# BLOOD PRESSURE VARIABILITY AND AGE-RELATED BLOOD PRESSURE PATTERNS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**ABSTRACT**

BACKGROUND

Despite the high prevalence of cardiovascular disease among patients with systemic lupus erythematosus, the relationship between age, blood pressure, and blood pressure variability (BPV) is not well understood. We studied visit-to-visit BPV, its relationship to age, clinical, demographic characteristics and its potential role as a cardiovascular risk factor in patients with SLE.

METHODS

We analyzed systolic and diastolic blood pressure measures in our cohort using mixed effects regression models. From these models, we then obtained estimates of the mean blood pressure, the visit-to-visit standard deviation and the between-person standard deviation. The estimated means were compared to general population using data from the National Health Statistics Reports from 2001-2008. In addition, we examined the relationship between blood pressures (means, variances), patient demographic, clinical characteristics, and subsequent cardiovascular events.

RESULTS

The mean systolic blood pressure (SBP) in SLE increased with age and was significantly higher in younger patients compared to the general population. BPV in systemic lupus was elevated across all age. BPV was significantly higher in African Americans, in patients with traditional cardiovascular risk factors, those with high disease activity, and in patients taking prednisone. Hydroxychloroquine was associated with significantly lower BPV. Within-person variability in diastolic blood pressure of ≥9mmHg was highly associated with cardiovascular events in a multivariate analysis.

CONCLUSION

Age-related blood pressure patterns in SLE differ from the general population. Increased visit-to-visit BPV is affected by many disease-specific and traditional cardiovascular factors. Increased diastolic BPV is highly associated with cardiovascular events in SLE.

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**ABBREVIATIONS**

SLE- Systemic Lupus Erythematosus

ACR- American College of Rheumatology

RR- Relative Risk

NHANES- National Health and Nutrition Examination Survey

SLICC- Systemic Lupus International Collaborating Clinics

SD- standard deviation

SBP- systolic blood pressure

DBP- diastolic blood pressure

SE- standard error

## INTRODUCTION

Based on 2007 to 2010 data, 33% of US adults over 20 years of age had hypertension. This represented 78 million US adults with hypertension (1). It is estimated that the implementation of the new 2017 American College of Cardiology and American Heart Association definition of hypertension (over 130/80 mmHg) will result in nearly half (46 percent) of the U.S. adult population being classified as hypertensive(2). The National Health and Nutritional Examination Survey (NHANES) (3) and the Framingham Study (4) demonstrated that aging in the general population is accompanied by steady increases in systolic blood pressure and gradual declines in diastolic blood pressure. Elderly hypertensive patients tend to exhibit isolated systolic hypertension and an elevated pulse pressure as a result of reduced arterial compliance, while hypertensive individuals younger than 50 years of age usually exhibit systolic and diastolic hypertension and a narrowed pulse pressure, reflecting increased peripheral vascular resistance(5).

Mean blood pressure is widely considered to be of primary importance as a risk factor for cardiovascular disease (6) and in diagnosis and treatment of hypertension (7). Visit-to-visit variability in blood pressure was previously considered an obstacle to the reliable estimation of usual blood pressure (8,9). Visit-to-visit variability in measured clinic blood pressure is common (10–12) and guidelines recommend continued monitoring or 24-hour ambulatory blood-pressure monitoring in patients with episodic hypertension (13,14) with treatment decisions based on mean blood pressure.

Rothwell et al. however demonstrated that visit-to-visit variability in blood pressure is increased in cohorts at high risk of stroke (11,15), that visit-to-visit variability in systolic blood pressure is a powerful predictor of stroke and coronary events independent of mean systolic blood pressure(16). Increased visit-to-visit blood pressure variability has been shown to be a predictor of all-cause mortality and cardiovascular mortality (17) and has been associated with decreased endothelial function (18), albuminuria and microalbuminuria (19), left ventricular diastolic dysfunction (20), and cognitive impairment (21).

Patients with systemic lupus erythematosus have a significantly increased risk of cardiovascular events due to atherosclerosis. The latest data from the Hopkins cohort estimates the risk of cardiovascular events among lupus patients to be 2.66 times higher compared to the general population (22). Traditional Framingham cardiovascular risk factors do not account for the entire risk in SLE patients (23). In the Hopkins Lupus cohort, 74 percent of patients are hypertensive (24). Over the first three years of follow up the percentage of hypertensive SLE patients in the SLICC inception cohort increased from 39.2 to 58.3 percent (25). Despite the high prevalence of cardiovascular events in SLE, it is not known whether blood pressure patterns are similar to the general population and differ with age, whether blood pressure variability is increased in SLE patients and whether it plays a role in the highly elevated cardiovascular risk in SLE patients. We thus hypothesized that the blood pressure patterns differ in SLE compared to the general population, that visit-to-visit blood pressure variability is increased and that it is an independent cardiovascular risk marker.

## METHODS

*Patients and Activity Indices.* As previously described (26), the Hopkins Lupus Cohort is a prospective cohort study of predictors of lupus flare, atherosclerosis, and health status in SLE. The study cohort includes all patients at the Hopkins Lupus Center who have a clinical diagnosis of SLE and give informed consent to participate in the study. Subjects enrolled in the cohort are followed quarterly or more frequently if clinically necessary. The clinical features, laboratory testing, and damage accrual data are recorded at the time of entry into the cohort and are updated at subsequent visits. The Hopkins Lupus Cohort has been approved by the Johns Hopkins University School of Medicine Institutional Review Board (NA_00039294) and complies with the Health Insurance Portability and Accountability Act. All patients gave written informed consent.

Ninety-five percent of patients fulfilled 4 or more of the American College of Rheumatology (ACR) 1982 revised classification criteria for SLE (27,28) and the SLICC classification criteria for SLE (29). Disease activity was measured with the SELENA revision of the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index instrument score (30) and the Physician Global Assessment (31).

Blood pressure was measured at each visit using a Carescape Dinamap V100 monitor which was calibrated once every 12 months according to manufacturer guidelines. Patients were in a seated position with the arm supported at heart level. Cuff sizes used included adult small (23-33cm) and adult large (31-40cm).

The analyses were based on different subsets of patients from the cohort. Each subset was approximately 92% female. Most (60%) were under 40 at cohort entry while a small proportion (6%) were 60 or older. Most were either Caucasian (55%) or African-American (38%).

*Statistical methods for estimating means and variances of blood pressure in lupus patients.* The mean systolic and diastolic blood pressure measures in this cohort were estimated using random intercept models, fit by restricted maximum likelihood. Using this approach, we obtained estimates of the mean blood pressure, the within-person standard deviation (i.e., the standard deviation of individual's blood pressure around their personal mean) and the between-person standard deviation (i.e., the standard deviation of the person-specific mean blood pressures.

To compare means with national data from 2001-2008, we analyzed data from 22,672 clinic visits of 1509 cohort members that took place between 2001 and 2008. Of the 1509 patients, 661 (44%) contributed less than 10 visits, 329 (22%) contributed 10-19 visits, and 520 (34%) contributed 20 or more visits. The estimated means were compared to the mean systolic and diastolic pressures in the general population using data from the National Health Statistics Reports (19,921 adults aged 18 and over with blood pressure estimates calculated using the mean of up to three measurements). (32) To obtain more precise estimates of the means and variances of blood pressure by age, we used a larger sample, including data from 52,791 cohort visits of 2128 patients seen from 1987 to 2013.

*Statistical methods for the analysis of the relationship between clinical and demographic characteristics and blood pressure variability.* This analysis was based on 63,890 clinic visits of 2525 cohort members from 1987 to 2018. Within and between-patient blood pressure variability was estimated using random intercept models. The statistical significance of differences between clinical subgroups with respect to blood pressure variability was determined using likelihood ratio tests.

*Statistical methods for the analysis of the relationship between blood pressure parameters and cardiovascular events.* This analysis was based on 1340 cohort members who had at least 8 clinical assessments of blood pressure in the cohort between 1987 and 2013. They were 1235 (92%) female. The average duration of follow-up per patient was 74 months (6.2 years) years. 459 (34%) were followed for less than 3 years, 331 (25%) were followed for 3-6 years, 210 (16%) were followed for 6-9 years, and 340 (25%) were followed for 10 or more years.

Cardiovascular events were defined as either stroke, myocardial infarction, incident angina, a coronary procedure (coronary artery bypass graft surgery or percutaneous coronary intervention), or claudication. Considering only the first cardiovascular event for each person, there were 105 events. This is a rate of 12.6 per thousand person-years. Of these, 60 were strokes, 23 were myocardial infarctions, 24 were angina or coronary procedures, 14 were claudications, and 3 were mixed.

For each month of follow-up for a patient in the cohort, the previous 8 blood pressure measurements were included in the analysis. The following variables were calculated based on those most recent past 8 measures: mean prior systolic blood pressure and diastolic blood pressure, standard deviation of prior systolic and diastolic blood pressure, and coefficient of variation of prior systolic and diastolic blood pressure. This information was then linked with whether the patient had a cardiovascular event in that month. Person-months were aggregated, and the risks of a cardiovascular events by monthly characteristics were calculated. Person-months after a previous cardiovascular event were excluded. In addition to adjusting for age, race, and sex, in this table, the rate ratios are also adjusted for diabetes, cholesterol>=240mg/dl, body mass index over 25, most recent prednisone dose, and past or current smoking.

## RESULTS

Table 1 compares the mean blood pressure in the Hopkins Lupus cohort to the NHANES mean blood pressure in broad age groups from 2001-2008 (32). The systolic blood pressure in SLE follows the trend of increase with age seen in the general population. Systolic blood pressure was significantly higher among young SLE patients, regardless of ethnicity or sex. With age, this difference narrowed, only to be reversed in women older than 60 years of age ($p<0.001$), but not in men.

Table 2 provides estimates of the mean and standard deviation of systolic and diastolic blood pressure in SLE patients in each decade of life. There are two components of standard deviation: 1) standard deviation within a person around his/her personal mean blood

pressure, and 2) standard deviation between people with respect to personal mean blood pressure. The total standard deviation is determined by the component standard deviations. Blood pressure variability in SLE is elevated across all age groups. Within- person standard deviation of systolic blood pressure increased with age and ranged between 12.2 mmHg among 20-year olds and 16.7 mmHg among 80-year olds, while diastolic blood pressure variability remained stable through all age groups and ranged between 8.7 mmHg and 8.9 mmHg. These values are substantially higher than the within-person blood pressure variability reported by NHANES, i.e 7.7 mmHg for systolic blood pressure and 5.8 mmHg for diastolic blood pressure(33), but is comparable to previously published data in stroke cohorts (34–36).

Table 3 shows the relationship between blood pressure variability and clinical and demographic characteristics. Blood pressure variability was statistically significantly higher ($p<0.0001$) in African-American patients. High disease activity (SLEDAI>4), positive anti-dsDNA, hypocomplementemia, and antiphospholipid antibodies were all significantly ($p<0.0001$) associated with higher blood pressure variability. Hypercholesterolemia, diabetes, and smoking were also associated with higher blood pressure variability ($p<0.0001$). Patients on hydroxychloroquine had significantly ($p<0.0001$) lower blood pressure variability, while blood pressure variability increased with prednisone dose and was significantly ($p<0.0001$) higher in patients taking prednisone >12.5 mg/day.

Table 4 shows the relationship between systolic and diastolic blood pressure summary measures (based on the prior eight blood pressure assessments) and rates of cardiovascular events in the Hopkins Lupus Cohort. Visit-to-visit systolic blood pressure variability of ≥14mmHg (RR=1.9 (1.0, 3.3), $p<0.05$) and diastolic blood pressure variability of ≥9mmHg (RR=2.5 (1.3, 4.9), $p<0.01$) were predictive of future cardiovascular events in a univariate analysis. After adjustment for age, ethnicity, sex, diabetes, hypercholesterolemia, body mass index over 25, most recent prednisone use, and smoking, diastolic blood pressure variability of ≥9mmHg (RR=2.1 (1.0, 4.1), $p<0.05$).

The mean systolic blood pressure in the previous 8 visits was a stronger predictor of cardiovascular events than any other blood pressure measurement. Table 5 shows the association between the other measures of recent blood pressure and cardiovascular events after adjustment for age, race, sex, and mean systolic blood pressure in past 8 visits. None of the measurements were significantly associated with events after these adjustments. In contrast, for every model shown in the table, mean systolic blood pressure was a significant predictor of cardiovascular events with odds ratios ranging from 1.5 to 1.7 per standard deviation increase.

## DISCUSSION

Accelerated atherosclerosis remains a major cause of morbidity and mortality in patients with systemic lupus and other autoimmune diseases(37). Traditional Framingham cardiovascular risk factors do not account for the entire risk in systemic lupus and the search for disease specific factors that elevate this risk has been ongoing for decades.

Compared to general population data from the National Health Statistics Reports, systolic blood pressure in SLE follows a similar trend of increase with age with substantially higher mean systolic blood pressure among the young (age 18-39) regardless of ethnicity. With age, we observe sex-specific patterns among SLE patients with elderly females (age 60+), regardless of ethnicity, having statistically significantly lower mean systolic blood pressure compared to their non-SLE counterparts. This trend of reversal is not seen among men, where SLE patients have higher mean systolic blood pressure among all age groups, although the difference loses its statistical significance among the elderly.

In contrast to mean systolic blood pressure, the mean diastolic blood pressure is higher in SLE patients among all age groups regardless of ethnicity or sex except for middle aged Caucasian women (age 40-59) who had a statistically significantly lower mean diastolic blood pressure. In contrast to women where all age groups had statistically significant differences in diastolic blood pressure compared to the general population, only elderly Caucasian men and young African American men had significantly higher mean diastolic blood pressure compared to their counterparts in NHANES.

Systolic blood pressure variability in SLE expressed as within-person standard deviation and between-person standard deviation rises with age in contrast to the diastolic blood pressure variability which remains unchanged. The average intraindividual standard deviations for systolic blood pressure were 14.1 in our cohort, comparable to data from stroke cohorts: 13.6 in UK-TIA trial(34), 15.0 in the Dutch TIA trial(38), and 13.9 mm Hg in the ECST(39). These values are substantially higher than the reported standard deviation for systolic blood pressure in the general population from the NHANES survey which was 7.7 mmHg(33). For diastolic blood pressure, the average intraindividual SD was 8.8, compared to 7.6, 7.8, and 7.4 mm Hg, respectively in stroke cohorts. These values are also higher than the within-person diastolic blood pressure variability reported by NHANES of 5.8 mmHg. It should be noted, however, that in NHANES, blood pressure variability was based on measures relatively close in time (median of 17 days apart) and based on averages of two measures at each visit.

Blood pressure variability in SLE is affected by both traditional cardiovascular risk factors and disease-specific factors. Among traditional cardiovascular risk factors, diabetes, hypercholesterolemia, and smoking were associated with higher blood pressure variability. Surprisingly, patients with a body mass index <20 had higher blood pressure variability than those with normal weight or obese patients, possibly related to higher disease activity in this subgroup. A SLEDAI>4, anti-dsDNA positivity, and hypocomplementemia were also associated with higher blood pressure variability. Blood pressure variability increased with higher prednisone doses and was highest in patients taking >12.5mg/day. Blood pressure variability was significantly higher among African Americans. Hydroxychloroquine use was protective and was associated with significantly lower blood pressure variability.

Visit-to-visit variability in systolic blood pressure ≥14mmHg and diastolic blood pressure ≥9mmHg were highly associated with cardiovascular events ($p<0.05$) in a univariate

analysis. After adjustments, only visit-to-visit diastolic blood pressure variability remained significantly ($p<0.05$) associated with cardiovascular events.

In contrast to the stroke populations, blood pressure variability in systemic lupus patients was not an independent cardiovascular risk factor- after adjusting for mean systolic blood pressure none of the studied measures was significantly associated with cardiovascular events.

There is no evidence that long-term blood pressure variability directly causes cardiovascular outcomes, but the current approach in patients with history of stroke or coronary artery disease is to consider correctable causes when unexpected blood pressure changes occur(40). Similarly, when faced with a lupus patient who has high blood pressure variability, one should consider correctable underlying causes, for example high dose prednisone or noncompliance with hydroxychloroquine. There is evidence of an antihypertensive drug class effect on blood pressure variability in stroke patients, namely that calcium channel blockers and thiazide diuretics decrease long term variability, while beta-blockers, angiotensin receptors blockers, and angiotensin converting enzyme inhibitors increase the blood pressure variability(41). It is intriguing to consider the future possibility of pharmacologically modifying blood pressure variability in lupus patients and the effect it could have on cardiovascular outcomes.

## SUMMARY

Age-related blood pressure patterns differ in patients with lupus with significantly higher mean systolic and diastolic blood pressure in younger patients, a difference that diminishes with age and reverses in women over 60 years of age. Visit-to-visit systolic and diastolic blood pressure variability in SLE rises with age and is comparable to the one described in stroke cohorts. Blood pressure variability in lupus is higher in patients with traditional cardiovascular risk factors, like diabetes, hypercholesterolemia, and smoking, but also in patients with high disease activity, those taking prednisone, and in patients of African American ethnicity. Hydroxychloroquine use is associated with significantly lower blood pressure variability. Increased visit-to-visit diastolic blood pressure variability is highly associated with cardiovascular events in systemic lupus, but mean blood pressure remains the dominant cardiovascular risk factor in this population.

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Table 1: Comparison of the Hopkins Lupus Cohort with the NHANES Sample with Respect to Mean Systolic and Mean Diastolic Blood Pressure from 2001-2008 by Age and Ethnicity

| Sex | Ethnicity | Age (years) | Mean (SE) SBP in Cohort | Mean (SE) SBP in NHANES | P-value | Mean (SE) DBP in Cohort | Mean (SE) DBP in NHANES | P-value |
|---|---|---|---|---|---|---|---|---|
| Female | Caucasian | 18-39 | 117.9 (0.5) | 109 (0.3) | <0.0001 | 71.1 (0.4) | 68 (0.3) | <0.0001 |
| | | 40-59 | 122.4 (0.6) | 120 (0.5) | 0.002 | 71.7 (0.4) | 74 (0.4) | <0.0001 |
| | | 60+ | 132.1 (1.2) | 138 (0.6) | <0.0001 | 70.7 (0.7) | 67 (0.4) | <0.0001 |
| | African American | 18-39 | 121.7 (0.7) | 114 (0.5) | <0.0001 | 74.4 (0.5) | 69 (0.4) | <0.0001 |
| | | 40-59 | 129.5 (0.8) | 128 (0.9) | 0.21 | 76.4 (0.4) | 75 (0.6) | 0.052 |
| | | 60+ | 134.6 (1.8) | 144 (1.2) | <0.0001 | 75.1 (1.1) | 70 (0.5) | <0.0001 |
| | | | | | | | | |
| Male | Caucasian | 18-39 | 125.7 (2.1) | 118 (0.3) | 0.0003 | 73.3 (1.7) | 70 (0.3) | 0.056 |
| | | 40-59 | 127.5 (1.5) | 124 (0.5) | 0.027 | 76.3 (0.9) | 76 (0.3) | 0.75 |
| | | 60+ | 135.7 (4.1) | 132 (0.6) | 0.37 | 75.6 (2.3) | 69 (0.4) | 0.0047 |
| | African American | 18-39 | 130.8 (2.2) | 121 (0.4) | <0.0001 | 77.3 (2.6) | 71 (0.4) | 0.017 |
| | | 40-59 | 133.4 (2.6) | 129 (0.8) | 0.11 | 79.1 (1.6) | 79 (0.6) | 0.95 |
| | | 60+ | 143.2 (9.5) | 137 (0.9) | 0.52 | 81.3 (7.9) | 71 (0.9) | 0.20 |

SE- standard error; SBP- systolic blood pressure; DBP- diastolic blood pressure

Table 2. Mean and Variance of Systolic and Diastolic Blood Pressure by Decade of Life in SLE.

| Decade of life | Mean (95%CI) SBP(mm Hg) | Within-person SD of SBP | Between-person SD of SBP | Total SD of SBP | Mean (95%CI) DBP (mmHg) | Within-person SD of DBP | Between-person SD of DBP | Total SD of DBP |
|---|---|---|---|---|---|---|---|---|
| 20's | 119.8 (119.0, 120.7) | 12.5 | 10.2 | 16.1 | 73.4 (72.8, 74.1) | 9.0 | 7.8 | 11.9 |
| 30's | 120.4 (119.7, 121.2) | 13.2 | 10.7 | 17.0 | 74.0 (73.4, 74.5) | 8.9 | 8.0 | 12.0 |
| 40's | 124.3 (123.6, 125.2) | 14.4 | 11.6 | 18.5 | 75.2 (74.6, 75.7) | 8.8 | 7.3 | 11.5 |
| 50's | 127.7 (126.6, 128.7) | 14.8 | 12.3 | 19.2 | 74.2 (73.4, 74.9) | 8.6 | 8.0 | 11.7 |
| 60's | 131.9 (130.3, 133.5) | 16.0 | 11.6 | 19.8 | 72.9 (71.9, 74.0) | 8.9 | 8.2 | 12.1 |
| 70's | 136.6 (133.7, 139.4) | 17.4 | 11.2 | 20.7 | 72.4 (70.5, 74.3) | 9.0 | 7.8 | 11.9 |
| 80's | 133.2 (125.0, 141.4) | 14.4 | 15.1 | 20.9 | 72.7 (66.6, 78.7) | 11.8 | 7.7 | 14.1 |

SD- standard deviation; SBP- systolic blood pressure; DBP- diastolic blood pressure

Table 3: Variability of blood pressure in subgroups of clinic visits defined by patient or clinical characteristics.

| Patient Characteristics | Number of Visits | Systolic Blood Pressure | | Diastolic Blood Pressure | |
|---|---|---|---|---|---|
| | | Within-person Standard Deviation | P-value | Within-person Standard Deviation | P-value |
| Sex | | | 0.027 | | 0.54 |
| Female | 58,853 | 14.3 | | 9.1 | |
| Male | 5,037 | 14.7 | | 9.2 | |
| Ethnicity | | | <0.0001 | | <0.0001 |
| White | 31,638 | 13.2 | | 8.5 | |
| Black | 29,368 | 15.7 | | 9.9 | |
| Other | 3,884 | 12.6 | | 8.5 | |
| Current SLEDAI | | | <0.0001 | | <0.0001 |
| 0 | 23,720 | 13.6 | | 8.7 | |
| 1-3 | 17,855 | 14.1 | | 8.9 | |
| 4+ | 21,950 | 15.2 | | 9.8 | |
| Current Prednisone dose (mg/day) | | | <0.0001 | | <0.0001 |
| 0 | 30,598 | 13.1 | | 8.3 | |
| 1-7.5 | 14,814 | 14.5 | | 9.0 | |
| 7.5-12.5 | 9,592 | 15.6 | | 9.8 | |
| >12.5 | 8,619 | 16.3 | | 10.9 | |
| BMI | | | <0.0001 | | <0.0001 |
| <20 | 8,513 | 14.9 | | 9.6 | |
| 20-24.9 | 18,406 | 14.0 | | 8.8 | |
| 25-29.9 | 17,052 | 14.3 | | 9.1 | |
| 30+ | 19.919 | 14.4 | | 9.4 | |
| Smoking history | | | <0.0001 | | <0.0001 |
| No | 38,451 | 13.6 | | 8.9 | |
| Yes | 25,439 | 15.4 | | 9.6 | |
| Current Anti-dsDNA | | | 0.0002 | | <0.0001 |
| No | 45,067 | 14.2 | | 8.9 | |
| Yes | 16,522 | 14.6 | | 9.6 | |
| Recent Low Comp | | | <0.0001 | | <0.0001 |
| No | 44,105 | 14.11 | | 8.9 | |
| Yes | 17,956 | 14.86 | | 9.7 | |
| Current Plaquenil Use | | | <0.0001 | | <0.0001 |
| No | 20,232 | 15.3 | | 9.8 | |
| Yes | 43,438 | 13.9 | | 8.8 | |
| History of Lupus Anticoagulant | | | <0.0001 | | <0.0001 |
| No | 41,992 | 14.2 | | 9.0 | |
| Yes | 21,221 | 14.7 | | 9.5 | |
| History of ACL | | | 0.0002 | | <0.0001 |
| No | 24,601 | 14.1 | | 9.0 | |

| | | | | | |
|---|---|---|---|---|---|
| Yes | 38,552 | 14.5 | | 9.2 | |
| Current Cholesterol>200 | | | <0.0001 | | <0.0001 |
| No | 39,652 | 13.7 | | 8.7 | |
| Yes | 18,523 | 15.3 | | 9.7 | |
| History of Diabetes | | | <0.0001 | | <0.0001 |
| No | 55,456 | 14.0 | | 9.0 | |
| Yes | 8,416 | 16.6 | | 10.1 | |

Table 4: Relationship between Systolic and Diastolic Blood Pressure Summary Measures and Rates of Cardiovascular Events in the Hopkins Lupus Cohort

| Subgroup | Observed Number of Cardiovascular events | Person-years of follow-up | Rate of events per 1000 person-years | Adjusted[1] Rate Ratios (95% CI) | P-value |
|---|---|---|---|---|---|
| Everyone | 105 | 8291 | 12.7 | | |
| Mean Prior SBP (mmHg) | | | | | |
| 1st quartile (<114) | 9 | 1969 | 4.6 | 1.0 (Ref Group) | |
| 2nd quartile (114-122) | 13 | 2021 | 6.4 | 1.2 (0.5, 2.9) | 0.68 |
| 3rd quartile (122-131) | 27 | 2144 | 12.6 | 1.6 (0.7, 3.8) | 0.23 |
| 4th quartile (131+) | 56 | 2156 | 26.0 | 2.5 (1.1, 5.5) | 0.024 |
| SD Prior SBP (mmHg) | | | | | |
| 1st quartile (<8.5) | 16 | 2129 | 7.5 | 1.0 (Ref. Group) | |
| 2nd quartile (8.5-10.9) | 24 | 2018 | 11.9 | 1.4 (0.7, 2.7) | 0.37 |
| 3rd quartile (10.9-14.0) | 23 | 2069 | 11.1 | 1.0 (0.5, 2.0) | 0.99 |
| 4th quartile (14.0+) | 42 | 2075 | 20.2 | 1.6 (0.9, 3.1) | 0.13 |
| CV Prior SBP (mmHg) | | | | | |
| 1st quartile (<.07) | 17 | 2021 | 8.4 | 1.0 (Ref. Group) | |
| 2nd quartile (.07-.089) | 28 | 2118 | 13.2 | 1.5 (0.8, 2.8) | 0.26 |
| 3rd quartile (.089-.112) | 23 | 2079 | 11.0 | 1.1 (0.6, 2.3) | 0.71 |
| 4th quartile (.112+) | 37 | 2074 | 17.8 | 1.6 (0.9, 3.1) | 0.13 |
| Mean Prior DBP (mmHg) | | | | | |
| 1st quartile (<68) | 11 | 2007 | 5.5 | 1.0 (Ref. Group) | |
| 2nd quartile (68-74) | 29 | 2233 | 13.0 | 2.2 (1.0, 4.5) | 0.038 |
| 3rd quartile (74-80) | 24 | 2109 | 11.4 | 1.6 (0.8, 3.5) | 0.21 |
| 4th quartile (80+) | 41 | 1943 | 21.1 | 2.6 (1.2, 5.3) | 0.0118 |
| SD Prior DBP (mmHg) | | | | | |
| 1st quartile (<5.4) | 13 | 2139 | 6.1 | 1.0 (Ref. Group) | |
| 2nd quartile (5.4-7.0) | 29 | 1982 | 14.6 | 1.9 (0.9, 3.7) | 0.082 |

| | | | | | |
|---|---|---|---|---|---|
| 3rd quartile (7.0-9.1) | 30 | 2184 | 13.7 | 1.9 (1.0, 3.7) | 0.069 |
| 4th quartile (9.1++) | 33 | 1986 | 16.6 | 2.1 (1.0, 4.1) | 0.036 |
| CV Prior DBP (mmHg) | | | | | |
| 1st quartile (<.117) | 17 | 2095 | 8.1 | 1.0 (Ref. Group) | |
| 2nd quartile (.117-.149) | 26 | 2083 | 12.5 | 1.3 (0.7, 2.5) | 0.46 |
| 3rd quartile (.149-.189) | 25 | 2049 | 12.2 | 1.1 (0.6, 2.2) | 0.74 |
| 4th quartile (.189+) | 37 | 2064 | 17.9 | 1.4 (0.7, 2.6) | 0.29 |

[1]Adjusted for age, race, sex, diabetes, cholesterol, BMI, smoking, and recent prednisone dose.

Table 5: Association between various recent blood pressure measurements and risk of a CVE after adjusting for age, race, sex, and the mean value of the 8 most recent systolic blood pressures.[1]

| Blood Pressure Measurement | Odds Ratio[2] (95% Confidence Interval) | P-value |
|---|---|---|
| Single most recent measure of SBP | 0.9 (0.7, 1.2) | 0.62 |
| Standard Deviation of 8 most recent SBP measures | 1.1 (0.9, 1.3) | 0.48 |
| Maximum of the 8 most recent SBP measures | 1.2 (0.8, 1.6) | 0.40 |
| Mean of the 8 most recent DBP | 1.1 (0.9, 1.5) | 0.42 |
| Single most recent measure of SBP | 1.0 (0.8, 1.2) | 0.88 |
| Standard Deviation of 8 most recent SBP measures | 1.1 (0.9, 1.3) | 0.39 |
| Maximum of the 8 most recent SBP measures | 1.1 (0.9, 1.5) | 0.36 |

[1] Each row in the model is based on a different regression model which included the measurement for that row as well as age, race, sex, and the mean value of the 8 most recent systolic blood pressures.

[2] Odds ratios are scaled so they are interpreted as the factor by which the odds changes for every on standard deviation increase in the measure.