

# Healthy Lifestyle and Blood Pressure Variability in Young Adults

Anna Maseli,<sup>1,2</sup> Stefanie Aeschbacher,<sup>1,2</sup> Tobias Schoen,<sup>1,2</sup> Andreas Fischer,<sup>1,2</sup> Manuel Jung,<sup>1</sup> Martin Risch,<sup>3,4</sup> Lorenz Risch,<sup>3,5,6</sup> and David Conen<sup>1,2,7,8</sup>

## BACKGROUND

The aim of this study was to assess the relationships between healthy lifestyle metrics and blood pressure variability (BPV) in young and healthy adults.

## METHODS

A population-based sample of 1,999 individuals aged 25–41 years was investigated. A lifestyle-score from 0 (most unhealthy) to 7 (most healthy) was calculated by giving one point for each of the following components: never smoking cigarettes, adhering to a healthy diet, performing moderate or intense physical activity, having a body mass index <25 kg/m<sup>2</sup>, a total cholesterol <200 mg/dl, a glycosylated hemoglobin <5.7%, or a conventional BP <120/80 mm Hg. Standardized ambulatory 24-hour BP measurements were obtained in all individuals. BPV was defined as the SD of all individual ambulatory BP recordings. We constructed multivariable linear regression models to assess the relationships between the lifestyle-score and BPV. None of the results were adjusted for multiple testing.

## RESULTS

Median age was 37 years and 46.8% were men. With increasing lifestyle-score, systolic and diastolic BPV is decreasing linearly (*P* for trend <0.0001), even after multivariable adjustment. Per 1-point increase in lifestyle-score, the  $\beta$ -coefficient (95% confidence interval) for systolic and diastolic 24-hour BPV was  $-0.03$  ( $-0.03$ ;  $-0.02$ ) and  $-0.04$  ( $-0.05$ ;  $-0.03$ ), respectively, both *P* for trend <0.0001. These relationships were attenuated but remained statistically significant after additional adjustment for mean individual BP.

## CONCLUSION

In this study of young and healthy adults, adopting a healthy lifestyle was associated with a lower BPV. These associations were independent of mean BP levels.

**Keywords:** blood pressure; blood pressure variability; healthy lifestyle; hypertension; lifestyle-score; population-based.

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Hypertension is a strong and independent predictor of cardiovascular morbidity and mortality,<sup>1,2</sup> and one of the most important cardiovascular risk factors worldwide.<sup>3</sup> In recent years, several publications suggested that not only the mean blood pressure (BP) level contributes to cardiovascular risk, but that also BP variability (BPV) is an important and independent predictor for the occurrence of cardiovascular events,<sup>4</sup> target organ damage,<sup>5</sup> and mortality.<sup>6,7</sup> Currently, BPV is mainly calculated using visit-to-visit BP, home BP, within visit BP or 24-hour BP. Both, short-term and long-term BPV have been implicated in this concept but not all studies have assessed whether the effect of BPV is independent of mean BP values.<sup>5,7–9</sup>

Current guidelines appropriately emphasize the importance of adopting healthy lifestyle habits,<sup>10,11</sup> given its profound

cardiovascular benefits. While a healthy lifestyle has important effects on several cardiovascular risk factors,<sup>12–14</sup> including BP, and on the reduction in cardiovascular events,<sup>15,16</sup> its overall effect on BPV is relatively unknown. Several studies have shown that an increased BPV is correlated with individual cardiovascular risk factors and/or sedentary lifestyle, but most of these studies were performed without using 24-hour BP measurement to quantify BPV and without adjusting the results for mean BP values.<sup>9,17</sup> Therefore, it remains unknown, whether the observed association just reflect a higher mean BP among those with higher BPV or whether there is an incremental association of BPV with cardiovascular risk factor that is independent of mean BP levels. In addition, the effect of a comprehensive healthy lifestyle on BPV in healthy populations is currently not very well known.<sup>18,19</sup>

Correspondence: David Conen ([conend@mcmaster.ca](mailto:conend@mcmaster.ca)).

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<sup>1</sup>Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, Basel, Switzerland; <sup>2</sup>Cardiology Division, Department of Medicine, University Hospital Basel, Basel, Switzerland; <sup>3</sup>Labormedizinisches Zentrum Dr Risch, Schaan, Principality of Liechtenstein; <sup>4</sup>Division of Laboratory Medicine, Kantonsspital Graubünden, Chur, Switzerland; <sup>5</sup>Division of Clinical Biochemistry, Medical University, Innsbruck, Austria; <sup>6</sup>Private University, Triesen, Principality of Liechtenstein; <sup>7</sup>Cardiology Division, St. Joseph's Healthcare, Hamilton, Ontario, Canada; <sup>8</sup>Population Health Research Institute, David Braley Cardiac, Vascular and Stroke Research Institute, Hamilton, Ontario, Canada.

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In this context, the aim of this study was to investigate in a large population-based sample of young and healthy adults whether a healthy lifestyle is associated with 24-hour BPV and whether this effect is independent of mean BP levels.

## METHODS

### Study participants

Study subjects included in this analysis are participants of the ongoing “genetic and phenotypic determinants of BP and other cardiovascular risk factors” (GAPP) study. A detailed description of the study design has been previously published.<sup>20</sup> Briefly, between 2010 and 2013, 2,170 inhabitants of the Principality of Liechtenstein aged 25 to 41 years were enrolled in a population-based prospective cohort study. Main exclusion criteria were known cardiovascular disease, including coronary artery disease, stroke, peripheral artery disease or renal failure, atrial fibrillation, current intake of insulin or antidiabetic drugs, daily intake of nonsteroidal anti-inflammatory drugs, regular intake of steroids, a body mass index (BMI) >35 kg/m<sup>2</sup>, known sleep apnea syndrome, or any other severe diseases.

For the present analysis, 171 participants were excluded because of missing or incomplete ambulatory BP recordings ( $n = 90$ ), treatment with BP lowering drugs ( $n = 34$ ), or missing covariates ( $n = 47$ ), such that 1,999 participants remained in the analysis. The study protocol was approved by the local ethics committee, and written informed consent was obtained from each participant.

### Assessment of BPV

Ambulatory 24-hour BP monitoring was obtained in every participant using a validated noninvasive device (Schiller BR-102 plus, Switzerland).<sup>20</sup> The device was set to measure BP every 15 minutes between 7:30 AM and 10:00 PM and every 30 minutes in the remaining period. Ambulatory BP recordings were repeated, whenever possible, if the number of BP measurements was <80% of expected values. Daytime and nighttime BP was individually defined based on 24-hour diaries. BPV was calculated as the SD of all individual BP values. Individual BPV estimates were calculated for systolic and diastolic daytime and nighttime BP. A daytime and nighttime weighted 24-hour BPV variable was calculated in order to remove the influence of the day–night BP difference using the following formula:  $[(\text{daytime SD} \times \text{hours daytime}) + (\text{nighttime SD} \times \text{hours nighttime})]/(\text{hours daytime} + \text{nighttime})$ .<sup>21</sup>

### Assessment of study variables

Standardized questionnaires were used to obtain information about personal medical, lifestyle, and nutritional factors.<sup>20</sup> Information on nutrition and diet were collected using the Swiss health survey questionnaire from 2007. The quantity of alcohol consumption was transformed into grams of alcohol consumed per day. Smoking status was categorized into current, past, or never and highest educational level achieved was classified into high school, college,

and university degree. Physical activity was estimated using the validated International Physical Activity Questionnaire (IPAQ).<sup>22</sup> Weight and height were directly measured in a standardized manner. BMI was calculated as body weight in kilogram divided by height in meters squared. Conventional systolic and diastolic BP were measured 3 times in a sitting position under standardized conditions. The average of the second and third measurement was used for all analyses.

Fasting venous blood samples were obtained to quantify high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and high-sensitivity C-reactive protein using standard methodologies (Roche Cobas 6000, F. Hoffmann-La Roche, Switzerland).<sup>20</sup> Glycated hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) was analyzed using high performance liquid chromatography (Biorad D10 Method, Bio-Rad Laboratories AG).<sup>20</sup>

### Lifestyle score

A previously validated score, which has shown to be strongly associated with cardiovascular and all-cause mortality in general population, was used in the current analysis.<sup>15,23,24</sup> This score is based on the criteria of ideal cardiovascular health, defined by the American Heart Association, and consists of 7 components, including behavioral and cardiovascular risk factors. The score is scaled from 0 (most unhealthy) to 7 (most healthy). One point was given for each of the following features: never smoking cigarettes, adopting a healthy diet, performing vigorous ( $\geq 75$  minutes per week) or moderate ( $\geq 150$  minutes per week) physical activity, and having a BMI <25 kg/m<sup>2</sup>, a total cholesterol <200 mg/dl, an HbA<sub>1c</sub> <5.7%, or a systolic/diastolic BP <120 mm Hg/<80 mm Hg, respectively. A healthy diet included 2 of the 3 following criteria: consumption of  $\geq 5$  portions of fruits and/or vegetables per day,  $\geq 2$  portions of fish per week, or <1500 mg of sodium per day.

### Statistical analysis

Baseline characteristics, including all BPV values, were stratified by lifestyle score. Additionally, median BPV values were stratified by every individual component of the lifestyle score. The distribution of continuous variables was assessed using skewness, kurtosis, and visual inspection of the histogram. Mean  $\pm$  SD was used to describe normally distributed variables and median (interquartile range) for skewed variables. Continuous variables were compared using student's *t*-test, analysis of variance, Wilcoxon rank sum test, or Kruskal–Wallis test, as appropriate. Categorical variables were expressed as numbers (percentage) and compared using Chi-square tests.

First, we assessed the relationship of individual lifestyle-score components with systolic and diastolic daytime and nighttime BPV using 2 different multivariable linear regression models. The first model consists of all lifestyle-score components and was adjusted for age, sex, educational status, alcohol consumption, and family history of cardiovascular disease. A second model was additionally adjusted for the corresponding BP values in order to investigate whether the observed associations are independent of the mean BP. For this analysis, the BP component of the score has been

**Table 1.** Baseline characteristics stratified by lifestyle-score

Lifestyle-score	0-1 (5%)		2 (12%)		3 (21%)		4 (27%)		5 (24%)		6-7 (11%)		P value*
	n		n		n		n		n		n		
Age, years	39.5 (34.4; 41.0)		37.7 (33.3; 40.8)		36.9 (31.6; 40.4)		36.8 (30.6; 40.0)		35.6 (30.1; 40.1)		35.7 (30.0; 39.2)		<0.0001
Male sex, %	88 (88%)		171 (69.2%)		262 (62.2%)		238 (44.8%)		147 (30.7%)		29 (13.1%)		<0.0001
Body mass index, kg/m <sup>2</sup>	28.3 ± 2.7		27.8 ± 3.2		25.9 ± 3.5		24.1 ± 3.5		22.4 ± 2.4		21.7 ± 2.1		<0.0001
Smoking, %													<0.0001
Current	55 (55%)		87 (35.2%)		119 (28.3%)		103 (19.4%)		70 (14.6%)		0 (0%)		
Past	39 (39%)		85 (34.4%)		125 (29.7%)		136 (25.6%)		80 (16.7%)		6 (2.7%)		
Never	6 (6%)		75 (30.4%)		177 (42.0%)		292 (55.0%)		329 (68.7%)		215 (97.3%)		
Conventional SBP, mm Hg	131.6 ± 11.6		128.5 ± 11.0		124.9 ± 11.8		119.3 ± 11.5		114.5 ± 10.8		108.8 ± 7.2		<0.0001
Conventional DBP, mm Hg	86.2 ± 8.1		83.3 ± 7.5		81.9 ± 8.6		77.8 ± 8.0		74.5 ± 7.4		71.2 ± 5.1		<0.0001
Daytime SBP, mm Hg	136.4 ± 10.0		133.9 ± 10.8		130.7 ± 11.5		126.5 ± 10.7		122.5 ± 10.6		117.4 ± 7.5		<0.0001
Nighttime SBP, mm Hg	116.3 ± 11.0		114.8 ± 11.1		113.1 ± 11.4		108.4 ± 10.2		105.3 ± 10.2		101.4 ± 8.3		<0.0001
Daytime DBP, mm Hg	88.5 ± 7.5		86.6 ± 7.7		84.3 ± 8.3		81.4 ± 7.5		78.7 ± 7.1		75.2 ± 5.8		<0.0001
Nighttime DBP, mm Hg	71.6 ± 8.0		70.9 ± 8.0		69.2 ± 8.3		65.9 ± 7.0		63.5 ± 6.9		61.4 ± 5.9		<0.0001
24-h SBP, mm Hg	132.2 ± 9.8		130.0 ± 10.4		127.03 ± 11.1		122.8 ± 10.2		118.9 ± 10.2		114.1 ± 7.3		<0.0001
24-h DBP, mm Hg	85.0 ± 7.3		83.4 ± 7.3		81.2 ± 7.9		78.2 ± 7.0		75.5 ± 6.7		72.3 ± 5.3		<0.0001
LDL-C, mmol/l	4.1 ± 0.8		3.6 ± 0.8		3.3 ± 0.9		2.9 ± 0.7		2.3 ± 0.6		2.4 ± 0.5		<0.0001
HDL-C, mmol/l	1.2 ± 0.3		1.4 ± 0.4		1.5 ± 0.4		1.6 ± 0.4		1.7 ± 0.4		1.7 ± 0.4		<0.0001
HbA <sub>1c</sub> , %	5.8 ± 0.4		5.6 ± 0.4		5.4 ± 0.4		5.4 ± 0.4		5.3 ± 0.3		5.3 ± 0.3		<0.0001
hs-CRP, mg/l	1.3 (0.8; 2.2)		1.4 (0.8; 2.8)		0.9 (0.5; 2.0)		0.9 (0.5; 1.7)		0.7 (0.4; 1.6)		0.7 (0.4; 1.3)		<0.0001
Education, %													0.0057
High school	11 (11%)		21 (8.5%)		35 (8.3%)		50 (9.4%)		24 (5.0%)		11 (4.9%)		
College	54 (54%)		135 (54.7%)		232 (55.1%)		297 (55.9%)		269 (56.2%)		100 (45.3%)		
University	35 (35%)		91 (36.8%)		154 (36.6%)		184 (34.7%)		186 (38.8%)		110 (49.8%)		

Data are presented as means ± SD, medians (interquartile range), or numbers (percentage). \*P value was based on analysis of variance or Kruskal-Wallis tests or Chi-square test, as appropriate. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HbA<sub>1c</sub>, glycated hemoglobin A1c; hs-CRP, high-sensitivity C-reactive protein.

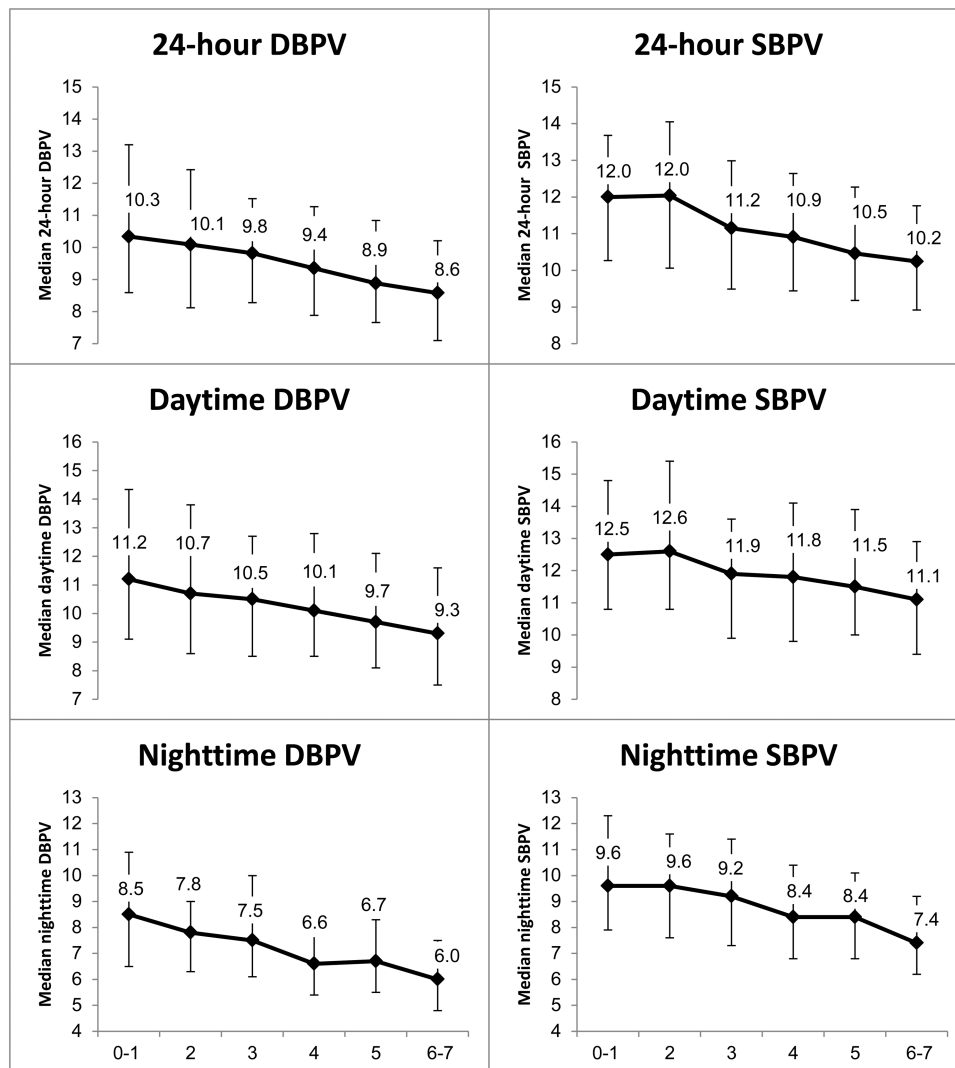
removed in order to avoid statistical collinearity. In a second step, the relationship between the lifestyle score and BPV was assessed using multivariable linear regression analysis. All models were adjusted for the above-mentioned covariates. A second model was additionally adjusted for individual BP values. Separate models were built for systolic and diastolic 24-hour, daytime, and nighttime BPV. For all analyses, we combined participants with lifestyle scores of 0–1 and 6–7 points, respectively, in order to have more balanced group sizes. Participants with a lifestyle score of 4 built the largest group and provide most statistical power. Therefore, this group was used as the reference. Because the observed associations were approximately linear, multivariable regression analyses were repeated using the lifestyle score as an ordinal variable. As all BPV variables had a skewed distribution they were log-transformed for all analyses.

Subgroup effects were assessed across predefined strata of age, sex, smoking status, and BMI. Formal differences

were evaluated using multiplicative interaction tests in the nonstratified models. SAS software version 9.4 (SAS Institute, Cary, NC) was used for all statistical analyses and a 2-tailed  $P$  value  $<0.05$  was considered to indicate statistical significance.

## RESULTS

Baseline characteristics were stratified by lifestyle score (Table 1) and sex (Supplementary Table S1). Overall, 935 (46.8%) participants were men and median age was 37 years. In general, individuals with a high lifestyle-score are younger, more often female and have lower BP and cholesterol levels compared to individuals with a low lifestyle-score. Median (interquartile range) values of systolic and diastolic BPV are decreasing linearly with increasing lifestyle score ( $P$  value  $<0.0001$ ) (Figure 1). In Supplementary Table S2, median BPV values stratified by individual lifestyle-score



**Figure 1.** Blood pressure variability stratified by lifestyle-score. Data are medians and whiskers are representing interquartile ranges. Abbreviations: DBPV, diastolic blood pressure variability; SBPV, systolic blood pressure variability.

components are presented. Significant differences in BPV were found for sex, smoking status, BMI, cholesterol, and HbA<sub>1c</sub> level. Overall, women had a higher lifestyle-score than men (Figure 2 and Supplementary Table S1). Five percent ( $n = 100$ ) of participants had a lifestyle-score of 0–1 (4.4% men, 0.6% women), whereas 11.1% ( $n = 221$ ) had a lifestyle-score of 6–7 (1.5% men, 9.6% women). Sex-differences in lifestyle-score are mainly based on the BP and BMI criteria (Supplementary Table S1). The median lifestyle-score was 4.

Using multivariable regression analysis, we found inverse associations between daytime and nighttime BPV with never smoking cigarettes and having an optimal BMI. These relationships persisted even after the additional adjustment for mean individual BP value, as shown in Table 2. Prediabetes was statistically significant associated with daytime BPV but not with nighttime BPV. None of the other individual components were independently related to BPV (Table 2).

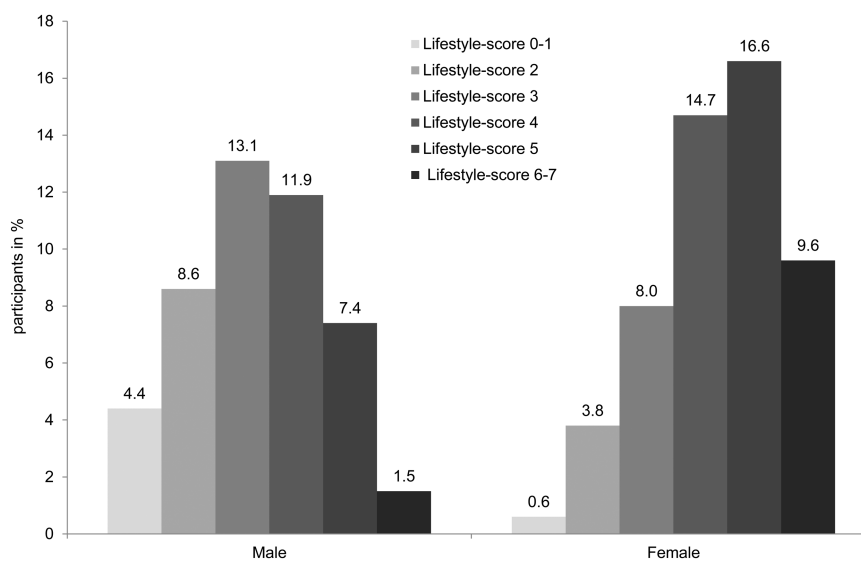
Results of the relationship between BPV and lifestyle-score are shown in Table 3. After multivariable adjustment, a statistically significant inverse and linear relationship was found between all BPV variables and lifestyle-score (all  $P$  for trend  $<0.0001$ ). Using a score of 4 as the reference group, the  $\beta$ -estimates (95% confidence interval) for 24-hour systolic BPV were 0.07 (0.02; 0.13), 0.08 (0.04; 0.11), 0.01 (–0.02; 0.05), –0.02 (–0.05; 0.01), and –0.06 (–0.09; –0.02) for a lifestyle-score of 0–1, 2, 3, 5, and 6–7 ( $P$  values for trend  $<0.0001$ ). Additional adjustment for mean BP attenuated these associations, but with the exception of systolic daytime BPV all relationships between BPV and lifestyle-score remained statistically significant, as shown in Table 3. Similar findings were obtained when the lifestyle-score was entered in the regression models as an ordinal variable (Figure 3). Per 1-point increase in lifestyle-score, the log-transformed 24-hour systolic BPV decreases by 0.03 ( $\beta$ -coefficient (95% confidence interval) –0.03 (–0.036; –0.019),  $P < 0.0001$ ). In nearly all analyses, BPV coefficients remained statistically significant after additional adjustment for mean BP levels.

Subgroup analyses are presented in Table 4. We found no evidence that age, sex, smoking status, or BMI modified the effect of lifestyle on systolic or diastolic 24-hour BPV.

## DISCUSSION

In this large population-based study of 1,999 young and healthy adults, a healthy lifestyle and individual health metrics were significantly associated with a lower BPV. These relationships were consistent for daytime, nighttime, and weighted 24-hour BPV. The effect of the relationship was attenuated but remained statistically significant after adjustment for mean BP levels, suggesting that the effect of healthy lifestyle on BP includes BPV and goes beyond mean BP levels. We suppose that a decrease in BPV might contribute to the beneficial effect of a healthy lifestyle regarding the prevention of cardiovascular events. However, further research is needed to improve the understanding of the underlying mechanisms. To the best of our knowledge, this is one of the first large population-based studies on the relationship between a healthy lifestyle and BPV that used 24-hour BP monitoring to quantify BPV and that systematically adjusted for mean BP levels. A few previous studies showed a significant relationship of BPV with cardiovascular risk factors beyond mean BP,<sup>8,9</sup> but without the use of 24-hour BP monitoring and in significantly older populations. Other studies have shown a positive relationship between BPV and several individual lifestyle factors.<sup>9,17,18</sup> Strengths of the present study that add additional insights compared to the prior data include the use of a well-validated comprehensive score of lifestyle factors and cardiovascular health metrics, availability of 24-hour BP measurements and comprehensive adjustment of the associations for potential confounders including mean BP levels.

The exact mechanisms of the relationship between a healthy lifestyle and BPV are not fully clear. Based on the strong individual relationship with BPV, smoking cigarettes,



**Figure 2.** Distribution of lifestyle-score categories among participants. Bars represent data as percentages for each lifestyle-score category among females and males.

**Table 2.** Relationship between daytime and nighttime BPV and individual components of the lifestyle-score

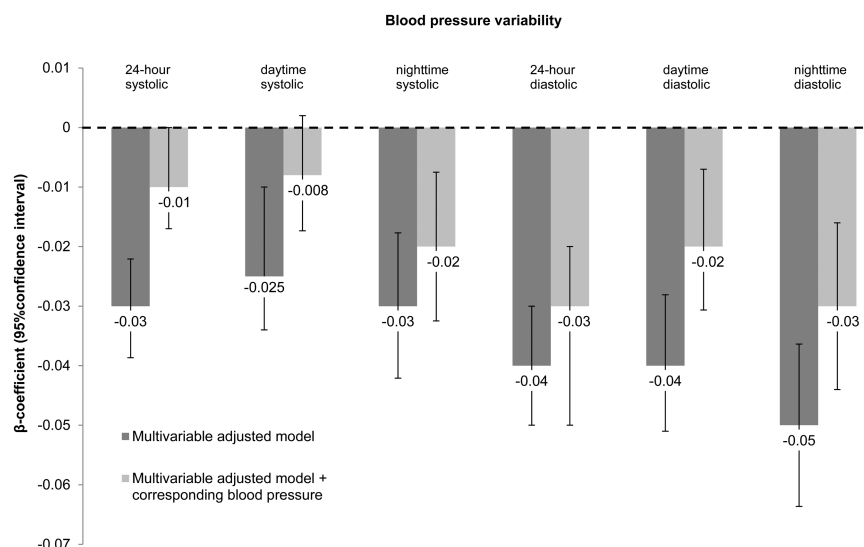
<i>n</i> = 1,999		Daytime SBPV	Daytime DBPV	Nighttime SBPV	Nighttime DBPV				
Never smoking	Model 1	-0.04 (-0.07; -0.20)	0.004	-0.06 (-0.09; -0.03)	<0.0001	-0.04 (-0.07; -0.01)	0.008	-0.07 (-0.10; -0.03)	<0.0001
	Model 2	-0.04 (-0.06; -0.01)	0.002	-0.05 (-0.08; -0.02)	0.0002	-0.04 (-0.07; -0.008)	0.01	-0.07 (-0.10; -0.03)	0.0001
BMI < 25 kg/m <sup>2</sup>	Model 1	-0.06 (-0.08; -0.03)	<0.0001	-0.10 (-0.14; -0.07)	<0.0001	-0.06 (-0.10; -0.03)	0.003	-0.09 (-0.13; -0.05)	<0.0001
	Model 2	-0.03 (-0.06; -0.009)	0.009	-0.07 (-0.10; -0.04)	<0.0001	-0.04 (-0.07; -0.007)	0.02	-0.07 (-0.11; -0.03)	0.0002
Regular physical activity	Model 1	0.004 (-0.02; 0.03)	0.77	0.007 (-0.03; 0.04)	0.68	-0.005 (-0.004; 0.03)	0.80	-0.002 (-0.04; 0.04)	0.94
	Model 2	0.002 (-0.03; 0.03)	0.86	0.01 (-0.02; 0.05)	0.56	-0.01 (-0.05; 0.03)	0.51	-0.004 (-0.05; 0.04)	0.84
Healthy diet	Model 1	0.05 (-0.01; 0.11)	0.12	0.008 (-0.006; 0.08)	0.83	0.04 (-0.04; 0.12)	0.33	-0.01 (-0.10; -0.04)	0.11
	Model 2	0.05 (-0.004; 0.11)	0.07	0.02 (-0.05; 0.09)	0.54	0.03 (-0.05; 0.11)	0.43	-0.01 (-0.10; 0.07)	0.73
Healthy BP level	Model 1	-0.006 (-0.03; 0.02)	0.66	0.004 (-0.03; 0.04)	0.83	-0.03 (-0.06; 0.01)	0.16	-0.04 (-0.07; 0.007)	0.11
	Model 2	-	-	-	-	-	-	-	-
Healthy cholesterol level	Model 1	-0.001 (-0.03; 0.02)	0.92	-0.01 (-0.04; 0.02)	0.52	-0.02 (-0.05; 0.01)	0.25	-0.03 (-0.07; 0.009)	0.13
	Model 2	0.009 (-0.02; 0.03)	0.48	0.008 (-0.02; 0.04)	0.61	-0.01 (-0.04; 0.02)	0.46	-0.01 (-0.05; 0.02)	0.44
No prediabetes	Model 1	-0.04 (0.07; -0.02)	0.002	-0.05 (-0.09; -0.02)	0.002	-0.03 (-0.06; 0.008)	0.13	-0.04 (-0.08; 0.001)	0.06
	Model 2	-0.04 (-0.07; -0.01)	0.003	-0.05 (-0.09; -0.02)	0.001	-0.02 (-0.06; 0.01)	0.21	-0.04 (-0.08; 0.003)	0.07

Data are  $\beta$  coefficients (95% confidence interval). Model 1 was adjusted for age, sex, educational status, alcohol consumption, and family history for cardiovascular disease. Model 2 was additionally adjusted for the corresponding blood pressure value, however, without including the variable "healthy blood pressure level". Abbreviations: BMI, body mass index; DBPV, diastolic blood pressure variability; SBPV, systolic blood pressure variability; regular physical activity, vigorous physical activity  $\geq 75$  or moderate physical activity  $\geq 150$  minutes per week; healthy diet, at least 2 of these components:  $\geq 5$  fruit or vegetable servings per day,  $\geq 2$  servings of fish per week, salt consumption  $< 1,500$  mg; healthy cholesterol level  $\leq 200$  mg/dl; pre-diabetes,  $HbA_{1c} > 5.6\%$ .

**Table 3.** Relationship between variables of the blood pressure variability and lifestyle/e-score

N = 1,999	Score = 0-1 (n = 100)	Score = 2 (n = 247)	Score = 3 (n = 421)	Score = 4 (n = 531)	Score = 5 (n = 479)	Score = 6-7 (n = 221)	P for trend
<b>24-h SBPV (mm Hg)</b>							
Model 1	0.07 (0.02; 0.13)	0.08 (0.04; 0.11)	0.01 (-0.02; 0.05)	Ref.	-0.02 (-0.05; 0.01)	-0.06 (-0.09; -0.02)	<0.0001
Model 2	0.04 (-0.008; 0.09)	0.05 (0.01; 0.08)	-0.00 (-0.03; 0.03)		0.001 (-0.03; 0.03)	-0.02 (-0.06; 0.02)	0.008
<b>Daytime SBPV (mm Hg)</b>							
Model 1	0.07 (0.01; 0.13)	0.07 (0.03; 0.11)	0.001 (-0.03; 0.04)	Ref.	-0.02 (-0.06; 0.01)	-0.06 (-0.10; -0.01)	<0.0001
Model 2	0.03 (-0.03; 0.09)	0.04 (-0.007; 0.08)	-0.01 (-0.05; 0.02)		-0.004 (-0.04; 0.03)	-0.02 (-0.06; 0.03)	0.07
<b>Nighttime SBPV (mm Hg)</b>							
Model 1	0.07 (-0.001; 0.15)	0.09 (0.04; 0.15)	0.05 (0.007; 0.10)	Ref.	-0.0002 (-0.04; 0.04)	-0.07 (-0.12; -0.01)	<0.0001
Model 2	0.05 (-0.03; 0.12)	0.07 (0.01; 0.12)	0.03 (-0.01; 0.08)		0.01 (-0.03; 0.06)	-0.04 (-0.10; 0.02)	0.004
<b>24-h DBPV (mm Hg)</b>							
Model 1	0.13 (0.07; 0.19)	0.09 (0.04; 0.13)	0.03 (-0.003; 0.07)	Ref.	-0.03 (-0.06; 0.007)	-0.10 (-0.15; -0.06)	<0.0001
Model 2	0.09 (0.03; 0.16)	0.05 (0.01; 0.10)	0.02 (-0.02; 0.05)		-0.01 (-0.05; 0.02)	-0.07 (-0.11; -0.02)	<0.0001
<b>Daytime DBPV (mm Hg)</b>							
Model 1	0.12 (0.05; 0.19)	0.07 (0.02; 0.12)	0.02 (-0.03; 0.06)	Ref.	-0.04 (-0.08; 0.0006)	-0.12 (-0.17; -0.06)	<0.0001
Model 2	0.07 (0.005; 0.14)	0.04 (-0.01; 0.08)	-0.002 (-0.04; 0.04)		-0.02 (-0.06; 0.02)	-0.07 (-0.12; -0.02)	0.0003
<b>Nighttime DBPV (mm Hg)</b>							
Model 1	0.16 (0.07; 0.24)	0.13 (0.07; 0.19)	0.09 (0.04; 0.14)	Ref.	0.004 (-0.04; 0.05)	-0.09 (-0.15; -0.02)	<0.0001
Model 2	0.13 (0.05; 0.21)	0.10 (0.04; 0.16)	0.07 (0.02; 0.12)		0.02 (-0.03; 0.07)	-0.06 (-0.12; 0.005)	<0.0001

Data are  $\beta$  coefficients (95% confidence intervals). Model 1: adjusted for age, sex, educational status, alcohol consumption and family history for cardiovascular disease. Model 2: additionally adjusted for BP. Abbreviations: BP, blood pressure; BPV, blood pressure variability; Ref., reference; 24-h SBPV, weighted systolic blood pressure variability over 24 hours; 24-h DBPV, weighted diastolic blood pressure variability over 24 hours.



**Figure 3.** Relationship between blood pressure variability and lifestyle-score. Bars represent  $\beta$  coefficients (95% confidence interval) per 1-point increase category increase in the lifestyle score. Model 1 was adjusted for age, sex, educational status, alcohol consumption and family history for cardiovascular disease. Model 2 was additionally adjusted for mean BP.

**Table 4.** Subgroup analysis for the relationship between blood pressure variability and the lifestyle-score

		<i>n</i>	24-h SBPV	<i>P</i> value for interaction	24-h DBPV	<i>P</i> value for interaction
Sex	Male	935	-0.01 (-0.02; 0.001)	0.90	-0.02 (-0.04; -0.007)	0.62
	Female	1,064	-0.01 (-0.03; 0.001)		-0.03 (-0.04; -0.01)	
Age	<36.7	992	-0.01 (-0.02; 0.001)	0.37	-0.03 (-0.04; -0.01)	0.92
	≥36.7	1,007	-0.01 (-0.02; -0.00)		-0.02 (-0.04; -0.007)	
Smoking	Current/past	905	-0.007 (-0.02; 0.008)	0.14	-0.02 (-0.04; -0.005)	0.11
	Never	1,094	-0.002 (-0.01; 0.01)		-0.01 (-0.03; 0.005)	
BMI	<25	1,202	-0.003 (-0.02; 0.01)	0.80	-0.01 (-0.03; 0.005)	0.55
	≥25	797	-0.007 (-0.02; 0.008)		-0.01 (-0.03; 0.006)	

Data are  $\beta$  coefficients (95% confidence interval). Model was adjusted for age, sex, educational status, alcohol consumption and family history for cardiovascular disease. Abbreviations: BMI, body mass index (kg/m<sup>2</sup>); BPV, blood pressure variability; 24-h SBPV, weighted systolic blood pressure variability over 24 hours; 24-h DBPV, weighted diastolic blood pressure variability over 24 hours.

and having a high BMI might be of particular importance regarding the relationship between a healthy lifestyle and BPV. Endothelial dysfunction, arterial stiffness, baroreceptor dysfunction, and increased sympathetic activity are mechanisms that potentially lead to a high BPV.<sup>25,26</sup> Additionally, genetic variations have to be taken into account.<sup>27</sup> Both obesity and smoking cigarettes may increase BPV through endothelial dysfunction, changes in baroreflex sensitivity and autonomic function.<sup>19,23,28–30</sup> Even though physical activity and a healthy diet were not independently associated with BPV in our study, it has still a favorable effect on the function and structure of the cardiovascular system and on body composition.<sup>31</sup> One previously published study showed an inverse relationship between BPV and healthy Mediterranean diet among patients with coronary artery disease, raising the possibility that diet assessment may somewhat depend on the type of questionnaire used.<sup>32</sup>

Weight reduction has shown to improve endothelial<sup>33</sup> and autonomic function<sup>34</sup> and to reduce BPV independently of the absolute BP value.<sup>33</sup> Interestingly, a drug-induced reduction of BPV was found to improve baroreflex sensitivity,<sup>35</sup> and showed a stronger association with a reduction of stroke risk compared to mean BP levels,<sup>36</sup> indicating that targeting BPV may help to optimize cardiovascular risk. But not only individual components are associated with BPV. Our results suggest an incremental effect of every health metric on BPV, even though not every component was individually associated with BPV. There is evidence showing that lifestyle modification, including physical activity and diet, may decrease BP<sup>37</sup> and prevents and reverses arterial stiffening,<sup>38</sup> potentially more effectively in healthy adults than in a patient population.<sup>39</sup> Thus, the consistent and strong results found in this study may be in part due to the exclusive assessment of young and healthy adults. Our results suggest



that an unhealthy lifestyle may have adverse effects on BPV already in young and healthy individuals. Thus, improving lifestyle measures in the community is particularly relevant in the context of our findings that only 11.1% (1.5% men vs. 9.6% women) of the study population were found to have a healthy lifestyle and optimal cardiovascular health metrics. BP and BMI are the main criteria that are responsible for the markedly lower lifestyle score among men compared to women.

Strengths of this study include the large and well-characterized population-based sample and the availability of ambulatory 24-hour BP recordings in all participants. However, several limitations should be acknowledged in the interpretation of the results. First, it is unclear whether our findings can be generalized to other populations with different baseline characteristics. Second, as in any cross-sectional study, the causality and directionality of our findings cannot be addressed. Third, type 1 errors are possible, even though our results are very consistent. Fourth, physical activity, dietary habits, and smoking status were self-assessed and although we used validated questionnaires, minor measurement errors can occur. We expect that if anything our results were slightly biased toward the null hypothesis.

In conclusion, in this large population-based study of young adults, a healthy lifestyle was strongly associated with a lower BPV, even after comprehensive multivariable adjustment and after taking into account mean BP values. Our findings provide an additional potential mechanism on how a healthy lifestyle reduces the occurrence of cardiovascular outcomes, thereby reinforcing the importance of widespread adoption of a healthy lifestyle in the community.

## SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

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## DISCLOSURES

The authors declared no conflict of interest.

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