Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods 1. Study Recruitment

We included population-based prospective longitudinal cohort studies in older people designed to evaluate incident dementia, from the 21st century EURODEM consortium. Four out of nine eligible cohorts could not participate, reasons being 1.) uncertainty regarding potential legal issues with off-site data sharing due to new European privacy regulations, 2.) insufficient time/manpower to comply with the data request, partly due to pressures from the Corona virus pandemic. Because the combined population of the four participating EURODEM studies was relatively limited to comprehensively assess the study's research question in detail with sufficient power over a broad age-range, we consulted our authors' personal networks to recruit additional population-based longitudinal cohort studies, specifically designed to study incident dementia in community-dwelling older people, that would meet inclusion criteria, and be able to provide data readily available for analysis on very short notice. This led to the inclusion of the preDIVA and ACT studies.

eMethods 2. Dementia Ascertainment and Follow-up in Participating Studies

LEILA75+:

The Leipzig Longitudinal Study of the Aged (LEILA 75+) is a populations-based prospective study of older adults in Leipzig, Germany. At baseline (1997), 1,692 subjects aged 75+ were enrolled: 1,500 through systematic random sampling from an age-ordered list provided by the local registry office, and 192 institutionalized participants as population representative proportion. During the baseline visit, face-to-face interviews were conducted by trained physicians and psychologists at the participants' homes. With regard to cognitively impaired participants, additional structured third-party interviews were conducted with proxies. Follow-up interviews were carried out for all eligible participants every 1.5 years during the study period of 8 years.

Cognitive status was assessed with the 30 items of the Mini-Mental State Examination (MMSE). Dementia was with the SIDAM (Structured Interview for Diagnosis of Dementia of Alzheimer type, Multi-infarct Dementia and Dementia of other Aetiology) according to DSM-IV criteria. The SIDAM comprises a cognitive test battery and a section for clinical judgement and third-party information on psychosocial impairment, including a scale for the assessment of activities of daily living with 14 items (SIDAM-ADL scale). The cognitive test battery consists of 55 items, including the 30 items of the MMSE. The criteria of a full work up of the SIDAM were an MMSE score lower than 24, and at least two impairment in the SIDAM-ADL scale. If it was not possible to administer the SIDAM at a follow-up assessment (e.g. because of death or severe weakness), a comprehensive structured proxy interview was offered including the Clinical Dementia Rating Scale (CDR). For each subject, consensus conferences of physicians and psychologists were held.

ZARADEMP:

The Zaragoza Dementia Project (ZARADEMP) is a longitudinal population-based study of dementia and depression in adults aged 55+. The study used a random, representative sample of population of Zaragoza, Spain (700,000 inhabitants) drawn from the official census lists. It included institutionalized individuals and was stratified with proportional allocation by age and sex. The refusal rate was 20.5%, and 4803 individuals were ultimately interviewed at baseline in 1994. Individuals with dementia and 'subsyndromal' dementia at baseline, according to the Geriatric Mental State (GMS), with its cognitive section and its Automated Geriatric Examination for Computer Assisted Taxonomy package (AGECAT) criteria, were excluded for the follow-up waves.

Dementia screening included a two-phase case finding. In phase I, well-trained and regularly supervised lay-interviewers administered the ZARADEMP interview at the participant's home or place of residence. In phase II, the trained research psychiatrist reassessed participants to confirm the suspected clinical diagnosis of dementia, as well as the presence of depression or anxiety identified in phase I. A similar procedure was implemented in the second, third, and fourth waves (2.5, 4.5, and 12 years later, respectively), in which interviewers were not aware of the results of the baseline interview described beforehand. Information on dementia status extended to the last available follow-up assessment.

Gothenburg H70:

The Gothenburg H70 studies are a number of multidisciplinary epidemiological studies examining representative birth cohorts of older populations in Gothenburg, Sweden drawn from the population register based on birthdates. This study included those examined at age 70, 75 and 79 at baseline in 2000. Individuals with dementia at baseline were excluded. Medical history was obtained by medical doctors or research nurses using semi-structured interviews including questions regarding disorders, symptoms and medication use. Physical examinations included measurements of blood pressure, anthropometry (e.g. height and weight) and

ECG. Blood pressure was measured in the right arm after five minutes rest in the seated position with a manual sphygmomanometer. Trained psychiatric research nurses performed neuropsychiatric examinations using semi-structured interviews that comprised questions about psychiatric disorders and symptoms, and cognitive tests. The neuropsychiatric examinations included assessments of psychiatric symptoms, signs of dementia, tests of mental functioning (e.g. memory, proverbs, language, visuospatial and executive abilities, apraxia, construction, and agnosia), the Mini-Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale (ADAS).

All participants were asked to provide contact information for a proxy-informant. The proxy-informant interviews were semi-structured and performed by telephone by a research nurse or a psychologist and included questions about medical history, changes in behaviour and intellectual function, as well as questions about age of onset and course of dementia when appropriate. Participants underwent 5-yearly follow-up assessments. Dementia diagnoses at each examination were based on the Diagnostic and Statistical Manual of Mental Disorders, third edition revised (DSM-III-R), using information from psychiatric examinations and proxy-informant interviews. Incident dementia was also based on information from the National Patient Register, which contains information about hospital discharge diagnoses with full national coverage of all Swedish inhabitants. The NPR is coded according to the Swedish version of the International Statistical Classification of Diseases and Related Health Problems (ICD-SE). Dementia diagnoses for individuals lost to follow-up were also informed by the NPR (ICD-10-SE codes: F00-03, G30). Death dates were obtained from the Swedish Tax Agency. Age of dementia onset was estimated based on information from proxy informants, the NPR and the psychiatric examinations.

Kungsholmen Project and SNAC-K:

The Kungsholmen Project (KP) and the Swedish National study on Aging and Care in Kungsholmen (SNAC-K) are both longitudinal population-based cohort studies in the Kungsholmen district of central Stockholm, Sweden, conducted at the Karolinska Instituted. They share some essential design elements and are therefore discussed here together.

KP is a community-based longitudinal study of aging and dementia. In 1987, all 2368 residents, who were 75 years of age or older, living at home or in institutions in the Kungsholmen district of Stockholm, were invited to attend the two-phase designed survey at baseline, and 1810 people (76.4%) participated. Of those, 110 declined to take part in the clinical phase, which aimed at identifying prevalent dementia cases. 225 were diagnosed with definite and questionable dementia, 2 had intellectual disability, and 1473 participants were included in the dementia-free cohort at KP baseline. Of these, 11.7% dropped out before the first follow-up. All participants in KP were followed up every 3 years until 1997-1998.

SNAC-K includes people aged ≥60, living at home or in institutions in the same geographical area as the KP participants. Of 5111 people randomly selected from 11 age cohorts, 4590 were alive/eligible, and 3363 (73.3%) participated in the baseline examination (2001-2004), aimed at identifying prevalent dementia cases. Of participants attending baseline who did not have definite or questionable dementia, 10.5% dropped out before the first follow-up. Younger cohorts (60, 66, and 72 years) were followed up every 6 years, and older cohorts (78, 81, 84, 87, and ≥90 years) every 3 years.

The KP and SNAC-K followed similar protocols for data collection. At baseline data on demographic characteristics (age, sex, and education), lifestyle factors (eg, smoking, alcohol consumption, and physical activity), work-related factors (eg, work complexity and psychosocial working condition), chronic medical conditions (eg, diabetes and hypertension), use of medications, and global cognitive function were collected through structured interviews, clinical examinations, and psychologic testing following the standard procedures. During examinations, the examining physician recorded the current use of medications (eg, antihypertensive and antidiabetic drugs) by inspecting the medication containers. The Stockholm patient registers were linked to the study databases to ascertain history of ischemic heart disease, atrial fibrillation, heart failure, and cerebrovascular disease at baseline.

In KP, a 2-phase procedure was used to identify baseline dementia cases. In the screening phase, all participants were screened using the Mini-Mental State Examination (MMSE). People with an MMSE score <24 (n = 314) and a random sample of those with an MMSE score ≥24 (n = 354) underwent the clinical phase that included comprehensive clinical examinations, laboratory testing, and cognitive testing. During the follow-up phases of KP, all participants were instead directly examined. Dementia diagnosis was made using the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) following a validated three-step procedure: two physicians independently made a preliminary diagnosis of dementia, and a third opinion was sought from a senior physician in case of disagreement between the first two diagnoses. In SNAC-K, all participants were examined using structured interviews, clinical examinations, and cognitive testing. The same three-step procedure as in KP was adopted in SNAC-K for the diagnosis of dementia following DSM-IV criteria. In both KP and SNAC-K, medical records and death certificates of participants who died during the follow-up period were collected and reviewed by physicians to determine whether the participants died with dementia. The sensitivity of these death records for incident dementia compared to the intensive cognitive screening during.

ACT:

The Adult Changes in Thought (ACT) study is a population-based longitudinal cohort study, recruited through the Kaiser Permanente Washington (formerly Group Health Cooperative) integrated healthcare delivery system located in Seattle, the United states. In 1995, 2581 community dwelling dementia-free participants randomly sampled from KPW members aged ≥65 were enrolled, with an additional 811 participants enrolled from 2000 through 2003. In 2005, the study began continuous enrolment to replace those who died or dropped out. Participants underwent assessment at study entry and every two years to evaluate cognitive function and collect demographic characteristics, medical history, health behaviours, and health status. Completeness of follow-up is very high (> 97%), in part because of the extensive KPW healthcare infrastructure. In addition, information on participants' health care utilization and medication dispensing is available from KPW electronic databases.

Cognitive function is assessed with the Cognitive Abilities Screening Instrument (CASI) at study entry and subsequent biennial visits. CASI scores range from 0 to 100, with higher scores indicating better cognitive performance. Participants with scores ≤85 undergo a standardized diagnostic evaluation for dementia, including a physical and neurological examination, and neuropsychological tests. Results of these evaluations and laboratory and imaging records are then reviewed in a multidisciplinary consensus conference. Dementia diagnoses are made using research criteria and according to DSM-IV, by an panel of dementia experts. Dementia status for participants who dropped-out or died were based on available medical records.

preDIVA:

Prevention of Dementia by Intensive Vascular Care (preDIVA) was a cluster-randomized controlled trial, evaluating the efficacy of nurse-led cardiovascular risk-management at the general practitioner level, over 6-8 years of follow-up. Since the intervention implemented standard cardiovascular guidelines and did not have an overall effect on dementia, the cohort is often employed as a longitudinal cohort study. All community-dwelling persons, registered with a participating GP were selected from electronic health registry. Persons were excluded if, according to their GP, they suffered from (probable) dementia, were terminally ill, did not understand Dutch, or had other conditions that could hinder successful long-term follow-up, like serious chronic diseases, cancer or alcoholism. Eligible individuals willing to participate underwent cognitive screening by trained research nurses at baseline using the MMSE and visual association test (VAT). Individuals with an MMSE <24 were referred to their GP for further clinical evaluation, and excluded in case of suspected possible dementia. Of the total eligible population between 70 and 78, 52·1% (3526/6762) participated (in 2006-2009). The baseline characteristics of the study population were comparable to those of other Dutch population representative community-dwelling cohorts.

During the pre-DIVA follow-up. General participant demographic and anthropomorphic characteristics, self-reported life-style factors, and medical history was collected based on participant interviews cross-referenced with the patients' electronic health records. Blood pressure was measured at the assessments twice, in sitting position, using a calibrated electronic device, according with standard general practice guidelines. Cognitive status was assessed at two-yearly follow-up assessments by a trained research nurse, using the MMSE and VAT. Also, clinical diagnoses were collected from the medical records. In cases of suspected (possible) dementia, all potentially relevant data on cognitive status, medical history, and follow-up investigation, were gathered, and presented independently to two members of a blinded outcome adjudication committee, comprising dementia specialized neurologists, general practitioners, and internists, to establish dementia status. Diagnoses were made according to DSM-IV criteria. In case of disagreement, a third member of the committee was consulted, blinded to the other members' adjudication. For individuals who died or dropped-out during the study, a dedicated research nurse gathered all the clinical information available on cognitive status at the end of the trial and/or prior to death from patients' electronic health databases and through contact with the general practitioner. Death records from the municipal registration were also consulted. All potentially relevant data regarding cognitive status before the time of death or at the end of the trial gathered were presented to the blinded outcome adjudication committee, who assessed dementia outcome according to the standard study procedure. Individuals with questionable dementia or insufficient information to establish cognitive status were left out of the analyses. Patients with a dementia diagnoses were followed-up after a year of the established date of diagnosis, to confirm the diagnosis.

eMethods 3. Models and Model Selection

Relationships between baseline blood and incident dementia were assessed using Cox regression, with dementia diagnosis/censoring age as timescale and baseline age as time of entry. Relationships of BP with incident dementia, mortality and dementia/mortality combined were evaluated within individual study populations using fixed effect models. For the combined population, mixed effects models with random study-specific baseline hazards (sometimes also referred to as frailty term or random intercept per study) were used. We evaluated the inclusion of random effects for baseline blood pressure per study, but this did not improve the model fit according to the Aikake Information Criterion (AIC).

The final R code used for the models amounted to:

coxme(Surv(Baseline_Age, Censoring_Age, Outcome) ~ ns(baseline_blood_pressure, df)+ sex + AHM + (1|Study))

Wherein 'df' is the degrees of freedom for the optimal non-linear model, AHM the use of antihypertensive medication coded as yes/no/unknown categorical variable, and 1|Study is the frailty (or random baseline hazard / random intercept) per study.

Systolic and diastolic BP were evaluated independently in separate models. Potential non-linear associations were examined using natural splines. Allowed degrees of freedom (df) ranged from 2 (1 knot at 50th percentile) to 4 (3 knots at 25th, 50th and 75th percentiles), the specific number chosen based on the best model fit according to the Akaike Information Criterion (AIC). A four df maximum was chosen because model generalizability may decrease with high df, while restriction to the minimal two df (a parabola-like shape) may mask biologically plausible relationships (e.g. HR 'plateauing' between certain BP levels). From the best fitting non-linear model, the BP associated with the lowest dementia risk (LR point) was recorded, with 95% confidence intervals (95%CI) calculated as the 2.5th and 97.5th percentiles from 1,000 bootstraps.

eMethods 4. Interpretation of Confidence Intervals

The interpretation of confidence intervals (CI) obtained from bootstrapped analyses from the BP (BP) estimates associated with the lowest risk (LR points) differs somewhat from those of the (linear) hazard ratio's. They can be asymmetrical and denote likely values (<2.5th / >97.5th percentile) beyond which the risk increases. Confidence interval width is not necessarily a reflection of power for the analyses, but also an indication of the shape of the association. Extreme values suggest uncertainty that the risk increases extending from the LR point. Consider the figures below.

They depict simulated U-shaped, J-shaped, L-shaped and negatively linear relationships of a normally distributed BP on the x axis (mean=150, SD=17.5), with a simulated risk on the y-axis. All these models are well-powered, with 5,000 individuals and a correlation between the shape of the relationship and the data points of approximately 0.2. The continuous red line is the modelled regression line, with its 95%CI in yellow. The p-value for the models' fit is <0.001. The 'true' LR point for all non-linear models is approximately 150 mmHg. Depicted in blue are the modelled lowest risk point (LR) and its 95% CI derived from 1,000 bootstraps.

Note that the (horizontal) 95%CI for the LR point do not directly depend on the (vertical) width of the yellow CI, but rather on whether the yellow CI include the risk at the LR point. As a rule of thumb for the depicted non-linear relationships: the lower and upper CI for the LR point are the points where the lowest yellow CI is (substantially) higher than the risk at the LR point.

In a perfect U-shaped relationship (A), the LR is accurately estimated with narrow CI (LR=149, 95%CI=146-152). In a J-shaped relation (B), the LR is estimated at a slightly higher BP value, with asymmetrical CI, slightly wider towards higher values (LR=153, 95%CI=148-159). This is caused by the right side of the relationship being 'flatter'. Therefore the exact point where the risks starts to rise again with higher BP is less clear. In the simulated L-shaped relationship (C), the true LR point is still 150 mmHg, but the increment in risk with higher BP from there is very small. The LR point is estimated at 156 mmHg and the 148 mmHg lower CI for the LR is comparable to the U- and J-shaped relationships the 207 mmHg upper CI for the LR is however extremely wide, extending to the highest observed BP value in the dataset. This is not due to a lack of power, but rather to uncertainty of the relationship to the right of the LR point. The relationship to the right of the LR may also be neutral, as illustrated by the lowest yellow CI to the right of the LR point never becoming substantially higher than the risk at the LR point. The depicted LR point of 156 mmHg with a CI=148-207 therefore conveys relative (percentile>2.5) certainty that a BP <148 mmHg is associated with increased risk compared to 156 mmHg, but uncertainty about whether BPs above 156 mmHg increase risk. This does not mean that an extremely high blood pressure values are favourable. Consider the negatively linear relationship (D). Theoretically, the lowest observed value in the data would be the value conveying the lowest risk. However, in practice, although negatively and positively linear associations are not uncommonly found in the literature, extremely high, but also low BP values should generally not be interpreted as ideal. Similarly, the extreme values in the CI for non-linear LR points should not be interpreted as signifying that extreme values are is nothing to worry about, but rather the best description of the relationship beyond the LR point may be neutral or negative.

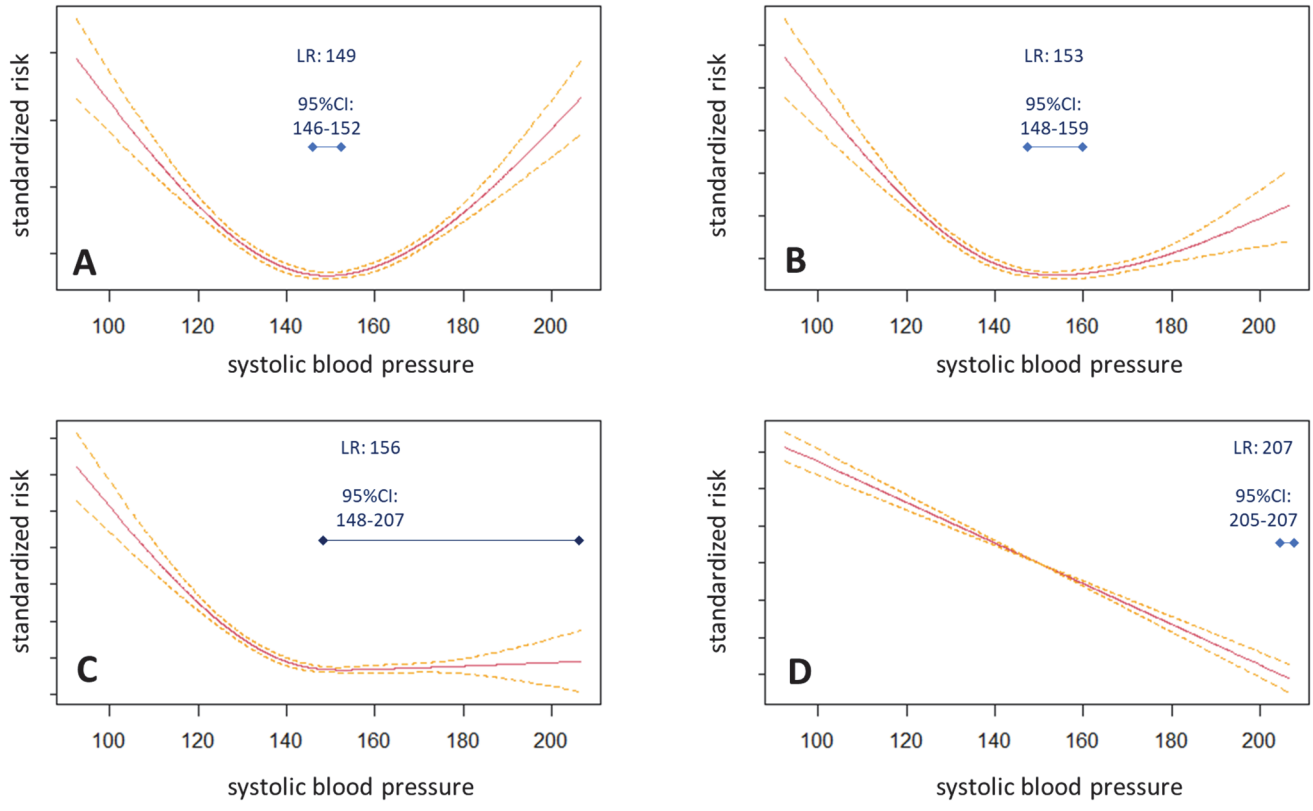


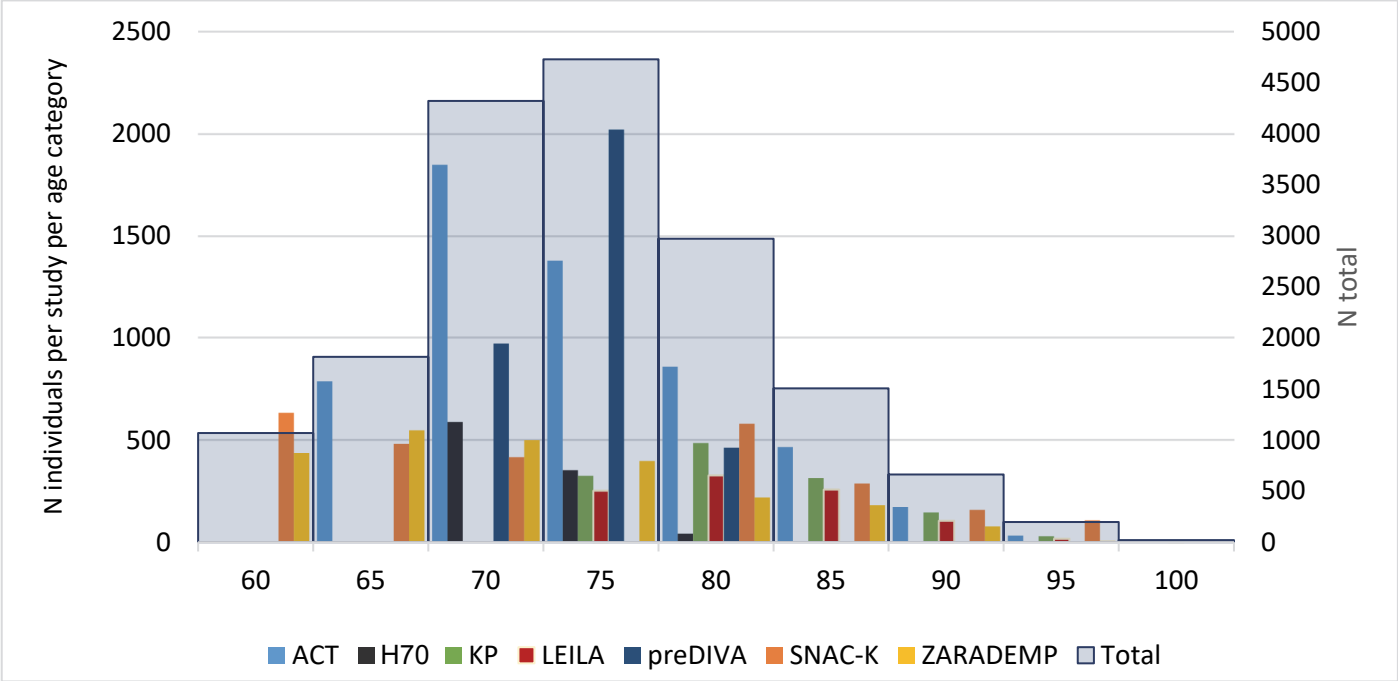
Illustration of the relation between association shapes and confidence intervals. Data derived from simulated relationships of 5,000 individuals. LR: blood pressure associated with the lowest risk, blue 95%CI: 95% confidence interval of LR estimate operationalised as the 2.5th and 97.5th percentile derived from 1,000 bootstraps

eMethods 5. Choice of Age-Bands and Shift in Analysis

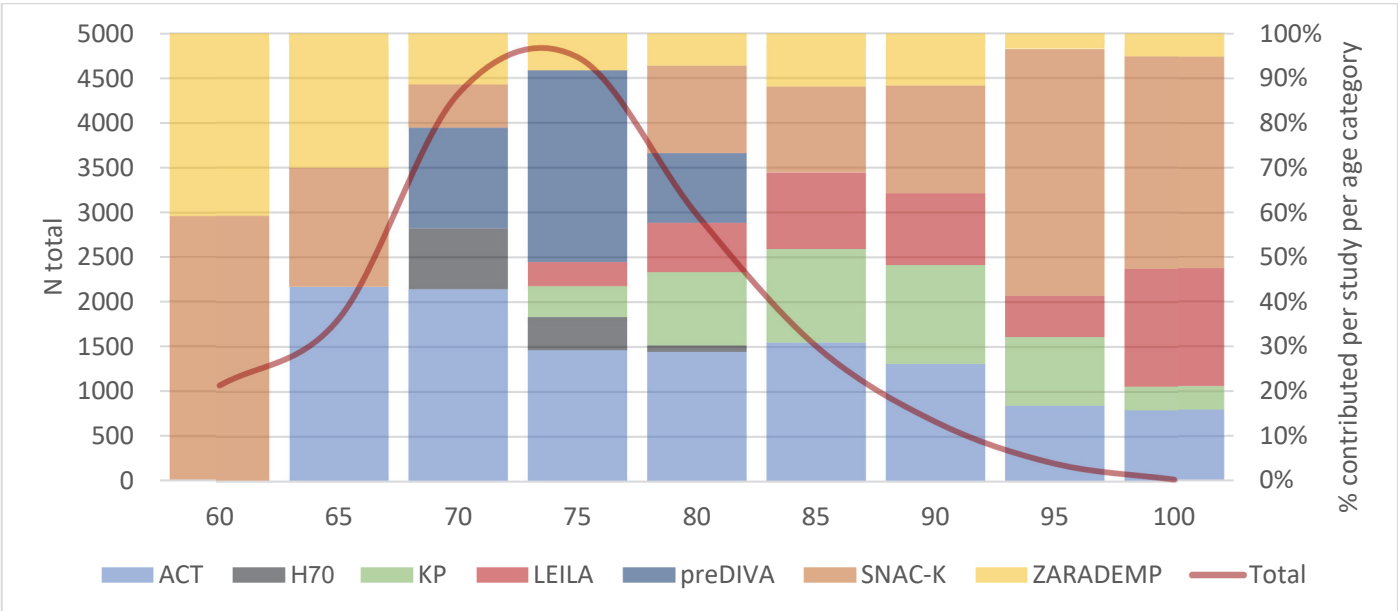
To investigate our hypothesis that the shape of the associations between blood pressure and dementia risk changed with baseline age, and that the blood pressures associated with the lowest risk were higher for older individuals, we performed subgroup analyses. We focussed on the age-range from 65 to 90 because we had relatively few participants/events outside of this bandwidth. Furthermore, we used 10-year age bands, but shifting them 5-years at a time, thereby studying overlapping age categories. The motivation for this was twofold:

1.) Our hypothesis was that the blood pressure associated with the lowest risk of dementia would gradually shift to higher levels with higher baseline age. By jumping 10-years at a time, we would only have 3 informative age bands (65-75, 75-85, and 85-95), the remaining ones having too small numbers of participants. We would therefore be unable to tell whether any difference in blood pressure associated with the lowest risk for the middle and the oldest category indeed represented a gradual shift with ageing, or was just based on chance. By shifting 5-year age bands at the time, we could better study whether there was an indication for such a gradual shift. However, if we would have used 5-year age bands, would have very much limited our statistical power. Using 10-year age bands but shifting them 5-years per step ensured we could study the gradual shift, while maintaining sufficient power.

2.) With the overlapping populations, we could better assess whether findings were caused by domination of single studies. For example, H70 and preDIVA only included participants aged approximately 70-80 years at baseline, and therefore may have a very strong impact on findings within this age band. Would we have only analysed this group, it would be difficult to tell whether findings would more likely be due to the shift in age or the shift in study populations. With the overlapping age bands, we can ensure that the inclusion of new study populations was gradual, and that results within one age band weren't caused by particular studies dominating that group.



eFigure 1. Participants per 5-Year Age Categories per Study. (narrow bars, left y-axis) and total (wide bars, right y-axis). Abbreviations: ACT: Adult Changes in Thought study, H70: Gothenburg H70 Birth Cohort, KP: Kungholmen Project, LEILA75+: Leipzig Longitudinal Study of the Aged 75+, preDIVA: Prevention of Dementia by Intensive Vascular Care study, SNAC-K: Swedish National Study on Aging and Care in Kungsholmen, ZARADEMP: Zaragoza Dementia Depression Project



eFigure 2. Percentage Contribution per Study per 5-Year Age Category. (coloured bar sections, percentage on right y-axis) to total number of participants (red line, number of individuals on left y-axis). Abbreviations: ACT: Adult Changes in Thought study, H70: Gothenburg H70 Birth Cohort, KP: Kungholmen Project, LEILA75+: Leipzig Longitudinal Study of the Aged 75+, preDIVA: Prevention of Dementia by Intensive Vascular Care study, SNAC-K: Swedish National Study on Aging and Care in Kungsholmen, ZARADEMP: Zaragoza Dementia Depression Project

Outcome	Baseline Age	Studies	Cases	Total	LR point (mmHg)	95%CI (mmHg)		p
Dementia	All	7	2735	16,860	139	80	139	0.16
	60-70	5	230	3720	130	86	130	0.07
	65-75	6	786	7656	130	62	130	0.36
	70-80	7	1352	9602	133	77	133	0.26
	75-85	7	1390	6449	139	128	139	0.048
	80-90	7	947	2922	110	79	139	0.17
	85-95	5	535	1504	96	68	136	0.36
	>90	5	121	345	79	46	120	0.77
Mortality	All	7	7683	16,856	84	80	97	**0.002**
	60-70	5	941	3720	82	78	88	**0.001**
	65-75	6	2547	7655	85	82	103	**<0.001**
	70-80	7	3914	3914	87	82	133	**0.01**
	75-85	7	3587	6446	85	80	133	**0.01**
	80-90	7	2309	2922	88	61	139	0.45
	85-95	5	1320	1504	96	47	136	0.39
	>90	5	328	345	87	76	120	0.2
Dem/Mort	All	7	8359	16,858	82	79	93	**0.01**
	60-70	5	1015	3720	83	79	99	**0.01**
	65-75	6	2805	7655	85	82	98	**<0.001**
	70-80	7	4357	9600	88	82	133	**0.02**
	75-85	7	3943	6448	87	82	139	**0.02**
	80-90	7	2461	2922	78	45	139	**0.02**
	85-95	5	1380	1504	86	71	136	0.29
	>90	5	333	345	84	73	120	0.42

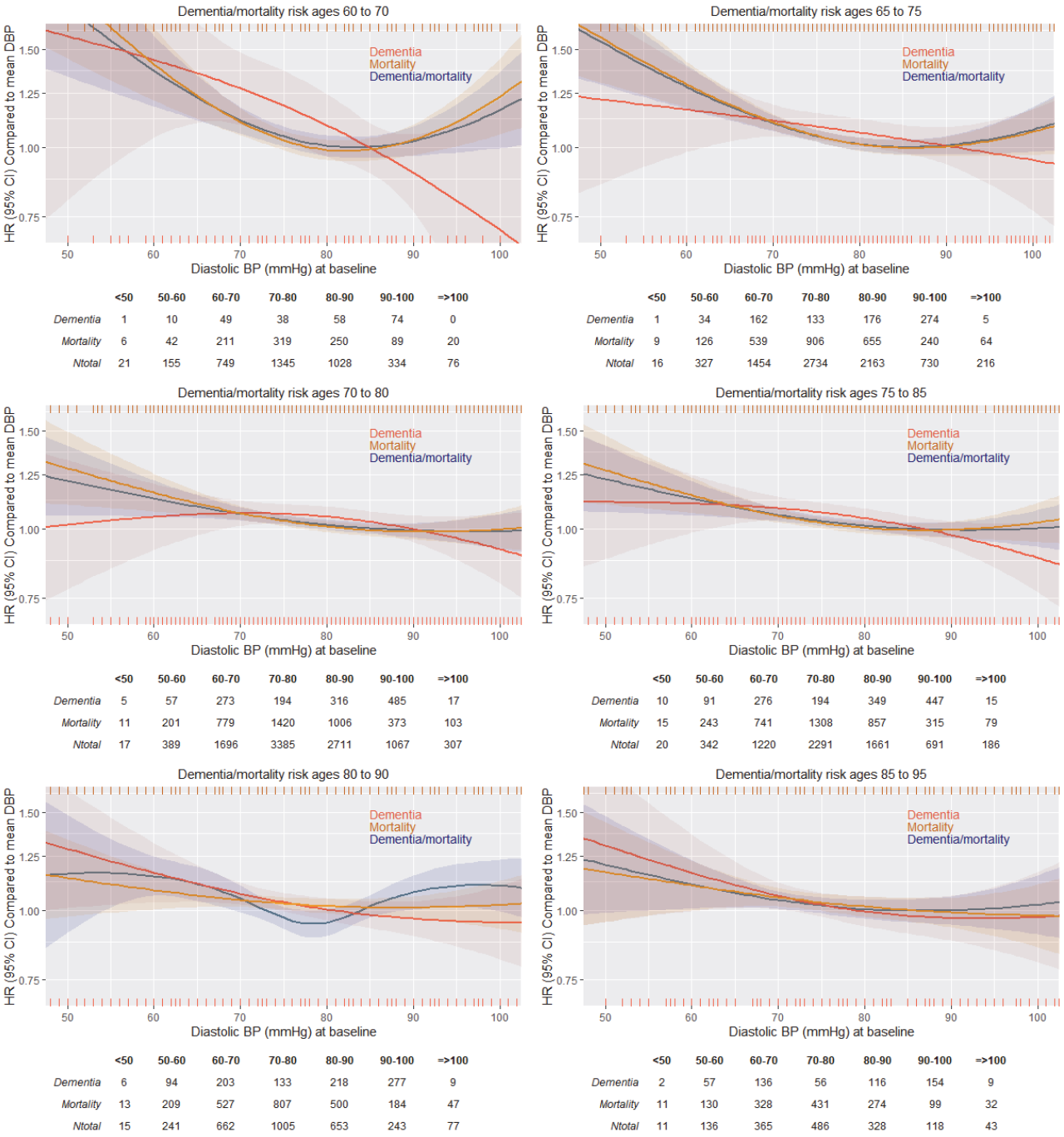
eTable 1. Relations for Diastolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality. Results are shown from non-linear models depending on optimal model fit in age-based subgroups. For each outome, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outome. Full data for comparison with linear models are provided in eTable 3. Relations are shown for the complete population (overall) and within 10 year age subgroups.

Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
								LR point	95%CI		p	HR	95%CI		P
Dementia	All	7	2738	16873	Linear	0.16	0.1	185	161	230	0.001	0.997	0.995	0.999	0.001
	60-70	5	230	3720	Linear	0.76	2.0	220	150	245	0.41	0.996	0.989	1.002	0.20
	65-75	6	786	7656	Linear	0.90	1.9	197	101	230	0.77	0.999	0.995	1.002	0.48
	70-80	7	1352	9602	Linear	0.48	1.5	224	107	260	0.09	0.997	0.995	1.000	0.04
	75-85	7	1390	6449	Non-linear	0.12	-0.4	170	160	260	0.004	0.996	0.993	0.999	0.003
	80-90	7	947	2922	Non-linear	0.001	-9.8	158	152	178	0.001	0.997	0.994	1.000	0.10
	85-95	5	535	1504	Non-linear	0.01	-4.4	162	153	240	0.01	0.996	0.993	1.000	0.07
	>90	5	121	345	Linear	0.72	1.9	160	87.8	231	0.93	1.000	0.992	1.008	0.92
Mortality	All	7	7698	16869	Non-linear	<0.001	-10.4	160	154	181	<0.001	0.998	0.997	1.000	0.008
	60-70	5	941	3720	Non-linear	0.01	-4.2	134	102	149	0.03	1.002	0.998	1.005	0.31
	65-75	6	2547	7655	Non-linear	0.01	-4.3	146	130	169	0.04	1.000	0.998	1.002	0.99
	70-80	7	3914	9598	Non-linear	0.10	-0.7	166	154	260	0.02	0.998	0.997	1.000	0.03
	75-85	7	3587	6446	Non-linear	0.004	-6.3	163	156	194	0.001	0.998	0.996	1.000	0.02
	80-90	7	2309	2922	Non-linear	<0.001	-12.2	155	150	166	<0.001	0.999	0.997	1.001	0.25
	85-95	5	1320	1504	Non-linear	0.01	-4.6	162	154	230	0.01	0.998	0.995	1.000	0.05
	>90	5	328	345	Linear	0.22	0.5	160	154	220	0.13	0.996	0.991	1.001	0.11
Dem/Mort	All	7	8375	16871	Non-linear	<0.001	-10.2	163	158	197	<0.001	0.998	0.997	0.999	<0.001
	60-70	5	1015	3720	Non-linear	0.06	-1.4	136	86	215	0.17	1.000	0.997	1.004	0.80
	65-75	6	2805	7655	Non-linear	0.02	-3.4	149	139	205	0.06	0.999	0.998	1.001	0.56
	70-80	7	4357	9600	Non-linear	0.08	-1.0	169	159	260	0.003	0.998	0.996	0.999	0.003
	75-85	7	3943	6448	Non-linear	<0.001	-10.7	164	157	192	<0.001	0.998	0.996	0.999	0.002
	80-90	7	2461	2922	Non-linear	<0.001	-16	157	151	167	<0.001	0.998	0.996	1.000	0.10
	85-95	5	1380	1504	Non-linear	0.047	-1.9	165	153	240	0.01	0.997	0.995	1.000	0.03
	>90	5	333	345	Linear	0.24	0.9	229	109	231	0.20	0.997	0.992	1.002	0.18

eTable 2. Complete Results Comparing Linear and Non-Linear Models for Systolic Blood Pressure. Listed are the results for both the linear and non-linear models in the main analyses for systolic blood pressure (see Table 1 in the manuscript). P-non-lin denotes the p-value for the difference between the linear models and the more complex non-linear models according to the likelihood ratio test. AIC difference denote the difference in AIC values between the linear and optimal non-linear model, with a negative AIC meaning that the non-linear model had a lower AIC (representing a better model fit) than the linear model. Results illustrate that when the best fitting model is linear, LR points for the best fitting non-linear models approximate the extreme values (i.e. highest or lowest values) of the SBP values measured (see eMethods 1).

Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
								LR point	95%CI		p	HR	95%CI		P
Dementia	All	7	2735	16860	Linear	0.57	1.7	139	80	139	0.16	0.997	0.994	1.001	0.16
	60-70	5	230	3717	Linear	0.67	1.9	130	86	130	0.07	0.984	0.97	0.998	**0.02**
	65-75	6	785	7647	Linear	0.90	2.0	130	62	130	0.36	0.995	0.988	1.002	0.16
	70-80	7	1350	9585	Linear	0.40	1.3	133	77	133	0.26	0.996	0.991	1.001	0.16
	75-85	7	1385	6426	Linear	0.23	1.0	139	128	139	0.048	0.994	0.989	0.999	**0.03**
	80-90	7	940	2899	Linear	0.49	1.6	110	79	139	0.17	0.995	0.989	1.001	0.08
	85-95	5	532	1492	Linear	0.40	1.3	96	68	136	0.36	0.996	0.988	1.003	0.24
	>90	5	121	343	Linear	0.50	1.6	79	46	120	0.77	1.002	0.986	1.018	0.78
Mortality	All	7	7683	16856	Non-linear	0.002	-7.5	84	80	97	**0.002**	0.998	0.996	1.000	0.063
	60-70	5	939	3717	Non-linear	<0.001	-11.1	82	78	88	**0.001**	0.984	0.97	0.998	0.023
	65-75	6	2541	7646	Non-linear	0.002	-8.0	85	82	103	**<0.001**	0.995	0.988	1.002	0.16
	70-80	7	3902	9581	Non-linear	0.04	-2.4	87	82	133	**0.01**	0.996	0.991	1.001	0.16
	75-85	7	3569	6423	Non-linear	0.01	-4.1	85	80	133	**0.01**	0.994	0.989	0.999	0.026
	80-90	7	2290	2899	Linear	0.35	1.2	88	61	139	0.45	0.998	0.995	1.002	0.39
	85-95	5	1310	1492	Linear	0.55	1.6	96	47	136	0.39	0.997	0.992	1.002	0.21
	>90	5	326	343	Linear	0.22	0.4	87	76	120	0.2	0.993	0.984	1.003	0.19
Dem/Mort	All	7	8359	16858	Non-linear	0.004	-6.3	82	79	93	**0.01**	0.999	0.997	1.001	0.30
	60-70	5	1013	3717	Non-linear	0.004	-6.0	83	79	99	**0.01**	0.996	0.99	1.003	0.25
	65-75	6	2799	7646	Non-linear	0.001	-8.5	85	82	98	**<0.001**	0.995	0.991	0.999	0.02
	70-80	7	4345	9583	Non-linear	0.14	-0.2	88	82	133	**0.02**	0.996	0.993	0.999	0.02
	75-85	7	3925	6425	Non-linear	0.08	-1.1	87	82	139	**0.02**	0.997	0.994	1.000	0.06
	80-90	7	2441	2899	Non-linear	0.02	-4.0	78	45	139	**0.02**	0.998	0.995	1.002	0.39
	85-95	5	1369	1492	Linear	0.20	0.4	86	71	136	0.29	0.998	0.993	1.003	0.37
	>90	5	331	343	Linear	0.27	0.8	84	73	120	0.42	0.996	0.987	1.006	0.47

eTable 3. Complete Results Comparing Linear and Non-Linear Models for Diastolic Blood Pressure. Listed are the results for both the linear and optimal fitting non-linear models for the main analyses on diastolic blood pressure (see eTable 3). P-non-lin denotes the p-value for the difference between the linear models and the more complex non-linear models according to the likelihood ratio test. AIC difference denote the difference in AIC values between the linear and optimal non-linear model, with a negative AIC meaning that the non-linear model had a lower AIC (representing a better model fit) than the linear model. Results illustrate that when the best fitting model is linear, LR points for the best fitting non-linear models approximate the extreme values (i.e. highest or lowest values) of the SBP values measured (see eMethods 1).



	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	1	10	49	38	58	74	0
Mortality	6	42	211	319	250	89	20
Ntotal	21	155	749	1345	1028	334	76

	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	1	34	162	133	176	274	5
Mortality	9	126	539	906	655	240	64
Ntotal	16	327	1454	2734	2163	730	216

	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	5	57	273	194	316	485	17
Mortality	11	201	779	1420	1006	373	103
Ntotal	17	389	1696	3385	2711	1067	307

	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	10	91	276	194	349	447	15
Mortality	15	243	741	1308	857	315	79
Ntotal	20	342	1220	2291	1661	691	186

	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	6	94	203	133	218	277	9
Mortality	13	209	527	807	500	184	47
Ntotal	15	241	662	1005	653	243	77

	<50	50-60	60-70	70-80	80-90	90-100	=>100
Dementia	2	57	136	56	116	154	9
Mortality	11	130	328	431	274	99	32
Ntotal	11	136	365	486	328	118	43

eFigure 3. Relations Between Diastolic Blood Pressure and Risk of Dementia/Mortality Combined. Results are presented in 10-year age-bands in the combined study population aged 60 to 95 years old. The coloured lines represent the relative hazard ratio (HR) on the y-axis, according to blood pressure in mmHg on the x-axis. Shaded areas represent 95% confidence intervals. Orange vertical stripes (top) represent one or multiple mortality cases at that specific DBP, red vertical stripes (bottom) represent one or multiple dementia cases at that specific BP. "HR compared to mean DBP" denotes that the HR is 1.00 at the mean DBP. Models fitted using natural splines, with degrees of freedom selected from 1 (linear model) upto a maximum of 4 (knots at 25th, 50th and 75th percentile), based on optimal model fit according to the Akaike Information Criterion (AIC). Models are adjusted for sex and antihypertensive use.

Subgroup	Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
									LR point	95%CI		p	HR	95%CI		P
AHM	Dementia	All	7	1102	6947	Non-linear	0.09	-4.5	178	160	230	0.002	0.995	0.993	0.998	0.002
users		60-70	5	84	1220	Linear	0.18	0.7	96	95	212	0.33	1.001	0.990	1.012	0.88
		65-75	6	311	3096	Linear	0.66	1.8	159	94	230	0.90	1.000	0.994	1.005	0.89
		70-80	7	553	4211	Linear	0.9	2.0	228	165	230	0.08	0.995	0.991	0.999	0.03
		75-85	7	556	2827	Non-linear	0.15	-0.5	**186**	**161**	**228**	0.004	0.994	0.990	0.998	0.003
		80-90	7	371	1241	Non-linear	0.002	-39.5	**167**	**153**	**180**	0.001	0.995	0.990	1.000	0.063
		85-95	5	226	663	Non-linear	0.03	-13.5	**173**	**157**	**230**	0.003	0.992	0.986	0.998	0.009
AHM	Dementia	All	7	1549	9523	Linear	0.63	1.7	222	150	225	0.15	0.998	0.995	1.000	0.998
non-users		60-70	5	145	2487	Linear	0.56	1.7	220	114	220	0.25	0.993	0.985	1.002	0.13
		65-75	6	473	4528	Linear	0.33	1.0	225	90	225	0.54	0.999	0.994	1.003	0.61
		70-80	7	769	5172	Linear	0.27	0.7	225	90	225	0.49	0.999	0.996	1.003	0.66
		75-85	7	777	3317	Linear	0.45	1.4	182	144	225	0.24	0.997	0.994	1.001	0.13
		80-90	6	522	1505	Non-linear	0.09	-4.5	**161**	**145**	**220**	0.10	0.997	0.993	1.001	0.20
		85-95	5	276	748	Non-linear	0.13	-1.5	**159**	**144**	**220**	0.19	0.997	0.991	1.003	0.30
AHM	Mortality	All	7	3249	6944	Non-linear	0.001	-43.5	**164**	**156**	**183**	**<0.001**	0.998	0.996	0.999	0.006
users		60-70	5	350	1220	Linear	0.04	2.3	**145**	**96**	**165**	**0.11**	1.001	0.995	1.006	0.76
		65-75	6	1044	3095	Linear	0.004	6.4	**157**	**147**	**169**	**0.01**	0.999	0.996	1.002	0.39
		70-80	7	1657	4208	Linear	0.02	3.7	**172**	**160**	**230**	**0.001**	0.996	0.994	0.999	0.002
		75-85	7	1523	2825	Non-linear	0.01	-23.5	**169**	**158**	**228**	**0.001**	0.996	0.994	0.999	0.006
		80-90	7	992	1241	Non-linear	0.01	-23	**158**	**146**	**176**	**0.03**	0.999	0.996	1.002	0.50
		85-95	5	589	663	Non-linear	0.22	-3.0	169	98	230	0.24	0.998	0.994	1.002	0.25
AHM	Mortality	All	7	4255	9522	Linear	0.06	1.7	156	144	225	0.0501	0.999	0.997	1.000	0.99
non-users		60-70	5	586	2487	Linear	0.06	1.7	134	90	149	0.10	1.002	0.998	1.007	0.31
		65-75	6	1492	4528	Linear	0.21	0.5	135	90	172	0.31	1.001	0.999	1.004	0.37
		70-80	7	2172	5171	Linear	0.95	2.0	220	90	225	0.87	0.999	0.997	1.002	0.61
		75-85	7	1928	3316	Non-linear	0.04	-2.2	**160**	**139**	**225**	**0.04**	0.998	0.996	1.001	0.14
		80-90	6	1216	1505	Non-linear	0.01	-31.0	**150**	**135**	**220**	**0.01**	0.998	0.995	1.001	0.20
		85-95	5	668	748	Linear	0.17	0.5	170	150	220	0.04	0.996	0.992	1.000	0.03

eTable 4. Relations for Systolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality in Age Groups, Stratified According to Antihypertensive Medication (AHM) Use. Results are shown from non-linear and linear models. For each outcome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. a p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model according to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95% CI) and p-value for the linear association of SBP with the outcome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given with 95% CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outcome. Relations are shown for the complete population (overall) and within 10 year age subgroups.

	Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
									LR point	95%CI		p	HR	95%CI		P
AHM	Dementia/	All	7	3528	6945	Non-linear	0.001	-43	**168**	**159**	**196**	**<0.001**	0.997	0.995	0.998	<0.001
users	Mortality	60-70	5	375	1220	Linear	0.07	1.3	**147**	**96**	**212**	**0.19**	0.999	0.994	1.005	0.84
		65-75	6	1154	3095	Linear	0.002	7.4	**159**	**151**	**180**	**0.003**	0.998	0.995	1.001	0.17
		70-80	7	1855	4209	Linear	0.03	3.0	**179**	**164**	**230**	**<0.001**	0.996	0.994	0.998	<0.001
		75-85	7	1668	2826	Non-linear	0.01	-27	**172**	**161**	**228**	**<0.001**	0.996	0.994	0.998	0.001
		80-90	7	1046	1241	Non-linear	0.001	-43.5	**158**	**150**	**171**	**0.003**	0.998	0.995	1.001	0.27
		85-95	5	613	663	Non-linear	0.26	-4.0	182	152	230	0.09	0.996	0.993	1.000	0.06
AHM	Dementia/	All	7	4623	9523	Linear	0.06	1.6	160	148	225	0.02	0.998	0.997	1.000	0.99
non-users	Mortality	60-70	5	635	2487	Linear	0.24	0.6	138	90	220	0.48	1.001	0.997	1.005	0.74
		65-75	6	1640	4528	Linear	0.38	1.2	138	90	225	0.52	1.001	0.998	1.003	0.46
		70-80	7	2406	5172	Linear	0.84	1.9	221	90	225	0.66	0.999	0.997	1.001	0.38
		75-85	7	2120	3317	Linear	0.02	3.5	**225**	**139**	**225**	**0.01**	0.998	0.995	1.000	0.03
		80-90	6	1296	1505	Non-linear	0.01	-33.0	**220**	**142**	**220**	**0.003**	0.998	0.995	1.000	0.07
		85-95	5	693	748	Linear	0.17	0.0	165	147	220	0.09	0.997	0.993	1.000	0.09

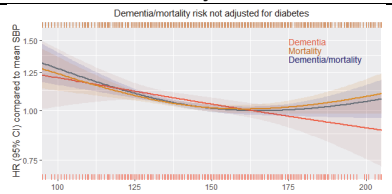
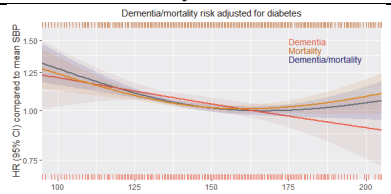
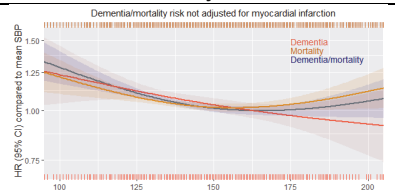
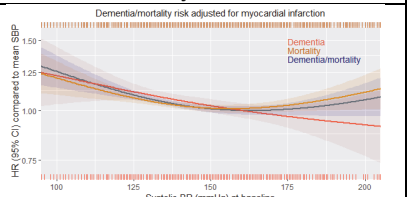
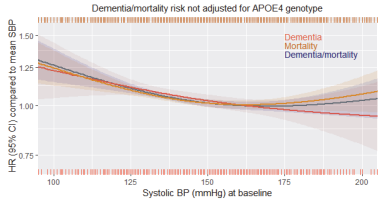
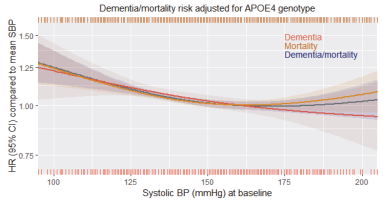
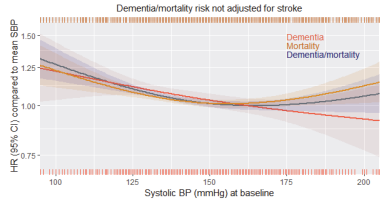
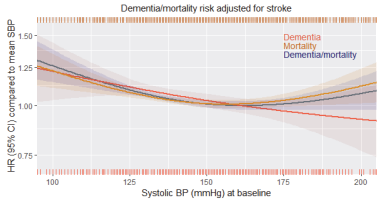
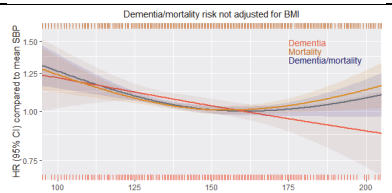
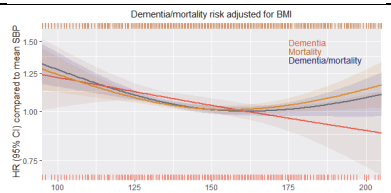
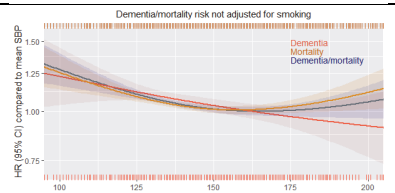
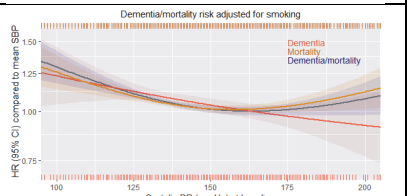
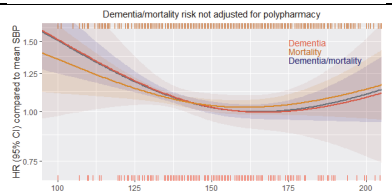
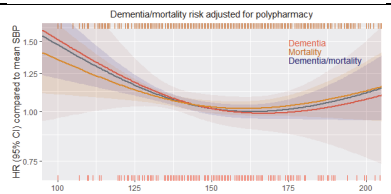
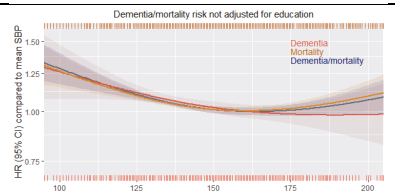
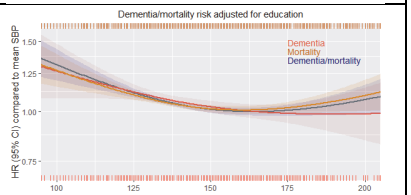
eTable 4. Relations for Systolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality in Age Groups, Stratified According to Antihypertensive Medication (AHM) Use. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. p-non-linear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of SBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups.

	Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results LR point	95%CI		p	Linear model results HR	95%CI		P
AHM	**Dementia**	All	7	1104	6939	Linear	0.42	1.3	123.5	45	124	0.33	0.997	0.991	1.002	0.21
users		60-70	5	84	1218	Linear	0.90	1.9	120	82	120	0.23	0.996	0.986	1.006	0.42
		65-75	6	311	3091	Linear	0.87	2.0	122	45	124	0.71	0.995	0.990	1.001	0.09
		70-80	7	554	4206	Linear	0.42	1.4	123.5	45	124	0.24	0.994	0.990	0.998	0.006
		75-85	7	556	2820	Linear	0.32	1.0	120	79	120	0.16	0.996	0.992	1.001	0.09
		80-90	7	369	1234	Linear	0.95	2.0	115	45	120	0.64	1.001	0.995	1.007	0.75
		85-95	5	227	666	Linear	0.96	1.9	120	80	120	0.32	0.996	0.989	1.003	0.30
AHM	**Dementia**	All	7	1545	9515	Linear	0.82	1.9	97.8	45	130	0.86	0.999	0.994	1.004	0.61
non-users		60-70	5	145	2490	Linear	0.26	1.3	125	93	125	0.2	0.995	0.988	1.003	0.26
		65-75	6	472	4531	Linear	0.78	1.9	125	45	130	0.56	0.997	0.992	1.002	0.28
		70-80	7	768	5171	Linear	0.97	2.0	111	45	130	0.94	0.999	0.995	1.003	0.64
		75-85	7	775	3313	Linear	0.77	1.9	119	45	128	0.51	0.997	0.993	1.001	0.13
		80-90	6	519	1496	Linear	0.35	1.1	87.5	47	120	0.39	0.996	0.991	1.001	0.15
		85-95	5	275	743	Non-linear	0.07	-1.2	47	46	119	0.12	0.998	0.991	1.005	0.59
AHM	**Mortality**	All	7	3243	6936	Linear	0.51	1.8	104.8	80	124	0.14	0.997	0.994	1.000	0.06
users		60-70	5	349	1218	Non-linear	0.01	-0.8	83	78	98	0.04	0.98	0.958	1.003	0.08
		65-75	6	1040	3090	Non-linear	0.09	-0.8	89	45	120	0.04	0.995	0.985	1.006	0.42
		70-80	7	1652	4203	Linear	0.99	1.9	123.5	92	124	0.004	0.994	0.986	1.002	0.14
		75-85	7	1516	2818	Non-linear	0.7	-0.5	120	85	120	0.049	0.994	0.986	1.001	0.11
		80-90	7	986	1234	Non-linear	0.55	-3.7	80	45	120	0.82	0.995	0.986	1.005	0.34
		85-95	5	593	666	Linear	0.50	1.8	87	53	120	0.50	0.991	0.979	1.003	0.13
AHM	**Mortality**	All	7	4244	9514	Non-linear	0.004	-6.5	81	76	90	0.01	0.999	0.996	1.002	0.44
non-users		60-70	5	586	2490	Non-linear	0.003	-4.2	81	76	90	0.01	0.988	0.97	1.005	0.16
		65-75	6	1492	4531	Non-linear	0.003	-7.0	82.2	78	91	0.004	0.995	0.986	1.004	0.30
		70-80	7	2171	5170	Non-linear	0.01	-2.0	80.5	73	90	0.04	0.999	0.992	1.006	0.73
		75-85	7	1923	3312	Non-linear	0.01	-2.6	81.5	75	99	0.04	0.996	0.989	1.003	0.26
		80-90	6	1207	1496	Linear	0.27	1.1	120	67	120	0.35	0.996	0.988	1.004	0.31
		85-95	5	663	743	Linear	0.98	0.6	119	46	120	0.65	0.997	0.987	1.008	0.64

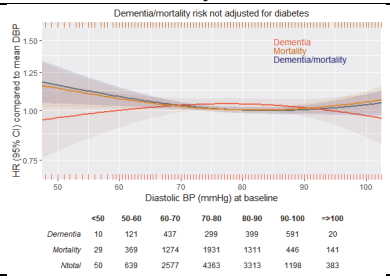
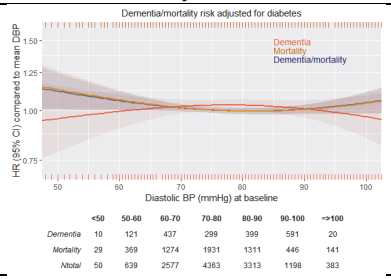
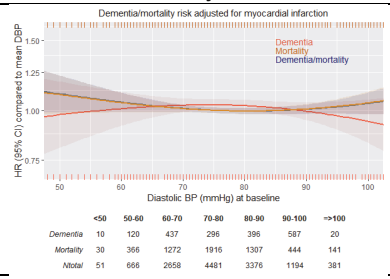
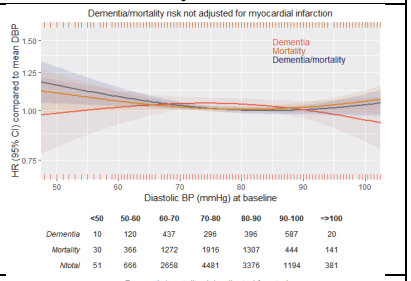
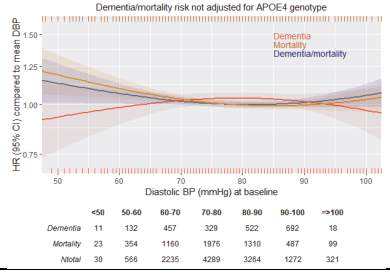
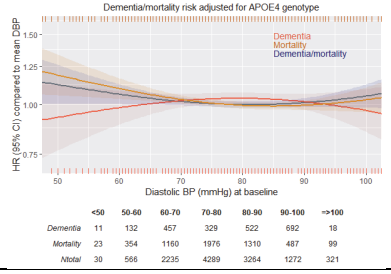
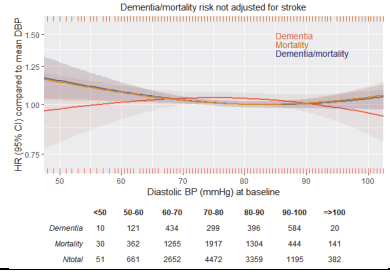
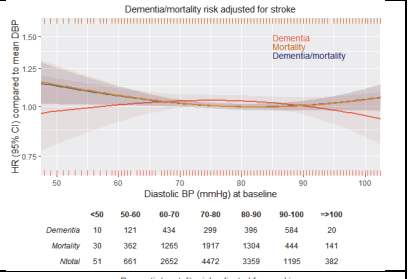
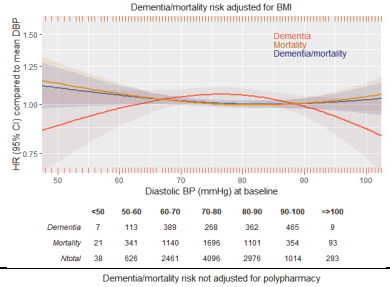
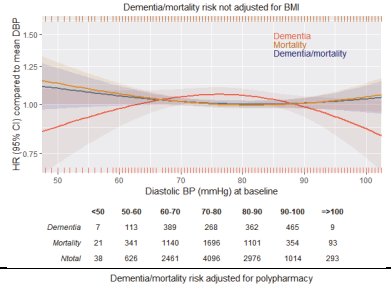
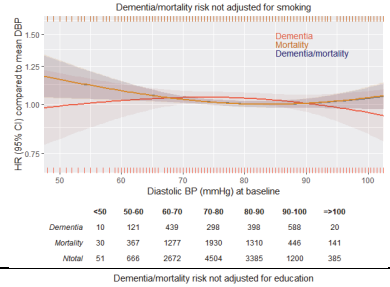
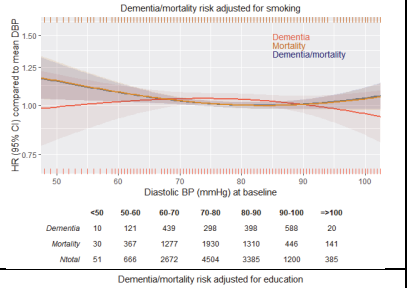
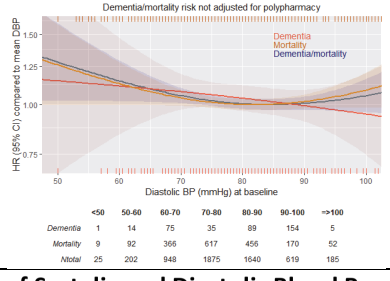
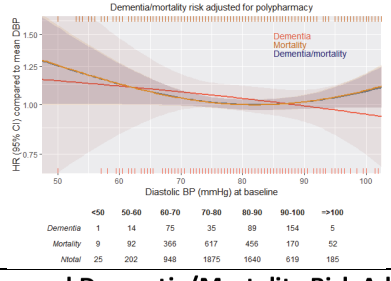
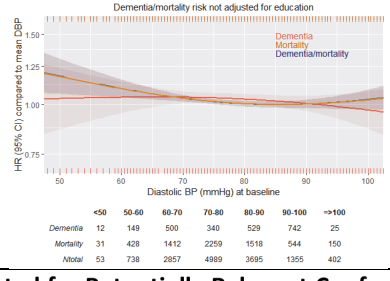
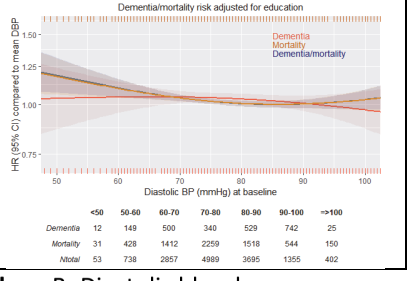
eTable 5. Relations for Diastolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality in Age groups, Stratified According to Antihypertensive Medication (AHM) Use. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of DBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of DBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups.

	Outcome	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
									LR point	95%CI		p	HR	95%CI		P
AHM	**Dementia/**	All	7	3521	6937	Linear	0.66	1.6	100	45	124	0.51	0.998	0.995	1.001	0.29
users	**Mortality**	60-70	5	374	1218	Non-linear	0.09	-4.3	85	74	120	0.17	0.996	0.986	1.007	0.49
		65-75	6	1150	3090	Non-linear	0.1	-0.9	90	82	124	0.06	0.995	0.989	1.000	0.07
		70-80	7	1850	4204	Linear	0.81	2	124	91	124	0.02	0.992	0.988	0.997	0.001
		75-85	7	1661	2819	Linear	0.09	1.8	120	115	120	0.053	0.994	0.99	0.999	0.02
		80-90	7	1039	1234	Linear	0.02	1.6	78	45	120	0.04	0.999	0.994	1.005	0.84
		85-95	5	616	666	Linear	0.62	1.5	100	51	120	0.51	0.996	0.989	1.004	0.34
		>90	5	141	146	Linear	0.93	1.9	110	50	115	0.91	0.995	0.980	1.010	0.53
AHM	**Dementia/**	All	7	4612	9515	Non-linear	0.003	-6.4	81	75	86.5	0.01	0.999	0.997	1.002	0.66
non-users	**Mortality**	60-70	5	635	2490	Non-linear	0.01	-6.6	83	77	115	0.02	0.996	0.988	1.005	0.38
		65-75	6	1640	4531	Non-linear	0.003	-7.1	82	77	90	0.01	0.997	0.991	1.002	0.19
		70-80	7	2405	5171	Non-linear	0.047	-4.5	82	69	124	0.12	1.000	0.995	1.004	0.89
		75-85	7	2115	3313	Non-linear	0.03	-4.1	85	79	128	0.03	0.998	0.994	1.003	0.49
		80-90	6	1287	1496	Linear	0.34	1.4	91	66	120	0.22	0.998	0.992	1.003	0.40
		85-95	5	688	743	Linear	0.23	2	81	47	120	0.43	0.997	0.990	1.004	0.35
		>90	5	173	177	Linear	0.12	0.9	79	69	120	0.25	0.989	0.975	1.003	0.13

eTable 5. Relations for Diastolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality in Age Groups, Stratified According to Antihypertensive Medication (AHM) Use. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of DBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of DBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups.

Confounder	Not Adjusted	Adjusted	Confounder	Not Adjusted	Adjusted
Diabetes			**Myocardial Infarction**		
APOE e4 genotye			**Stroke**		
BMI			**(Former) smoking**		
Polypharmacy			**Education**		

eFigure 4. Analyses of Systolic and Diastolic Blood Pressure and Dementia/Mortality Risk Adjusted and Not Adjusted for Potentially Relevant Confounders. A. Systolic blood pressure. Depicted are results for optimal non-linear models. The 'Not Adjusted' figures show results of the main analyses without additional adjustment, in the subpopulation for which the confounding variable was available (i.e. not missing). The 'adjusted' figures show results of the main analyses (which were adjusted for sex and antihypertensive medication use) additionally adjusted for the individual tabulated confounders. The coloured lines represent the relative hazard ratio (HR) on the y-axis, according to blood pressure in mmHg on the x-axis. Shaded areas represent 95% confidence intervals. Orange vertical stripes (top) represent one or multiple mortality cases at that specific SBP, red vertical stripes (bottom) represent one or multiple dementia cases at that specific BP. "HR compared to mean SBP" denotes that the HR is 1.00 at the mean SBP. Models fitted using natural splines, with degrees of freedom selected from 1 (linear model) upto a maximum of 4 (knots at 25th, 50th and 75th percentile), based on optimal model fit according to the Akaike Information Criterion (AIC). Models are adjusted for sex and antihypertensive use.

Confounder	Not Adjusted	Adjusted	Confounder	Not Adjusted	Adjusted
Diabetes			**Myocardial Infarction**		
APOE e4 genotype			**Stroke**		
BMI			**(Former) smoking**		
Polypharmacy			**Education**		

eFigure 4. Analyses of Systolic and Diastolic Blood Pressure and Dementia/Mortality Risk Adjusted and Not Adjusted for Potentially Relevant Confounders. B, Diastolic blood pressure. Depicted are results for optimal non-linear models. The 'Not Adjusted' figures show results of the main analyses without additional adjustment, in the subpopulation for which the confounding variable was available (i.e. not missing). The 'adjusted' figures show results of the main analyses (which were adjusted for sex and antihypertensive medication use) additionally adjusted for the individual tabulated confounders. The coloured lines represent the relative hazard ratio (HR) on the y-axis, according to blood pressure in mmHg on the x-axis. Shaded areas represent 95% confidence intervals. Orange vertical stripes (top) represent one or multiple mortality cases at that specific DBP, red vertical stripes (bottom) represent one or multiple dementia cases at that specific BP. "HR compared to mean DBP" denotes that the HR is 1.00 at the mean DBP. Models fitted using natural splines, with degrees of freedom selected from 1 (linear model) upto a maximum of 4 (knots at 25_{th}, 50_{th} and 75_{th} percentile), based on optimal model fit according to the Akaike Information Criterion (AIC). Models are adjusted for sex and antihypertensive use.

		Systolic BP		Diastolic BP	
Subgroup	**Outcome**	**AIC difference**	**P-value**	**AIC difference**	**P-value**
Sex	Dementia/Mortality	2.39	0.54	2.73	0.39
	Dementia	1.42	0.20	1.78	0.64
	Mortality	0.79	0.28	2.05	0.20
Antihypertensives	Dementia/Mortality	-5.12	0.01	1.39	0.27
	Dementia	1.40	0.27	3.61	0.82
	Mortality	-2.24	0.04	-302.20	<0.001
Diabetes	Dementia/Mortality	5.38	0.07	6.18	0.04
	Dementia	1.45	0.45	1.93	0.78
	Mortality	6.52	0.03	5.82	0.05
History of myocardial infarction	Dementia/Mortality	7.64	0.02	3.48	0.22
	Dementia	2.27	0.41	1.13	0.35
	Mortality	6.17	0.04	3.57	0.20
History of stroke	Dementia/Mortality	9.93	<0.001	6.53	0.03
	Dementia	-1.88	0.048	0.87	0.28
	Mortality	9.52	0.01	6.72	0.03
APOE e4 genotype	Dementia/Mortality	5.67	0.06	5.45	0.06
	Dementia	1.72	0.60	0.58	0.24
	Mortality	7.61	0.02	6.99	0.03
Polypharmacy	Dementia/Mortality	5.76	0.05	4.13	0.14
	Dementia	5.67	0.66	1.92	0.76
	Mortality	5.24	0.07	4.45	0.12

eTable 6. Model Improvement Stratified According to Subgroups. Akaike Information Criterion (AIC) difference denotes the improvement of the model including an interaction term blood pressure*subgroup variable compared to a model adjusted for the subgroup variable. Comparisons include linear and non-linear models (i.e. the best fitting model was selected for each subgroup, which could be either linear or non-linear). Negative AIC denotes better and positive AIC worse model fit when stratified. P-value denotes significance of difference between models. Subgroups with a significantly ($p<0.05$) better (i.e. AIC<0) model fit were considered relevant modifiers of the relation between blood pressure and each outcome (bold and shaded in grey). BP: blood pressure.

BP	Outcome	Subgroup	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC difference	Non-linear model results				Linear model results			
									LR point	95%CI		p	HR	95%CI		P
SBP	Dementia	Stroke	5	106	710	Linear	0.78	1.9	100	100	216	0.24	1.008	0.999	1.017	0.09
		No Stroke	5	1764	12092	Linear	0.92	2.0	229	161	229	0.03	0.997	0.995	0.999	0.01
	Mortality	Stroke	5	358	710	Linear	0.45	1.5	158	100	216	0.66	0.999	0.993	1.004	0.60
		No Stroke	5	5129	12088	Non-linear	0.01	-5.4	148	136	158	0.03	1.000	0.999	1.001	0.84
	Dem/mort	Stroke	5	392	710	Linear	0.62	1.8	153	100	216	0.88	1.000	0.995	1.005	0.99
		No Stroke	5	5600	12090	Non-linear	0.01	-5.6	154	144	170	0.01	0.999	0.998	1.001	0.27
DBP	Dementia	Stroke	5	105	708	Linear	0.3	1.0	75	40	131	0.49	1.008	0.999	1.017	0.09
		No Stroke	5	1761	12090	Linear	0.41	1.3	143	45	143	0.54	0.997	0.995	0.999	0.01
	Mortality	Stroke	5	355	708	Linear	0.72	1.8	82	40	131	0.92	0.999	0.993	1.004	0.60
		No Stroke	5	5125	12086	Non-linear	0.004	-6.1	80	72	89	0.02	1.000	0.999	1.001	0.84
	Dem/mort	Stroke	5	389	708	Linear	0.77	1.9	76	40	131	0.92	1.000	0.995	1.005	0.99
		No Stroke	5	5595	12088	Non-linear	0.01	-5.3	81	73	89	0.03	0.999	0.998	1.001	0.27

eTable 7. Subgroup Analyses in Individuals With/Without a History of Stroke. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. a p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of DBP/SBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of DBP/SBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups. BP: blood pressure, SBP: stystolic blood pressure, DBP: diastolic blood pressure

Outcome	Excluding	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
								LR point	95%CI		p	HR	95%CI		P
Dementia	ACT	6	1491	11442	Non-linear	0.004	-32	167	157	219	0.001	0.997	0.995	1.000	0.02
	Got	6	2660	15893	Linear	0.19	0.3	193	162	230	0.001	0.997	0.995	0.998	<0.001
	KP	6	2310	15607	Linear	0.37	1.2	230	167	230	0.001	0.996	0.994	0.998	<0.001
	LEILA	6	2533	15973	Linear	0.27	0.8	206	162	225	0.002	0.997	0.995	0.999	0.001
	PreDIVA	6	2507	13433	Non-linear	0.13	-1.5	182	158	230	0.004	0.997	0.995	0.999	0.004
	SNAC	6	2316	14216	Linear	0.45	1.4	195	157	230	0.09	0.998	0.996	1.000	0.04
	ZARADEMP	6	2613	14684	Linear	0.35	1.1	221	164	230	0.01	0.997	0.995	0.999	0.002
Mortality	ACT	6	4696	11438	Non-linear	<0.001	-10.7	166	158	194	<0.001	0.998	0.996	0.999	0.001
	Got	6	7184	15889	Non-linear	0.005	-6.0	162	153	203	0.001	0.999	0.997	1.000	0.01
	KP	6	6845	15603	Non-linear	0.001	-9.4	160	152	177	<0.001	0.998	0.997	1.000	0.009
	LEILA	6	7215	15969	Non-linear	<0.001	-10.1	158	152	174	<0.001	0.999	0.997	1.000	0.02
	PreDIVA	6	7153	13433	Non-linear	<0.001	-11.9	157	150	169	<0.001	0.999	0.998	1.000	0.04
	SNAC	6	6406	14212	Non-linear	0.002	-7.6	159	151	176	0.001	0.999	0.998	1.000	0.053
	ZARADEMP	6	6699	14680	Non-linear	0.001	-9.2	163	155	189	<0.001	0.998	0.997	0.999	0.004
Dementia/	ACT	6	5144	11440	Non-linear	<0.001	-11.9	167	160	184	<0.001	0.997	0.996	0.999	<0.001
Mortality	Got	6	7852	15891	Non-linear	0.004	-6.2	168	158	219	<0.001	0.998	0.997	0.999	<0.001
	KP	6	7388	15605	Non-linear	0.002	-7.5	165	156	203	<0.001	0.998	0.997	0.999	<0.001
	LEILA	6	7818	15971	Non-linear	0.001	-9.2	162	154	185	<0.001	0.998	0.997	0.999	<0.001
	PreDIVA	6	7645	13433	Non-linear	<0.001	-11.4	160	153	177	<0.001	0.998	0.997	0.999	0.003
	SNAC	6	7050	14214	Non-linear	0.001	-9.1	162	153	182	<0.001	0.998	0.997	0.999	0.003
	ZARADEMP	6	7363	14682	Non-linear	0.002	-7.3	167	158	205	<0.001	0.998	0.997	0.999	<0.001

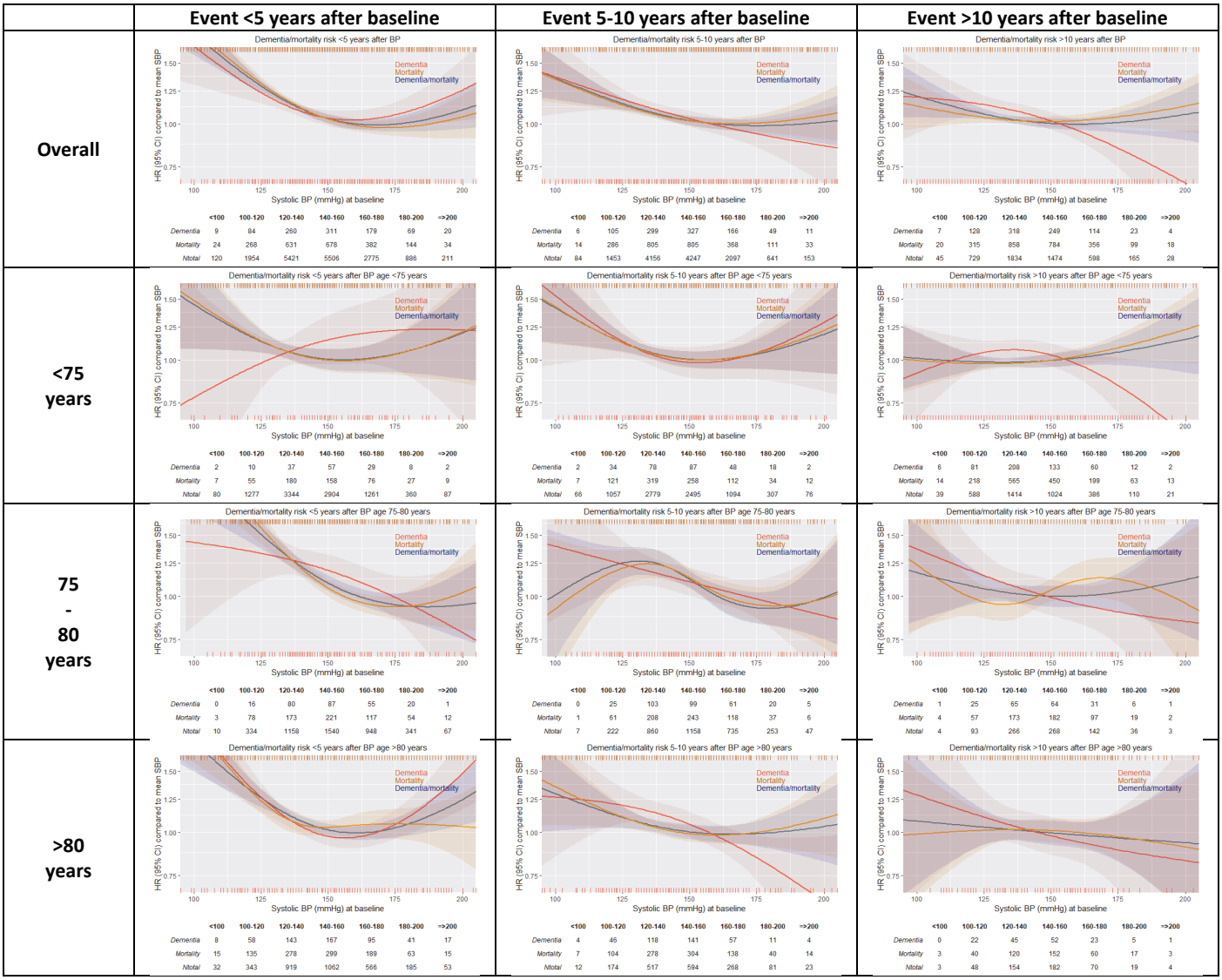
eTable 8. Leave-One-Out Analyses. A, Systolic blood pressure. Overall analyses results when leaving out the individual study populations listed one at a time. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. a p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of SBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups. BP: blood pressure, SBP: stystolic blood pressure

Outcome	Excluding	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
								LR point	95%CI		p	HR	95%CI		P
Dementia	ACT	6	1484	11410	Linear	0.29	0.9	103	86	150	0.06	0.995	0.99	1.000	0.04
	Got	6	2651	15853	Linear	0.48	1.5	139	74	139	0.28	0.997	0.994	1.001	0.15
	KP	6	2304	15571	Linear	0.39	1.2	139	78	139	0.35	0.998	0.994	1.002	0.25
	LEILA	6	2528	15936	Linear	0.22	0.5	120	45	120	0.23	0.998	0.994	1.002	0.24
	PD	6	2498	13392	Linear	0.57	1.6	143	76	143	0.39	0.998	0.994	1.001	0.21
	SNAC	6	2307	14175	Linear	0.47	1.5	141	45	141	0.53	0.998	0.994	1.002	0.39
	ZARADEMP	6	2604	14647	Linear	0.48	1.5	141	45	141	0.53	0.998	0.995	1.002	0.38
Mortality	ACT	6	4673	11406	Non-linear	0.001	-8.5	90	84	102	<0.001	0.997	0.994	1.000	0.02
	Got	6	7153	15849	Non-linear	0.01	-5.5	85	80	104	0.01	0.998	0.996	1.000	0.13
	KP	6	6818	15567	Non-linear	0.003	-6.6	85	80	108	0.003	0.998	0.996	1.000	0.09
	LEILA	6	7187	15932	Non-linear	0.01	-5.1	83	78	96	0.01	0.998	0.996	1.001	0.16
	PD	6	7122	13392	Non-linear	0.01	-5.6	84	79	99	0.01	0.998	0.996	1.001	0.14
	SNAC	6	6374	14171	Non-linear	0.03	-2.5	86	78	139	0.04	0.998	0.996	1.001	0.14
	ZARADEMP	6	6670	14643	Non-linear	0.004	-6.2	87	81	114	0.001	0.997	0.995	1.000	0.02
Dementia/	ACT	6	5119	11408	Non-linear	0.002	-7.9	86	82	95	0.003	0.998	0.996	1.001	0.20
Mortality	Got	6	7820	15851	Non-linear	0.01	-5.0	83	77	96	0.02	0.999	0.997	1.001	0.38
	KP	6	7360	15569	Non-linear	0.01	-5.2	82	76	93	0.02	0.999	0.997	1.002	0.56
	LEILA	6	7790	15934	Non-linear	0.04	-2.1	85	77	120	0.08	0.999	0.997	1.001	0.37
	PD	6	7613	13392	Non-linear	0.01	-5.1	82	75	93	0.02	0.999	0.997	1.002	0.57
	SNAC	6	7017	14173	Non-linear	0.02	-3.1	86	80	139	0.02	0.998	0.996	1.000	0.12
	ZARADEMP	6	7333	14645	Non-linear	0.01	-5.0	84	79	100	0.02	0.999	0.997	1.001	0.24

eTable 8. Leave-One-Out Analyses. B, Diastolic blood pressure. Overall analyses results when leaving out the individual study populations listed one at a time. Results are shown from non-linear and linear models. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. a p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of DBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of DBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups. BP: blood pressure, DBP: diastolic blood pressure

BP	Time to event	Outcome	Studies	Cases	Total	Optimal shape	p-non-lin	AIC difference	LR	95% CI		p-val	HR	95%CI	P	HR
SBP	**<5 years**	**Dementia**	7	932	16873	Non-llinear	0.004	-6.2	160	150	200	0.01	0.998	0.995	1.001	0.25
		Mortality	7	2161	16869	Non-llinear	<0.001	-13.1	169	160	200	<0.001	0.995	0.993	0.997	<0.001
		Dem/Mort	7	2745	16870	Non-llinear	<0.001	-17.6	166	159	185	<0.001	0.996	0.994	0.998	<0.001
	5-10 years	**Dementia**	7	962	12821	Linear	0.82	2.0	225	162	225	0.03	0.996	0.993	0.999	0.01
		Mortality	7	2420	12819	Non-llinear	0.09	-1.0	161	145	225	0.06	0.998	0.996	1.000	0.10
		Dem/Mort	7	2819	12820	Non-llinear	0.11	-0.7	166	152	225	0.02	0.998	0.996	1.000	0.02
	>10 years	**Dementia**	6	842	4869	Linear	0.21	0.3	218	214	218	0.01	0.995	0.992	0.999	0.01
		Mortality	6	2448	4869	Linear	0.19	0.3	143	91	214	0.36	1.001	0.999	1.003	0.60
		Dem/Mort	6	2597	4869	Non-llinear	0.14	-0.2	153	92	218	0.24	0.999	0.997	1.001	0.41
DBP	**<5 years**	**Dementia**	7	933	16860	Linear	0.62	1.7	131	83	139	0.20	0.998	0.995	1.001	0.25
		Mortality	7	2154	16856	Non-llinear	0.001	-9.8	91	85	114	<0.001	0.995	0.993	0.997	<0.001
		Dem/Mort	7	2737	16857	Non-llinear	0.002	-7.8	93	87	139	<0.001	0.996	0.994	0.998	<0.001
	5-10 years	**Dementia**	7	961	12820	Linear	0.85	2.0	100	45	125	0.74	0.996	0.993	0.999	0.01
		Mortality	7	2417	12818	Linear	0.61	1.7	84	45	125	0.82	0.998	0.996	1.000	0.10
		Dem/Mort	7	2814	12819	Linear	0.42	1.3	82	45	125	0.71	0.998	0.996	1.000	0.02
	>10 years	**Dementia**	6	841	4869	Non-llinear	0.07	-1.4	120	45	120	0.13	0.995	0.992	0.999	0.01
		Mortality	6	2445	4869	Linear	0.71	1.9	45	45	67	<0.001	1.001	0.999	1.003	0.60
		Dem/Mort	6	2594	4869	Linear	0.91	2.0	45	45	56	<0.001	0.999	0.997	1.001	0.41

eTable 9. Relations for Systolic and Diastolic Blood Pressure With Risk of Dementia, Mortality, and Dementia/Mortality According to Time to Event in the Total Population. Relations between systolic and diastolic blood pressure and risk of events occuring in the listed follow-up time windows. Time windows (<5 years, 5-10 years, <10 years) were based on tertiles of dementia events across follow-up time. Results are shown from non-linear and linear models in age-based subgroups. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. a p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of SBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups. BP: blood pressure, SBP: stystolic blood pressure, DBP: diastolic blood pressure



eFigure 5. Analyses for Systolic Blood Pressure According to Time to Event in the Total Population and Within Age Subgroups. Depicted are results for optimal non-linear models on relations between systolic blood pressure and risk of events occuring in the listed follow-up time windows, and for the listed age categories. Time windows (<5 years, 5-10 years, <10 years) and age categories (<75, 75-80, >80 years) were based on tertiles of dementia events across follow-up time and across baseline age. For age categories, the age window was increased by steps of 2.5 years to avoid abrupt changes in the study population influencing results, analogous the to the overall age stratified analyes.

eTable 10. Sensitivity Analyses Adjusting for Multiple Confounders in Together in Single Models

Study	n	Sex	AHM	BMI	DM	Smoking	Stroke	MI	N med	Edu	APOE
ZARADEMP	2189	0	0	410	15	1	49	31	0	12	2189
Kungsholmen	1275	0	0	1275	1275	1275	1275	1275	1275	0	306
SNAC-K.	2657	0	0	2657	2657	2657	2657	2657	2657	2657	152
LEILA	891	0	0	891	1	5	1	4	891	19	647
H70	980	0	0	17	0	18	27	0	487	20	35
PreDIVA	3449	0	0	2	0	7	44	23	632	34	546
ACT	5432	0	0	102	367	13	15	41	5432	1	999

A, Missing confounders per study. N denotes the total number of participants, the number under each confounder listed the number of individuals with missing data. Abbreviation: AHM: antihypertensive medication, BMI: Body Mass Index, DM: diabetes, MI: Myocardial infarction history, N med: number of medication, Edu: education, APOE: APOE-genotype

Method	Outcome	Studies	Cases	Total	Optimal shape	P-non-lin	AIC diffeerence	LR	95%CI		p	HR	95%CI		p
Original	Dem	7	2738	16873	Linear	0.16	0.1	185	161	230	0.001	0.997	0.995	0.999	0.001
Analyses	Mortality	7	7698	16869	Non-linear	<0.001	-10.4	160	154	181	<0.001	0.998	0.997	1.000	0.008
	Dem/Mort	7	8375	16871	Non-linear	<0.001	-10.2	163	158	197	<0.001	0.998	0.997	0.999	<0.001
Minimal	Dem	5	1843	12247	Linear	0.58	1.7	230	178	230	0.01	0.997	0.995	0.999	0.01
Dataset	Mortality	5	5399	12243	Non-linear	0.004	-6.3	151	147	184	0.01	1.000	0.998	1.001	0.51
	Dem/Mort	5	5893	12245	Non-linear	0.003	-7.1	159	149	168	0.002	0.999	0.998	1.000	0.06
'Unknown'	Dementia	7	2738	16873	Linear	0.2	0.4	230	185	230	0.001	0.997	0.995	0.999	0.001
Category	Mortality	7	7698	16869	Non-linear	0.002	-7	161	156	170	0.001	0.999	0.998	1.000	0.04
	Dem/Mort	7	8375	16871	Non-linear	0.002	-7.2	159	149	168	<0.001	0.998	0.997	0.999	0.001
Propensity	Dementia	7	2738	16873	Linear	0.18	0.3	230	161	230	0.003	0.997	0.995	0.999	0.003
Score	Mortality	7	7698	16869	Non-linear	0.001	-8.2	154	149	159	0.002	0.999	0.998	1.000	0.12
	Dem/Mort	7	8375	16871	Non-linear	0.001	-8.3	163	161	176	<0.001	0.999	0.997	1.000	0.01

B, Results for systolic blood pressure models adjusted for multiple additional confounders using different methods for handling missing data. *Original analyses:* main analyses in the paper, adjusted for age, sex and antihypertensive use only. *Minimal dataset:* additionally adjusted for age, sex, antihypertensive use, diabetes mellitus, smoking, history of myocardial infarction, history of stroke, and education (tertiles of levels within study). Missing values left out of analyses (pairwise), these analyses exclude the Kungsholmen and SNAC-K studies completely. *'Unknown' category:* additionally adjusted for BMI (<25, 25-30, 30+), number of medications used, and APOE-genotype. *Propensity score:* analyses adjusted for a propensity score handling missing data using missing pattern approach, comprising the relation between confounders and systolic BP levels, specifically calculated for each missing data pattern in the confounders.

Method	Outcome	Studies	Cases	Total	Optimal shape	P-non-lin	AIC diffeerence	LR	95%CI		p	HR	95%CI		p
Original	Dem	7	2735	16860	Linear	0.57	1.7	139	80	139	0.16	0.997	0.994	1.001	0.16
analyses	Mortality	7	7683	16856	Non-linear	0.002	-7.5	84	80	97	**0.002**	0.998	0.996	1.000	0.063
	Dem/Mort	7	8359	16858	Non-linear	0.004	-6.3	82	79	93	**0.01**	0.999	0.997	1.001	0.30
Minimal	Dem	5	1840	12235	Linear	0.37	1.1	139	45	139	0.70	0.999	0.995	1.003	0.70
dataset	Mortality	5	5388	12231	Non-linear	0.06	-1.6	73	45	83	0.051	1.002	0.999	1.005	0.12
	Dem/Mort	5	5882	12233	Non-linear	0.047	-1.9	74	45	82	0.046	1.002	0.999	1.004	0.14
'Unknown'	Dementia	7	2735	16860	Linear	0.41	1.3	139	45	139	0.34	0.998	0.995	1.002	0.34
category	Mortality	7	7683	16856	Non-linear	0.02	-3.1	80	66	94	0.07	1	0.998	1.002	0.81
	Dem/Mort	7	8359	16858	Non-linear	0.03	-2.5	74	45	82	0.07	1.001	0.999	1.003	0.38
Propensity	Dementia	7	2735	16860	Linear	0.57	1.7	139	45	139	0.24	0.998	0.994	1.001	0.24
score	Mortality	7	7683	16856	Non-linear	0.002	-7.8	82	76	89	0.01	0.999	0.997	1.002	0.59
	Dem/Mort	7	8359	16858	Non-linear	0.01	-5.8	80	72	87	0.02	1	0.998	1.002	0.94

C, Results for diastolic blood pressure models adjusted for multiple additional confounders using different methods for handling missing data. *Original analyses:* main analyses in the paper, adjusted for age, sex and antihypertensive use only. *Minimal dataset:* additionally adjusted for age, sex, antihypertensive use, diabetes mellitus, smoking, history of myocardial infarction, history of stroke, and education (tertiles of levels within study). Missing values left out of analyses (pairwise), these analyses exclude the Kungsholmen and SNAC-K studies completely. *'Unknown' category:* additionally adjusted for BMI (<25, 25-30, 30+), number of medications used, and APOE-genotype. *Propensity score:* analyses adjusted for a propensity score handling missing data using missing pattern approach, comprising the relation between confounders and diastolic BP levels, specifically calculated for each missing data pattern in the confounders.

Blood pressure	Baseline Age	Studies	Cases	Total	Optimal Shape	P-non-lin	AIC Difference	Non-linear model results				Linear model results			
								LR point	95%CI		p	HR	95%CI		P
Systolic	All	7	2,738	16,873	Linear	0.33	1.05	195	158	230	0.03	0.998	0.996	1.000	0.015
	60-70	5	231	3813	Linear	0.89	1.99	260	157	260	0.22	0.998	0.997	1.000	0.08
	65-75	6	786	7656	Linear	0.57	1.68	230	86	230	0.75	0.999	0.996	1.003	0.60
	70-80	7	1352	9602	Linear	0.40	1.29	260	179	260	0.09	0.997	0.995	1.000	0.047
	75-85	7	1390	6449	Linear	0.27	0.79	197	163	260	0.008	0.996	0.994	0.999	0.004
	80-90	7	947	2922	Non-linear	0.001	-9.14	160	153	189	0.001	0.997	0.994	1.001	0.10
	85-95	5	535	1504	Non-linear	0.005	-5.94	162	152	195	0.004	0.997	0.993	1.001	0.11
	>90	5	121	345	Linear	0.72	1.82	231	79	231	0.76	0.999	0.991	1.007	0.73
Diastolic	All	7	2735	16860	Linear	0.99	2.00	139	91	139	0.01	0.995	0.991	0.998	0.003
	60-70	5	231	3811	Linear	0.21	0.60	130	115	130	0.16	0.989	0.976	1.003	0.12
	65-75	6	786	7651	Linear	0.31	0.97	130	27	130	0.16	0.994	0.988	1.001	0.11
	70-80	7	1351	9598	Linear	0.27	0.76	130	114	139	0.14	0.996	0.991	1.001	0.11
	75-85	7	1386	6442	Linear	0.55	1.07	130	108	139	0.06	0.995	0.990	0.999	0.03
	80-90	7	944	2914	Non-linear	0.07	-0.54	105	87	139	0.03	0.994	0.989	1.000	0.04
	85-95	5	535	1503	Non-linear	0.12	-0.99	93	74	173	0.13	0.997	0.990	1.004	0.37
	>90	5	121	345	Linear	0.92	1.97	30	30	120	0.96	1.002	0.987	1.018	0.79

eTable 11. Results for Fine-Gray Analyses of Dementia Accounting for the Competing Risk of Mortality in the Overall Population and Baseline Age Groups. Results of the main analyses for systolic blood pressure and diastolic blood pressure on the outcome of dementia, accounting for mortality as competing risk. Results are shown from non-linear and linear models overall and in age-based subgroups. For each outome, the optimal shape is given, with the p-value comparing the optimal non-linear model to the optimal linear model (i.e. p-non-lnear value >0.05 denotes that the non-linear model was not significantly better than the linear model acccording to the log-likelihood ratio test). For linear models, the hazard ratio (HR) per mmHg increment, 95% confidence intervals (95%CI) and p-value for the linear association of SBP with the outome are given. For non-linear models, the blood pressure associated with the lowest risk (LR) point estimated from the model is given, with 95%CI based on 1,000 bootstraps, and the p-value for the non-linear association of SBP with the outome. Relations are shown for the complete population (overall) and within 10 year age subgroups.

