

ONLINE SUPPLEMENT**Population impact of different hypertension management guidelines based on the prospective population-based Heinz Nixdorf Recall study**

Janine Gronewold, Ph.D.¹, Rene Kropp, MSc;¹ Nils Lehmann, PhD;² Andreas Stang, MD;^{2,3} Amir A. Mahabadi, MD;⁴ Christian Weimar, MD;¹ Martin Dichgans, MD;^{5,6} Susanne Moebus, PhD;² Knut Kröger, MD;⁷ Barbara Hoffmann, MD;⁸ Karl-Heinz Jöckel, PhD;² Raimund Erbel, MD;² Dirk M. Hermann, MD;¹ on behalf of the Heinz Nixdorf Recall Study Investigative Group.

1: Department of Neurology, University Hospital Essen, Essen, Germany; 2: Institute for Medical Informatics, Biometry and Epidemiology, University Hospital Essen, University Duisburg-Essen, Essen, Germany; 3: Boston University School of Public Health, Department of Epidemiology, Boston, USA; 4: West German Heart and Vascular Center Essen, Department of Cardiology and Vascular Medicine, University Hospital Essen, Essen, Germany; 5: Institute for Stroke and Dementia Research, University Hospital, Ludwig-Maximilians-Universität LMU, Munich, Germany; 6: Munich Cluster of Systems Neurology (SyNergy), Munich, Germany; 7: Department of Angiology, Helios-Klinikum Krefeld, Krefeld, Germany; 8: Environmental Epidemiology Group, Institute of Occupational, Social and Environmental Medicine, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Correspondence: Dr. Janine Gronewold & Prof. Dr. Dirk M. Hermann, janine.gronewold@uk-essen.de

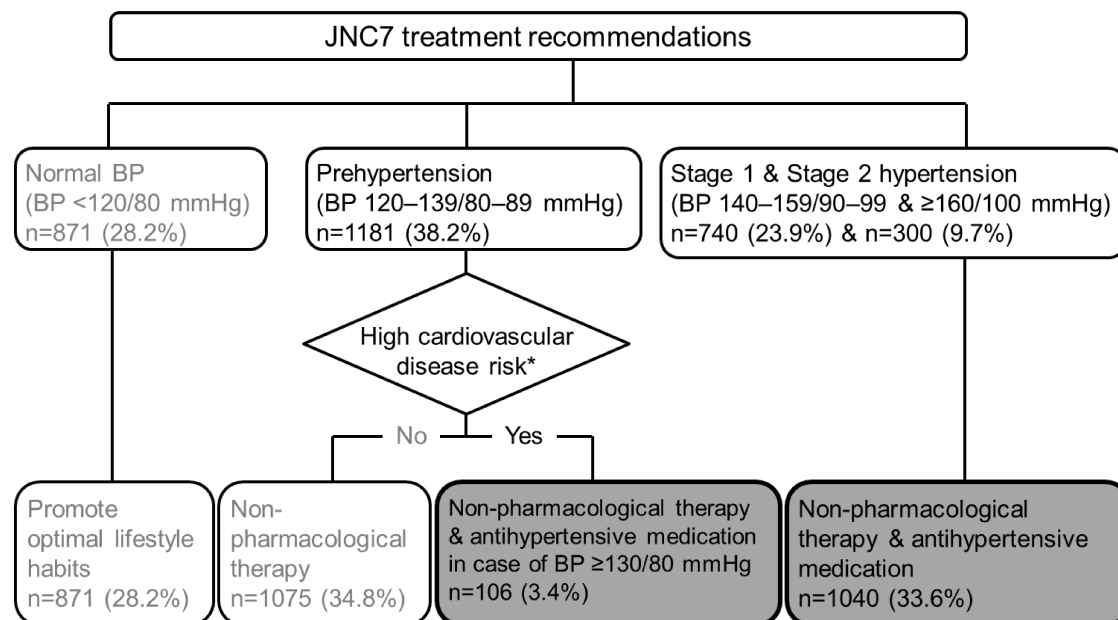
Online methods: measurement of vascular risk factors

For the assessment of ankle-brachial index (ABI), systolic BP measurements were performed using an 8-MHz Doppler transducer on subjects resting on a flat couch for 15 minutes (Logidop, Kranzbühler, Germany). Ankle pressures were measured above the posterior tibial and dorsal foot arteries, brachial pressures above the cubital segment of both brachial arteries. ABI was calculated per leg as a ratio of the highest ankle artery pressure recorded either in the posterior tibial or dorsal foot artery and the highest systolic pressure measured in the right and left arm. For further analyses, the lower ABI of both legs was used. For the assessment of common carotid artery intima-media thickness (CIMT), B-mode images were obtained with a Vivid FiVe ultrasound system (GE Ultrasound Europe, Solingen, Germany) using a linear 10-MHz scanner. In longitudinal two-dimensional images, CIMT measurements were made at the far wall of both common carotid arteries for a 10-mm distance proximal to the bifurcation. Focal plaques were excluded from the analysis. Average values were calculated for the left and right vessel, of which mean values were formed. Left ventricular hypertrophy and atrial fibrillation were assessed by standardized digital 12-lead resting surface ECG sampled at 250 Hz and recorded on a MAC 5000[®] electrocardiograph (ECG) recorder (GE Healthcare, Freiburg, Germany) and defined automatically according to 12SL-Code[®] definitions.¹ Body mass index (BMI, kg/m²) was calculated from standardized measurements of height and weight, overweight was defined as BMI ≥ 30 kg/m². Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides were measured with standardized enzymatic methods using the ADVIA 1650 System (Siemens Healthcare Diagnostics, Eschborn, Germany). We defined high LDL cholesterol/high triglycerides as LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL. Blood glucose was measured after overnight fasting with a mean of 9.7 ± 4.9 h (median 12 h). Participants were classified as diabetic when fasting glucose exceeded 126 mg/dL or non-fasting glucose exceeded 200 mg/dL, or the use of insulin or oral hypoglycaemic agents was reported. Serum creatinine was measured (Advia Clinical Chemistry Analyzer, Siemens HealthCare Diagnostics, Erlangen, Germany) and glomerular filtration rate (GFR, in mL/min/1.73 m²) was estimated using the abbreviated Modification of Diet in Renal Disease equation. Chronic kidney disease was defined by GFR <60 mL/min/1.73 m². Smoking was defined as history of cigarette smoking during the past year,² and physical inactivity was defined as not regularly performing any type of physical activity, which was assessed in standardized computer-assisted personal interviews. History of stroke, coronary heart disease (myocardial infarction or coronary intervention), heart failure, peripheral artery disease as well as history of myocardial infarction in first-degree relatives and the age of the last period (menopause) was assessed in standardized questionnaires. We defined early-onset menopause as menopause in participants <45 years. Participants were asked to bring all the medications they had been taking during the 7 days prior to the examination appointment. Medications were coded according to the Anatomical Therapeutic Chemical Classification Index.³ Antidiabetic medications included all medications with ATC Code A10. The 10-year atherosclerotic cardiovascular disease (ASCVD, including coronary heart disease and stroke) risk score⁴ and the 10-year European fatal cardiovascular disease risk score (SCORE [Systematic COronary Risk Evaluation])⁵ were calculated. All above-mentioned measures available in the Heinz Nixdorf Recall study were used to calculate frequencies and percentages of participants recommended for antihypertensive medication as well as frequencies and percentages of participants exhibiting blood pressure above treatment goal.

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Online Figures and Tables

**Figure S1: JNC7 treatment recommendations**

*High cardiovascular disease risk defined by (a) diabetes mellitus or (b) chronic kidney disease (glomerular filtration rate <60 mL/min per 1.73 m², urine albumin >300 mg/day or >200 mg/g creatinine). BP=blood pressure; JNC=Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

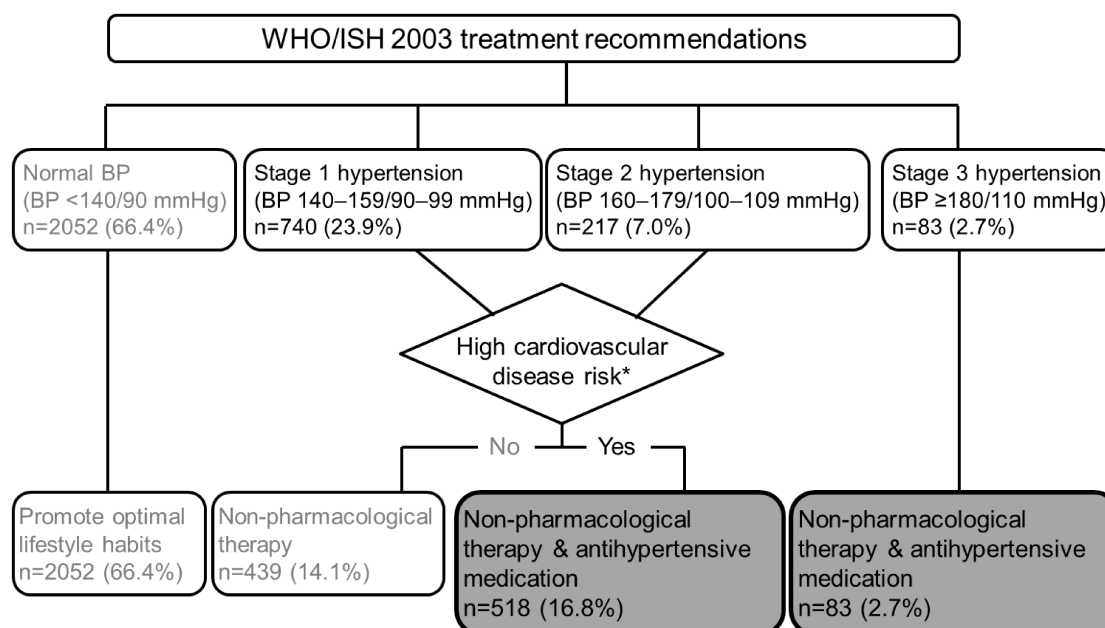


Figure S2: WHO/ISH 2003 treatment recommendations

*High cardiovascular disease risk defined by (a) three or more of the following cardiovascular disease risk factors: age >55/>65 years for males/females, smoking, total cholesterol >240 mg/dL, LDL cholesterol >60 mg/dL, high-density lipoprotein cholesterol <40/<45 mg/day for males/females, history of cardiovascular disease in first-degree relatives before age 50 years, or obesity or physical inactivity; (b) target-organ damage: left ventricular hypertrophy on electrocardiogram or echocardiogram, urine albumin 20–300 mg/day, radiological or ultrasound evidence of extensive atherosclerotic plaque (aorta, carotid, coronary, iliac, or femoral arteries), or hypertensive retinopathy grade III or IV; or (c) associated clinical conditions: diabetes, cerebrovascular disease (ischaemic stroke, cerebral haemorrhage, or transient ischaemic attack), heart disease (myocardial infarction, angina, coronary revascularisation, or congestive heart failure), renal disease (plasma creatinine >1.5/>1.4 mg/dL for males/females or urine albumin > 300 mg/day), or peripheral vascular disease. BP=blood pressure; ISH=International Society of Hypertension; WHO=World Health Organization.

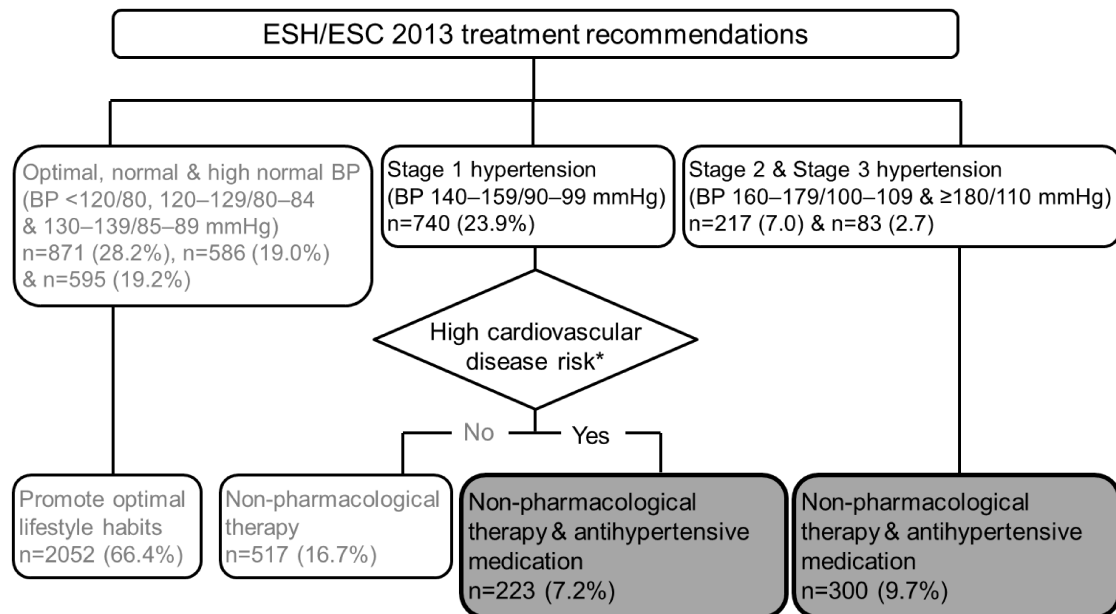


Figure S3: ESH/ESC 2013 treatment recommendations

*High cardiovascular disease risk defined by (a) asymptomatic organ damage: pulse pressure ≥ 60 mmHg in the elderly ≥ 80 years, left ventricular hypertrophy (electrocardiographic Sokolow–Lyon index > 3.5 mV, RaVL > 1.1 mV, Cornell voltage duration product > 244 mV*ms, or echocardiographic left ventricular mass index $> 115/95$ g/m² for males/females), carotid wall thickening (common-carotid artery intima-media thickness > 0.9 mm or plaque), carotid–femoral pulse wave velocity > 10 m/s, ankle–brachial index < 0.9 , glomerular filtration rate 30–60 mL/min/1.73 m², or urine albumin 30–300 mg/day or 30–300 mg/g creatinine; (b) diabetes mellitus: (fasting plasma glucose ≥ 126 mg/dL on two repeated measurements, glycated haemoglobin (HbA_{1c}) $> 7\%$, or post-load plasma glucose > 198 mg/dL); or (c) established cardiovascular or renal disease: cerebrovascular disease (ischaemic stroke, cerebral haemorrhage, or transient ischaemic attack), coronary heart disease (myocardial infarction, angina, myocardial revascularisation with percutaneous coronary intervention, or coronary artery bypass graft), heart failure (with or without preserved ejection fraction), symptomatic lower extremities peripheral artery disease, glomerular filtration rate < 30 mL/min/1.73 m² or urine protein > 300 mg/day, or advanced retinopathy (haemorrhage, exudate, or papilloedema). For elderly people, defined by age ≥ 80 years, treatment is recommended in case of systolic BP ≥ 160 mm Hg. BP=blood pressure; ESC=European Society of Cardiology; ESH=European Society of Hypertension.

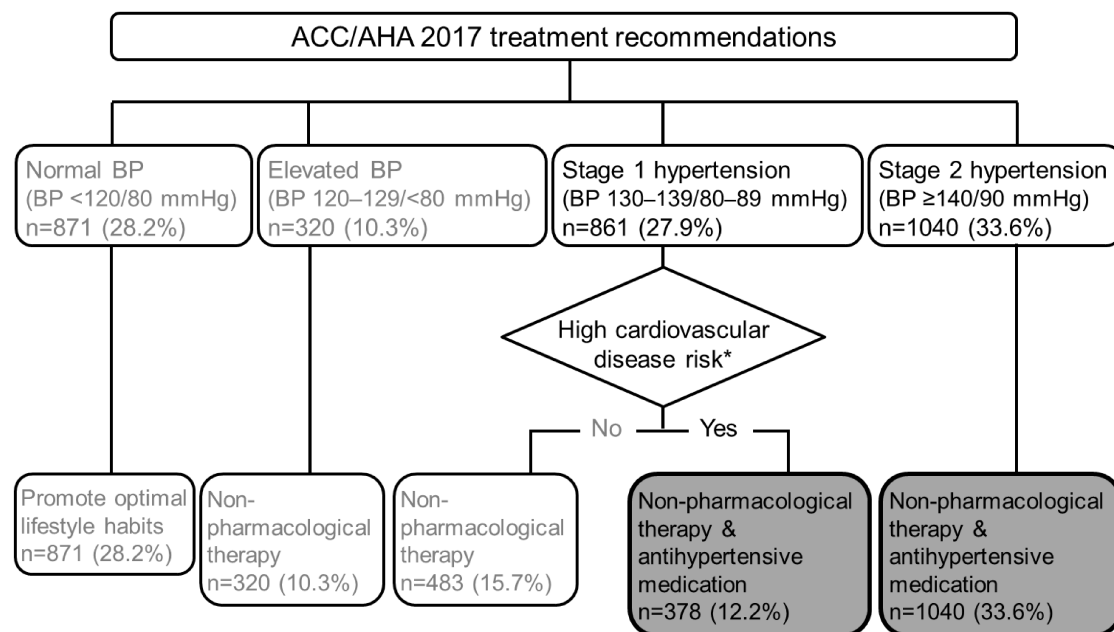


Figure S4: ACC/AHA 2017 treatment recommendations

*High cardiovascular disease risk defined by (a) estimated 10-year atherosclerotic cardiovascular disease (ASCVD, including coronary heart disease and stroke) risk $\geq 10\%$ using the ACC/AHA pooled cohort equations;⁴ (b) history of cardiovascular disease (coronary heart disease, heart failure, or stroke); or (c) peripheral artery disease; or (d) diabetes mellitus; or (e) chronic kidney disease (glomerular filtration rate < 60 mL/min/1.73 m² or urine albumin ≥ 300 mg/g creatinine). For non-institutionalised, ambulatory, community-living adults ≥ 65 years, treatment is recommended in the case of systolic BP ≥ 130 mm Hg. BP = blood pressure; ACC = American College of Cardiology; AHA = American Heart Association.

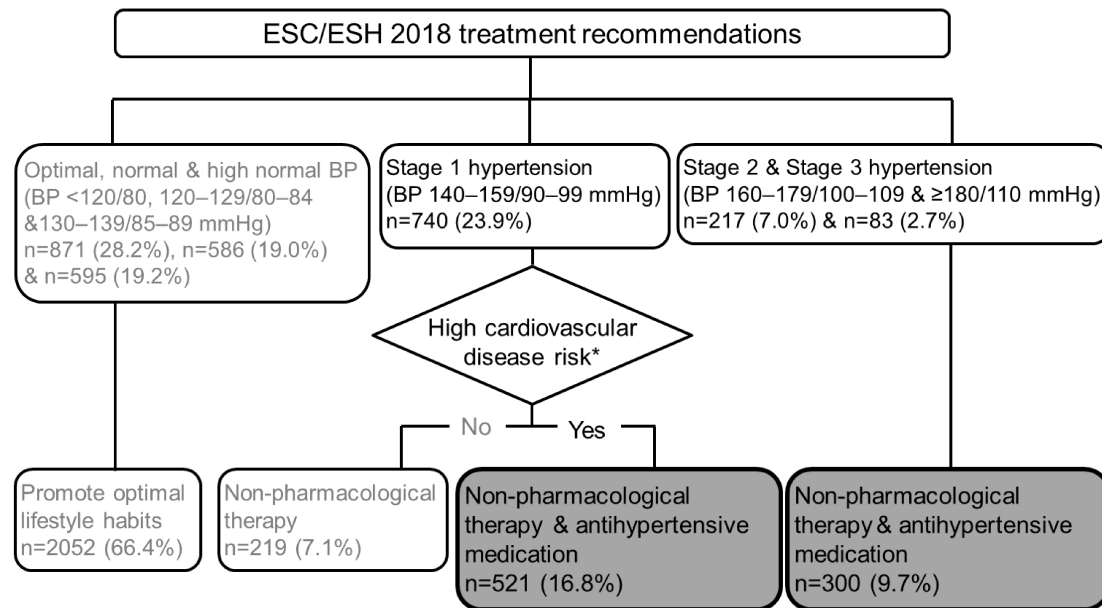


Figure S5: ESC/ESH 2018 treatment recommendations.

*High cardiovascular disease risk defined by (a) 10-year risk of fatal cardiovascular disease $\geq 5\%$ using the European SCORE equation; (b) clinical cardiovascular disease (acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularisation, stroke, transitory ischaemic attack, aortic aneurysm, or peripheral artery disease); (c) unequivocal documented cardiovascular disease on imaging (including significant plaque, i.e. $>50\%$ stenosis on angiography or ultrasound not including increase in carotid intima-media thickness) or chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m²); (d) marked cholesterol elevation (>310 mg/dL or familial hypercholesterolaemia); (e) diabetes mellitus; (f) hypertensive left ventricular hypertrophy; (g) hypertension-mediated organ damage (HMOD, previously termed target-organ damage, defined by pulse pressure [in the elderly] ≥ 60 mmHg, carotid–femoral pulse wave velocity >10 m/s, urine albumin 30–300 mg/day or 30–300 mg/g creatinine, ankle–brachial index <0.9 or advanced retinopathy [haemorrhages, exudates, or papilloedema]), or (h) fit elderly people ≥ 65 to <80 years. For fit elderly people ≥ 80 years, treatment is recommended in the case of systolic BP ≥ 160 mm Hg. BP=blood pressure; ESC=European Society of Cardiology; ESH=European Society of Hypertension; SCORE= Systematic COronary Risk Evaluation.

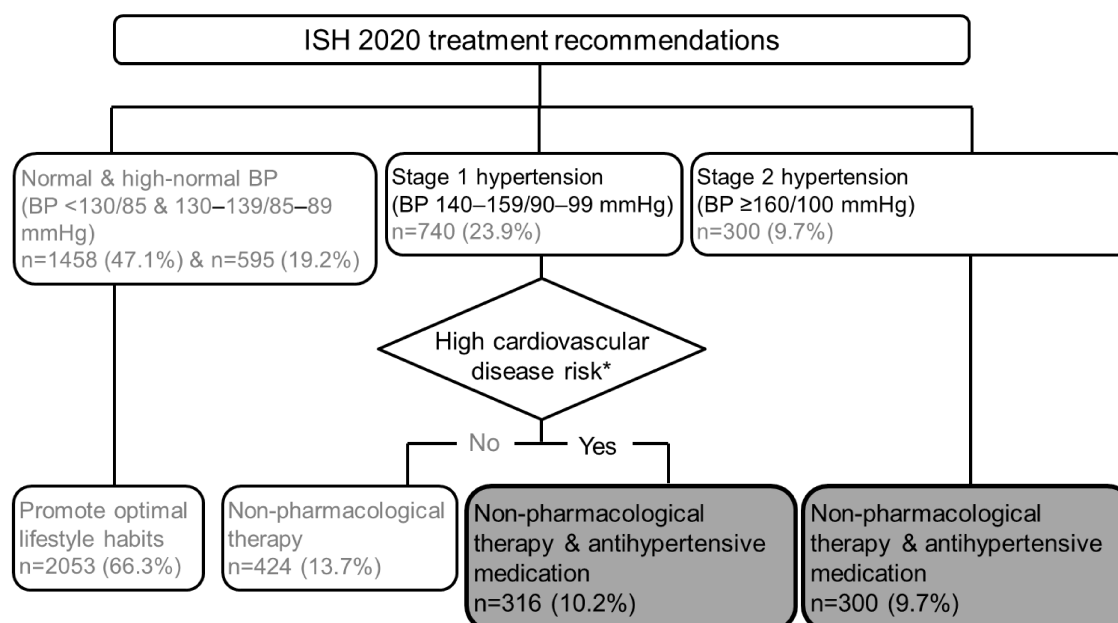


Figure S6: ISH 2020 treatment recommendations.

*High cardiovascular disease risk defined by (a) three or more of the following cardiovascular disease risk factors: age >65 years, male sex, heart rate (>80 beats/min), overweight, high LDL-C/triglyceride, family history of cardiovascular disease, family history of hypertension, early-onset menopause, smoking, psychosocial or socioeconomic factors; (b) hypertension-mediated organ damage (HMOD) or cardiovascular disease (CVD): left ventricular hypertrophy on electrocardiogram or echocardiogram, atrial fibrillation, diabetes, chronic kidney disease, history of coronary heart disease, stroke, peripheral artery disease or heart failure. BP=blood pressure; ISH=International Society of Hypertension.

Table S1: Baseline characteristics of the total Heinz Nixdorf Recall study cohort

| | Total (n=4814) | Missing n (%) |
|--------------------------------------------------------------------|--------------------|------------------|
| Age, years | 59.6±7.8 | 0 (0.00) |
| >55/>60 years for males/females, n (%) | 2218 (46.1) | 0 (0.00) |
| >65 years, n (%) | 1423 (29.6) | 0 (0.00) |
| Male sex, n (%) | 2395 (49.8) | 0 (0.00) |
| Systolic blood pressure, mmHg | 133.1±20.9 | 15 (0.31) |
| Diastolic blood pressure, mmHg | 81.4±10.9 | 14 (0.29) |
| Total cholesterol, mg/dL | 229.1±39.2 | 22 (0.46) |
| Total cholesterol >310 mg/dL, n (%) | 123 (2.6) | 22 (0.46) |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/day, n (%) | 1990 (41.6) | 31 (0.64) |
| LDL cholesterol, mg/dL | 145.5±36.2 | 37 (0.77) |
| HDL cholesterol, mg/dL | 58.0±17.2 | 24 (0.50) |
| HDL <40/45 mg/dL for males/females, n (%) | 732 (15.3) | 24 (0.50) |
| Triglycerides, mg/dL, median (IQR) | 124.0 (90.0–179.0) | 25 (0.52) |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 4442 (92.9) | 30 (0.62) |
| Glucose, mg/dL | 111.6±28.3 | 26 (0.54) |
| Diabetes mellitus, n (%) | 655 (13.6) | 0 (0.00) |
| Serum creatinine, mg/dL | 0.91±0.24 | 26 (0.54) |
| GFR, mL/min/1.73 m ² | 79.7±18.5 | 26 (0.54) |
| CKD, n (%) | 421 (8.8) | 26 (0.54) |
| Smoking, n (%) | 1128 (23.5) | 10 (0.21) |
| BMI, kg/m ² | 27.9±4.6 | 29 (0.60) |
| Overweight, n (%) | 1323 (27.6) | 29 (0.60) |
| Physical inactivity, n (%) | 2360 (49.0) | 0 (0.00) |
| Overweight or physical inactivity, n (%) | 2947 (61.3) | 7 (0.15) |
| CIMT, mm | 0.68±0.13 | 1035 (21.5) |
| CIMT >0.9 mm, n (%) | 217 (5.7) | 1035 (21.5) |
| ABI | 1.12±0.16 | 76 (1.58) |
| ABI <0.9, n (%) | 258 (5.4) | 76 (1.58) |
| Left ventricular hypertrophy on ECG, n (%) | 129 (2.7) | 108 (2.24) |
| Atrial fibrillation on ECG, n (%) | 80 (1.7) | 0 (0.00) |
| Stroke history, n (%) | 135 (2.8) | 19 (0.39) |
| CHD history, n (%) | 327 (6.8) | 15 (0.31) |
| Heart failure history, n (%) | 169 (3.5) | 23 (0.48) |
| Peripheral artery disease history, n (%) | 108 (2.3) | 82 (1.70) |
| MI history in first-degree relatives, n (%) | 1235 (27.8) | 371 (7.71) |
| Early-onset menopause, n (%) | 453 (9.5) | 35 (0.73) |
| Antihypertensive medications, n (%) | 1699 (35.4) | 16 (0.33) |
| Antidiabetic medications, n (%) | 265 (5.9) | 310 (6.44) |
| ASCVD score, %, median (IQR) | 8.9 (3.9–17.1) | 56 (1.16) |
| SCORE, %, median (IQR) | 4.0 (2.0–8.0) | 40 (0.83) |
| Cardiovascular event, n (%) | 123 (2.6) | 152 (3.2) |

Unless stated otherwise, values are presented as mean±standard deviation. ABI=ankle-brachial index; ASCVD=atherosclerotic cardiovascular disease; BMI=body mass index; CHD=coronary heart disease; CIMT=common-carotid artery intima-media thickness; CKD=chronic kidney disease; ECG=electrocardiography; GFR=glomerular filtration rate; HDL=high-density lipoprotein cholesterol; IQR=interquartile range; LDL=low-density lipoprotein cholesterol; MI=myocardial infarction; SCORE=Systematic COronary Risk Evaluation score.

Table S2: Treatment goals of antihypertensive medication therapy according to the different hypertension management guidelines

| |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>2003 Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7):</p> <p>SBP <140 mmHg and DBP <90 mmHg in all patients, SBP <140 mmHg and DBP <80 mmHg in patients with diabetes mellitus or chronic kidney disease</p> |
| <p>2003 World Health Organization (WHO) and International Society of Hypertension (ISH):</p> <p>SBP <140 mmHg and DBP <90 mmHg in all patients</p> |
| <p>2013 European Society of Hypertension (ESH) and European Society of Cardiology (ESC):</p> <p>SBP <140 mmHg and DBP <90 mmHg in all patients, SBP <140 mmHg and DBP <85 mmHg in patients with diabetes mellitus</p> |
| <p>2017 American College of Cardiology (ACC) and American Heart Association (AHA):</p> <p>SBP <130 mmHg and DBP <80 mmHg in all patients, SBP <130 mmHg in non-institutionalized, ambulatory, community-living adults ≥65 years</p> |
| <p>2018 European Society of Cardiology (ESC) and European Society of Hypertension (ESH):</p> <p>SBP <140 mmHg and DBP <90 mmHg in all patients, SBP <130 mmHg and DBP <80 mmHg or lower in most patients provided that the treatment is well tolerated</p> |
| <p>2020 International Society of Hypertension (ISH):</p> <p>Essential: SBP <140 mmHg and DBP <90 mmHg in all patients</p> <p>Optimal: SBP <130 mmHg and DBP <80 mmHg (but SBP > 120 mmHg and DBP > 70 mmHg, especially in heart failure patients) in patients <65 years if tolerated, SBP <140 mmHg and DBP <90 mmHg in patients ≥65 years if tolerated</p> |

DBP=diastolic blood pressure; SBP=systolic blood pressure.

Table S3: Missing information regarding antihypertensive medication recommendation and blood pressure above treatment goal according to the different hypertension management guidelines in the Heinz Nixdorf Recall study cohort

| | JNC7 2003 | WHO/ISH 2003 | ESH/ESC 2013 | ACC/AHA 2017 | ESC/ESH 2018 | ISH 2020 |
|--------------------------------------------------------------------------------------------------|-----------|---------------------------------------------|---------------------------------------------|--------------|--------------|----------|
| Missing antihypertensive medication recommendation among participants hitherto untreated*, n (%) | 15 (0.5) | 133 (4.3) [33 (1.1) if CIMT is excluded] | 149 (4.8) [38 (1.2) if CIMT is excluded] | 0 (0.0) | 14 (0.5) | 16 (0.5) |
| Blood pressure above treatment goal among participants already treated†, n (%) | 8 (0.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

ACC=American College of Cardiology; AHA=American Heart Association; ESC=European Society of Cardiology; ESH=European Society of Hypertension; JNC7=Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 7; ISH=International Society of Hypertension; WHO=World Health Organization.

*n=3092.

†n=1691.

Table S4: Baseline characteristics of the Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the JNC7 guideline

| | No (n=1931) | Yes (n=1146) | p |
|-------------------------------------------------------------------|--------------------|--------------------|------------------|
| Age, years | 56.8±7.3 | 60.2±7.5 | <0.001 |
| >55/>65 years for males/females, n (%) | 563 (29.1) | 617 (53.8) | <0.001 |
| >65 years, n (%) | 319 (16.5) | 348 (30.4) | <0.001 |
| Male sex, n (%) | 810 (41.9) | 690 (60.2) | <0.001 |
| Systolic blood pressure, mmHg | 119.1±12.3 | 150.0±16.0 | <0.001 |
| Diastolic blood pressure, mmHg | 75.7±7.4 | 90.1±9.4 | <0.001 |
| Total cholesterol, mg/dL | 228.1±38.6 | 235.8±38.9 | <0.001 |
| Total cholesterol >240 mg/dL, n (%) | 42 (2.2) | 39 (3.4) | 0.039 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 764 (39.6) | 552 (48.3) | <0.001 |
| LDL cholesterol, mg/dL | 144.5±36.3 | 150.3±36.7 | <0.001 |
| HDL cholesterol, mg/dL | 61.1±17.3 | 57.7±17.3 | <0.007 |
| HDL <40/45 mg/dL for males/females, n (%) | 202 (10.5) | 178 (15.6) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 106.0 (79.0–152.0) | 135.0 (96.0–194.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 1758 (91.2) | 1085 (94.9) | <0.001 |
| Glucose, mg/dL | 103.7±16.5 | 114.8±29.5 | <0.001 |
| Diabetes mellitus, n (%) | 59 (3.1) | 206 (18.0) | <0.001 |
| Serum creatinine, mg/dL | 0.90±0.24 | 0.93±0.19 | <0.001 |
| GFR, mL/min/1.73 m ² | 80.9±17.9 | 81.9±19.3 | 0.157 |
| CKD, n (%) | 87 (4.5) | 103 (9.0) | <0.001 |
| Smoking, n (%) | 547 (28.3) | 265 (23.1) | 0.002 |
| BMI, kg/m ² | 26.4±3.9 | 28.3±4.3 | <0.001 |
| Overweight, n (%) | 309 (16.1) | 336 (29.5) | <0.001 |
| Physical inactivity, n (%) | 830 (43.0) | 588 (51.3) | <0.001 |
| Overweight or physical inactivity, n (%) | 993 (51.5) | 731 (63.8) | <0.001 |
| CIMT, mm | 0.64±0.12 | 0.70±0.14 | <0.001 |
| CIMT >0.9 mm, n (%) | 44 (2.8) | 66 (7.6) | <0.001 |
| ABI | 1.15±0.13 | 1.13±0.15 | <0.001 |
| ABI <0.9, n (%) | 36 (1.9) | 60 (5.4) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 16 (0.8) | 42 (3.8) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 12 (0.9) | 9 (0.8) | 0.653 |
| Stroke history, n (%) | 20 (1.0) | 23 (2.0) | 0.026 |
| CHD history, n (%) | 23 (1.2) | 26 (2.3) | 0.021 |
| Heart failure history, n (%) | 23 (1.2) | 13 (1.1) | 0.888 |
| Peripheral artery disease history, n (%) | 14 (0.7) | 27 (2.4) | <0.001 |
| MI history in first-degree relatives, n (%) | 498 (28.5) | 271 (25.6) | 0.102 |
| Early-onset menopause, n (%) | 197 (10.3) | 89 (7.8) | 0.025 |
| Antidiabetic medications, n (%) | 22 (1.2) | 67 (6.4) | <0.001 |
| ASCVD score, %, median (IQR) | 4.5 (2.1–9.1) | 12.1 (6.2–20.7) | <0.001 |
| SCORE, %, median (IQR) | 2.0 (1.0–4.0) | 6.0 (3.0–12.0) | <0.001 |
| Cardiovascular event, n (%) | 26 (1.4) | 26 (2.3) | 0.060 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. JNC=Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; for other abbreviations see Table S1.

Table S5: Baseline characteristics of Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the WHO/ISH 2003 guideline

| | No (n=2358) | Yes (n=601) | p |
|--------------------------------------------------------------------------------|--------------------|---------------------|------------------|
| Age, years | 57.2±7.3 | 61.2±7.5 | <0.001 |
| >55/>65 years for males/females, n (%) | 745 (31.6) | 393 (65.4) | <0.001 |
| >65 years, n (%) | 422 (17.9) | 214 (35.6) | <0.001 |
| Male sex, n (%) | 1040 (44.1) | 412 (68.6) | <0.001 |
| Systolic blood pressure, mmHg | 123.3±15.4 | 154.8±17.2 | <0.001 |
| Diastolic blood pressure, mmHg | 77.9±8.8 | 91.7±10.4 | <0.001 |
| Total cholesterol, mg/dL | 228.3±38.5 | 241.1±39.6 | <0.001 |
| Total cholesterol >310 mg/dL, n (%) | 53 (2.3) | 25 (4.2) | 0.009 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 913 (39.0) | 356 (59.3) | <0.001 |
| LDL cholesterol, mg/dL | 144.3±36.1 | 156.9±37.2 | <0.001 |
| HDL cholesterol, mg/dL | 61.0±17.2 | 54.6±17.4 | <0.001 |
| HDL <40/45 mg/dL for males/females, n (%) | 242 (10.3) | 135 (22.5) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 109.0 (81.0–156.0) | 142.5 (103.0–211.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 2146 (91.0) | 580 (96.7) | <0.001 |
| Glucose, mg/dL | 105.1±18.7 | 118.9±33.6 | <0.001 |
| Diabetes mellitus, n (%) | 132 (5.6) | 132 (22.0) | <0.001 |
| Serum creatinine, mg/dL | 0.91±0.23 | 0.94±0.20 | 0.003 |
| GFR, mL/min/1.73 m ² | 80.4±17.6 | 82.4±18.2 | 0.021 |
| CKD, n (%) | 142 (6.1) | 40 (6.7) | 0.576 |
| Smoking, n (%) | 608 (25.8) | 186 (30.9) | 0.011 |
| BMI, kg/m ² | 26.6±4.0 | 28.8±4.3 | <0.001 |
| Overweight, n (%) | 407 (17.3) | 215 (36.0) | <0.001 |
| Physical inactivity, n (%) | 1006 (42.7) | 374 (62.2) | <0.001 |
| Overweight or physical inactivity, n (%) | 1206 (51.2) | 467 (77.7) | <0.001 |
| CIMT, mm | 0.65±0.12 | 0.73±0.14 | <0.001 |
| CIMT >0.9 mm, n (%) | 47 (2.4) | 63 (13.7) | <0.001 |
| ABI | 1.15±0.13 | 1.11±0.17 | <0.001 |
| ABI <0.9, n (%) | 40 (1.7) | 57 (9.7) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 17 (0.7) | 41 (7.0) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 14 (0.6) | 7 (1.2) | 0.168 |
| Stroke history, n (%) | 22 (0.9) | 20 (3.3) | <0.001 |
| CHD history, n (%) | 26 (1.1) | 23 (3.8) | <0.001 |
| Heart failure history, n (%) | 25 (1.1) | 10 (1.7) | 0.213 |
| Peripheral artery disease history, n (%) | 17 (0.7) | 24 (4.1) | <0.001 |
| MI history in first-degree relatives, n (%) | 568 (26.6) | 185 (33.4) | 0.001 |
| Early-onset menopause, n (%) | 241 (10.3) | 36 (6.0) | 0.002 |
| Antidiabetic medications, n (%) | 45 (2.0) | 44 (8.1) | <0.001 |
| ASCVD score, %, median (IQR) | 5.0 (2.4–9.9) | 16.6 (9.9–24.5) | <0.001 |
| SCORE, %, median (IQR) | 2.0 (1.0–5.0) | 9.0 (5.0–15.0) | <0.001 |
| Cardiovascular event, n (%) | 37 (1.6) | 12 (2.1) | 0.474 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. WHO/ISH=World Health Organization and International Society of Hypertension; for other abbreviations see Table S1.

Table S6: Baseline characteristics of Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the ESH/ESC 2013 guideline

| | No (n=2420) | Yes (n=523) | p |
|-------------------------------------------------------------------|--------------------|--------------------|------------------|
| Age, years | 57.3±7.3 | 61.2±7.4 | <0.001 |
| >55/>65 years for males/females, n (%) | 795 (32.8) | 323 (61.8) | <0.001 |
| >65 years, n (%) | 439 (18.1) | 186 (35.6) | <0.001 |
| Male sex, n (%) | 1090 (45.0) | 352 (67.3) | <0.001 |
| Systolic blood pressure, mmHg | 123.5±14.9 | 159.1±17.4 | <0.001 |
| Diastolic blood pressure, mmHg | 77.9±8.5 | 93.9±10.7 | <0.001 |
| Total cholesterol, mg/dL | 229.2±38.7 | 236.9±39.4 | <0.001 |
| Total cholesterol >310 mg/dL, n (%) | 57 (2.4) | 18 (3.5) | 0.152 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 985 (40.9) | 257 (49.4) | <0.001 |
| LDL cholesterol, mg/dL | 145.2±36.5 | 152.5±37.0 | <0.001 |
| HDL cholesterol, mg/dL | 60.5±17.2 | 56.3±17.4 | <0.001 |
| HDL <40/45 mg/dL for males/females, n (%) | 277 (11.5) | 88 (16.9) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 111.0 (82.0–158.0) | 140.0 (99.0–206.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 2208 (91.8) | 499 (96.0) | 0.001 |
| Glucose, mg/dL | 105.2±18.6 | 120.2±35.6 | <0.001 |
| Diabetes mellitus, n (%) | 133 (5.5) | 132 (25.2) | <0.001 |
| Serum creatinine, mg/dL | 0.91±0.22 | 0.95±0.22 | <0.001 |
| GFR, mL/min/1.73 m ² | 80.7±17.4 | 81.9±20.3 | 0.190 |
| CKD, n (%) | 127 (5.3) | 63 (12.1) | <0.001 |
| Smoking, n (%) | 655 (27.1) | 124 (23.7) | 0.113 |
| BMI, kg/m ² | 26.7±4.1 | 28.7±4.4 | <0.001 |
| Overweight, n (%) | 439 (18.2) | 177 (34.0) | <0.001 |
| Physical inactivity, n (%) | 1077 (44.5) | 274 (52.4) | 0.001 |
| Overweight or physical inactivity, n (%) | 1296 (53.6) | 349 (66.7) | <0.001 |
| CIMT, mm | 0.65±0.12 | 0.73±0.15 | <0.001 |
| CIMT >0.9 mm, n (%) | 47 (2.3) | 63 (15.8) | <0.001 |
| ABI | 1.15±0.13 | 1.10±0.17 | <0.001 |
| ABI <0.9, n (%) | 40 (1.7) | 57 (11.1) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 17 (0.7) | 41 (8.1) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 13 (0.5) | 8 (1.5) | 0.022 |
| Stroke history, n (%) | 23 (1.0) | 20 (3.8) | <0.001 |
| CHD history, n (%) | 26 (1.1) | 23 (4.4) | <0.001 |
| Heart failure history, n (%) | 26 (1.1) | 10 (1.9) | 0.110 |
| Peripheral artery disease history, n (%) | 17 (0.7) | 24 (4.7) | <0.001 |
| MI history in first-degree relatives, n (%) | 622 (28.2) | 118 (24.4) | 0.089 |
| Early-onset menopause, n (%) | 244 (10.1) | 32 (4.4) | 0.006 |
| Antidiabetic medications, n (%) | 45 (2.0) | 44 (9.4) | <0.001 |
| ASCVD score, %, median (IQR) | 5.2 (2.4–10.4) | 16.7 (8.4–25.8) | <0.001 |
| SCORE, %, median (IQR) | 3.0 (1.0–5.0) | 9.0 (5.0–16.0) | <0.001 |
| Cardiovascular event, n (%) | 39 (1.6) | 12 (2.4) | 0.354 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. ESH/ESC=European Society of Hypertension and European Society of Cardiology; for other abbreviations see Table S1.

Table S7: Baseline characteristics of Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the ACC/AHA 2017 guideline

| | No (n=1674) | Yes (n=1418) | p |
|-------------------------------------------------------------------|----------------------|------------------------|------------------|
| Age, years | 56.0±6.9 | 60.5±7.4 | <0.001 |
| >55/>65 years for males/females, n (%) | 365 (21.8) | 821 (57.9) | <0.001 |
| >65 years, n (%) | 214 (12.8) | 458 (32.3) | <0.001 |
| Male sex, n (%) | 600 (35.8) | 905 (63.8) | <0.001 |
| Systolic blood pressure, mmHg | 117.1±11.8 | 146.5±16.3 | <0.001 |
| Diastolic blood pressure, mmHg | 74.8±7.3 | 88.5±9.4 | <0.001 |
| Total cholesterol, mg/dL | 226.7±37.7 | 235.9±39.7 | <0.001 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 30 (1.8) | 51 (3.6) | 0.002 |
| LDL cholesterol, mg/dL | 142.7±35.5 | 151.3±37.3 | <0.001 |
| HDL cholesterol, mg/dL | 62.5±17.3 | 56.6±16.9 | <0.001 |
| HDL <40/45 mg/dL for males/females, n (%) | 151 (9.1) | 230 (16.3) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 103.0 (77.0–143.0) | 135.0 (96.0–194.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 1502 (90.4) | 1343 (95.2) | <0.001 |
| Glucose, mg/dL | 103.6±17.1 | 112.9±27.4 | <0.001 |
| Diabetes mellitus, n (%) | 59 (3.5) | 206 (14.5) | <0.001 |
| Serum creatinine, mg/dL | 0.90±0.25 | 0.93±0.19 | <0.001 |
| GFR, mL/min/1.73 m ² | 80.5±17.9 | 82.3±18.9 | 0.008 |
| CKD, n (%) | 87 (5.2) | 103 (7.3) | 0.017 |
| Smoking, n (%) | 441 (26.4) | 371 (26.2) | 0.902 |
| BMI, kg/m ² | 26.2±4.0 | 28.1±4.2 | <0.001 |
| Overweight, n (%) | 255 (15.3) | 392 (27.8) | <0.001 |
| Physical inactivity, n (%) | 694 (41.1) | 731 (51.6) | <0.001 |
| Overweight or physical inactivity, n (%) | 836 (50.0) | 897 (63.3) | <0.001 |
| CIMT, mm | 0.63±0.11 | 0.70±0.13 | <0.001 |
| CIMT >0.9 mm, n (%) | 25 (1.9) | 85 (7.7) | <0.001 |
| ABI | 1.15±0.13 | 1.13±0.15 | <0.001 |
| ABI <0.9, n (%) | 25 (1.5) | 72 (5.2) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 12 (0.7) | 46 (3.3) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 9 (0.5) | 12 (0.8) | 0.380 |
| Stroke history, n (%) | 10 (0.6) | 33 (2.3) | <0.001 |
| CHD history, n (%) | 18 (1.1) | 31 (2.2) | 0.014 |
| Heart failure history, n (%) | 12 (0.7) | 24 (1.7) | 0.011 |
| Peripheral artery disease history, n (%) | 7 (0.4) | 34 (2.4) | <0.001 |
| MI history in first-degree relatives, n (%) | 450 (29.8) | 322 (24.5) | 0.002 |
| Early-onset menopause, n (%) | 191 (11.5) | 99 (7.0) | <0.001 |
| Antidiabetic medications, n (%) | 22 (1.4) | 67 (5.2) | <0.001 |
| ASCVD score, %, median (IQR) | 3.7 (1.8–6.8) | 12.5 (7.1–19.6) | <0.001 |
| SCORE, %, median (IQR) | 2.0 (1.0–3.0) | 7.0 (4.0–11.0) | <0.001 |
| Cardiovascular event, n (%) | 18 (1.1) | 34 (2.5) | 0.005 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. ACC/AHA=American College of Cardiology and American Heart Association; for other abbreviations see Table S1.

Table S8: Baseline characteristics of Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the ESC/ESH 2018 guideline

| | No (n=2257) | Yes (n=821) | p |
|-------------------------------------------------------------------|--------------------|--------------------|------------------|
| Age, years | 56.7±7.2 | 62.0±7.0 | <0.001 |
| >55/>65 years for males/females, n (%) | 621 (27.5) | 565 (68.8) | <0.001 |
| >65 years, n (%) | 349 (15.5) | 323 (39.3) | <0.001 |
| Male sex, n (%) | 941 (41.7) | 561 (68.3) | <0.001 |
| Systolic blood pressure, mmHg | 121.7±13.7 | 154.8±15.4 | <0.001 |
| Diastolic blood pressure, mmHg | 77.3±8.3 | 91.2±10.1 | <0.001 |
| Total cholesterol, mg/dL | 228.1±38.6 | 238.6±38.9 | <0.001 |
| Total cholesterol >310 mg/dL, n (%) | 49 (2.2) | 32 (3.9) | 0.008 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 895 (39.9) | 415 (50.9) | <0.001 |
| LDL cholesterol, mg/dL | 144.1±36.3 | 155.5±36.5 | <0.001 |
| HDL cholesterol, mg/dL | 60.9±17.4 | 56.8±17.0 | <0.001 |
| HDL <40/45 mg/dL for males/females, n (%) | 254 (11.3) | 127 (15.6) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 109.0 (81.0–156.0) | 139.0 (98.0–198.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 2045 (91.2) | 786 (96.3) | <0.001 |
| Glucose, mg/dL | 105.2±19.1 | 115.2±30.0 | <0.001 |
| Diabetes mellitus, n (%) | 133 (5.9) | 132 (16.1) | <0.001 |
| Serum creatinine, mg/dL | 0.91±0.23 | 0.95±0.19 | <0.001 |
| GFR, mL/min/1.73 m ² | 80.9±18.3 | 81.9±18.1 | 0.220 |
| CKD, n (%) | 127 (5.7) | 63 (7.7) | 0.036 |
| Smoking, n (%) | 618 (27.4) | 191 (23.3) | 0.021 |
| BMI, kg/m ² | 26.7±4.1 | 28.3±4.1 | <0.001 |
| Overweight, n (%) | 405 (18.0) | 238 (29.2) | <0.001 |
| Physical inactivity, n (%) | 995 (44.1) | 424 (51.6) | <0.001 |
| Overweight or physical inactivity, n (%) | 1203 (53.4) | 522 (63.6) | <0.001 |
| CIMT, mm | 0.64±0.12 | 0.72±0.14 | <0.001 |
| CIMT >0.9 mm, n (%) | 51 (2.8) | 59 (9.5) | <0.001 |
| ABI | 1.15±0.13 | 1.12±0.16 | <0.001 |
| ABI <0.9, n (%) | 40 (1.8) | 57 (7.1) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 17 (0.8) | 41 (5.1) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 12 (0.5) | 9 (1.1) | 0.133 |
| Stroke history, n (%) | 23 (1.0) | 20 (2.4) | 0.003 |
| CHD history, n (%) | 26 (1.2) | 23 (2.8) | 0.001 |
| Heart failure history, n (%) | 27 (1.2) | 9 (1.1) | 0.831 |
| Peripheral artery disease history, n (%) | 17 (0.8) | 24 (2.9) | <0.001 |
| MI history in first-degree relatives, n (%) | 582 (28.5) | 185 (24.1) | 0.021 |
| Early-onset menopause, n (%) | 242 (10.8) | 47 (5.6) | <0.001 |
| Antidiabetic medications, n (%) | 45 (2.1) | 44 (5.9) | <0.001 |
| ASCVD score, %, median (IQR) | 4.6 (2.2–9.1) | 15.1 (9.5–22.8) | <0.001 |
| SCORE, %, median (IQR) | 2.0 (1.0–4.0) | 9.0 (5.0–15.0) | <0.001 |
| Cardiovascular event, n (%) | 33 (1.5) | 19 (2.4) | 0.114 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. ESC/ESH=European Society of Cardiology and European Society of Hypertension, for other abbreviations see Table S1.

Table S9: Baseline characteristics of Heinz Nixdorf Recall study cohort stratified by antihypertensive medication recommendation according to the ISH 2020 guideline

| | No (n=2304) | Yes (n=772) | p |
|----------------------------------------------------------------------------|--------------------|--------------------|------------------|
| Age, years | 57.1±7.2 | 60.8±7.7 | <0.001 |
| >55/>65 years for males/females, n (%) | 711 (30.9) | 469 (60.8) | <0.001 |
| >65 years, n (%) | 384 (16.7) | 284 (36.8) | <0.001 |
| Male sex, n (%) | 969 (42.1) | 532 (68.9) | <0.001 |
| Systolic blood pressure, mmHg | 122.4±14.3 | 154.8±16.1 | <0.001 |
| Diastolic blood pressure, mmHg | 77.4±8.2 | 92.0±10.0 | <0.001 |
| Total cholesterol, mg/dL | 228.8±38.8 | 236.9±38.2 | <0.001 |
| Total cholesterol >240 mg/dL, n (%) | 56 (2.4) | 24 (3.1) | 0.360 |
| Total cholesterol >240 mg/dL or LDL cholesterol >160 mg/dL, n (%) | 917 (40.0) | 390 (50.8) | <0.001 |
| LDL cholesterol, mg/dL | 144.4±36.5 | 152.8±35.3 | <0.001 |
| HDL cholesterol, mg/dL | 61.1±17.3 | 55.9±17.1 | <0.001 |
| HDL <40/45 mg/dL for males/females, n (%) | 247 (10.8) | 134 (17.4) | <0.001 |
| Triglycerides, mg/dL, median (IQR) | 109.0 (81.0–156.0) | 139.5 (98.0–201.0) | <0.001 |
| LDL cholesterol >100 mg/dL or triglycerides >150 mg/dL, n (%) | 2088 (91.2) | 744 (96.7) | <0.001 |
| Glucose, mg/dL | 105.1±18.8 | 115.9±30.6 | <0.001 |
| Diabetes mellitus, n (%) | 132 (5.7) | 132 (17.1) | <0.001 |
| Serum creatinine, mg/dL | 0.91±0.23 | 0.95±0.20 | <0.001 |
| GFR, mL/min/1.73 m ² | 80.8±18.0 | 82.3±19.1 | 0.050 |
| CKD, n (%) | 127 (5.5) | 63 (8.2) | 0.010 |
| Smoking, n (%) | 598 (26.0) | 212 (27.5) | 0.422 |
| BMI, kg/m ² | 26.5±3.9 | 28.8±4.4 | <0.001 |
| Overweight, n (%) | 366 (16.0) | 277 (36.1) | <0.001 |
| Physical inactivity, n (%) | 1005 (43.6) | 413 (53.5) | <0.001 |
| Overweight or physical inactivity, n (%) | 1195 (52.0) | 528 (68.4) | <0.001 |
| CIMT, mm | 0.65±0.12 | 0.71±0.14 | <0.001 |
| CIMT >0.9 mm, n (%) | 56 (3.1) | 53 (8.9) | <0.001 |
| ABI | 1.15±0.13 | 1.12±0.16 | <0.001 |
| ABI <0.9, n (%) | 45 (2.0) | 52 (6.9) | <0.001 |
| Left ventricular hypertrophy on ECG, n (%) | 17 (0.8) | 41 (5.5) | <0.001 |
| Atrial fibrillation on ECG, n (%) | 12 (0.5) | 9 (1.2) | 0.075 |
| Stroke history, n (%) | 22 (1.0) | 20 (2.6) | 0.001 |
| CHD history, n (%) | 26 (1.1) | 23 (3.0) | <0.001 |
| Heart failure history, n (%) | 25 (1.1) | 10 (1.3) | 0.694 |
| Peripheral artery disease history, n (%) | 17 (0.7) | 24 (3.1) | <0.001 |
| MI history in first-degree relatives, n (%) | 548 (26.2) | 221 (30.7) | 0.020 |
| Early-onset menopause, n (%) | 230 (10.0) | 59 (7.7) | 0.054 |
| Antidiabetic medications, n (%) | 45 (2.1) | 44 (6.3) | <0.001 |
| ASCVD score, %, median (IQR) | 4.8 (2.3–9.7) | 15.1 (8.3–23.1) | <0.001 |
| SCORE, %, median (IQR) | 2.0 (1.0–5.0) | 8.0 (5.0–15.0) | <0.001 |
| Cardiovascular event, n (%) | 34 (1.5) | 18 (2.3) | 0.145 |

Unless stated otherwise, values are presented as mean±standard deviation. Variables shown in bold are included in the recommendation. ISH=International Society of Hypertension, for other abbreviations see Table S1.