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ASSOCIATION BETWEEN WITHIN-VISIT SYSTOLIC BLOOD PRESSURE VARIABILITY AND DEVELOPMENT OF PRE-DIABETES AND DIABETES AMONG OVERWEIGHT/OBESE INDIVIDUALS

Kaumudi J. Joshipura, BDS, MS, ScD^{a,b}, Francisco J. Muñoz-Torres, MPH^a, Maribel Campos, MD, MSc, MBA^a, Alba D. Rivera-Díaz, MD, LND^a, and Juan C. Zevallos, MD^c

^aCenter for Clinical Research and Health Promotion, University of Puerto Rico Medical Sciences Campus, School of Dental Medicine, San Juan, Puerto Rico

^bDepartment of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, United States

^cDepartment of Medical and Population Sciences Research, Herbert Wertheim College of Medicine, Florida International University, Miami, FL, United States

Abstract

Short-term blood pressure variability is associated with pre-diabetes/diabetes cross-sectionally, but there are no longitudinal studies evaluating this association. The objective of this study is to evaluate the association between within-visit systolic and diastolic blood pressure variability and development of pre-diabetes/diabetes longitudinally. The study was conducted among eligible participants from the San Juan Overweight Adults Longitudinal Study (SOALS), who completed the three-year follow-up exam. Participants were Hispanics, 40–65 years of age, and free of diabetes at baseline. Within-visit systolic and diastolic blood pressure variability was defined as the maximum difference between three measures, taken a few minutes apart, of systolic and diastolic blood pressure respectively. Diabetes progression was defined as development of pre-diabetes/diabetes over the follow-up period. We computed multivariate incidence rate ratios adjusting for baseline age, gender, smoking, physical activity, waist circumference and hypertension status. Participants with systolic blood pressure variability ≥ 10 mm Hg compared to those with < 10 mm Hg, showed higher progression to pre-diabetes/diabetes (RR=1.77, 95% CI: 1.30–2.42). The association persisted among never smokers. Diastolic blood pressure variability ≥ 10 mm Hg (compared to < 10 mm Hg) did not show an association with diabetes status progression (RR=1.20, 95% CI: 0.71–2.01). Additional adjustment of baseline glycemia, C-

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Corresponding author: Kaumudi J. Joshipura, BDS, MS, ScD, Center for Clinical Research and Health Promotion, University of Puerto Rico Medical Sciences Campus, School of Dental Medicine; Department of Epidemiology, Harvard T. H. Chan School of Public Health. Mailing address: Center for Clinical Research and Health promotion, Office A107, University of Puerto Rico Medical Sciences Campus, School of Dental Medicine, PO Box 365067 San Juan, PR, 00936-5067, Tel: 787-237-0009; 787-758-2525 ext. 2585 Fax: 787-763-4868, kaumudi.joshipura@upr.edu.

Conflict of Interest

The authors have nothing to disclose.

reactive protein, and lipids (reported dyslipidemia or baseline HDL or triglycerides) did not change the estimates. Systolic blood pressure variability may be a novel independent risk factor and an early predictor for diabetes, which can be easily incorporated into a single routine outpatient visit at none to minimal additional cost.

Keywords

Within-visit blood pressure variability; pre-diabetes; diabetes; hypertension; overweight; obesity

Introduction

The published literature has shown that blood pressure (BP) is not constant, and it undergoes natural oscillations (modulation) over the long-term (visit-to-visit) and short-term (within-visit or within 24 hours) (1–8). Several studies have shown that high visit-to-visit blood pressure variability (BPV) and high BP are strongly associated with increased cardiometabolic disorders including carotid artery atherosclerosis and stiffness, stroke, organ damage, and all-cause mortality (2, 3, 9, 10). One recent study among Japanese adults, where long-term visit-to-visit BPV was computed across baseline and three annual visits, showed a small elevated risk of diabetes of around 10% for an increment of 1 standard deviation (SD) or of 6 mm mercury (Hg) for systolic blood pressure variability (SBPV), and an increment of 1 SD or 4 mm Hg for diastolic (DBPV) (11). A study comparing 24 hour ambulatory blood pressure between 18 diabetics and 18 non-diabetics showed significantly higher crude systolic (SBP), diastolic (DBP) and mean daytime arterial blood pressure among diabetics compared to non-diabetics (5). Another small study also showed increased BP variability among diabetics during the day (12).

A bi-directional relationship between high BP and diabetes is suggested (13). A recent report showed that 20 mm Hg higher SBP and 10 mm Hg higher DBP were associated with a 58% and a 52% higher risk of diabetes respectively in a large cohort (14). The same report also showed a 77% higher pooled relative risk of diabetes for a 20 mm Hg higher than usual SBP in a meta-analysis among 30 studies with 17,388 incident diabetes events (14). Within-visit BPV assessed from repeated measures over a few minutes during an outpatient visit reflects a physiological transient fluctuation of autonomic stimulation, leading to a humoral response (1). Results from two cross-sectional studies suggest that higher within-visit BPV is associated with higher fasting plasma glucose, and with pre-diabetes/diabetes (8, 15).

Although there is evidence relating high blood pressure and long-term BPV with increased risk of diabetes, there are no longitudinal studies published to date evaluating within-visit BPV as a cause or consequence of pre-diabetes/diabetes. Although the causality may be bidirectional, in our study we hypothesized that the autonomic dysfunction, seen as short-term BPV, may impact the diagnosis of diabetes. Short-term BPV can be assessed easily during a routine clinical visit, with minimal if any additional cost compared to a single BP measure. Hence, within-visit BPV, could be potentially used in identifying subjects at increased risk of developing diabetes, and may have large potential for impacting clinical practice. Accordingly, we evaluate within-visit SBPV and DBPV as potential predictors of

development of pre-diabetes/diabetes within the San Juan Overweight Adults Longitudinal Study (SOALS).

Materials and Methods

Study overview

These analyses include SOALS participants who completed key components of the baseline and follow-up examination. The study was approved by the University of Puerto Rico Human Research Subjects Protection Office Institutional Review Board, and participants signed a written informed consent. SOALS is a longitudinal study conducted among civilian, non-institutionalized Hispanic adults recruited primarily from San Juan metropolitan area using flyers and various other means. The sample size was pre-determined for the primary aims relating periodontitis and pre-diabetes. Recruitment and baseline data collection started in 2011 and the follow up exam (planned for around 3 year follow up period) was completed in 2016. Our study population consists of multiracial individuals of Hispanics ethnicity, who reported their race as White (25%), Black (14%), and Mixed race (61%). A total of 1451 came for the baseline exam. Eligibility criteria for this cohort study include: 1) age between 40 and 65 years, 2) overweight or obese (body mass index of at least 25.0 kg/m²), 3) free of clinically diagnosed diabetes prior to the baseline exam. The baseline exclusion criteria are as follows: 1) physician-diagnosed type 1 or type 2 diabetes or taking either insulin or oral anti-hyperglycemic agents; 2) pregnancy; 3) physician-diagnosed hypoglycemia, congenital heart murmurs, heart valve disease, congenital heart disease, endocarditis, rheumatic fever, and hemophilia or bleeding disorders; 4) active dialysis treatment; 5) having undergone procedures related to cardiovascular disease; 6) severe health conditions or psychological or physical disabilities that would interfere with participation in the study; and 7) plans on moving away in the next three-year period. Participants with a provisional diagnosis of type 2 diabetes based on fasting plasma glucose ≥ 7 mmol/l (126 mg/dl), two-hour oral glucose tolerance ≥ 11.1 mmol/l (200 mg/dl), or HbA1c $> 6.5\%$ (48 mmol/mol), detected from the baseline blood tests, were further excluded. We completed baseline blood samples, interviews, and anthropometric measurements among 1206 participants who provided extensive contact information including additional contacts. Retention efforts included phone calls, letters and tokens. The follow-up exam had similar data collection procedures. From the 1206 participants, 950 (79%) who came to the follow-up visit were included; of the remaining, 6 were deceased, 68 refused to participate, 87 were not reached by phone, letters or e-mail, 41 moved out of Puerto Rico, 53 were reached but were unable to come (see figure 1), and 1 excluded from the analyses for missing physical activity data.

Blood Pressure Variability Assessment

Study nurses experienced in clinical research were individually trained utilizing audiovisual techniques to minimize observer bias. The double stethoscope was also utilized for training purposes and to reduce within and between observer variability (16). Calibration was conducted between the trainees and an experienced trainer using the double stethoscope simultaneously. Retraining was conducted as necessary during the three-year study follow-up. The criteria for passing the training (17), which includes 4 readings of a videotape and 3 simultaneous reading using a double stethoscope with an experienced trainer, were as

follows. a) The overall systolic and diastolic mean must lie within 1.96 SD from the standard mean. This criterion detects consistent bias in blood pressure readings. b) No more than one systolic or diastolic pair difference may lie beyond ± 1.96 SD from the expected zero value. This criterion tests the repeatability of blood pressure readings, which corresponds to an allowable range of ± 2 mm Hg. The gold standard Korotkoff auscultatory method with a mercury sphygmomanometer was utilized to assess the blood pressure of each participant after 5 minutes of rest in a quiet and relaxing setting (18). The palpatory method was used to obtain an approximation of the SBP and to ensure an adequate level of inflation (19). At the baseline exam, three serial measurements (with intervals of 1 minute between measures) were conducted in the upper arm of all participants in a sitting position, after the appropriate sphygmomanometer cuff width was selected based on the mid-arm circumference. The three readings were recorded and averaged for SBP and DBP. Several different measures of SBPV have been used in the literature such as standard deviation or coefficient of variation; we chose the maximum difference between the three measures taken over few minutes apart as the simplest and most clinically translatable measure. A cross-sectional report used cutoffs as follows: low-BPV (≤ 10 mmHg), moderate-BPV (11–20 mmHg), and high-BPV (> 20 mmHg) for evaluating the association between BPV and progression to pre-diabetes/diabetes (15). In our study, over 90% had SBPV and DBPV below 10 mm Hg; hence, individuals were categorized as having high (≥ 10 mm Hg) or low (< 10 mm Hg) SBPV and DBPV.

Glycemia assessment

Glucose and insulin levels were evaluated at baseline and follow-up at fasting, and after administration of a 75-g glucose load at 30, 60 and 120 minutes. Glucose was measured using an enzymatic colorimetric assay. Plasma insulin concentrations were analyzed using an immunochemiluminometric assay. The lab staff conducting these assays were unaware of the participants' BPV status, hence assessments were unbiased. Insulin resistance was estimated using HOMA-IR (Fasting glucose \times Fasting insulin)/405. HbA1c was measured with an assay based on a latex immunoagglutination inhibition method (DCA 2000+ Analyzer, Siemens Healthcare Diagnostics, NY, US).

We defined diabetes at each visit based on American Diabetes Association thresholds as having fasting glucose ≥ 7 mmol/l (126 mg/dl), 2-hour post load glucose ≥ 11.1 mmol/l (200 mg/dl) or HbA1c $\geq 6.5\%$ (48 mmol/mol); pre-diabetes as having fasting glucose ≥ 5.6 mmol/l (100 mg/dl) but < 7 mmol/l (126 mg/dl), 2-hour post load glucose ≥ 7.8 mmol/l (140 mg/dl) but < 11.1 mmol/l (200 mg/dl) or HbA1c $\geq 5.7\%$ (39 mmol/mol) but $< 6.5\%$ (48 mmol/mol); and normal glycemia if the three measurements were below the mentioned thresholds. We defined diabetes progression as a change in the diabetes classification from normal glycemia to pre-diabetes or from normal or pre-diabetes to diabetes during the follow-up period. In addition, participants who reported physician diagnosed diabetes during the follow-up period were classified as having diabetes progression at the follow-up exam.

Covariate assessment

Anthropometric measurements were taken in duplicate according to the NHANES III procedures, a third measure was taken when the first two measures differed by 5.0 mm, and the measures recorded were averaged for each individual. Body weight was measured using

a Tanita scale (Tanita Body Composition Analyzer-TBF-310A), and height was measured using a portable stadiometer (Seca Corporation, Hanover, MD). Body Mass Index (BMI) was calculated as weight in kg/height in m². Waist circumference was measured with a Gulick tape. A questionnaire was administered by trained interviewers and included socio-demographic characteristics, lifestyle factors, medical and family history, and time and frequency of physical activity during a typical week. Each activity was assigned a metabolic equivalent (MET) score based on the intensity. Activities from 3.0 to 6.0 metabolic equivalents (METs) were classified as moderate and activities with more than 6 METs as vigorous. Physical activity was categorized as meeting or not meeting WHO recommendations of at least 150 minutes of moderate-intensity aerobic physical activity per week, or at least 75 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination of moderate and vigorous activity (20). Participants were classified as hypertensive if they had physician diagnosis of hypertension, if they reported taking high blood pressure medication, and/or had high blood pressure at the baseline exam with systolic blood pressure (SBP) \geq 140 or diastolic blood pressure (DBP) \geq 90 (mmHg). Participants were classified as pre-hypertensive if they were not classified as hypertensive nor reported high blood pressure medication, and had SBP between 120 and 140 or DBP between 80 and 90 (mmHg).

Data analyses methods

The proportional hazards assumption for Cox was violated with crossing hazards, but the assumptions for the Poisson models were met. The results were similar for Cox and Poisson, and we present only the Poisson results here, which inherently factors variations in follow-up time (21, 22). Since we were analyzing a binary outcome, we obtained robust standard errors for the Poisson parameter estimates (23).

Major potential confounders were selected and included based on the literature (age, gender, smoking, physical activity, waist circumference, and hypertension status). Several additional potential confounders including fasting glucose, 2-hour post load glucose, HbA1c, insulin resistance measured as HOMA, C-reactive protein, or lipids (reported dyslipidemia or baseline HDL or triglycerides), family history of diabetes, dietary factors (fiber rich foods including fruits, vegetable, whole grain bread, and beans), and alcohol intake, were considered using the change in estimate procedure. We also explored the associations between SBPV and diabetes progression among sub-groups defined by age (\geq 55 vs. <55 years), gender, smoking (ever vs. never), physical activity (compliance with the WHO recommendations), BMI (overweight vs. obese), SBP (< 120 vs. \geq 120 mmHg) and DBP (< 80 vs. \geq 80 mmHg).

Results

For this cohort study, the mean follow-up was 2.97 years (SD = 0.24, range: 2.26–4.48, median = 2.96 years). From the 951 participants who completed follow-up, 1 person was excluded for missing physical activity data; the remaining 950 with complete data on the key variables were included in the analyses. The SBPV ranged from 0–36 mm Hg (mean=4.3, SD=3.4) and DBPV ranged from 0–28 mm Hg (mean=3.5 and SD=2.8). Table 1 presents the

description of participant characteristics at baseline, by high and low SBPV and DBPV. The group with SBPV ≥ 10 mm Hg was older, more physically active, less obese, more likely to have prior hypertension diagnosis, and smoked more compared to persons with SBPV < 10 mm Hg. The group with DBPV ≥ 10 mm Hg was more physically active, less obese, higher alcohol consumption, and sleep disordered breathing compared with persons with DBPV < 10 mm Hg. The groups with SBPV ≥ 10 mm Hg and with DBPV ≥ 10 mm Hg had higher diabetes status progression compared to low SBPV and low DBPV groups. The group with high SBPV also showed higher DBPV and vice versa. Individual SBP and DBP measures reduced with each subsequent measure in all groups. SBP was higher in groups with higher SBPV or DBPV, but there was no consistent difference for DBP.

A total of 213 participants developed pre-diabetes/diabetes. Of the normoglycemic individuals at baseline, 35% developed pre-diabetes and 2% developed diabetes; of the persons with pre-diabetes at baseline, 12% developed diabetes in the 3 years of follow-up. Table 2 shows results from multivariate Poisson models adjusted for important confounders. Participants with SBPV ≥ 10 mm Hg showed higher progression to diabetes compared to those with SBPV < 10 mm Hg (RR=1.77, 95% CI: 1.30–2.42) after adjustment for major risk factors for diabetes including age, gender, smoking, physical activity, waist circumference, and hypertension status. Participants with DBPV ≥ 10 mm Hg (compared to those with DBPV < 10 mm Hg) did not show a significant association with diabetes status progression (RR=1.20, 95% CI: 0.71–2.01) after similar adjustment. Adjustment of baseline fasting glucose, 2-hour post load glucose, HbA1c, insulin resistance measured as HOMA, C-reactive protein, or lipids (reported dyslipidemia or baseline HDL or triglycerides), family history of diabetes, dietary factors (fiber rich foods including fruits, vegetable, whole grain bread, and beans) and alcohol intake, showed that none had a substantial impact on the associations. Additional adjustment for mean SBP or DBP, or for hypertension medications associated with BPV in the literature (24) (calcium channel blocker and diuretics) also did not change the estimates.

The data is sparse to draw conclusions about differences in effects estimates across subgroups (not shown in tables), but importantly, the SBPV and diabetes progression association persisted among never smokers (RR=1.85, 95% CI: 1.21–2.84), and among people who did not take calcium channel blocker and diuretics (RR=1.83, 95% CI: 1.33–2.54). All sub-groups showed elevated diabetes status progression among high SBPV compared to low SBPV. Although the association was not significant among several sub-groups due to small numbers, consistency of the association within different subgroups suggest robustness of the associations.

Discussion

Our study shows a 77% higher progression to pre-diabetes/diabetes over a three-year follow-up period among participants with SBPV ≥ 10 mm Hg compared to participants with SBPV < 10 mm Hg. These results are independent of major risk factors and stronger than findings from a previously published cross-sectional study showing significant associations between high vs. low SBPV (> 10 mm Hg vs. ≤ 10 mm Hg) and pre-diabetes (16%) and diabetes

(40%) as detected by HbA1c (15). We did not find a significant association relating DBPV with diabetes status progression.

SBPV is associated with progression to pre-diabetes/diabetes independently of major risk factors for diabetes including age, low physical activity, adiposity, and baseline SBP, baseline glycemia, insulin resistance and dyslipidemia. The individual SBP and DBP measures reduced over time as may be expected with subsequent measurements in the same visit. Importantly, the SBPV association was not driven by SBP or DBP, which were controlled in the analyses.

The SBPV association remained similar after controlling for C-reactive protein, suggesting that the association was not likely to be explained by inflammation, although we do not have data on IL-6 or TNF- α or oxidative stress markers, which may be more important in this context. Known risk factors for BPV include extrinsic environmental and behavioral risk factors such as, physical activity, sleep disturbances and emotional stimuli such as stress(25–28); and intrinsic cardiovascular regulatory mechanisms such as autonomic dysfunction, disturbed baroreceptor sensitivity, humoral response and rheological factors have also been proposed (29). Another potential risk factor for BPV may be neuroendocrine system stimulation via increase of sympathetic tone. Emotional stress elicits autonomic response, which increase sympathetic activity, resulting in elevated blood pressure. Prolonged stimulation and eventual dysregulation of the sympathetic stimuli may lead to BPV (28, 30, 31). Based on our crude descriptive data presented in Table 1, SBPV seems associated with smoking and physical activity in our study, whereas DBPV is positively associated with male gender, physical activity, alcohol consumption and sleep disturbances, and inversely related with hypertension diagnosis and medications. The exact mechanism of physiological and environmental factors involved in the variability of blood pressure has not been well described (32). The primary mechanism of blood pressure modulation, which impacts BPV, is postulated to occur via autonomic nervous system outflow and humoral response (33). Diabetes free participants who presented an increase of 10 mmHg in SBPV at baseline, had significantly higher risk of developing pre-diabetes/diabetes approximately 3 years later. The potential association between high BPV and increased risk of pre-diabetes/diabetes may be mediated by persistent autonomic dysregulation, which in turn may lead to a humoral response by the pancreas (34, 35). Increased sympathetic tone has been proposed as a mechanism of increased reactivity of vasculature of the neuroendocrine system (36). BPV is a promoter of endothelial dysfunction (37), and autonomic dysregulation resulting from SBPV may lead to end organ damage and increased glycemia.

Since some of the factors impacting BPV may also independently increase the risk for hyperglycemia, it is possible that such unmeasured common risk factors may explain part of the association between SBPV and pre-diabetes/diabetes. One important such factor is arterial stiffness or lack of arterial distensibility (38). Although the assessment of clinical and neuroendocrine markers of arterial stiffness such as pulse pressure or hormone modulation was beyond the scope of this study and we did not collect resting heart rate measures at baseline, we did control for several well recognized contributing risk factors for arterial stiffness, such as age, obesity, physical activity and blood pressure. The association between short term systolic BPV and pre-diabetes/diabetes remained significant independent

of such factors. Measures of arterial stiffness are not easy to assess at the primary care level, whereas, the capacity to determine the blood pressure variability is within reach of the most basic clinic settings, and can be easily assessed in day to day clinical practice. Importantly, this is the first longitudinal study suggesting that SBPV may be an early predictor of pre-diabetes/diabetes, independent of major traditional risk factors for diabetes and may be a surrogate for arterial stiffness.

The association between SBP and pre-diabetes/diabetes is seen within different subgroups defined by age, gender, smoking, physical activity, overweight/obese, SBP and DBP (suggesting robustness, although power to detect significant associations is limited in many subgroups). Importantly, the association is significant among never smokers and among people who did not take pertinent hypertension medications, suggesting that it is independent of confounding by smoking and medications that may affect BPV.

In this population of overweight/obese adults, high systolic blood pressure variability showed a significant association with subsequent increased progression to pre-diabetes/diabetes. The associations between BPV and pre-diabetes/diabetes need to be replicated in additional longitudinal studies, in different populations, and mechanistic pathways need to be evaluated. Regardless of whether the association is causal, High SBPV could alert the health care provider to consider the patient as high risk for diabetes. SBPV could thus be an important marker for progression of diabetes in a population and could be used for identifying high-risk groups for preventive interventions. Among people identified with high SBPV, promotion of preventive lifestyle measures could help delay or prevent diabetes; furthermore, timely screening for diabetes as appropriate for this high risk group, could help delay or prevent diabetes related comorbidities. The potential return of investment through the prevention or delay in onset of diabetes and associated co-morbid conditions justifies targeted additional health promotion, screening and follow up efforts in such high risk individuals.

In conclusion, the findings suggest that high BPV could potentially be a novel modifiable risk factor amenable to lifestyle and pharmacological intervention, which could impact both cardiovascular as well as metabolic health through the prevention or delay of development of pre-diabetes/diabetes. BPV could be easily assessed clinically to identify individuals for primary and secondary prevention interventions.

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Summary Table

What is known about this topic?

- Several studies have shown that high visit-to-visit blood pressure variability (BPV) and high blood pressure (BP) are strongly associated with increased cardiometabolic disorders, stroke, organ damage, and all-cause mortality.
- Long-term visit-to-visit BPV and variation in BP assessed by ambulatory blood pressure monitoring has been associated with elevated cardiometabolic risk.
- Only two published cross-sectional studies evaluated within-visit BPV, and found higher within visit BPV associated with higher fasting plasma glucose, and with pre-diabetes/diabetes.

What this study adds?

- This is the first longitudinal study evaluating whether within-visit BPV is associated with development of pre-diabetes/diabetes.
- The results show that within visit systolic blood pressure variability was associated with 77% higher pre-diabetes/diabetes, independent of major diabetes risk factors.
- This study suggests a novel early predictor and potential novel risk factor for pre-diabetes/diabetes that can be easily evaluated in routine clinical visits with none to minimal cost.

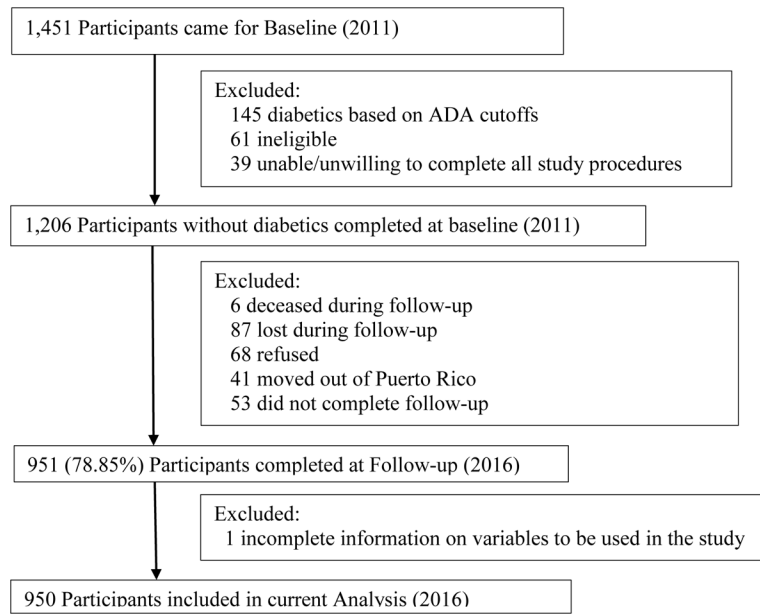


Figure 1. Flow Chart of the San Juan Adults Longitudinal Study (SOALS) Participants' Tracking

Table 1

Baseline Characteristics by Blood Pressure Variability

	SBPV < 10, mm Hg (N = 867)	SBPV ≥ 10, mm Hg (N = 83)	DBPV < 10, mm Hg (N = 912)	DBPV ≥ 10, mm Hg (N = 38)
Age, mean (SD), years	50.4 (6.8)	52.6 (6.8)	50.6 (6.8)	49.7 (6.4)
Female, No. (%)	638 (73.6)	66 (79.5)	680 (74.6)	24 (63.2)
Current smoker, No. (%)	154 (17.8)	19 (22.9)	167 (18.3)	6 (15.8)
Meeting WHO physical activity goals, No. (%)	472 (54.4)	51 (61.5)	499 (54.7)	24 (63.2)
Obese, No. (%)	558 (64.4)	48 (57.8)	586 (64.3)	20 (52.6)
Waist circumference, mean (SD), mm	1062.1 (144.4)	1048.5 (130.3)	1061.2 (142.6)	1052.3 (158.2)
Alcohol consumption, mean (SD), grams per day	2.3 (5.8)	2.0 (4.2)	2.2 (5.6)	3.5 (6.5)
Sleep breathing disorder, No. (%)	38 (4.4)	3 (3.6)	37 (4.1)	4 (10.5)
Hypertension status, No. (%)				
Pre-hypertension	271 (31.3)	21 (25.3)	282 (30.9)	10 (26.3)
Hypertension	404 (46.6)	44 (53.0)	430 (47.2)	18 (47.4)
SBPV, mean (SD), mm Hg	3.6 (2.1)	12.3 (4.2)	4.2 (3.3)	7.2 (5.0)
DBPV, mean (SD), mm Hg	3.3 (2.5)	5.3 (4.6)	3.1 (2.0)	12.3 (4.8)
Fasting glucose, mean (SD), mmol/L	5.1 (0.5)	5.2 (0.5)	5.1 (0.5)	5.2 (0.5)
2-hour post load glucose, mean (SD), mmol/L	6.4 (1.6)	6.5 (1.7)	6.4 (1.7)	6.1 (1.6)
HbA1c % (SD) mmol/mol	5.7 (0.3)	5.7 (0.3)	5.7 (0.3)	5.7 (0.3)
HOMA-IR, mean (SD)	2.5 (1.7)	2.3 (1.3)	2.5 (1.7)	2.1 (0.9)
C reactive protein, mean (SD), mmol/L	55.8 (60.7)	42.4 (43.8)	55.7 (60.2)	28.2 (26.3)
Diabetes status progression, No. (%)	182 (21.0)	31 (37.4)	202 (22.2)	11 (29.0)
SBP 1 st measurement	128.6(16.6)	136.8(22.9)	129.2(17.4)	132.3(17.9)
SBP 2 nd measurement	127.9(16.4)	133.4(22.4)	128.2(17.0)	130.8(18.9)
SBP 3 rd measurement	127.5(16.1)	130.0(21.8)	127.6(16.5)	130.5(21.1)
DBP 1 st measurement	81.0(9.6)	82.0(12.5)	81.0(9.7)	85.4(13.4)
DBP 2 nd measurement	80.8(9.8)	80.6(12.6)	80.8(9.7)	80.6(16.8)
DBP 3 rd measurement	80.7(9.6)	79.6(12.0)	80.7(9.6)	79.6(14.6)

SD= Standard Deviation. SBPV= Systolic Blood Pressure Variability. DBPV= Diastolic Blood Pressure Variability. HbA1c= Hemoglobin A1C. HOMA=Homeostatic Model Assessment-Insulin Resistance Index.

Table 2

Incidence Rate Ratios (IRR) relating within-visit blood pressure variability and diabetes status progression

SBPV 10 mm Hg (Ref = SBPV < 10 mm Hg)	Diabetes status progression	
	IRR	95% CI
Adjusted for age, gender and smoking	1.81	1.33–2.47
Multivariate *	1.77	1.30–2.42
DBPV 10 mm Hg (Ref = DBPV < 10 mm Hg)	IRR	95% CI
Adjusted for age, gender and smoking	1.24	0.75–2.07
Multivariate *	1.20	0.71–2.01

SBPV= Systolic Blood Pressure Variability

DBPV= Diastolic Blood Pressure Variability

* Adjusted for age (years), gender, smoking (never, former, current), physical activity (meeting WHO guidelines), waist circumference (mm), and hypertension status: hypertension if reported physician diagnosis of hypertension or high blood pressure medication, and/or high blood pressure at the baseline exam with systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 (mmHg); and pre-hypertension if no hypertension and either SBP between 120 and 140 or DBP between 80 and 90 (mmHg).

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