

# Association of 24-Hour Blood Pressure With Urinary Sodium Excretion in Healthy Adults

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## BACKGROUND

While the positive relationship between urinary sodium excretion and blood pressure (BP) is well established for middle-aged to elderly individuals using office BP, data are limited for younger individuals and ambulatory BP measurements.

## METHODS

Our analysis included 2,899 individuals aged 18 to 90 years from 2 population-based studies (GAPP, Swiss Kidney Project on Genes in Hypertension [SKIPOGH]). Participants with prevalent cardiovascular disease, diabetes, or on BP-lowering treatment were excluded. In SKIPOGH, 24-hour urinary sodium excretion was used as a measure of sodium intake, while in GAPP it was calculated from fasting morning urinary samples using the Kawasaki formula. Multivariable linear regression models were used to assess the relationships of 24-hour urinary salt excretion with office and ambulatory BP measurements.

## RESULTS

Mean age, ambulatory BP, sodium excretion, and estimated glomerular filtration rate in GAPP and SKIPOGH were 35 and 44 years, 123/78

and 118/77 mm Hg, 4.2 and 3.3 g/d, and 110 and 99 ml/min/1.73 m<sup>2</sup>, respectively. A weak linear association was observed between 24-hour ambulatory systolic BP and urinary sodium excretion ( $\beta$  (95% confidence interval [CI]) per 1 g increase in sodium excretion (0.33 % (0.09; 0.57);  $P = 0.008$ ). No significant relationships were observed for 24-hour ambulatory diastolic BP ( $\beta$  (95% CI) (0.13 % (-0.15; 0.40)  $P = 0.37$ ). When repeating the analyses in different age groups, all BP indices appeared to have stronger relationships in the older age groups (>40 years).

## CONCLUSIONS

In these large cohorts of healthy adults, urinary sodium excretion was only weakly associated with systolic 24-hour ambulatory BP.

**Keywords:** blood pressure; epidemiology; 24-hour ambulatory blood pressure; hypertension; Kawasaki; office blood pressure; urinary salt excretion.

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With hypertension affecting approximately 1 billion people worldwide and being a major cause for death, myocardial infarction, congestive heart failure, stroke, and renal disease,

knowledge about factors modifying this disease are crucial.<sup>1-4</sup> Large population-based studies have shown that salt intake is a strong determinant of hypertension.<sup>5-8</sup> Therefore,

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current guidelines by the WHO recommend a low salt intake of less than 6 g of salt per day for the entire population.<sup>9</sup> However, little data exists for applying these recommendations to younger, healthy individuals. In addition, limited evidence exists for the relationship between ambulatory blood pressure (BP) monitoring and urinary sodium excretion.<sup>10–15</sup>

Knowledge on these factors is important for at least 2 reasons. First, 24-hour ambulatory BP measurements (24-h ABPM) correlate better with cardiovascular outcomes than conventional office BP.<sup>16–19</sup> Second, it is currently unknown whether the same salt intake cutoffs should be applied to the entire population, independent of age or baseline sodium consumption.

To our knowledge, there are no large studies investigating the relationship of sodium excretion and ambulatory BP in a younger and healthy population. In order to address this knowledge gap, we assessed this relationship in 2 large and well-characterized cohorts.

## METHODS

### GAPP

**Study participants.** The genetic and phenotypic determinants of BP and other cardiovascular risk factors (GAPP) study is a population-based cohort in the Principality of Liechtenstein. The recruitment period started in June 2010 and all inhabitants aged between 25 and 41 years were invited to participate. Main exclusion criteria were prevalent diabetes, a body mass index (BMI) >35 kg/m<sup>2</sup> or prevalent cardiovascular disease. Participants were mainly of Caucasian origin. Complete details about design and methodology, including all exclusion criteria have been published previously.<sup>20</sup> Informed consent was obtained from each participant. The local ethics committee approved the study protocol.

**BP measurements.** Conventional BP was obtained by 3 consecutive measurements after at least 5 minutes of rest using a validated oscillometric device (Microlife BP3AG1, Microlife AG, Switzerland). The mean of the second and third BP measurement were used for all analyses. 24-H ABPM was performed using a validated automatic device (BR-102 plus, Schiller AG, Switzerland). BP was obtained every 15 minutes from 07.30 to 22.00 and every 30 minutes during the remainder. If participants had less than 80% of valid BP measurements, ABPM was repeated if possible. Daytime and nighttime BP were defined according to individually completed diaries. Individuals with less than 10 valid daytime or less than 5 valid nighttime measurements were considered to have insufficient ABPM and were excluded from the analysis.

**Sodium excretion.** A morning fasting urine sample was used to estimate 24-h urinary sodium excretion using the Kawasaki formula.<sup>21</sup> A recent study showed that this formula was the most valid and least biased method of estimating 24-h sodium excretion from single morning fasting urine.<sup>22</sup>

**Assessment of other study variables.** Standardized questionnaires were used to gather information on personal characteristics and medical background including education, smoking and alcohol, and fruit/vegetable consumption. Education was divided into 3 groups (high/middle/low). Alcohol consumption was divided into drinkers and nondrinkers. Fruit and vegetable consumption was divided into more than 5 portions per day or less. Smoking was divided into 3 groups (current/past/never). Weight and height were directly measured using standardized devices. BMI was calculated as body weight in kilograms divided by body height in meters squared.

**Blood sampling.** Fasting venous blood samples were obtained from every participant by venipuncture. Creatinine, low-density lipoproteins, and high-density lipoproteins cholesterol were measured using standard methods and estimated glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.<sup>23</sup>

### SKIPOGH

**Study population and design.** The Swiss Kidney Project on Genes in Hypertension (SKIPOGH) study is a multicenter family-based population study initiated in 2009 to explore the genetic and environmental determinants of BP.<sup>24</sup>

Study participants were recruited in the cantons of Bern and Geneva and the city of Lausanne. Recruitment began in December 2009 and ended in April 2013. Inclusion criteria were: (i) written informed consent, (ii) minimum age of 18 years, (iii) Caucasian origin, and (iv) at least one, and preferably 3, first-degree family members also willing to participate. At the end of the recruitment period, the study population included 1,128 participants from 271 distinct family pedigrees. Of the individuals asked to participate in Bern, Geneva, and Lausanne, 21%, 22%, and 20% agreed, respectively. The SKIPOGH study was approved by the ethical committees of Lausanne University Hospital, Geneva University Hospital, and the University Hospital of Bern.

**BP and sodium excretion measurements.** BP was measured with a nonmercury auscultatory sphygmomanometer (A&D UM-101, A&D Company, Ltd., Toshima Ku, Tokyo, Japan) that has passed the International Protocol for validation of BP measuring devices of the European Society of Hypertension (ESH). BP was measured after 10 minutes of rest in the sitting position in each arm. Subsequently, 5 consecutive BP measurements were taken on the side with the highest BP. In this study, each subject's office BP was defined as the mean of the last 4 office BP readings.

24-Hour APBM was measured using a validated Diasys Integra device (Novacor, Rueil-Malmaison, France) that has fulfilled the validation criteria set forth by the British Hypertension Society and Association for the Advancement of Medical Instrumentation (AAMI) protocols. Measurements were taken every 15 minutes during the day, and every 30 minutes during the night (from 10 PM to 7 AM). Participants were included in the analyses if they had at least 10 systolic BP (SBP) and diastolic BP (DBP) measurements during the

day and at least 5 readings during the night, in accordance with ESH recommendations. Day and night periods were obtained from participants' diaries over the 24-h period. Mean 24-h BP readings were subsequently calculated using the valid daytime and nighttime measurements.

Participants were asked to collect a 24-h urine sample for the measurement of urine volume and sodium excretion. Participants with incomplete collections as previously defined were excluded.<sup>24</sup>

**Assessment of other study variables.** Participants filled in a standardized questionnaire at home. The questionnaire focused on a variety of issues including lifestyle habits as well as medical and drug history. Education was divided into 3 groups (high/middle/low). Alcohol consumption was divided into drinkers and nondrinkers. Fruit and vegetable consumption was divided into more than 5 portions per day or less. Smoking was divided into 3 groups (current/past/never). The CKD-EPI formula was used to calculate the estimated glomerular filtration rate. Body weight and height were measured using precision electronic scales (Seca, Hamburg, Germany). Blood venous samples were drawn after an overnight fast. Serum high-density lipoproteins, low-density lipoproteins, and creatinine were measured by standard clinical laboratory methods.

**Merging of the data sets.** To increase the similarity between the 2 cohorts, we applied the key GAPP exclusion criteria to the SKIPOGH cohort. Namely, we excluded SKIPOGH individuals with a BMI >35 kg/m<sup>2</sup>, treated for hypertension, with any known cardiovascular disease, with current intake of antidiabetic drugs or insulin, current pregnancy, with known obstructive sleep apnea syndrome, with daily intake of nonsteroidal anti-inflammatory drugs, regular intake of steroids, or suffering of cancer. A total of 885 individuals were left.

In GAPP, of 2,135 participants, complete covariate data were available for 2,091 (98%) participants for office BP, and 1,993 participants (93.3%) for ambulatory BP. In SKIPOGH, of 885 participants, complete covariate data were available for 808 (91.3%) participants for office BP and 761 (86%) for ambulatory BP.

### Statistical analysis

Baseline characteristics were stratified by the individual cohorts. The association between urinary sodium excretion and BP measurements (ambulatory/office and systolic/diastolic) was investigated for GAPP and SKIPOGH separately using a 2-step procedure. In the first step, we explored whether a linear association was present. Multivariable linear regression analyses were used to model the relationship of each BP measurement with urinary sodium excretion. All models were adjusted for age, gender, BMI, smoking, fruit and vegetable consumption (to reflect potassium intake), low-density lipoproteins and high-density lipoproteins cholesterol, education, alcohol intake, estimated glomerular filtration rate (to reflect kidney function), and 24-h creatinine excretion (to reflect quality of urine collection). In SKIPOGH, the urinary volume and center were also added

as covariates, and a random effect for family was taken into account. Once separate models were constructed for each cohort, the association between urinary sodium excretion and each BP outcome were pooled across cohorts using a fixed-effect meta-analysis method.<sup>25</sup> We evaluated the assumptions underlying linear regression modeling and found a slight to moderate skewness of the residuals. BP was log transformed subsequently to optimize the distribution of the residuals. Multivariable linear regression analyses were repeated with awake and sleep BP using the same variables mentioned above. To assess a possible age-dependent effect, participants were divided into 3 subgroups (20–30 years of age, >30–40 years of age, and >40–50 years of age) and the same models were constructed in each subgroup separately. A *P* value of <0.05 was predefined to indicate statistical significance.

**Table 1.** Baseline characteristics divided by study group

	GAPP, n = 2,093	SKIPOGH, n = 810	<i>P</i> value
24-Hour sodium excretion, g	4.17 (1.31)	3.27 (1.36)	<0.001
24-Hour systolic BP, mm Hg	123 (11)	118 (14)	<0.001
24-Hour diastolic BP, mm Hg	78 (8)	77 (8)	0.003
Office systolic BP, mm Hg	120 (13)	114 (15)	<0.001
Office diastolic BP, mm Hg	78 (9)	75 (9)	<0.001
Awake systolic aBP, mm Hg	127 (12)	122 (14)	<0.001
Awake diastolic aBP, mm Hg	82 (8)	80 (9)	<0.001
Sleep systolic aBP, mm Hg	109 (11)	106 (14)	<0.001
Sleep diastolic aBP, mm Hg	66 (8)	68 (8)	<0.001
Age, years	35.4 (5.2)	43.7 (16.1)	<0.001
Female sex	1,126 (54)	447 (54)	1
Education			0.034
Low	163 (8)	87 (11)	
Middle	1,142 (54)	420 (51)	
High	788 (38)	315 (38)	
eGFR (CKD-EPI-formula)	110 (12)	99 (17)	<0.001
Any alcohol consumption	1080 (52)	522 (64)	<0.001
BMI, kg/m <sup>2</sup>	24.5 (3.7)	24.0 (3.6)	0.002
Fruit/vegetable consumption (≥5 portions/day)	412 (20)	259 (32)	<0.001
LDL, mmol/l	3 (0.9)	3.1 (0.9)	<0.001
HDL, mmol/l	1.5 (0.4)	1.5 (0.4)	0.36
Never	1,148 (55)	379 (47)	<0.001
Smoking			
Former	489 (23)	320 (39)	
Current	456 (22)	111 (14)	
Urinary creatinine, mmol	13.8 (4.2)	12.8 (4.0)	<0.001

Data are mean (SD) or number (percentage). Abbreviations: aBP, ambulatory BP; BMI, body mass index; BP, blood pressure; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SKIPOGH, Swiss Kidney Project on Genes in Hypertension.

Additionally, as an alternative approach to a fixed-effect meta-analysis method a likelihood ratio test was used to assess a linear relationship. To assess whether a nonlinear relationship was present between sodium excretion and BP, a piece-wise (2 segments) linear association model was created and the Akaike Information Criterion was used to select the most plausible model for our data. Details are described in the Supplementary Methods.

R version 3.2.2 was used for all statistical analyses.

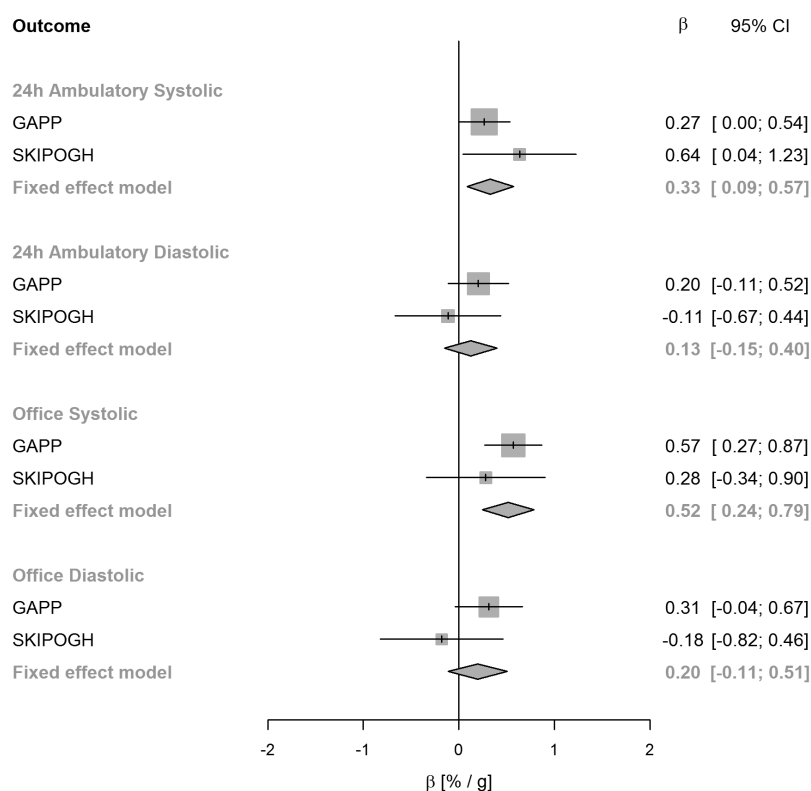
## RESULTS

Baseline characteristics of the 2,093 participants in GAPP and 810 in SKIPOGH stratified by study cohort are shown in Table 1. Individuals in GAPP were younger, had a better kidney function, and a higher mean sodium excretion (4.17 g) compared to individuals in SKIPOGH (3.27 g). SBP was higher in GAPP (24-h BP 123 mm Hg; office BP 120 mm Hg) compared to SKIPOGH (24-h BP 118 mm Hg; office BP 114 mm Hg). DBP was also higher in GAPP (24-h BP 78 mm Hg; office 78 mm Hg) compared to SKIPOGH (24-h BP 77 mm Hg; office 75 mm Hg).

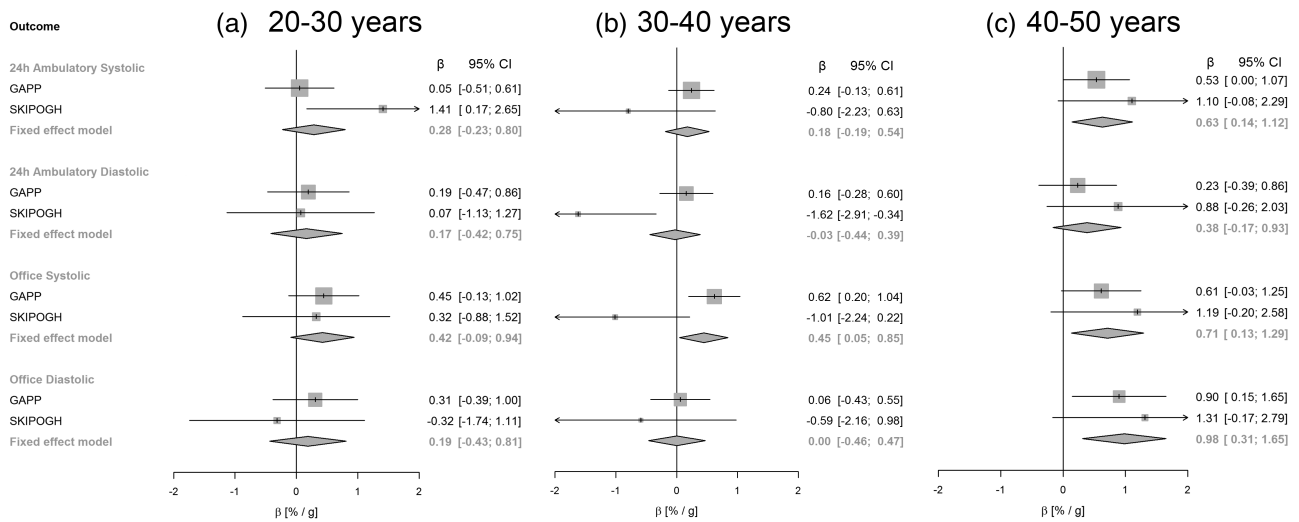
Associations between sodium excretion and BP outcomes as pooled and cohort-wise  $\beta$  coefficients (95% confidence interval [CI]) per 1 g increase in sodium excretion are shown in Figure 1. Pooled  $\beta$  coefficients (95% CI) were 0.33 (0.09; 0.57) ( $P = 0.008$ ) for 24-h SBP, 0.52 (0.24; 0.79) ( $P = 0.0002$ ) for office SBP, 0.13 (-0.15; 0.40) ( $P = 0.34$ ) for 24-h DBP and 0.20 (-0.11; 0.51) ( $P = 0.21$ ) for office DBP. There was a significant interaction of age and sodium excretion with 24-h DBP ( $P = 0.002$ ) and office DBP ( $P = 0.006$ ). There was a trend with 24-h SBP ( $P = 0.09$ ).

Association between sodium excretion and BP outcomes across 3 different age strata are shown in Figure 2. Pooled coefficients (95% CI) for 24-h SBP increased from 0.28 (-0.23; 0.80) ( $P = 0.28$ ) in the youngest group to 0.63 (0.14; 1.12) ( $P = 0.01$ ) in the oldest group. Office SBP increased from 0.42 (-0.09; 0.94) ( $P = 0.11$ ) in the youngest group to 0.71 (0.13; 1.29) ( $P = 0.02$ ) in the oldest group. 24-H DBP remained nonsignificant in all subgroups. Office DBP increased from 0.19 (-0.43; 0.81) ( $P = 0.55$ ) in the youngest group to 0.98 (0.31; 1.65) ( $P = 0.004$ ) in the oldest group.

For the association between sodium excretion and awake BP, as shown in Figure 3, pooled coefficients (95% CI) were 0.36 (0.11; 0.61) ( $P = 0.005$ ) for systolic and 0.16 (-0.13;



**Figure 1.** Multivariable linear regression analysis for the association of sodium excretion with log-transformed BP outcomes.  $\beta$  corresponds to the % BP difference per 1 g of sodium excretion. As an example, an office systolic BP of 100 mm Hg would correspond to a 0.52 mm Hg increase per 1 g of sodium excretion.  $\beta$  refers to the corresponding regression coefficient in a multivariable model including age, sex, BMI, smoking (current/former/never), fruit and vegetable consumption (more or less than 5 portions/day), LDL, HDL, eGFR, urinary creatinine, education (high/middle/low), alcohol (yes/no). Cohort-wise betas are drawn with gray squares and pooled estimated with gray diamond. The size of the square is related to the weight that study/cohort has on the pooled estimate. Ambulatory BP:  $n = 1,993$  (GAPP);  $n = 761$  (SKIPOGH). Office BP:  $n = 2,091$  (GAPP);  $n = 808$  (SKIPOGH). Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SKIPOGH, Swiss Kidney Project on Genes in Hypertension.



**Figure 2.** (a) Ambulatory BP:  $n = 406$  (GAPP);  $n = 205$  (SKIPOGH). Office BP:  $n = 436$  (GAPP);  $n = 214$  (SKIPOGH). (b) Ambulatory BP:  $n = 1,028$  (GAPP);  $n = 135$  (SKIPOGH). Office BP:  $n = 1,074$  (GAPP);  $n = 120$  (SKIPOGH). (c) Ambulatory BP:  $n = 559$  (GAPP);  $n = 147$  (SKIPOGH). Office BP:  $n = 581$  (GAPP);  $n = 158$  (SKIPOGH). Multivariable linear regression analysis for the association of sodium excretion with log-transformed BP outcomes in individuals between 20–30, 30–40, and 40–50 years of age.  $\beta$  corresponds to the % BP difference per 1 g of sodium excretion. As an example, an office systolic BP of 100 mm Hg in a population aged 30–40 years would correspond to a 0.45 mm Hg increase per 1 g of sodium excretion.  $\beta$  refers to the corresponding regression coefficient in a multivariable model including age, sex, BMI, smoking (current/former/never), fruit and vegetable consumption (more or less than 5 portions/day), LDL, HDL, eGFR, urinary creatinine, education (high/middle/low), alcohol (yes/no). Cohort-wise betas are drawn with gray squares and pooled estimated with gray diamond. The size of the square is related to the weight that study/cohort has on the pooled estimate. Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SKIPOGH, Swiss Kidney Project on Genes in Hypertension.

0.45) ( $P = 0.27$ ) for DBP. Pooled coefficients (95% CI) for sleep BP were 0.39 (0.09; 0.68) ( $P = 0.01$ ) for systolic and 0.23 (–0.11; 0.56) ( $P = 0.19$ ) for DBP. There was a significant relationship between awake and sleep SBP only. The odds ratio for hypertension combined across cohorts was not significant as reported in the Supplementary Results.

For ambulatory and office SBP, the likelihood ratio tests were significant with a chi-squared ( $\chi^2$ ) value of 13.5 ( $P = 0.009$ ) and 19.4 ( $P = 0.0007$ ), respectively, showing the presence of a linear relationship. For ambulatory and office DBP, the likelihood ratio test was nonsignificant, similar to the fixed-effect meta-analysis method. Using the Akaike Information Criterion, there was no strong evidence for a nonlinear relationship between sodium excretion and any BP indices in our data as can be seen in the Supplementary Results.

## DISCUSSION

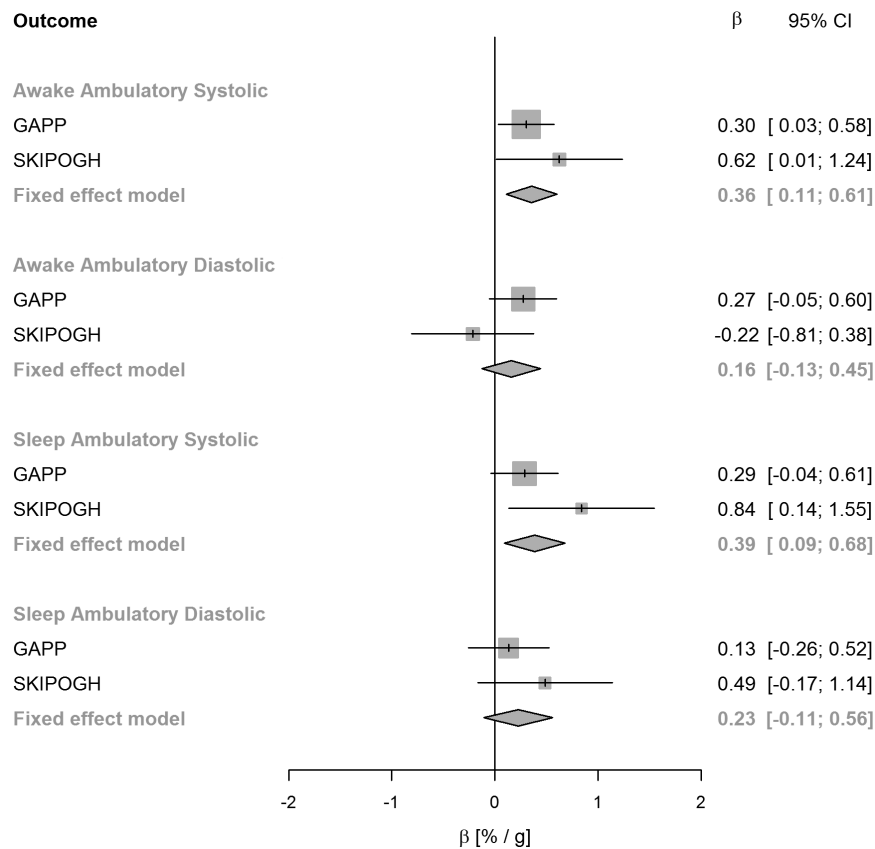
In this large sample of healthy individuals from the general population, we found a weak but statistically significant relationship between urinary sodium excretion and ambulatory systolic 24-h BP. A weak but statistically significant association was also found between sodium excretion and systolic office BP. DBP was not associated with sodium excretion. This study extends previous findings between sodium excretion and BP to young and middle-aged individuals and suggests that reductions in salt consumption might only lead to small BP changes in this population. Furthermore, our data did not confirm prior evidence suggesting a nonlinear relationship between BP and 24-h sodium excretion.<sup>26</sup>

For 1 g increment of sodium excretion (i.e., 2.5 g of sodium chloride), we found a small but significant increase

in ambulatory SBP of 0.33%. Although the relationship between office SBP and sodium excretion was somewhat stronger, the overall relationship was still weak (0.52% increase for every 1 g increment in sodium excretion). In comparison, effect sizes for systolic office BP increase in PURE, INTERSALT, and a large meta-analysis of observational studies was 1.46 mm Hg, 0.94 mm Hg, and 1.6 mm Hg per 1 g increments of sodium excretion, respectively.<sup>5,6,26</sup>

Differences in age and kidney function might explain the observed differences across cohorts. For example, the average age in the PURE study at baseline was 51 years compared to 35 years in GAPP and 44 years in SKIPOGH.<sup>26</sup> Even in PURE, the relationship between BP and sodium excretion was significantly weaker among individuals under the age of 45 years, hinting toward an age-dependent effect.<sup>26</sup> Our results suggesting a stronger relationship among individuals aged 40–50 years compared to those aged 20–30 years provide further evidence of an age-dependent difference and extend these findings to a large cohort with available 24-h ambulatory BP measurements. Ambulatory and office BP produced similar results in our population. Younger individuals have slightly lower office BP compared to ambulatory BP, while this difference is inverted and augmented in the elderly.<sup>27</sup> Further studies are needed to see whether salt consumption may be implicated in these findings.

Kidney function probably plays an important role in this context as it decreases with age and has an important influence on sodium excretion and BP.<sup>28</sup> Persons in our study had a normal estimated glomerular filtration rate. This variable was not universally used in previous studies.<sup>5,6,26</sup> These studies also included individuals reporting hypertension as well as taking antihypertensive medication, like



**Figure 3.** Multivariable linear regression analysis for the association of sodium excretion with awake and sleep blood pressure measures.  $\beta$  corresponds to the % BP difference per 1 g of sodium excretion. As an example, sleep ambulatory systolic BP of 100 mm Hg would correspond to 0.39 mm Hg increase per 1 g of sodium excretion.  $\beta$  refers to the corresponding regression coefficient in a multivariable model including age, sex, BMI, smoking (current/former/never), fruit and vegetable consumption (more or less than 5 portions/day), LDL, HDL, eGFR, urinary creatinine, education (high/middle/low), alcohol (yes/no). Cohort-wise betas are drawn with gray squares and pooled estimated with gray diamond. The size of the square is related to the weight that study/cohort has on the pooled estimate. Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

angiotensin-converting-enzyme-inhibitors and diuretics which may have a significant effect on sodium excretion.<sup>29,30</sup>

Currently, the WHO recommends an intake of no more than 2.3 g of sodium per day.<sup>9</sup> The mean sodium excretion in GAPP and SKIPOGH were substantially higher. Interventional trials such as dietary approaches to stop hypertension have shown that by changing dietary patterns, while maintaining low sodium intake of about 3 g/d, a significant BP reduction was achieved.<sup>31</sup> It remains unclear to what degree sodium and age played a role in these results. Furthermore, the current WHO recommendations make no distinction between age groups or comorbidities. As mentioned above, data from previous studies as well as our study hint toward an age-dependent effect. Additionally, the WHO does not account for salt sensitivity in their recommendations. Our results suggest that lowering salt consumption in young and healthy adults might only have a small effect on BP, and it is currently unknown whether this strategy has an effect on hard cardiovascular endpoints particularly in this population stratum.

While the effects of dietary sodium intake on BP and subsequent cardiovascular outcomes have been widely mentioned and extensively published, it is important to note that dietary sodium has a much wider range of effects on the body which

also play an important role in cardiovascular outcomes. These effects include glomerular injury, cardiac hypertrophy, diastolic dysfunction, endothelial dysfunction, fibrosis in the blood vessels, and changes in the plasma concentration of renin, aldosterone, adrenaline, noradrenaline, and triglycerides.<sup>32–35</sup>

Whether estimating 24-h sodium excretion from fasting urinary samples is accurate remains controversial as is the use of the Kawasaki formula.<sup>22,36</sup> It is therefore important to highlight that despite the different methods used to calculate 24-h urinary excretion across the 2 cohorts, the estimated relationships with BP were very similar independent of the methodology used to quantify sodium excretion.

We excluded individuals with hypertension, diabetes, and a BMI >35 kg/m<sup>2</sup>. In the general population of Liechtenstein and Switzerland, in the age range of 15–34 year olds, prevalence for hypertension and diabetes were 4.2% and <1%, respectively. In the age range of 35–49 year olds, the prevalence rose to 7.1% and 1.8%, respectively. Obesity, defined as a BMI at or above 30 kg/m<sup>2</sup> was present in around 10% of the population, however, having a higher prevalence in the elderly.<sup>37</sup> We therefore believe that our population sample is a good reflection of the general young adult population, being slightly healthier than average in Liechtenstein and Switzerland.

## Strengths and Limitations

Major strengths of this study include the population-based study design with a large number of well-characterized young and healthy participants resulting in a homogenous sample, including the availability of 24-h ambulatory BP.

Potential limitations include the fact that we performed a cross-sectional analysis which does not allow to draw causal inferences or to assess the directionality of the observed effects. Therefore, our results may not necessarily reflect effects seen in an interventional study. Nonetheless, our findings are consistent with the very modest BP differences that have been observed in other studies despite substantial sodium intake differences. Furthermore, residual confounding can be an issue in every observational study. Also, the great majority of enrolled individuals were Caucasian and the generalizability of our results to other population groups is uncertain. Finally, potassium intake is also associated with BP but was not available in all participants.

While previous studies in hypertensive individuals have shown that 24-h ABPM can potentially be used to assess salt sensitivity risk groups,<sup>38</sup> it is unclear whether this interesting concept can be applied to our population.

In conclusion, 24-h sodium excretion was weakly but significantly associated with both systolic 24-h ambulatory BP and office BP in 2 large cohorts of young and healthy individuals. In order to validate our results and to assess the population impact of reducing sodium intake, adequately powered randomized trials will be needed to show the potential beneficial effect on BP and whether age specific recommendations are needed.

## SUPPLEMENTARY MATERIALS

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

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## DISCLOSURE

The authors declared no conflict of interest.

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