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The International Database of Central Arterial Properties for Risk Stratification: Research Objectives and Baseline Characteristics of Participants

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Abstract:	Objective: To address to what extent central hemodynamic measurements improve risk stratification, and determine outcome-based diagnostic thresholds, we constructed the International Database of Central Arterial Properties for Risk Stratification (IDCARS), allowing a participant-level meta-analysis. The purpose of this article was to describe the characteristics of IDCARS participants and to highlight research perspectives. Methods: Longitudinal or cross-sectional cohort studies with central blood pressure measured with the SphygmoCor devices and software were included. Results: The database included 10930 subjects (54.8% women; median age 46.0 years) from thirteen studies in Europe, Africa, Asia and South America. The prevalence of office hypertension was 4446 (40.1%), of which 2713 (61.0%) were treated, and of diabetes mellitus was 629 (5.8%). The peripheral and central systolic/diastolic blood pressure averaged 129.5/78.7 mm Hg and 118.2/79.7 mm Hg, respectively. Mean aortic pulse wave velocity was 7.3 meter per seconds. Among 6871 participants enrolled in 9 longitudinal studies, the median follow-up was 4.2 years (5th–95th percentile interval, 1.3–12.2 years). During 38957 person-years of follow-up, 339 participants experienced a composite cardiovascular event and 212 died, 67 of cardiovascular disease. Conclusions: IDCARS will provide a unique opportunity to investigate hypotheses on central hemodynamic measurements that could not reliably be studied in individual studies. The results of these analyses might inform guidelines and be of help to clinicians involved in the management of patients with suspected or established hypertension.
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The International Database of Central Arterial Properties for Risk Stratification: Research Objectives and Baseline Characteristics of Participants

Running title: IDCARS database and study design

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ABSTRACT

Objective: To address to what extent central hemodynamic measurements improve risk stratification, and determine outcome-based diagnostic thresholds, we constructed the International Database of Central Arterial Properties for Risk Stratification (IDCARS), allowing a participant-level meta-analysis. The purpose of this article was to describe the characteristics of IDCARS participants and to highlight research perspectives.

Methods: Longitudinal or cross-sectional cohort studies with central blood pressure measured with the SphygmoCor devices and software were included.

Results: The database included 10930 subjects (54.8% women; median age 46.0 years) from thirteen studies in Europe, Africa, Asia and South America. The prevalence of office hypertension was 4446 (40.1%), of which 2713 (61.0%) were treated, and of diabetes mellitus was 629 (5.8%). The peripheral and central systolic/diastolic blood pressure averaged 129.5/78.7 mm Hg and 118.2/79.7 mm Hg, respectively. Mean aortic pulse wave velocity was 7.3 meter per seconds. Among 6871 participants enrolled in 9 longitudinal studies, the median follow-up was 4.2 years (5th–95th percentile interval, 1.3–12.2 years). During 38957 person-years of follow-up, 339 participants experienced a composite cardiovascular event and 212 died, 67 of cardiovascular disease.

Conclusions: IDCARS will provide a unique opportunity to investigate hypotheses on central hemodynamic measurements that could not reliably be studied in individual studies. The results of these analyses might inform guidelines and be of help to clinicians involved in the management of patients with suspected or established hypertension.

KEYWORDS

Cardiovascular outcome; central blood pressure; hemodynamics; pulse wave analysis; pulse wave velocity

Introduction

Blood pressure is the major modifiable cardiovascular risk factor.[1] The Global Burden of Diseases Study reported that hypertension is the leading risk factor for ill health, causing 10.8 million deaths worldwide each year, which is more than half of the total cardiovascular mortality.[2] Based on the seminal work by Michel Safar[3] and Michael O'Rourke,[4] the perception that cardiovascular events are closer related to central than to brachial blood pressure has become a mainstream idea. The anatomical proximity of the aorta to the heart, brain and kidney, systolic augmentation from the central to the peripheral arteries, and the degradation of the arterial elastic properties with advancing age also contributed to the growing interest in the pathophysiological role of central blood pressure.

While theoretically sound,[5-7] the evidence supporting the association of cardiovascular events with central blood pressure, over and beyond brachial blood pressure, remains controversial. Roughly half of the published studies had a cross-sectional design with preclinical outcomes.[8-15] The longitudinal studies related a wide array of outcomes with central blood pressure, but applied different technologies to quantify the risk marker and not always accounted for peripheral blood pressure.[10,11,16-25] Other factors limiting the interpretation of the available literature are a sample size of less than 200 study participants,[8,9,17,18,26-29] a follow-up of 12 months or less,[16-18] selective enrollment of patients with hypertension,[8,13,21,22,26,27,30,31] chronic kidney disease[9,12,18] or coronary heart disease.[16,17,20] To address this knowledge gap, we constructed the International Database of Central Arterial Properties for Risk Stratification (IDCARS), allowing a participant-level meta-analysis. The purpose of this article was to describe the baseline characteristics of IDCARS participants and to highlight research perspectives that will be pursued in the future, using the IDCARS resource.

Methods

Identification of studies

Longitudinal cohort studies qualified for inclusion if information on brachial and central blood pressure and cardiovascular risk factors was available at baseline, if the central blood pressure had been tonometrically measured, using SphygmoCor devices and software (AtCor Medical Pty. Ltd., West Ryde, New South Wales, Australia and AtCor Medical Inc., Itasca, IL), if follow-up included both fatal and nonfatal endpoints, if study reports had been published in peer-reviewed articles, and if the study participants had been sampled from a population or in case of a convenience sample they were representative for the community from which they were enrolled. Cross-sectional studies of populations and hypertensive patients without information on fatal and nonfatal outcomes also qualified, provided that all other eligibility criteria were met. We identified studies qualifying for inclusion in the IDCARS resource by approaching investigators networked in the International Databases on Ambulatory (IDACO)[32] and Home (IDHOCO)[33] Blood Pressure in Relation to Cardiovascular Outcome.

All studies complied with the Helsinki Declaration on research in humans[34] and were approved by the competent Institutional Review Boards. Participants provided informed written consent. Before transfer to the coordinating office in Leuven, Belgium, the data were stripped from all personal identifiers, and if required by national legislations, additional ethical clearances were obtained. The online-only Data Supplement provides further study-specific information on the catchment areas, sampling strategies, recruitment, participation rate, the number of participants enrolled and related literature sources (**Table S1** and **Table S2** available in the online-only Data Supplement).

Brachial blood pressure

Office blood pressure was measured in the sitting position by auscultation of the Korotkoff sounds or oscillometrically according to contemporary national or European guidelines, which did not substantially change over time.[35] Up to five consecutive readings were recorded (**Table S3**), but for analysis only the first two were averaged. In some instances, only a single office reading was available. Office hypertension was a blood pressure of at least 140 mm Hg systolic or 90 mm Hg diastolic or use of antihypertensive drugs irrespective of the blood pressure level. Estimates of central blood pressure were calibrated, using one or the average of three additional blood pressure readings, which were obtained after the participants had rested in the supine position for at least 5 minutes, but in most instances for a longer period up to 15 minutes. If two blood pressure readings were obtained, the second was employed for calibration (**Table S3**).

Pulse wave analysis

In most cohorts, experienced observers recorded the radial arterial waveform at the dominant arm during an 8-second period by applanation tonometry. They used a high fidelity SPC-301 micromanometer (Millar Instruments Inc., Houston, TX) interfaced with a SphygmoCor CvMS device and a laptop computer running SphygmoCor software. If multiple recordings were available from an individual, the record with the highest quality was selected for inclusion in the IDCARS database.

From the radial signal, the SphygmoCor software calculates the aortic pulse wave by means of a validated generalized transfer function.[36,37] The software returns the central systolic, diastolic and pulse pressure, and the pressure at the first and second peak (shoulder) of the central waveform (**Figure S1**). The augmentation ratio and index are quotients of the second over the first peak of the central blood pressure wave and of the

absolute difference between the second and first peak over central pulse pressure, both expressed as a percentage. For future analyses, a pressure-based triangular-flow wave separation algorithm will be applied,[38] as implemented in the SphygmoCor software, version 10, which allows computing the forward and backward pulse pressure amplitudes (**Figure S1**) and the timing of their peak height, relative to the electrocardiographic QRS complex. Similarly, reimporting the SphygmoCor data files into software version 10 will also enable recalibrating the pulse wave analysis based on mean arterial pressure defined as diastolic blood pressure plus either 33% or 40% of pulse pressure, the difference between systolic and diastolic blood pressure.[39] The reflection index is the ratio of the backward to the forward pulse pressure amplitude, expressed as percentage.

In the cohort enrolled at Potchefstroom, South Africa, central blood pressure was recorded by the SphygmoCor XCEL, according to the procedures recommended by the manufacturer (www.youtube.com/watch?v=cjps2t1f6X8). This automated device has been validated against invasive recordings of central blood pressure[40,41] and manual tonometric measurements.[42]

Pulse wave velocity

In most cohorts, aortic pulse wave velocity was measured by sequential electrocardiographically gated recordings of the arterial pressure waveform at the carotid and femoral arteries. The observers measured the distance from the suprasternal notch to the carotid sampling site (distance A), and from the suprasternal notch to the femoral sampling site (distance B). Pulse wave travel distance was calculated as distance B minus distance A.[43] Pulse transit time was the average of 10 consecutive beats.[44] Carotid-femoral pulse wave velocity is the ratio of the travel distance in meters to transit time in seconds. Pulse wave velocity was discarded if the standard error of the mean of 10 beats

was more than 10%. Participants enrolled at Potchefstroom, South Africa, had their pulse wave velocity measured using the SphygmoCor XCEL, according to the instructions of the manufacturer (www.youtube.com/watch?v=7SPFDToCR0U). This device has been validated for assessment of pulse wave velocity.[42,45] Carotid pulse waves were registered with a tonometer, as with the SphygmoCor device, whereas the femoral pulse wave was recorded, using a partially inflated oscillometric cuff positioned around the thigh.[46,47] Thus, in contrast to the SphygmoCor CvMS, the SphygmoCor XCEL allows simultaneous registration of the carotid and femoral pulse waves.

Other baseline measurements

Data collection at baseline included information on each individual's medical history, smoking and drinking habits, and intake of medications. Body mass index was body weight in kilograms divided by height in meters squared. Serum levels of total and high-density lipoprotein (HDL) cholesterol and creatinine and blood glucose were determined at the study sites by automated techniques in certified laboratories. Diabetes mellitus was a self-reported diagnosis, a fasting or non-fasting blood glucose level of at least 126 mg per deciliter (7.0 mmol per liter) or 200 mg per deciliter (11.1 mmol per liter) or higher, or use of antidiabetic drugs.[48]

Primary and secondary outcomes

The primary endpoint in future analyses will be a composite cardiovascular endpoint, including cardiovascular mortality, nonfatal myocardial infarction, heart failure and stroke, and surgical or percutaneous coronary revascularization or pacemaker implantation. Secondary endpoints include (i) all-cause, cardiovascular and noncardiovascular mortality, (ii) coronary events (mortality from ischemic heart disease and sudden death, nonfatal myocardial infarction, acute coronary syndrome and coronary revascularization, including or

not including stable angina pectoris); (iii) cardiac events (coronary events, fatal and nonfatal heart failure, pacemaker implantation and other cardiac deaths), (iv) and cerebrovascular events (fatal and nonfatal stroke, including or not including transient ischemic attack).

In terms of coding according to the international classification of diseases (ICD), stroke is defined as ICD-8 or ICD-9 codes 430–434 or 436, or ICD-10 codes I60–I64. Myocardial infarction is coded ICD-8 or ICD-9 code 410 or ICD-10 codes I21–I22, and heart failure as ICD8 codes 4270, 4271, 4280, 4290, 5191 or 7824, or ICD-9 codes 429 or 5184, or ICD-10 codes I50 or J81. Sudden death is ICD-8 code 4272 or 795, or ICD-9 code 4275 or 798, or ICD-10 codes I46 or R96. Peripheral arterial disease corresponds with ICD-8 or ICD-9 codes 441–444, or ICD-10 codes I71–I74, and includes surgical or peripheral revascularization procedures. In case ICD codes were unavailable in the transferred data, the definition of events as provided by the investigators were accepted with reference to the publications on each cohort in the peer-reviewed literature.

Statistical analysis

For database management and statistical analysis, SAS software, version 9.4 (SAS Institute, Cary, NC) was used. For longitudinal studies, median follow-up time was estimated by the reverse Kaplan-Meier method. We standardized the time-dependent hemodynamic measurements, including the augmentation index and pressure amplification to a heart rate of 75 beats per minute. Means and proportions were compared between groups by the large sample z-test or ANOVA and by the χ^2 statistic, respectively. Statistical methods also included single and multiple regression analysis.

After stratification for cohort and sex, we interpolated missing values of body mass index and serum cholesterol levels from the regression slopes on age. In participants with unknown status of smoking, drinking, antihypertensive treatment, diabetes mellitus, or

unknown history of cardiovascular disease, we set the indicator (dummy) variable to the cohort- and sex-specific mean of the codes (0, 1). Information on alcohol intake was not available for the cohort recruited in Buenos Aires, Argentina. Following methods applied in previous publications,[49] we extrapolated alcohol consumption in adult Argentinians from data stratified by sex and age.[50-52]

Results

Characteristics of studies

Thirteen studies were included in the IDCARS database, of which eleven were population studies. Among the population studies (Table S1), six were conducted in Europe, three in Africa, one in Asia, and one in South America. The sampling of participants was random, using a family-based (n = 7) or age-stratified (n = 1) sampling frame or, in the case of Finland and South Africa, a two-stage cluster sampling method with the goal to enroll individuals representative of the Finnish population (n = 1) or a random sample of Black residents of Johannesburg (n=1) or a convenience sample of healthy volunteers, aged 20-30 years, who were stratified by ethnicity and recruited in Potchefstroom (n = 1). Of the population studies (**Table S1**), eight applied epidemiological and phenotyping methods similar to those used in the Flemish Study on Environment and Genes in Relation to Health Outcomes. The IDCARS database included two studies of hypertensive patients, respectively recruited in Buenos Aires, Argentina, and in Gdańsk, Poland. **Table S2** and the reference list available in the online-only Data Supplement provide the literature sources describing the design characteristics of the 13 studies in detail.

Assessment of the central hemodynamics

Published articles describing the procedures for measuring the central hemodynamics are available for each study in **Table S2**. In 12 studies (**Table S3**), the central hemodynamics were recorded by SphygmoCor CvMS devices and software versions ranging from 6.2 to 9.0. In Potchefstroom, South Africa, investigators used the SphygmoCor XCEL and software version 1.3 to acquire the hemodynamic data. To calibrate the pulse wave analysis with the signal recorded by the SphygmoCor CvMS approach, investigators measured brachial blood pressure by either Omron 705CP, Omron M6 or Omron 714/7220 devices, or by a standard mercury sphygmomanometer after participants had rested in the supine position for intervals ranging from 5 to 15 minutes (**Table S3**). The number of readings obtained ranged from 1 to 3, but only the average or the last of two readings was used for calibration of the central pulse wave in IDCARS. At the acquisition stage, the pulse wave analysis was calibrated on brachial systolic and diastolic blood pressure, but recalibration will be effected, if appropriate, using software version 10.0.

Clinical and biochemical characteristics of participants

At the time of writing of this article, the IDCARS database included 10930 individuals. Missing values at baseline, i.e., the date at which the hemodynamic measurements were obtained, were interpolated for body mass index (n = 32), total (n = 483) and high-density lipoprotein (n = 828) serum cholesterol, serum creatinine (n = 704), blood glucose (n = 322), smoking (n = 344) and drinking (n = 1243) status, use of antihypertensive medications at baseline (n = 77), and history of cardiovascular disease (n = 513).

The whole study population included 5994 women (54.8%). The self-reported ethnicity was White in 6391 participants (58.5%), Black in 2389 (21.9%), Chinese in 2069 (18.9%) and mixed or other in 81 (0.7%). The prevalence of office hypertension was 4446 (40.7%),

of which 2713 (61.0%) were treated; 629 (5.8%) participants had diabetes. A history of cardiovascular disease, ischemic heart disease or stroke was reported in 1052 (10.1%), 241 (2.6%) and 130 (1.3%) participants.

Mean age at baseline was 46.0 years (5th-95th percentile interval, 21.0–76.2 years). In all study participants (**Table 1**), mean values were 26.1 kg/m^2 (5th–95th percentile interval [PI_{5-95}] 19.0–36.7kg/m^2) for body mass index, 127.5/78.8 mm Hg (PI_{5-95}, 100.0–166.0/61.0–98.5 mm Hg) for office systolic/diastolic blood pressure, 68.4 beats per minute (PI_{5-95}, 52–87 beats per minute) for pulse rate, 184.8 mg/dL (PI_{5-95}, 116.9–257.7 mg/dL) and 55.3 mg/dL (PI_{5-95}, 31.9–83.6 mg/dL) for total and HDL serum cholesterol, 0.9 mg/dL (PI_{5-95}, 0.6–1.3 mg/dL for serum creatinine, and 88.8 mg/dL (PI_{5-95}, 60.5-117.0 mg/dL) for blood glucose. The prevalence of smoking and drinking was 660 (11.4%) and 1845 (35.1%) among women and 1558 (32.6%) and 2864 (64.7%) among men. The waist-to-hip ratio averaged 0.83 (PI_{5-95}, 0.7–1.0) in women and 0.89 (PI_{5-95}, 0.8–1.0) in men. **Tables S4-S16** provide detailed information on the baseline measurements in each of the 13 cohorts.

Hemodynamic measurements

Table 2 lists mean values of the peripheral (brachial) blood pressure levels as recorded in the supine position just prior to the hemodynamic assessment, the central blood pressure levels, and the time-dependent hemodynamic measurement. The peripheral supine blood pressure averaged 129.5 mm Hg systolic and 78.7 mm Hg diastolic. The corresponding central values were 118.2 mm Hg and 79.7 mm Hg, respectively. Mean aortic pulse wave velocity was 7.3 meters per second. **Tables S4-S16** provide the similar information for each cohort and **Table S17** highlights the sex differences in the peripheral and central blood pressure and in the time dependent hemodynamic measurements.

Incidence of events

Among 6871 participants enrolled in 9 longitudinal studies, the median follow-up was 4.2 years (PI_{5-95}, 1.3–12.2 years). Across cohorts (**Table S1**), the median follow-up ranged from 2.3 years (PI_{5-95}, 1.4–3.1) to 14.1 years (PI_{5-95}, 8.5–14.4 years). During 38957 person-years of follow-up, 339 participants experienced a composite cardiovascular event (8.7 per 1000 person-years) and 212 participants died (5.4 per 1000 person-years), 67 (1.7 per 1000 patient-years) of cardiovascular disease. **Table 3** lists the number of events by category that had accrued at the time of writing of this manuscript.

Discussion

This article describes the construction of the IDCARS database and the characteristics of the studies and participants enrolled. Of the 13 included studies, eight applied epidemiological and phenotyping methods similar to those used in the Flemish Study on Environment and Genes in Relation to Health Outcomes. This is an important advantage, which greatly facilitated data harmonization. As shown in Supplemental Tables 4–16, IDCARS covers a wide diversity of ethnicities, the whole blood pressure spectrum from normotension up to hypertension, and an age span ranging from teenagers to the very old.

Meta-analytic methods involve combining and analyzing quantitative evidence from related studies to produce “new” results based on a whole body of research. As such, meta-analyses are an integral part of evidence-based medicine.[53] Traditional meta-analyses synthesize aggregate data obtained from study publications or study authors, while IDCARS was designed as meta-analysis of individual participant data, in which raw data from each study were obtained and will be used for analysis. Although being more resource-intensive and time-consuming than aggregate level approach, individual data-based meta-analyses

have more power, allow the use of the same statistical approach across contributiong studies, give more flexibility to extend or refine the planned analyses, and to account for heterogeneity across cohorts.[53] IDCARS, like its predecessors IDACO[32] and IDHOCO[33] should provide investigators the opportunity to investigate several hypotheses linking cardiovascular outcomes to central hemodynamic indexes that could not be reliably studied in the smaller cohorts of the contributing studies.

Stratifying individuals by brachial pressure revealed considerable overlap in aortic pressure, 70% of individuals with high-normal brachial pressure had similar aortic pressures as those with stage-1 hypertension. These data demonstrate that central pressure cannot be simply inferred from peripheral pressure.[54] Central compared with peripheral blood pressure was more closely associated with hypertensive target organ damage.[54] Nonetheless, the added prognostic value of peripheral versus central blood pressure still remains controversial.[6] A first IDCARS report demonstrated that associations of the primary and secondary cardiovascular endpoints with central systolic blood pressure and pulse pressure were not closer than their peripheral counterparts in adults older than 30 years.[55] Future IDCARS analyses will enable to address several issues. First , we will investigate the prognostic information generated by various indexes derived from the radial, carotid and central pulse waveforms, such as but not limited to forward and backward pulse pressure amplitude, the augmentation indexes, and pulse wave velocity. Next, for the indexes showing association with adverse health outcomes, we will derive outcome-driven thresholds and construct predictive models in an attempt to clarify whether these arterial phenotypes improve currently applied risk scores.[56,57]

One of the strengths of IDCARS, is the use of a single noninvasive system (SphygmoCor) for the estimation of central hemodynamics via a validated generalized transfer function.[36,37] As stated in the Methods, quality control of the arterial phenotypes was rigorously

standardized. In addition, various calibration methods to estimate central blood pressure,[55] for instance using brachial systolic and diastolic blood pressure or using brachial mean arterial pressure and diastolic blood pressure, could be employed via re-analyzing the raw data of the pulse waveforms. The difference between the calibration methods in terms of central blood pressure level and risk prediction could therefore be tested in the same IDCARS population. Future analyses will also address potential limitations. First, the anthropometric characteristics, the time of recruitment, and the availability of endpoint data differed between cohorts. However, analyses will be adjusted for cohort as a random effect and analyses stratified by cohort, as appropriate. Second, the reconstruction of the aortic pulse wave from the radial or brachial pulse wave requires the application of a generalized transfer function, which has been validated,[37] but also has been criticized.[58] Finally, confounding factors, such as antihypertensive treatment, smoking and drinking status, or renal dysfunction, were only assessed at baseline so that they cannot be accounted for in a time dependent manner. However, we intend to update the IDCARS database at 5-year intervals in the same way as we did for IDACO[32] and IDHOCO.[33]

Conclusions

In conclusion, IDCARS is a unique data resource that will provide an opportunity to investigate several hypotheses relating adverse health outcomes to central hemodynamic indexes with greater statistical power and generalizability than possible in the individual studies included in the database. Results of such analyses might inform guidelines and be of help to clinicians involved in the management of patients with suspected or established arterial disease and cardiovascular risk factors, such as hypertension.

Appendix

Argentina, Buenos Aires: LS Aparicio, J Barochiner;

Belgium, Noordkempen: B Mujaj, L Thijs, JA Staessen, F-F Wei, W-Y Yang, Z-Y Zhang;

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References

1. Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, Brauer M, Kutty VR, Gupta R, Wielgosz A, AlHabib KF, Dans A, Lopez-Jaramillo P, Avezum A, Lanas F, Oguz A, Kruger IM, Diaz R, Yusoff K, Mony P, Chifamba J, Yeates K, Kelishadi R, Yusufali A, Khatib R, Rahman O, Zatonska K, Iqbal R, Wei L, Bo H, Rosengren A, Kaur M, Mohan V, Lear SA, Teo KK, Leong D, O'Donnell M, McKee M, Dagenais G. Modifiable risk factors, cardiovascular disease, and mortality in 155722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet* 2020;395:795–808.

2. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1223–1249.

3. Safar ME, Toto-Moukouo JA, Bouthier JA, Asmar RE, Levenson JA, Simon AC, London GM. Arterial dynamics, cardiac hypertrophy, and antihypertensive treatment. *Circulation* 1987;75:I156–I161.

4. O'Rourke MF. Influence of ventricular ejection on the relationship between central aortic and brachial pressure pulse in man. *Cardiovasc Res* 1970;4:291–300.

5. Avolio AP, Van Bortel LM, Boutouyrie P, Cockcroft JR, McEniery CM, Protogerou AD, Roman MJ, Safar ME, Segers P, Smulyan H. Role of pulse pressure amplification in arterial hypertension : experts' opinion and review of the data. *Hypertension* 2009;54:375–383.

6. McEniery CM, Cockcroft JR, Roman MJ, Franklin SS, Wilkinson IB. Central blood pressure: current evidence and clinical importance. *Eur Heart J* 2014;35:1719–1725.

7. Kollias A, Lagou S, Zeniodi ME, Boubouchairopoulou N, Stergiou GS. Association of central versus brachial blood pressure with target-organ damage: Systematic review and meta-analysis. *Hypertension* 2016;67:183–190.

8. Boutouyrie P, Bussy C, Lacolley P, Girerd X, Laloux B, Laurent S. Association between local pulse pressure, mean blood pressure, and large-artery remodeling. *Circulation* 1999;100:1387–1393.

9. Covic A, Goldsmith DJA, Panahhiu L, Covic M, Sedor J. Analysis of the effect of hemodialysis on peripheral and central arterial pressure waveforms. *Kidney Intern* 2000;57:2634–2643.

10. Roman MJ, Devereux RB, Kizer JR, Lee ET, Galloway JM, Ali T, Umans JG, Howard BV. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure. The Strong Heart study. *Hypertension* 2007;50:197–203.

11. Wang KL, Cheng HM, Chuang SY, Spurgeon HA, Ting CT, Lakatta EG, Yin FCP, Chou P, Chen CH. Central or peripheral systolic or pulse pressure: which best relates to target organs and future mortality? *J Hypertens* 2009;27:461–467.

12. DeLoach SS, Appel LJ, Chen J, offe MM, Gadegbeku CA, Mohler ERI, Parsa A, Perumal K, Rafey MA, Steigerwalt SP, Teal V, Townsend R, Rosas SE. Aortic pulse pressure is associated with carotid IMT in chronic kidney disease: report from chronic renal insufficiency cohort. *Am J Hypertens* 2009;22:1235–1241.

13. Manisty CH, Zambanini A, Parker KH, Davies JE, Francis DP, Mayet J, McG Thom SA, Hughes AD, on behalf of the Anglo-Scandinavian Cardiac Outcome Trial Investigators. Differences in the magnitude of wave reflection account for differential effects of amlodipine- versus atenolol-based regimens on central blood pressure. An Anglo-Scandinavian Cardiac Outcome Trial substudy. *Hypertension* 2009;54:724–730.

14. Roman MJ, Okin PM, Kizer JR, Lee ET, Howard BV, Devereux RB. Relations of central and brachial blood pressure to left ventricular hypertrophy and geometry: the Strong Heart Study. *J Hypertens* 2010;28:384–388.

15. Wohlfahrt P, Wichterle D, Seidlerová J, Filipovský J, Bruthans J, Adámková V, Cífková R. Relation of central and brachial blood pressure to left ventricular hypertrophy. The Czech Post-MONICA Study. *J Hum Hypertens* 2012;26:14–19.

16. Nakayama Y, Tsumura K, Yamashita N, Yoshimaru K, Hayashi T. Pulsatility of ascending aortic pressure waveform is a powerful predictor of restenosis after percutaneous transluminal coronary angioplasty. *Circulation* 2000;101:470–472.

17. Lu TM, Hsu NW, Chen YH, Lee WS, Wu CC, Ding YA, Chang MS, Lin SJ. Pulsatility of ascending aorta and restenosis after coronary angioplasty in patients >60 years of age with stable angina pectoris. *Am J Cardiol* 2001;88:964–968.

18. Safar ME, Blacher J, Pannier B, Guerin AP, Marchais SJ, Guyonvarc'h PM, London GM. Central pulse pressure and mortality in end-stage renal disease. *Hypertension* 2002;39:735–738.

19. Hansen TW, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, Jeppesen J. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. *Circulation* 2006;113:664–670.

20. Chirinos JA, Zambrano JP, Chakko S, Veerani A, Schob A, Willens HJ, Perez G, Mendez AJ. Aortic pressure augmentation predicts adverse cardiovascular events in patients with established coronary artery disease. *Hypertension* 2005;45:980–985.

21. Adji A, O'Rourke MF. Determination of central aortic systolic and pulse pressure from the radial artery pressure waveform. *Blood Press Monit* 2004;9:115–121.

22. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, Hugues AD, Thurston H, O'Rourke M. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation* 2006;113:1213–1225.

23. Jankowski P, Kawecka-Jaszcz K, Czarnecka D, Brzozowska-Kiszka M, Styczkiewicz K, Loster M, Kloch-Badelek M, Wilinski J, Curylo AM, Dudek D, on behalf of the Aortic Blood Pressure and Survival Study Group. Pulsatile but not steady component of blood pressure predicts cardiovascular events in coronary patients. *Hypertension* 2008;51:848–855.

24. Redelinghuys M, Norton GR, Scott L, Maseko MJ, Brooksband R, Majane OHI, Sareli P, Woodiwiss AJ. Relationship between urinary salt excretion and pulse pressure and central aortic hemodynamics independent of steady state pressure in the general population. *Hypertension* 2010;56:584–590.

25. Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, Hamburg NM, Vila JA, Levy D, Benjamin EJ. Arterial stiffness and cardiovascular events: the Framingham Heart Study. *Circulation* 2010;121:505–511.

26. Boutouyrie P, Bussy C, Hayoz D, Hengstler J, Dartois N, Laloux B, Brunner H, Laurent S. Local pulse pressure and regression of arterial wall hypertrophy during long-term antihypertensive treatment. *Circulation* 2000;101:2601–2606.

27. De Luca N, Asmar RG, London GM, O'Rourke MF, Safar ME, on behalf of the REASON project investigators. Selective reduction of cardiac mass and central blood pressure on low-dose combination perindopril/indapamide in hypertensive subjects. *J Hypertens* 2004;22:1623–1630.

28. Drüeke T, Witko-Sarsat V, Massy Z, Descamps-Latscha B, Guerin AP, Marchais SJ, Gausson V, London GM. Iron therapy, advanced oxidation protein products, and carotid rtery intima-media thickness in end-stage renal disease. *Circulation* 2002;106:2212–2217.

29. Pini R, Cavallini C, Palmieri V, Marchionni N, Di Bari M, Devereux RB, Masotti G, Roman MJ. Central but not brachial blood pressure predicts cardiovascular events in an unselected geriatric population. The ICARe Dicomano Study. *J Am Coll Cardiol* 2008;51:2432–2439.

30. Dart AM, Gatzka CD, Kingwell BA, Willson K, Cameron JD, Liang YL, Berry KL, Wing LMH, Reid CM, Ryan P, Beilin LJ, Jennings GLR, Johnston CI, McNeil JJ, MacDonald GJ, Morgan TO, West MJ. Brachial blood pressure but not carotid arterial

waveforms predict cardiovascular events in elderly femal hypertensives. *Hypertension* 2006;47:785–790.

31. Sharman JE, Marwick TH, Gilroy D, Otahal P, Abhayaratna WP, Stowasser M, Value of Central Blood Pressure for GUIDing ManagEment of Hypertension Study Investigators. Randomized trial of guiding hypertension management using central aortic blood pressure compared with best-practice care: principal findings of the BP GUIDE study. *Hypertension* 2013;62:1138–1145.

32. Li Y, Thijs L, Zhang ZY, Asayama K, Hansen TW, Boggia J, Björklund-Bodegård K, Yang WY, Niiranen TJ, Ntineri A, Wei F-F, Kikuya M, Ohkubo T, Dolan E, Hozawa A, Tsuji I, Stolarz-Skrzypek K, Haung QF, Melgarejo JD, Tikhonoff V, Malyutina S, Casiglia E, Nikitin Y, Lind L, Sandoya E, Aparicio L, Barochiner J, Gilis-Malinowska N, Narkiewicz K, Kawecka-Jaszcz K, Maestre GE, Jula AM, Johansson JK, Kuznetsova T, Filipovský J, Stergiou G, Wang JG, Imai Y, O'Brien E, Staessen AJ, on behalf of the Internatioanl Database on Ambulatory and Home Blood Pressure in Relation to Cardiovascular Outcome Investigators. Opposing age-related trends in absolute and relative risk of adverse health outcomes associated with out-of-office blood pressure. *Hypertension* 2019;74:1333–1342.

33. Niiranen TJ, Asayama K, Thijs L, Johansson JK, Ohkubo T, Kikuya M, Boggia J, Hozawa A, Sandoya E, Stergiou GS, Tsuji I, Jula AM, Imai Y, Staessen JA, for the Database of HOme blood pressure in relation to Cardiovascular Outcome Investigators. Outcome-driven thresholds for home blood pressure measurement : International Database for HOme blood pressure in relation to Cardiovascular Outcome. *Hypertension* 2013;61:27–34.

34. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *J Am Med Ass* 2013;310:2191–2194.

35. O'Brien E, Asmar R, Beilin L, Imai Y, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, Verdecchia P, on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. *J Hypertens* 2005;23:697–701.

36. Karamanoglu M, O'Rourke MF, Avolio AP, Kelly PJ. An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. *Eur Heart J* 1993;14:160–167.

37. Pauca AL, O'Rourke M, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform *Hypertension* 2001;38:932–937.

38. Lieber A, Millasseau S, Bourhis L, Blacher J, Protogerou A, Levy IL, Safar ME. Aortic wave reflection in women and men. *Am J Physiol Heart Circ Physiol* 2010;H236–H242.

39. Bos WJ, Verrij E, Vincent HH, Westerhof BE, Parati G, van Montfrans GA. How to assess mean blood pressure properly at the brachial artery level. *J Hypertens* 2007;25:751–755.

40. Shoji T, Nakagomi A, Okada S, Ohno Y, Kobayashi Y. Invasive validation of a novel brachial cuff-based oscillometric device (SphygmoCor XCEL) for measuring central blood pressure. *J Hypertens* 2017;35:69–75.

41. Nakagomi A, Shoji T, Okada S, Ohno Y, Kobayashi Y. Vailidity of the augmentation index and pulse pressure amplification as determined by the SphygmoCor XCEL device: a comparison with invasive measurements. *Hypertens Res* 2018;41:27–32.

42. Stabouli S, Printza N, Zervas C, Dotis J, Chrysaidou K, Maliahova O, Antza C, Papachristou F, Kotsis V. Comparison of the SphygmoCor XCEL device with applanation tonometry for pulse wave velocity and central blood pressure assessment in youth. *J Hypertens* 2019;37:30–36.

43. Weber T, Ammer M, Rammer M, Adji A, O'Rourke MF, Wassertheurer S, Rosenkranz S, Eber B. Noninvasive determination of carotid-femoral pulse wave velocity depends critically on assessment of travel distance: a comparison with invasive measurement. *J Hypertens* 2009;27:1624–1630.

44. Laurent S, Cockcroft J, Bortel LV, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson L, Struijker-Boudier H, European Network for Non-invasive Investigation of Large Arteries. Expert consensus document on arterial stiffness : methodological issues and clinical applications. *Eur Heart J* 2006;27:2588–2605.

45. Milan A, Zocaro G, Leone D, Tosello F, Buraioli I, Schiavone D, Veglio F. Current assessment of pulse wave velocity: comprehensive review of validation studies. *J Hypertens* 2019;37:1547–1557.

46. Weber T, Wassertheurer S, Hametner B, Parragh S, Eber B. Noninvasive methods to assess pulse wave velocity: comparison with the invasive gold standard and relationship with organ damage. *J Hypertens* 2015;33:1023–1031.

47. Butlin M, Qasem A. Large artery stiffness assessment using ShygmoCor technology. *Pulse* 2016;4:180–192.

48. Roglic G, Resnikoff S, Strong K, Unwin N, Alberti KGMM, Bennett PH, Borch-Johnsen K, Colagiuri S, Engelgau M, Home P, Metelko Z, Mohan V, Pan CY, Qiao Q, Ramaija K, Shaw J, Schmidt MI, Tuomilehto J, Vistisen D, Zimmet P. What diagnostic tests should be used to define glycaemic status? In *Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia.*Geneva, Switzerland, World Health Organization, 2006, pp 1-9.

49. Asayama K, Thijs L, Brguljan Hitij J, Niiranen TJ, Hozawa A, Boggia J, Aparicio LS, Hara A, Johansson JK, Ohkubo T, Tzourio C, Stergiou GS, Sandoya E, Tsuji I, Jula AM, Imai Y, Staessen JA, on behalf of the International Database on HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO) Investigators. Risk stratification by self-measured home blood pressure across categories of the conventional blood pressure: a participant-level meta-analysis. *PLOS Medicine* 2014;11:e1001591.

50. Munné MI. Social consequences of alcohol consumption in Argentina. In Obot IS, Room I (eds): *Alcohol, Gender and Drinking Problems. Perspectives from Low and Middle Income Countries.* Geneva, Switzerland, World Health Organization, 2005, pp 25-48.

51. Wilsnack RW, Willsnack SC, Krisjanson AF, Vogeltanz ND, Gmel G. Gender and alcohol consumption : patterns from the multinational GENACIS project. *Addiction* 2009;104:1487–1500.

52. World Health Organization. *Global status report on alcohol and health 2018.* Geneva, Switzerland, World Health Organization, 2018,

53. Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. *Br Med J* 2010;340:c221.

54. McEniery CM, Yasmin, McDonnell B, Munnery M, Wallace SM, Rowe CV, Cockcroft JR, Wilkinson IB. Central pressure: variability and impact of cardiovascular risk factors: the Anglo-Cardiff Collaborative Trial II. *Hypertension* 2008;51:1476–1482.

55. Huang QF, Aparicio LS, Thijs L, Wei FF, Melgarejo JD, Cheng YB, Sheng CS, Yang WY, Gilis-Malinowska N, Boggia J, Niiranen TJ, Wojciechowska W, Stolarz-Skrzypek K, Barochiner J, Ackermann D, Tikhonoff V, Ponte B, Pruijm M, Casiglia E, Narkiewicz K, Filipovsky J, Czarnecka D, Kawecka-Jaszcz K, Jula AM, Bochud M, Vanassche T, Verhamme P, Struijker-Boudier HAJ, Wang JG, Zhang ZY, Li Y, Staessen JA. Cardiovascular end points and mortality are not closer associated with central than peripheral pulsatile blood pressure components. *Hypertension* 2020;76:350–358.

56. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, De Bacquer D, Ducimetière P, Jousilahti P, Keil U, Njølstad I, Oganov RG, Thomson T, Tunstall-Pedoe H, Tverdal A, Wedel H, Whincup P, Wilhelmsen L, Graham IM, on behalf of

the SCORE project group. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J* 2003;24:987–1003.

57. D'Agostino RB, Jr., Grundy S, Sullivan LM, Wilson P, for the CHD Risk Prediction Group. Validation of the Framingham coronary heart disease predictions scores. Results of a multiple ethnic groups investigation. *J Am Med Assoc* 2001;286:180–187.

58. Segers P, Mahieu D, Kips J, Van Bortel LM. The use of a generalized transfer function : different processing, different results! *J Hypertens* 2007;25:1783–1787.

Figure legend

Figure. Geographical spread of IDCARS participants. Two cohorts were enrolled in Poland and South Africa.

Table 1. Characteristics of 10930 participants enrolled in 13 studies

Characteristic	No	Statistic before interpolation	Statistic with interpolation
No (%) of participants with characteristic			
Women	10930	5995 (54.8)	5995 (54.8)
Region of enrolment			
Europe	10930	4140 (37.9)	4140 (37.9)
JingNing, China	10930	2069 (18.9)	2069 (18.9)
Africa	10930	2968 (27.2)	2968 (27.2)
South America	10930	1753 (16.0)	1753 (16.0)
Current smoking	10586	2218 (21.0)	2218 (20.3)
Drinking alcohol	9687	4709 (48.6)	5226 (47.8)
Hypertension	10930	4446 (40.1)	4446 (40.1)
On antihypertensive treatment	10853	2713 (61.0)	2713 (61.0)
Diabetes mellitus	10930	629 (5.8)	629 (5.8)
History of cardiovascular disease	10417	1052 (10.1)	1052 (10.0)
Mean (±SD) characteristic			
Age, y	10930	46.0 ± 18.0	46.0 ± 18.0
Body mass index, kg/m^2	10898	26.1 ± 5.6	26.0 ± 5.6
Office systolic blood pressure, mm Hg	10734	127.5 ± 20.4	127.5 ± 20.4
Office diastolic blood pressure, mm Hg	10733	78.8 ± 11.3	78.8 ± 11.3
Heart rate, beats per minute	9569	68.4 ± 11.0	68.4 ± 11.0
Serum total cholesterol, mg/dL	10447	184.8 ± 43.2	185.1 ± 42.3
Serum high-density lipoprotein cholesterol, mg/dL	10102	55.3 ± 16.1	55.2 ± 15.8
Total-to-high-density-lipoprotein cholesterol ratio	10097	3.6 ± 2.6	3.6 ± 2.5
Serum creatinine, mg/dL	10226	0.9 ± 0.3	0.9 ± 0.3
Blood glucose, mg/dL	10608	88.8 ± 24.8	89.0 ± 24.5

Characteristics refers to baseline data of 6871 participants enrolled in 9 longitudinal cohort studies or to data at recruitment in 4059 participants enrolled in 4 cross-sectional studies. No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 9787 participants or based on a single reading in 947 participants. Body mass index was body weight in kilogram divided by height in meters squared.

Table 2. Hemodynamic characteristics of **10930** participants enrolled in **13** studies

Characteristic	No	Statistic
Peripheral blood pressure		
Systolic pressure, mm Hg	10834	129.5 ± 20.4
Diastolic pressure, mm Hg	10836	78.7 ± 11.2
Pulse pressure, mm Hg	10834	50.7 ± 15.6
Mean arterial pressure, mm Hg	9637	97.3 ± 14.4
Central blood pressure		
Systolic pressure, mm Hg	10834	118.2 ± 20.9
Diastolic pressure, mm Hg	10835	79.7 ± 11.3
Pulse pressure, mm Hg	10833	38.5 ± 15.1
Mean arterial pressure, mm Hg	10835	96.1 ±14.2
Time dependent central hemodynamics		
Augmentation index, %	10812	22.2 ±15.6
Augmentation index 75, %*	9908	17.8 ± 15.2
Augmentation ratio, %	10810	134.0 ± 27.4
Pressure amplification, mm Hg	10811	9.9 ± 9.3
Pressure amplification 75, mm Hg*	7320	8.3 ± 8.0
Aortic pulse wave velocity, m/s	7601	7.3 ± 2.3

Values are mean ± SD. Hemodynamic characteristics refers to measurements obtained at baseline in 6871 participants enrolled in 9 longitudinal cohort studies or to measurements obtained at recruitment in 4059 participants enrolled in 4 cross-sectional studies. No indicates the number of participants with available measurements. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. These measurement were used to calibrate the central hemodynamic measurements. Mean arterial pressure was diastolic blood pressure plus one third of pulse pressure, the difference between systolic and diastolic blood pressure. * The time-dependent hemodynamic variables were standardized to a heart rate of 75 beats per minute.

Table 3. Incidence of events in 6871 participants enrolled in 9 longitudinal studies

Event	n	Fatal	Nonfatal
Total mortality	…	212	…
Cardiovascular mortality	…	67	…
Sudden death	…	7	…
Ischemic heart disease	…	10	…
Heart failure	…	14	…
Peripheral arterial disease	…	2	…
Other cardiovascular disease	…	6	…
Stroke	…	28	…
Noncardiovascular mortality	…	123	…
Death from renal failure	…	3	…
Cause of death unknown	…	19	…
Composite cardiovascular endpoint			
Coronary heart disease	176		
Sudden death	7	7	…
Myocardial infarction	43	5	38
Coronary revascularization	73	…	73
Other ischemic heart disease	53	…	53
Heart failure	70	14	56
Stroke	93	28	65
Other nonfatal cardiovascular outcomes			
Atrial fibrillation	61	…	61
Pacemaker implantation	13	…	13
Transient ischemic attack	22	…	22

Median follow-up of **6871** participants was **4.2** years (5th to 95th percentile interval, **1.3**–**12.2** years). The composite and nonfatal events do not add up, because within each category only the first event was analyzed. An ellipsis indicates not applicable.

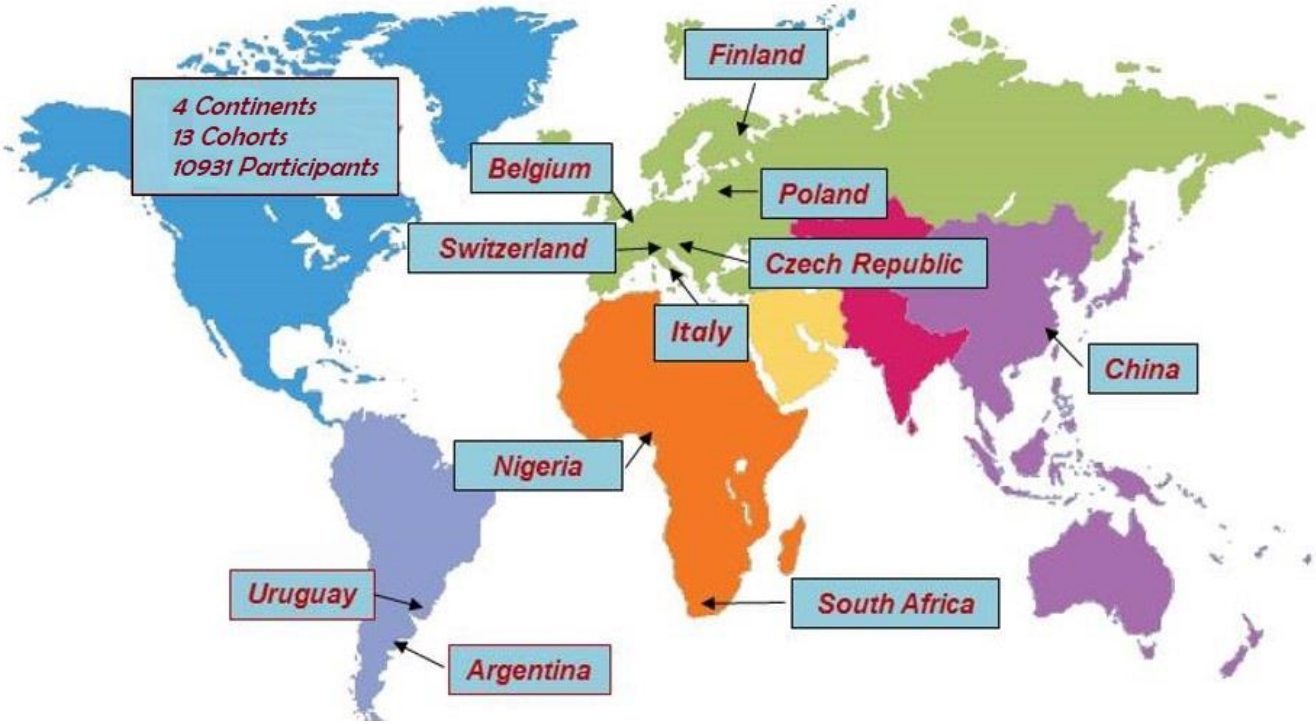

Figure.

Geographical spread of IDCARS participants. Two cohorts were enrolled in Poland and South Africa.

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Data Supplement

This Data Supplement formed part of the original submission and has been peer reviewed.
Supplement to: "*The International Database of Central Arterial Properties for Risk Stratification: Research Objectives and Baseline Characteristics of Participants*".

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Table S1. Methods of recruitment and follow-up of participants by study

Study	Recruitment			Vascular examination (years)	Included in IDCARS	Follow-up	
	Sampling method	Starting point for sample	IPR (%)			Until (year)	Median in years (5–95th percentile interval)
Argentina, Buenos Aires	NA	Out-patient clinic	NA	2011-2015	1428	2018	3.2 (0.4–4.5)
Belgium, Noordkempen	Random sample of families	Address lists	78	2005–2015	1365	2018	8.8 (3.3–12.3)
China, Zhejiang, JingNing	Random sample of families	All villagers invited	62	2003–2008	2069	2012	4.0 (3.6 –7.6)
Czech Republic, Pilsen	Random sample of families	Address list	82	2000–2006	206	2015	14.1 (8.5–14.4)
Finland, Finrisk	Random sample of community	Population register	70	2007	488	2014	6.9 (6.8–6.9)
Italy, Padova	Random sample of families	Address lists	73	2006–2008	302	2013	6.6 (5.9–7.1)
Nigeria, Abuja	Random sample of families	Lugbe Housing Estate	80	2013– 2016	366	CS	CS
Poland, Gdańsk	Random sample of families	Address list	90	2008–2010	297	2017	6.1 (4.8–8.6)
Poland, Kraków, Niepolomice	Random sample of families	Address list	54	2001–2008	391	2014	12.0 (6.1–12.2)
South Africa, Johannesburg	Random sample of residents of Black ancestry	Municipal population register	NoF	2002–2016	1400	CS	CS
South Africa, Potchefstroom	Convenience sample of healthy volunteers (20-30 years) stratified by ethnicity	Public advertisement	64	2013–2017	1202	CS	CS
Switzerland	Random sample of families	Municipal address lists	26	2009-2013	1091	CS	CS
Uruguay, Montevideo	Age-stratified random sample	Members of a health insurance organization	78	2013-2016	325	2016	2.3 (1.4–3.1) *

Abbreviation: IPR, initial participation rate. The European Project on Genes in Hypertension included participants recruited in Kraków, Gdańsk, Pilsen and Padova. Participants from Padova were recruited in Mirano in the province of Venice and in Torrebelvicino and Valli del Pasubio in the province of Vicenza. The Swiss cohort was recruited in Bern, Geneva and Lausanne. Sample size refers to the number of participants, who underwent an assessment of central hemodynamics at least once. NA indicates not applicable and NoF not on file. Participants enrolled in longitudinal studies were only included in the IDCARS database, if follow-up data had been collected. CS indicates cross-sectional study without follow-up data. *In Uruguay, follow-up was available in a subset of 137 participants. For the longitudinal studies, the timing of the vascular examination constitutes baseline.

Table S2. Literature sources by study

Study identification		Literature sources	
Location	Name	Design/Methods	PWA/PWV
Argentina, Buenos Aires	Hospital Italiano de Buenos Aires	[1]	[2] [1]
Belgium, Noordkempen	Flemish Study on Environment Genes and Health Outcomes (FLEMENGHO)	[3] [4] [5]	[6] [7]
China, Zhejiang, JingNing	JingNing Population Study (JNPS)	[8] [9] [10] [11]	[12] [13] [14]
Czech Republic, Pilsen	European Project on Genes in Hypertension (EPOGH)	[4] [15]	[16]
Southwestern Finland	National Cardiovascular Risk Factor Survey in Finland (FINRISK)	[17]	[18]
Italy, Padova	European Project on Genes in Hypertension (EPOGH)	[4] [15]	[16]
Nigeria, Abuja	Nigerian Population Research on Environment, Genes and Health (NIPREGH)	[19] [20] [21]	[22]
Poland, Gdańsk	European Project on Genes in Hypertension (EPOGH); CARE NORTH	[15] [23]	[16] [24]
Poland, Kraków, Niepolomice	European Project on Genes in Hypertension (EPOGH)	[4] [15]	[16]
South Africa, Johannesburg	African Project on Genes in Hypertension (APOGH)	[25] [26]	[13] [27] [28] [29]
South Africa, Potchefstroom	The African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African-PREDICT)	[30] [31] [32]	[33] [34] [35] [36]
Switzerland	Swiss Kidney Project on Genes in Hypertension (SKIPOGH)	[5] [37] [38] [39]	[40] [41]
Uruguay, Montevideo	Genotipo, Fenotipo y Ambiente de la Hipertensión Arterial en Uruguay (GEFA-HT-UY)	[42] [43] [44]	[45] [46]

References are listed starting on page S20.

Table S3. Assessment of central hemodynamics

Study	SphygmoCor device		Blood pressure measurement performed for calibration		
	Type	Software	Monitor	Supine rest (minutes)	No of readings
Argentina, Buenos Aires	CvMS	9.0	Omron 705 CP	5	1-3
Belgium, Noordkempen	CvMS	7.1	Omron 705 CP	15	2
China, Zhejiang, JingNing	CvMS	6.3, 7.1	Omron 705 CP	5	3
Czech Republic, Pilsen	CvMS	7.1	Omron 705 CP	15	2
Southwestern Finland	CvMS	7.1	Omron M6	5	3
Italy, Padova	CvMS	7.1	Omron 705 CP	15	2
Nigeria, Abuja	CvMS	7.1	Mercury sphygmomanometer	15	1
Poland, Gdańsk	CvMS	7.1	Mercury sphygmomanometer	5	1
Poland, Kraków, Niepolomice	CvMS	7.1	Omron 705 CP	15	2
South Africa, Johannesburg	CvMS	6.2, 8.0, 9.0	Mercury sphygmomanometer	15	1
South Africa, Potchefstroom	XCEL	1.3	SphygmoCor XCEL	5	2-3
Switzerland	CvMS	8.0, 8.2	Omron 705 CP	15	2
Uruguay, Montevideo	CvMS	8.2	Omron 714, 7220	15	1

Software refers to the version used for data acquisition. Recalibration was done, using software version 10.0.

Table S4. Characteristics of **1428** participants enrolled in Buenos Aires, Argentina

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	839	58.8	Systolic pressure, mm Hg	139.3	18.7
Current smoking	156	10.9	Diastolic pressure, mm Hg	79.2	10.6
Drinking alcohol	535	37.5	Pulse pressure, mm Hg	60.1	17.5
Hypertension	1211	84.8	Mean arterial pressure, mm Hg	100.1	12.0
On antihypertensive treatment	1183	97.7	End systolic pressure, mm Hg	103.8	13.7
Diabetes mellitus	157	11.0	Central blood pressure		
History of cardiovascular disease	351	25.1	Systolic pressure, mm Hg	127.0	18.4
Mean (±SD) characteristic			Diastolic pressure, mm Hg	80.3	10.7
Age, y	60.4	18.1	Pulse pressure, mm Hg	46.7	17.0
Body mass index, kg/m^2	27.9	5.0	Mean arterial pressure, mm Hg	100.1	12.0
Waist-to-hip ratio	n/a	n/a	End systolic pressure, mm Hg	115.2	15.3
Office systolic blood pressure, mm Hg	135.6	18.5	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	77.8	11.1	Augmentation index, %	25.6	14.6
Heart rate, beats per minute	75.6	13.7	Augmentation index 75, %*	23.3	13.1
Serum total cholesterol, mg/dL	191.9	40.6	Augmentation ratio, %	139.4	27.2
Serum HDL cholesterol, mg/dL	54.3	14.8	Pressure amplification, mm Hg	13.3	10.5
Total-to-HDL cholesterol ratio	4.0	7.0	Pressure amplification 75, mm Hg*	11.2	8.3
Serum creatinine, mg/dL	0.9	0.3	Aortic pulse wave velocity, m/s	8.6	2.5
Blood glucose, mg/dL	99.5	17.7	Ejection duration, msec	303.7	30.2

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 305 participants or based on a single reading in 944 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75.

Table S5. Characteristics of **1365** participants enrolled in Noordkempen, Belgium

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	700	51.3	Systolic pressure, mm Hg	129.8	18.8
Current smoking	238	17.4	Diastolic pressure, mm Hg	78.8	9.7
Drinking alcohol	966	70.8	Pulse pressure, mm Hg	50.9	15.9
Hypertension	622	45.6	Mean arterial pressure, mm Hg	96.5	12.2
On antihypertensive treatment	327	52.6	End systolic pressure, mm Hg	99.1	13.9
Diabetes mellitus	62	4.5	Central blood pressure		
History of cardiovascular disease	159	11.7	Systolic pressure, mm Hg	120.0	19.5
Mean (±SD) characteristic			Diastolic pressure, mm Hg	79.6	9.9
Age, y	51.0	15.7	Pulse pressure, mm Hg	40.4	15.9
Body mass index, kg/m^2	26.4	4.4	Mean arterial pressure, mm Hg	96.4	12.2
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	108.1	16.4
Office systolic blood pressure, mm Hg	131.4	18.0	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	80.7	10.0	Augmentation index, %	25.8	15.9
Heart rate, beats per minute	63.8	9.4	Augmentation index 75, %*	18.5	15.4
Serum total cholesterol, mg/dL	196.3	37.0	Augmentation ratio, %	140.9	30.9
Serum HDL cholesterol, mg/dL	56.3	14.7	Pressure amplification, mm Hg	11.8	9.8
Total-to-HDL cholesterol ratio	3.7	1.1	Pressure amplification 75, mm Hg*	7.8	7.6
Serum creatinine, mg/dL	0.9	0.2	Aortic pulse wave velocity, m/s	7.6	2.0
Blood glucose, mg/dL	86.2	13.1	Ejection duration, msec	337.8	24.8

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 1365 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75.

Table S6. Characteristics of **2069** participants enrolled in JingNing, Zhejiang, China

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	1087	52.5	Systolic pressure, mm Hg	132.7	25.6
Current smoking	621	30.0	Diastolic pressure, mm Hg	79.4	12.1
Drinking alcohol	903	43.6	Pulse pressure, mm Hg	53.3	17.2
Hypertension	611	29.5	Mean arterial pressure, mm Hg	98.3	17.1
On antihypertensive treatment	183	30.0	End systolic pressure, mm Hg	100.1	19.1
Diabetes mellitus	34	1.6	Central blood pressure		
History of cardiovascular disease	172	8.3	Systolic pressure, mm Hg	121.2	26.4
Mean (±SD) characteristic			Diastolic pressure, mm Hg	80.5	12.4
Age, y	46.5	14.7	Pulse pressure, mm Hg	40.7	17.4
Body mass index, kg/m^2	22.4	2.9	Mean arterial pressure, mm Hg	98.3	17.1
Waist-to-hip ratio	0.8	0.1	End systolic pressure, mm Hg	109.7	22.8
Office systolic blood pressure, mm Hg	128.1	24.6	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	77.2	12.6	Augmentation index, %	24.1	15.4
Heart rate, beats per minute	71.2	10.3	Augmentation index 75, %*	20.6	14.3
Serum total cholesterol, mg/dL	183.3	37.5	Augmentation ratio, %	137.1	28.0
Serum HDL cholesterol, mg/dL	60.7	16.1	Pressure amplification, mm Hg	11.5	10.5
Total-to-HDL cholesterol ratio	3.2	1.0	Pressure amplification 75, mm Hg*	9.2	8.5
Serum creatinine, mg/dL	1.0	0.4	Aortic pulse wave velocity, m/s	7.4	1.7
Blood glucose, mg/dL	80.9	19.8	Ejection duration, msec	314.9	23.2

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 2056 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75.

Table S7. Characteristics of **206** participants enrolled in Pilsen, Czech Republic

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	108	52.4	Systolic pressure, mm Hg	123.1	16.7
Current smoking	53	25.7	Diastolic pressure, mm Hg	80.7	10.6
Drinking alcohol	131	63.6	Pulse pressure, mm Hg	42.4	10.8
Hypertension	73	35.4	Mean arterial pressure, mm Hg	96.1	12.8
On antihypertensive treatment	42	57.5	End systolic pressure, mm Hg	n/a	n/a
Diabetes mellitus	10	4.9	Central blood pressure		
History of cardiovascular disease	9	4.4	Systolic pressure, mm Hg	112.1	16.8
Mean (±SD) characteristic			Diastolic pressure, mm Hg	82.0	10.7
Age, y	38.3	13.8	Pulse pressure, mm Hg	30.1	9.7
Body mass index, kg/m^2	26.2	4.8	Mean arterial pressure, mm Hg	96.1	12.8
Waist-to-hip ratio	0.8	0.1	End systolic pressure, mm Hg	104.4	15.6
Office systolic blood pressure, mm Hg	123.3	15.9	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	80.0	11.3	Augmentation index, %	14.7	17.3
Heart rate, beats per minute	68.5	9.4	Augmentation index 75, %*	n/a	n/a
Serum total cholesterol, mg/dL	204.2	44.9	Augmentation ratio, %	122.7	26.0
Serum HDL cholesterol, mg/dL	56.4	14.2	Pressure amplification, mm Hg	5.3	6.5
Total-to-HDL cholesterol ratio	3.8	1.2	Pressure amplification 75, mm Hg*	n/a	n/a
Serum creatinine, mg/dL	1.0	0.1	Aortic pulse wave velocity, m/s	7.8	2.6
Blood glucose, mg/dL	98.1	20.6	Ejection duration, msec	309.2	25.2

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 206 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75.

Table S8. Characteristics of **488** participants enrolled in southwestern Finland

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	253	51.8	Systolic pressure, mm Hg	129.8	18.0
Current smoking	71	14.5	Diastolic pressure, mm Hg	76.6	9.4
Drinking alcohol	342	70.1	Pulse pressure, mm Hg	53.2	12.7
Hypertension	187	38.3	Mean arterial pressure, mm Hg	94.8	12.5
On antihypertensive treatment	84	44.9	End systolic pressure, mm Hg	97.8	14.5
Diabetes mellitus	35	7.2	Central blood pressure		
History of cardiovascular disease	19	3.9	Systolic pressure, mm Hg	118.9	19.0
Mean (±SD) characteristic			Diastolic pressure, mm Hg	77.4	9.6
Age, y	49.7	14.2	Pulse pressure, mm Hg	41.5	13.3
Body mass index, kg/m^2	26.6	4.6	Mean arterial pressure, mm Hg	94.8	12.5
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	106.9	16.8
Office systolic blood pressure, mm Hg	131.3	19.0	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	77.0	10.8	Augmentation index, %	23.7	13.4
Heart rate, beats per minute	69.1	11.6	Augmentation index 75, %*	16.2	13.5
Serum total cholesterol, mg/dL	200.0	36.7	Augmentation ratio, %	135.1	23.7
Serum HDL cholesterol, mg/dL	55.2	13.6	Pressure amplification, mm Hg	10.9	8.3
Total-to-HDL cholesterol ratio	3.8	1.1	Pressure amplification 75, mm Hg*	6.9	6.6
Serum creatinine, mg/dL	0.9	0.2	Aortic pulse wave velocity, m/s	7.4	2.0
Blood glucose, mg/dL	104.5	15.2	Ejection duration, msec	336.5	21.1

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 487 participants or based on a single reading in 1 participant. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75.

Table S9. Characteristics of **302** participants enrolled in Padova, Italy

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	158	52.3	Systolic pressure, mm Hg	126.9	16.5
Current smoking	57	18.9	Diastolic pressure, mm Hg	79.8	10.6
Drinking alcohol	174	57.6	Pulse pressure, mm Hg	47.1	11.9
Hypertension	143	47.4	Mean arterial pressure, mm Hg	96.7	13.3
On antihypertensive treatment	74	51.7	End systolic pressure, mm Hg	97.3	15.1
Diabetes mellitus	13	4.3	Central blood pressure		
History of cardiovascular disease	53	17.6	Systolic pressure, mm Hg	116.1	17.5
Mean (±SD) characteristic			Diastolic pressure, mm Hg	80.9	10.7
Age, y	47.8	14.3	Pulse pressure, mm Hg	35.3	11.5
Body mass index, kg/m^2	26.7	4.6	Mean arterial pressure, mm Hg	96.7	13.3
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	105.4	17.0
Office systolic blood pressure, mm Hg	126.2	17.6	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	82.5	10.5	Augmentation index, %	21.2	16.7
Heart rate, beats per minute	67.8	9.3	Augmentation index 75, %*	n/a	n/a
Serum total cholesterol, mg/dL	190.3	38.8	Augmentation ratio, %	131.9	28.0
Serum HDL cholesterol, mg/dL	58.2	14.8	Pressure amplification, mm Hg	8.5	8.1
Total-to-HDL cholesterol ratio	3.5	1.1	Pressure amplification 75, mm Hg*	n/a	n/a
Serum creatinine, mg/dL	0.8	0.2	Aortic pulse wave velocity, m/s	7.1	2.1
Blood glucose, mg/dL	90.9	20.0	Ejection duration, msec	333.2	20.9

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 302 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75.

Table S10. Characteristics of **366** participants enrolled in Lugbe, Abuja, Nigeria

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	175	47.8	Systolic pressure, mm Hg	115.1	16.0
Current smoking	7	1.9	Diastolic pressure, mm Hg	73.6	11.7
Drinking alcohol	121	33.1	Pulse pressure, mm Hg	41.5	10.4
Hypertension	77	21.0	Mean arterial pressure, mm Hg	87.7	12.8
On antihypertensive treatment	46	59.7	End systolic pressure, mm Hg	87.9	13.9
Diabetes mellitus	31	8.5	Central blood pressure		
History of cardiovascular disease	n/a	n/a	Systolic pressure, mm Hg	103.8	15.9
Mean (±SD) characteristic			Diastolic pressure, mm Hg	74.6	11.8
Age, y	40.6	11.5	Pulse pressure, mm Hg	29.3	9.1
Body mass index, kg/m^2	26.8	5.1	Mean arterial pressure, mm Hg	87.7	12.8
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	94.9	15.0
Office systolic blood pressure, mm Hg	115.8	17.0	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	74.0	11.6	Augmentation index, %	15.9	12.3
Heart rate, beats per minute	73.1	9.8	Augmentation index 75, %*	12.2	11.9
Serum total cholesterol, mg/dL	185.7	33.8	Augmentation ratio, %	121.5	18.6
Serum HDL cholesterol, mg/dL	n/a	n/a	Pressure amplification, mm Hg	5.3	5.1
Total-to-HDL cholesterol ratio	n/a	n/a	Pressure amplification 75, mm Hg*	3.9	4.4
Serum creatinine, mg/dL	n/a	n/a	Aortic pulse wave velocity, m/s	n/a	n/a
Blood glucose, mg/dL	97.5	32.0	Ejection duration, msec	320.3	25.0

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 365 participants or based on a single reading in 1 participant. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available *standardized to a heart rate of 75.

Table S11. Characteristics of **297** participants enrolled in Gdańsk, Poland

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	133	44.8	Systolic pressure, mm Hg	128.9	17.0
Current smoking	80	26.9	Diastolic pressure, mm Hg	77.2	11.0
Drinking alcohol	141	47.5	Pulse pressure, mm Hg	51.7	12.4
Hypertension	117	39.4	Mean arterial pressure, mm Hg	94.5	13.2
On antihypertensive treatment	48	41.0	End systolic pressure, mm Hg	94.9	15.6
Diabetes mellitus	24	8.1	Central blood pressure		
History of cardiovascular disease	26	8.8	Systolic pressure, mm Hg	115.3	18.1
Mean (±SD) characteristic			Diastolic pressure, mm Hg	78.2	11.2
Age, y	41.2	15.2	Pulse pressure, mm Hg	37.1	11.5
Body mass index, kg/m^2	26.3	4.7	Mean arterial pressure, mm Hg	94.5	13.2
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	103.2	17.3
Office systolic blood pressure, mm Hg	131.9	16.9	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	76.8	10.2	Augmentation index, %	16.9	17.1
Heart rate, beats per minute	75.0	10.5	Augmentation index 75, %*	12.1	16.6
Serum total cholesterol, mg/dL	195.4	40.8	Augmentation ratio, %	125.8	27.9
Serum HDL cholesterol, mg/dL	49.8	12.9	Pressure amplification, mm Hg	7.3	8.4
Total-to-HDL cholesterol ratio	4.1	1.2	Pressure amplification 75, mm Hg*	4.9	7.0
Serum creatinine, mg/dL	0.9	0.2	Aortic pulse wave velocity, m/s	6.9	1.6
Blood glucose, mg/dL	94.2	17.0	Ejection duration, msec	328.8	21.7

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 295 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75

Table S12. Characteristics of **391** participants enrolled in Kraków, Poland

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	211	54.0	Systolic pressure, mm Hg	130.1	18.8
Current smoking	96	24.6	Diastolic pressure, mm Hg	79.9	12.6
Drinking alcohol	124	31.7	Pulse pressure, mm Hg	50.2	12.6
Hypertension	130	33.3	Mean arterial pressure, mm Hg	96.4	14.9
On antihypertensive treatment	79	60.8	End systolic pressure, mm Hg	97.2	16.3
Diabetes mellitus	15	3.8	Central blood pressure		
History of cardiovascular disease	41	10.5	Systolic pressure, mm Hg	116.0	19.8
Mean (±SD) characteristic			Diastolic pressure, mm Hg	80.8	12.4
Age, y	37.9	14.9	Pulse pressure, mm Hg	35.0	11.7
Body mass index, kg/m^2	25.4	5.0	Mean arterial pressure, mm Hg	96.2	14.5
Waist-to-hip ratio	0.8	0.1	End systolic pressure, mm Hg	105.8	18.4
Office systolic blood pressure, mm Hg	126.6	18.4	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	78.5	11.2	Augmentation index, %	14.6	17.3
Heart rate, beats per minute	70.5	10.1	Augmentation index 75, %*	n/a	n/a
Serum total cholesterol, mg/dL	192.0	43.3	Augmentation ratio, %	121.9	26.0
Serum HDL cholesterol, mg/dL	59.5	15.3	Pressure amplification, mm Hg	6.3	8.1
Total-to-HDL cholesterol ratio	3.4	1.2	Pressure amplification 75, mm Hg*	n/a	n/a
Serum creatinine, mg/dL	0.9	0.2	Aortic pulse wave velocity, m/s	7.3	2.1
Blood glucose, mg/dL	84.3	20.9	Ejection duration, msec	301.4	25.5

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 391 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75

Table S13. Characteristics of **1400** participants enrolled in Johannesburg, South Africa

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	931	66.5	Systolic pressure, mm Hg	128.4	22.1
Current smoking	213	15.2	Diastolic pressure, mm Hg	83.3	12.5
Drinking alcohol	291	20.8	Pulse pressure, mm Hg	45.0	15.5
Hypertension	678	48.4	Mean arterial pressure, mm Hg	99.7	15.5
On antihypertensive treatment	352	51.9	End systolic pressure, mm Hg	n/a	n/a
Diabetes mellitus	156	11.1	Central blood pressure		
History of cardiovascular disease	34	2.4	Systolic pressure, mm Hg	119.7	22.0
Mean (±SD) characteristic			Diastolic pressure, mm Hg	84.2	12.7
Age, y	44.5	18.2	Pulse pressure, mm Hg	35.4	14.4
Body mass index, kg/m^2	29.7	8.0	Mean arterial pressure, mm Hg	99.7	15.5
Waist-to-hip ratio	0.8	0.1	End systolic pressure, mm Hg	110.7	19.5
Office systolic blood pressure, mm Hg	130.6	22.0	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	83.7	12.4	Augmentation index, %	27.1	12.5
Heart rate, beats per minute	69.6	10.7	Augmentation index 75, %*	22.7	12.1
Serum total cholesterol, mg/dL	178.1	38.9	Augmentation ratio, %	141.2	24.8
Serum HDL cholesterol, mg/dL	54.1	15.2	Pressure amplification, mm Hg	10.5	7.6
Total-to-HDL cholesterol ratio	3.5	1.8	Pressure amplification 75, mm Hg*	n/a	n/a
Serum creatinine, mg/dL	0.8	0.3	Aortic pulse wave velocity, m/s	6.3	2.6
Blood glucose, mg/dL	93.1	42.9	Ejection duration, msec	322.3	25.4

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 1400 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75

Table S14. Characteristics of **1202** participants enrolled in Potchefstroom, South Africa

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	624	51.9	Systolic pressure, mm Hg	122.7	10.4
Current smoking	286	23.8	Diastolic pressure, mm Hg	73.4	7.8
Drinking alcohol	674	56.1	Pulse pressure, mm Hg	49.3	7.8
Hypertension	137	11.4	Mean arterial pressure, mm Hg	n/a	n/a
On antihypertensive treatment	0	0.0	End systolic pressure, mm Hg	n/a	n/a
Diabetes mellitus	3	0.3	Central blood pressure		
History of cardiovascular disease	8	0.7	Systolic pressure, mm Hg	108.1	9.6
Mean (±SD) characteristic			Diastolic pressure, mm Hg	74.1	7.8
Age, y	25.0	3.1	Pulse pressure, mm Hg	34.0	5.7
Body mass index, kg/m^2	25.1	5.6	Mean arterial pressure, mm Hg	87.2	8.5
Waist-to-hip ratio	0.8	0.1	End systolic pressure, mm Hg	96.5	10.1
Office systolic blood pressure, mm Hg	119.3	12.1	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	78.5	7.9	Augmentation index, %	11.0	11.5
Heart rate, beats per minute	63.3	10.5	Augmentation index 75, %*	4.5	12.8
Serum total cholesterol, mg/dL	144.5	46.1	Augmentation ratio, %	116.0	10.1
Serum HDL cholesterol, mg/dL	44.5	16.0	Pressure amplification, mm Hg	4.0	4.4
Total-to-HDL cholesterol ratio	3.5	1.3	Pressure amplification 75, mm Hg*	n/a	n/a
Serum creatinine, mg/dL	0.8	0.2	Aortic pulse wave velocity, m/s	6.3	0.9
Blood glucose, mg/dL	73.1	19.1	Ejection duration, msec	n/a	n/a

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 1202 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. n/a data not available. *standardized to a heart rate of 75

Table S15. Characteristics of **1091** participants enrolled in Bern, Geneva and Lausanne, Switzerland

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	569	52.2	Systolic pressure, mm Hg	125.0	18.0
Current smoking	271	24.8	Diastolic pressure, mm Hg	77.7	9.5
Drinking alcohol	691	64.0	Pulse pressure, mm Hg	47.3	14.3
Hypertension	297	27.2	Mean arterial pressure, mm Hg	94.5	12.4
On antihypertensive treatment	217	73.1	End systolic pressure, mm Hg	97.1	14.4
Diabetes mellitus	47	4.3	Central blood pressure		
History of cardiovascular disease	127	11.8	Systolic pressure, mm Hg	115.2	18.9
Mean (±SD) characteristic			Diastolic pressure, mm Hg	78.6	9.7
Age, y	47.3	17.5	Pulse pressure, mm Hg	36.6	14.4
Body mass index, kg/m^2	24.9	4.5	Mean arterial pressure, mm Hg	94.5	12.4
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	104.7	16.7
Office systolic blood pressure, mm Hg	119.0	17.1	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	75.6	9.8	Augmentation index, %	22.8	16.0
Heart rate, beats per minute	66.3	11.1	Augmentation index 75, %*	15.9	16.3
Serum total cholesterol, mg/dL	195.3	40.8	Augmentation ratio, %	135.2	29.1
Serum HDL cholesterol, mg/dL	58.4	16.5	Pressure amplification, mm Hg	9.7	9.1
Total-to-HDL cholesterol ratio	3.6	1.1	Pressure amplification 75, mm Hg*	6.4	7.4
Serum creatinine, mg/dL	0.8	0.2	Aortic pulse wave velocity, m/s	8.0	2.3
Blood glucose, mg/dL	92.5	13.0	Ejection duration, msec	338.0	21.6

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 1089 participants. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75

Table S16. Characteristics of **325** participants enrolled in Montevideo, Uruguay

Clinical and biochemical characteristics			Hemodynamic characteristics		
Item	No	Statistic	Item	No	Statistic
No (%) of participants with characteristic			Peripheral blood pressure		
Women	206	63.4	Systolic pressure, mm Hg	130.5	18.9
Current smoking	69	21.2	Diastolic pressure, mm Hg	82.4	12.7
Drinking alcohol	119	36.6	Pulse pressure, mm Hg	48.1	14.0
Hypertension	163	50.2	Mean arterial pressure, mm Hg	99.5	14.4
On antihypertensive treatment	123	75.5	End systolic pressure, mm Hg	99.6	15.9
Diabetes mellitus	44	13.5	Central blood pressure		
History of cardiovascular disease	53	16.3	Systolic pressure, mm Hg	120.1	19.3
Mean (±SD) characteristic			Diastolic pressure, mm Hg	83.5	12.8
Age, y	54.5	17.4	Pulse pressure, mm Hg	36.6	13.3
Body mass index, kg/m^2	29.5	6.2	Mean arterial pressure, mm Hg	99.5	14.4
Waist-to-hip ratio	0.9	0.1	End systolic pressure, mm Hg	108.8	17.6
Office systolic blood pressure, mm Hg	129.8	22.9	Time dependent central hemodynamics		
Office diastolic blood pressure, mm Hg	81.6	11.8	Augmentation index, %	23.9	15.8
Heart rate, beats per minute	72.0	9.3	Augmentation index 75, %*	21.4	15.3
Serum total cholesterol, mg/dL	205.5	44.5	Augmentation ratio, %	137.1	29.9
Serum HDL cholesterol, mg/dL	51.3	14.8	Pressure amplification, mm Hg	9.8	8.6
Total-to-HDL cholesterol ratio	4.3	1.3	Pressure amplification 75, mm Hg*	8.4	7.6
Serum creatinine, mg/dL	0.8	0.2	Aortic pulse wave velocity, m/s	8.0	4.2
Blood glucose, mg/dL	97.9	28.0	Ejection duration, msec	321.2	24.6

No indicates the number of participants with available measurements. Hypertension was an office BP of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs. Diabetes mellitus was use of antidiabetic drugs, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L), a self-reported diagnosis, or diabetes documented in practice or hospital records. Office blood pressure was the average of two readings in 324 participants or based on a single reading in 1 participant. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *standardized to a heart rate of 75

Table S17. Hemodynamic measurements in 5943 women and 4893 men

Hemodynamic variable	Women		Men		Δ	
	No	Statistic	No	Statistic	Δ (95% CI)	*P*
Peripheral blood pressure						
Systolic pressure, mm Hg	5942	127.9 ± 21.7	4892	131.4 ± 18.6	3.5 (2.8-4.3)	<0.0001
Diastolic pressure, mm Hg	5943	77.7 ± 11.3	4893	80.0 ± 10.9	2.2 (1.8-2.7)	<0.0001
Pulse pressure, mm Hg	5942	50.1 ± 16.5	4892	51.4 ± 14.2	1.3 (0.7-1.9)	<0.0001
Mean arterial pressure, mm Hg	5321	96.7 ± 15.0	4316	97.9 ± 13.6	1.2 (0.6-1.8)	<0.0001
Central blood pressure						
Systolic pressure, mm Hg	5942	118.0 ± 22.2	4892	118.4 ± 19.2	0.4 (-0.4-1.2)	0.3
Diastolic pressure, mm Hg	5942	78.7 ± 11.5	4893	80.9 ± 11.1	2.2 (1.7-2.6)	<0.0001
Pulse pressure, mm Hg	5941	39.3 ± 16.2	4892	37.6 ± 13.6	-1.7 (-2.3-[-1.2])	<0.0001
Mean arterial pressure, mm Hg	5942	95.6 ± 14.8	4893	96.7 ± 13.5	1.1 (0.6-1.6)	<0.0001
Time dependent central hemodynamics						
Augmentation index, %	5931	25.9 ± 14.6	4881	17.7 ± 15.5	-8.2 (-8.8-[-7.7])	<0.0001
Augmentation index 75, %*	5457	22.4 ± 13.8	4451	12.2 ± 15.0	-10.2 (-10.8-[-9.6])	<0.0001
Augmentation ratio, %	5929	140.3 ± 27.6	4881	126.3 ± 25.1	-14.0 (-15.0-[-13.0])	<0.0001
Pressure amplification, mm Hg	5930	11.5 ± 9.5	4881	7.8 ± 8.6	-3.7 (-4.0-[-3.3])	<0.0001
Pressure amplification 75, mm Hg*	3907	10.5 ± 8.1	3413	5.8 ± 7.1	-4.7 (-5.1-[-4.4])	<0.0001
Aortic pulse wave velocity, m/s	4250	7.1 ± 2.3	3351	7.5 ± 2.3	0.4 (0.3-0.5)	<0.0001
Ejection duration, msec	5319	325.0 ± 27.7	4314	318.0 ± 27.5	-7.0 (-8.2-[-5.9])	<0.0001

Δ reported with 95% confidence interval (95 % CI) refers the difference (men minus women). No indicates the number of participants with available measurements. Peripheral blood pressure was measured in the supine position immediately prior to the tonometric assessment of participants. *The time-dependent measurements were standardized to a heart rate of 75 beats per minute.

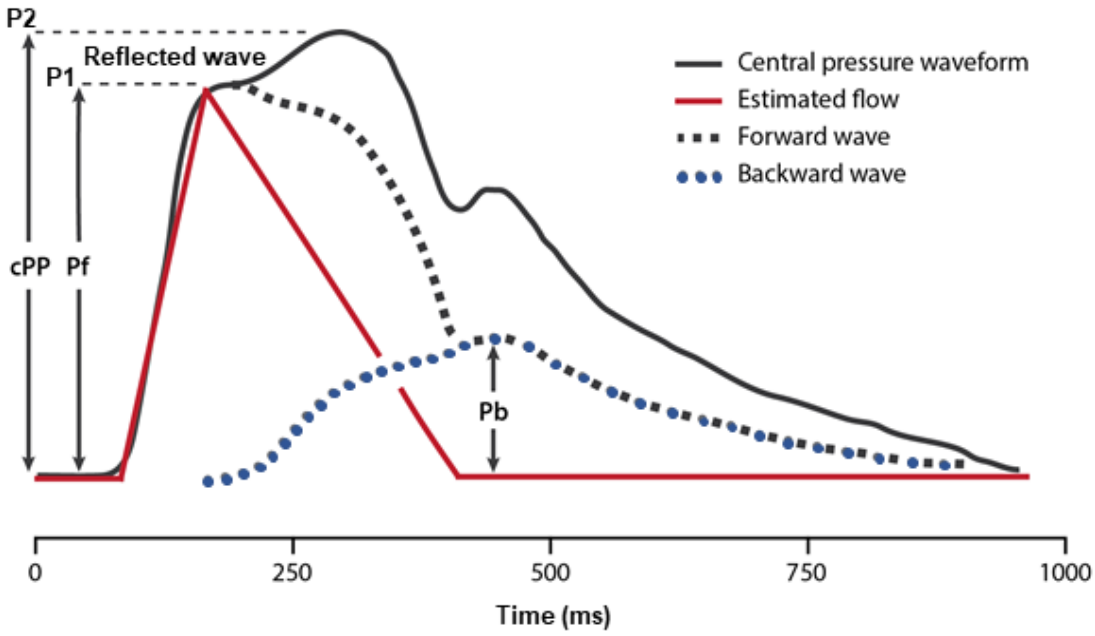

Figure S1.

Pressure-only pulse wave analysis. The central waveform is derived from the radial waveform by means of a validated transfer function. P1 and P2 indicate the first and second peak of the central waveform, cPP the central pulse pressure, and Pf and Pb the forward and reflected pulse wave amplitude. The central pressure waveform can be separated in its forward and backward pulse wave component using a triangular-shaped flow estimate. Start, peak and end of the estimated flow curve are derived from the ejection period and the first shoulder (P1) of the central pressure curve.

References

1. Aparicio LS, Barochiner J, Peuchot VA, Giunta DH, Martínez R, Morales MS et al. Comparing office, central, home and ambulatory blood pressure in predicting left ventricular mass. *Hipertens Riesgo Vasc* 2019; 36:5-13.

2. Cuffaro P, Morales M, Barochiner J, Rada M, Alfie J, Aparicio L et al. Validation of a new pizoelectric device for noninvasive measurement of central aortic systolic blood pressure. *Blood Press Monit* 2018; 23:49-51.

3. Jin Y, Kuznetsova T, Maillard M, Richter T, Thijs L, Bochud M et al. Independent relations of left ventricular structure with the 24-hour urinary excretion of sodium and aldosterone. *Hypertension* 2009; 54:489-495.

4. Stolarz-Skrzypek K, Kuznetsova T, Thijs L, Tikhonoff V, Seidlerova J, Richart T et al. Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. *J Am Med Ass* 2011; 305:1777-1785.

5. Wei FF, Trenson S, Monney P, Yang WY, Pruijm M, Zhang ZY et al. Epidemiological and histological findings implicate matrix Gla protein in diastolic left ventricular dysfunction. *PLoS One* 2018; 13:e0193967.

6. Liu YP, Thijs L, Kuznetsova T, Gu YM, Asayama K, Stolarz-Skrzypek K et al. Central systolic augmentation indexes and urinary sodium in a white population. *Am J Hypertens* 2013; 26:95-103.

7. Liu YP, Gu YM, Thijs L, Asayama K, Jin Y, Jacobs L et al. Do level and variability of systolic blood pressure predict arterial properties or vice versa? *J Hum Hypertens* 2013; 28:316-322.

8. Li Y, Wang JG, Nawrot T, Wang GL, Qian YS, Staessen JA et al. Are published characteristics of the ambulatory blood pressure generalizable to rural Chinese ? The JingNing population study. *Blood Press Monit* 2005; 10:125-134.

9. Li Y, Thijs L, Kuznetsova T, Zagato L, Struijker-Boudier H, Bianchi G et al. Cardiovascular risk in relation to a-addicin Gly460Trp polymorphism and systolic pressure. A prospective population study.1708. Hypertension 2005; 46:527-532.

10. Li Y, Staessen JA, Li LH, Gao PJ, Thijs L, Brand E et al. Blood pressure and urinary sodium excretion in relation to the A-1984G adrenomedullin polymorphism in a Chinese population. Kidney Intern 2006; 69:1153-1158.

11. Li Y, Wang JG, Gao PJ, Wang GL, Qian YS, Zhu DL et al. Interaction between body mass index and alcohol intake in relation to blood pressure in HAN and SHE Chinese. *Am J Hypertens* 2006; 19:448-453.

12. Li Y, Staessen JA, Sheng CS, Huang QF, O'Rourke M, Wang JG. Age dependency of peripheral and central systolic pressures: cross-sectional and longitudinal observations in a Chinese population. *Hypertens Res* 2012; 35:115-122.

13. Chirinos JA, Kips JG, Roman MJ, Medina-Lezama J, Li Y, Woodiwiss AJ et al. Ethnic differences in arterial wave reflections and normative equations for augmentation index. *Hypertension* 2011; 57:1108-1116.

14. Wang Y, Zhang DY, Guo QH, Cheng YB, Huang QF, Sheng CS et al. Short-term reproducibility of the 24-h ambulatory monitoring of brachial and central hemodynamics in untreated Chinese. *Blood Press* 2019; 28:250-257.

15. Kuznetsova T, Staessen JA, Kawecka-Jaszcz K, Babeanu S, Casiglia E, Filipovsky J et al. Quality control of the blood pressure phenotype in the European Project on Genes in hypertension. *Blood Press Monit* 2002; 7:215-224.

16. Wojciechowska W, Staessen JA, Nawrot T, Cwynar M, Sleidlerová J, Stolarz K et al. Reference values in White Europeans for the arterial pulse wave recorded by means of the ShygmoCor device. *Hypertens Res* 2006; 29:475-483.

17. Vartiainen E, Laatikainen T, Peltonen M, Juolevi A, Männistö S, Sundvall J et al. Thirty-five-year trends in cardiovascular risk factors in Finland. *Int J Epidemiol* 2010; 39:504-518.

18. Johansson JK, Puukka PJ, Jula AM. Interarm blood pressure difference and target organ damage in the general population. *J Hypertens* 2014; 32:260-266.

19. Odili AN, Ogedengbe JO, Nwegbu M, Anumak FO, Asala S, Staessen JA. Nigerian Population Research on Environment, Gene and Health (NIPREGH) — objectives and protocol. *J Biomed Res* 2014; 28:360-367.

20. Odili AN, Ameh VO, Ogedengbe J, Staessen JA. Quality of blood pressure phenotype in the Nigerian population research on environment gene and health. *Blood Press Monit* 2014; 19:220-225.

21. Odili AN, Thijs L, Hara A, Wei FF, Ogedengbe JO, Nwegbu MM et al. Prevalence and determinants of masked hypertension among black Nigerians compared with a reference population. *Hypertension* 2016; 67:1249-1255.

22. Odili AN, Chori BS, Danladi B, Yang WY, Zhang ZY, Thijs L et al. Electrocardiographic left ventricular hypertrophy in relation to peripheral and central blood pressure indices in a Nigerian population. *Blood Press* 2020; 29:39-46.

23. Świerblewska E, Wolf J, Kunicka K, Graff B, Polonis K, Hoffmann M et al. Prevalence and distribution of left ventricular diastolic dysfunction in treated patients with long-lasting hypertension. *Blood Press* 2018; 27:376-384.

24. Polonis K, Hoffmann M, Szyndler A, Wolf J, Nowak R, Becari C et al. A multilocus genetic risk score is associated with arterial stiffness in hypertensive patients : the CARE NORTH study. *J Hypertens* 2018; 36:1882-1888.

25. Majane OHI, Norton GR, Maseko M, Makaula S, Crowther N, Paiker J et al. The association of waist circumference with ambulatory blood pressure is independent of alternative adiposity indices. *J Hypertens* 2007; 23:1798-1806.

26. Norton GR, Maseko M, Libhaber E, Libhaber CD, Majane OHI, Dessein P et al. Is prehypertension an independent predictor of target organ damage in young-to-middle-aged persons of African descent? *J Hypertens* 2008; 26:2279-2287.

27. Shiburi CP, Staessen JA, Maseko M, Wojciechowska W, Thijs L, Van Bortel LM et al. Reference values for SphygmoCor measurements in South Africans of African ancestry. *Am J Hypertens* 2006; 19:40-46.

28. Redelinghuys M, Norton GR, Scott L, Maseko MJ, Brooksband R, Majane OHI et al. Relationship between urinary salt excretion and pulse pressure and central aortic hemodynamics independent of steady state pressure in the general population. *Hypertension* 2010; 56:584-590.

29. Booysen HL, Woodiwiss AJ, Sibiya MJ, Hodson B, Raymond A, Libhaber E et al. Indexes of aortic pressure augmentation markedly underestimate the contribution of reflected waves toward variation in aortic pressure and left ventricular mass. *Hypertension* 2015; 65:540-546.

30. Schutte AE, Huismans HW, van Rooyen JM, Malan L, Malan NT, Fourie CMT et al. A significant decline in IGF-I may predispose young Africans to subsequent cardiometabolic vulnerability. *J Clin Endocrinol Metab* 2010; 95:2503-2507.

31. Schutte AE, Schutte R, Huisman HW, van Rooyen JM, Fourie CMT, Malan NT et al. Are behavioural risk factors to be blamed for the conversion from optimal blood pressure to hypertensive status in Black South Africans? *Int J Epidemiol* 2012;1114-1123.

32. Wei FF, Drummen NEA, Schutte AE, Thijs L, Jacobs L, Petit T et al. Vitamin K dependent protection of renal function in multi-ethnic population studies. *EBioMed* 2016; 4:162-169.

33. Breet Y, Huisman HW, Kruger R, van Rooyen JM, Gafane-Matemane LF, Ware LJ et al. Pulse pressure amplification and its relationship with age in young, apparently healthy black and white adults. The African-PREDICT study. *Int J Cardiol* 2017; 249:387-391.

34. Maritz M, Fourie CMT, van Rooyen JM, Moss SJ, Schutte AE. Large artery stiffness is associated with gamma-glutamyltransferase in young, healthy adults: the African-PREDICT study. *J Am Soc Hypertens* 2016; 10:772-781.

35. Strauss M, Smith W, Wei W, Bagrov AY, Fedorova OV, Schutte AE. Large artery stiffness is associated with marinobufagenin in young adults: the African-PREDICT study. *J Hypertens* 2018; 36:2333-2339.

36. Mels CM, Delles C, Louw R, Schutte AE. Central systolic pressure and a nonessential amino acid metabolomics profile : the African Prospectie Study on the Early Detection

and Identification of Cardiovascular Disease and Hypertension. *J Hypertens* 2019; 37:1157-1166.

37. Alwan H, Pruijm M, Ponte B, Ackermann D, Guessous I, Ehret G et al. Epidemiology of masked hypertension and white-coat hypertension : the family-based SKIPOGH study. *PLoS One* 2014; 9:e92522.

38. Pruijm M, Ponte B, Ackermann D, Paccaud F, Guessous I, Ehret G et al. Associations of urinary uromodulin with clinical characteristics and markers of tubular function in the general population. *Clin J Am Soc Nephrol* 2016; 11:70-80.

39. van der Stouwe JG, Carmeli C, Aeschbacher S, Schoen T, Krisai P, Wenger G et al. Association of 24-hour blood pressure with urinary sodium excretion in healthy adults. *Am J Hypertens* 2018; 31:784-791.

40. Pivin E, Ponte B, Pruijm M, Ackermann D, Guessous I, Ehret G et al. Inactive matrix Gla-protein is associated with arterial stiffness in an adult population-based study. *Hypertension* 2015; 66:85-92.

41. Ponte B, Pruijm M, Ackermann D, Vuistiner P, Eisenberger U, Guessous I et al. Reference values and factors associated with renal resistive index in a family-based population study. *Hypertension* 2014; 63:136-142.

42. Luzardo L, Lujambio I, Sottolano M, da Rosa A, Robaina S, Arce F et al. Cohorte GEFA-HT-UY (GEnotipo, Fenotipo y Ambiente de la HiperTensión arterial en UruguaY). Protocolo and primeros resultatos. *Rev Méd Urug* 2013; 29:103-113.

43. Luzardo L, Sottolano M, Lujambio I, Robaina S, Thijs L, da Rosa A et al. Quality of the blood pressure phenotype in the GEnotipo, Fenotipo y Ambiente de la hipertensión arterial en UruguaY (GEFA-HT-UY) study. *Blood Press Monit* 2014; 19:339-345.

44. Lujambio I, Sottolano M, Luzardo L, Robaina S, Krul N, Thijs L et al. Estimation of glomerular filtration rate based on serum cystatin c vs. creatinine in a Uruguayan population. *Int J Nephrol* 2014; 837106.

45. Luzardo L, Lujambio I, Sottolano M, da Rosa A, Thijs L, Noboa O et al. 24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation : a feasibility study. *Hypertens Res* 2012; 35:980-987.

46. Boggia J, Luzardo L, Lujambio I, Sottolano M, Robaina S, Thijs L et al. The diurnal profile of central hemodynamics in a general Uruguayan population. *Am J Hypertens* 2016; 29:737-746.