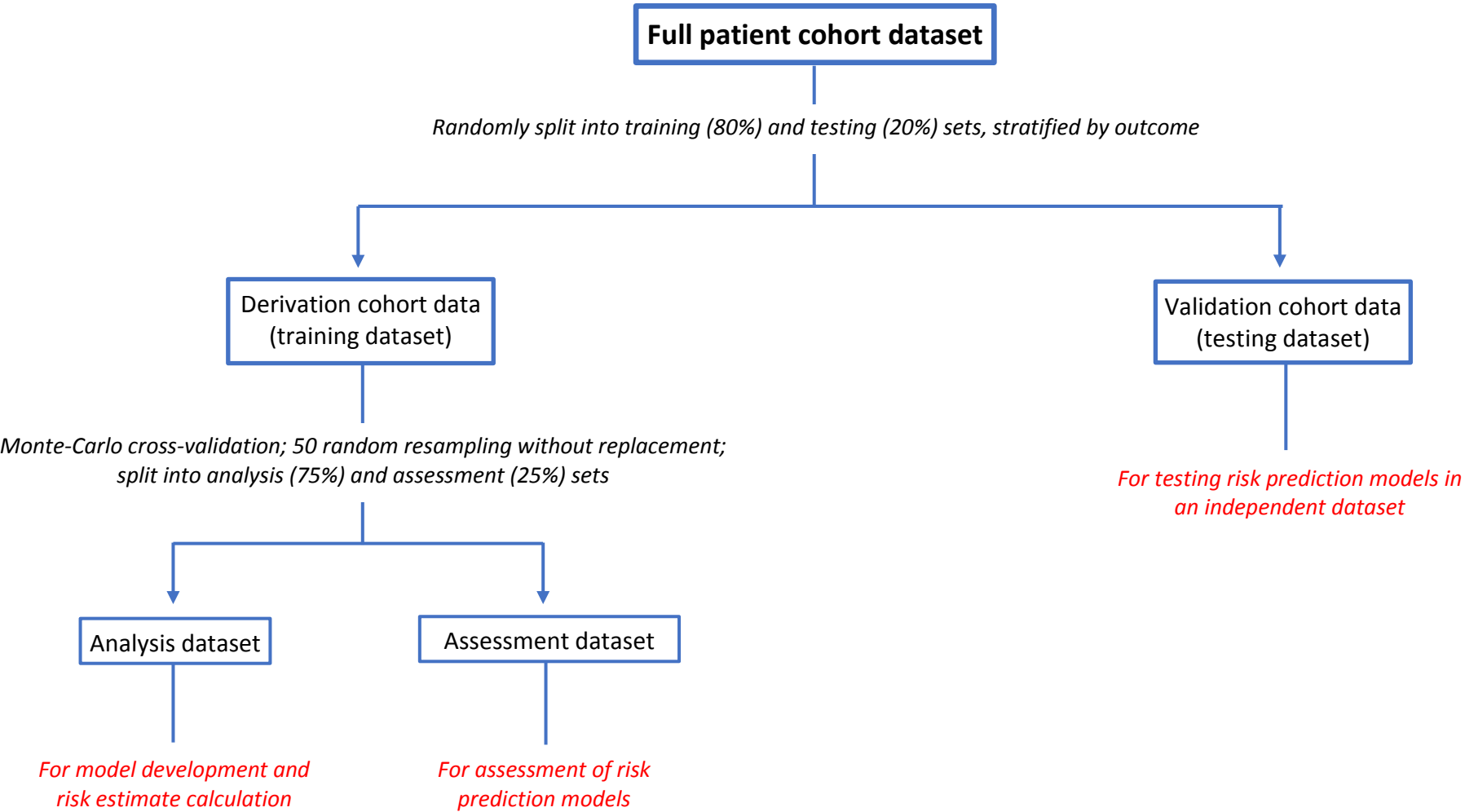
Baseline covariate capture period (within one year of baseline): 

Figure S2. Schematic diagram showing the use of data in model derivation and validation.



Reference S1:

1. Clarke R, Shipley M, Lewington S, et al. Underestimation of risk associations due to regression dilution in long-term follow-up of prospective studies. *Am J Epidemiol* 1999; **150**(4): 341-53.
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5. Smith T, Noble M, Noble S, Wright G, McLennan D, Plunkett E. The English Indices of Deprivation 2015. London: Crown Copyright; 2015. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/464597/English_Indices_of_Deprivation_2015_-_Research_Report.pdf. Accessed on May 14, 2018.