# Population Effects on Individual Systolic Blood Pressure: A Multilevel Analysis of the World Health Organization MONICA Project

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Received for publication September 16, 2003; accepted for publication January 12, 2004.

Individuals from the same population share a number of contextual circumstances that may condition a common level of blood pressure over and above individual characteristics. Understanding this population effect is relevant for both etiologic research and prevention strategies. Using multilevel regression analyses, the authors quantified the extent to which individual differences in systolic blood pressure (SBP) could be attributed to the population level. They also investigated possible cross-level interactions between the population in which a person lived and pharmacological (antihypertensive medication) and nonpharmacological (body mass index) effects on individual SBP. They analyzed data on 23,796 men and 24,986 women aged 35–64 years from 39 worldwide Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study populations participating in the final survey of this World Health Organization project (1989–1997). SBP was positively associated with low educational achievement, high body mass index, and use of antihypertensive medication and, for women, was negatively associated with smoking. About 7–8% of all SBP differences between subjects were attributed to the population level. However, this population effect was particularly strong (i.e., 20%) in antihypertensive medication users and overweight women. This empirical evidence of a population effect on individual SBP emphasizes the importance of developing population-wide strategies to reduce individual risk of hypertension.

analysis of variance; antihypertensive agents; blood pressure; body mass index; education; hypertension; population; world health

Abbreviations: BMI, body mass index; MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease; SBP, systolic blood pressure; SBP-SD, standard deviation of SBP measurements in each population; VPC, variance partition coefficient.

Individuals from the same population may be more similar to each other than to those from other populations because they share a number of socioeconomic, health care, genetic, and lifestyle factors, which may partly condition a collective and common level of health over and above individual variation. Based on the ideas of Emile Durkheim (1858–1917) (1), these aspects were developed in Rose's seminal discourse on the importance of distinguishing between the causes of individual cases of disease within a population and the causes of differences in the rates of disease across populations (2, 3).

Therefore, even if blood pressure level is an individual characteristic, population factors may condition a common level of blood pressure over and above individual characteristics. Understanding this collective phenomenon is relevant for both etiologic research and prevention strategies.

There are two main strategies for preventing blood pressure-related cardiovascular diseases (2). The "high-risk strategy" aims at detection and treatment (often by pharmacological methods) of individuals with established hypertension. The "mass strategy" aims to shift the whole blood

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pressure distribution in the population in a favorable direction (often by lifestyle and nonpharmacological-related approaches such as maintaining a normal body weight) (4). Even so, population factors may determine differences in the effectiveness of these approaches, and these differences need to be understood when developing prevention strategies. For instance, it is known that individual weight reduction reduces systolic blood pressure (SBP), but the effect of weight reduction may be more intense in some populations than in others.

Most comparative studies of population determinants of blood pressure have had a pure ecologic design (5) or performed separate individual and ecologic analyses in the same study (6-8). However, even when the focus of the investigation is on the population level, ecologic analyses or combined individual and ecologic analysis—in contrast to multilevel analyses—are unable to discern whether population characteristics influence SBP over and above individual factors or whether between-population variation in blood pressure level is due to differences in the individual composition of the populations. Ecologic analysis also cannot detect whether individual characteristics affect blood pressure differently in different populations (9, 10).

The World Health Organization multinational project known as Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) collected individual information on blood pressure from a large number of populations. The data collection procedures were uniform and were subjected to detailed quality assessments (for more information, refer to the following website: http://www.ktl.fi/ monica/index.html). Large differences in mean SBP are known to exist between the MONICA study populations (11). Therefore, the MONICA database is particularly valuable for conducting multilevel analyses to investigate the influence of individual and contextual factors on blood pres-

We aimed to quantify the extent to which individual differences in SBP were attributable to the population in which a person lived. Another goal was to determine the size of this population effect.

## **MATERIALS AND METHODS**

# Study population

The analyses were based on data obtained during the last MONICA Project risk factor survey, performed among 39 worldwide MONICA study populations during 1989-1997. (Refer to the Appendix for a list of the sites and key personnel.) Each study population was a geographically defined community in which it was feasible to conduct surveillance for all suspected heart attacks and, in some cases, strokes. The MONICA study populations were not necessarily representative of the countries in which they were located. In each population, a random sample of persons aged 35-64 years, stratified by sex and age, was invited to participate. The median participation rate was 75 percent (first-third quartiles, 68-78 percent). Of the 50,697 participants, we excluded those for whom information was missing on blood pressure (n = 1,196), demographic characteristics (n = 713), or both (n = 6). Therefore, we performed the study by using data on 48,782 subjects (23,796 men and 24,986 women) for whom information on these variables was complete.

Detailed information about the World Health Organization MONICA Project sampling frames, study design and characteristics, and data quality is available in the MONICA manual, quality control reports, and other MONICA publications. For more information, refer to the http://www.ktl.fi/ monica website.

#### Assessment of variables

Standardized examinations including a questionnaire, anthropometric and blood pressure measurements, and collection of blood samples were performed during all population surveys. The variables were measured by following a common protocol and were subjected to strict quality controls. Detailed information about the variables used is available at http://www.ktl.fi/publications/monica/index.html.

Age was calculated at the date of the examination and was categorized into three groups: 35-44, 45-54, and 55-64 years. In the comparisons, we used the youngest group as the reference.

Relative body weight was expressed as body mass index (BMI; weight (kg)/height (m)<sup>2</sup>). In the analysis, BMI was centered on the overall mean. For 0.4 percent (199/48,782) of the participants, information on BMI was missing.

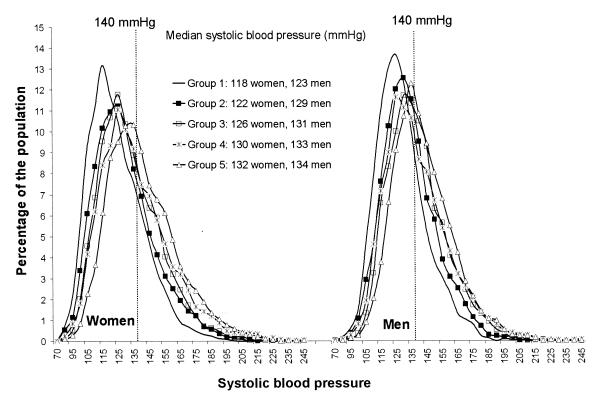
SBP was measured to the nearest 2 mmHg. Recorded values represented the mean of two readings on the right arm with the subject in a sitting position after at least 5 minutes at rest. Blood pressure was measured by means of standard sphygmomanometers in 23, and by random zero sphygmomanometers in 16, of the MONICA study populations. The random zero sphygmomanometer gives SBP readings that tend to underestimate those obtained from the standard devices (12).

Participants were asked whether they were taking antihypertensive medication. For 0.8 percent (366/48,782) of them, information on antihypertensive medication was not available.

An important population-level measure of health is the extent of health inequality among the people in that population. For example, Rose (13) observed that an unfavorable average population level of health was often accompanied by larger within-population variation. In this paper, we used the standard deviation of SBP measurements in each population (SBP-SD) as an indicator of health inequality and investigated the association between population SBP-SD and SBP level.

We classified the participants according to their smoking habits as smokers (daily or occasional) and nonsmokers. Former smokers were included with nonsmokers. For 0.1 percent (62/48,782) of the participants, information on smoking habits was not obtained.

Measurement of educational achievement was based on years of schooling categorized according to a standard approach developed by the MONICA Project. This approach groups years of schooling into tertiles (for each sex and 10year age group) within each MONICA study population. For 3,497 persons from three MONICA study populations, infor-



**FIGURE 1.** Distribution of systolic blood pressure in the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study populations that participated in the final survey of the World Health Organization MONICA Project, 1989–1997.

mation on educational achievement was missing. In the analysis, the highest category of educational achievement was used as the reference.

### Statistical analysis

Distribution of individual SBP. To compare the distributions of SBP across populations, we followed a method similar to that used by Rose (13). We ranked the MONICA study populations by median SBP and created five groups of increasing SBP. Then, we calculated the percentage of persons in each 5-mmHg SBP category and plotted the distributions (figure 1).

Multilevel analysis. Individual SBP was analyzed by using multilevel linear regression models (10, 14, 15), with individuals at the first level and MONICA study populations at the second level. The associations between the variables studied and SBP (and their uncertainty) were appraised by using beta coefficients (95 percent confidence intervals) in the fixed-effects part of the models.

We fitted three models. Model i did not include any explanatory variables and focused on describing only individual and population components of variance in SBP. In model ii, we included individual age to adjust for age-related differences in SBP, and we studied the association of SBP with BMI, antihypertensive medication use, smoking, and educational achievement. Finally, in model iii, we extended model ii and adjusted for two population characteristics:

measurement techniques (i.e., random zero sphygmomanometer) and population variation in SBP (i.e., SBP-SD).

In models ii and iii, the coefficients for BMI and antihypertensive medication use were taken as random at the MONICA study population level, allowing for possible between-population differences in the association between these variables and SBP in each population (i.e., random slopes analysis). That is, we investigated random cross-level interactions by determining whether the MONICA study population level modified the individual-level association 1) between BMI and SBP and also 2) between antihypertensive medication use and SBP. The association between SBP and BMI was also allowed to vary at the individual level, since between-individual differences in SBP may not be constant for all BMI values (i.e., presence of individual heteroscedasticity).

We computed the first-level variance (i.e., differences between individuals in MONICA study populations) and the second-level variance (i.e., differences between MONICA study populations). We calculated the variance partition coefficient (VPC), a measure of the extent to which individuals in a MONICA study population resemble each other more than they resemble those from other MONICA study populations in terms of SBP level. The VPC provides an estimate of the extent to which population-level factors may explain individual differences in SBP. The VPC is the percentage of the variance in SBP attributed to the MONICA

study population level and is therefore a measure of population effect.

In its simplest form (model i), the VPC corresponds to the intraclass correlation. It is a measure of general clustering of individual SBP in the MONICA study populations:

$$VPC = \frac{V_{MSP}}{V_{MSP} + V_I} \times 100,$$

where  $V_I$  = variance between individuals (first-level variance) and  $V_{\rm MSP}$  = variance between MONICA study populations (MSP) (second-level variance).

A large VPC would indicate that differences between the MONICA study populations account for an appreciable part of the individual differences observed in the combined MONICA populations (i.e., the MONICA study populations are important to understanding individual differences). On the other hand, a VPC close to zero would indicate that the MONICA study population exerts only a small influence on individual SBP variance (14).

At the population level, the variance of the coefficient measuring the association between SBP and any of the other variables (i.e., the random slopes variance) can be interpreted as the between-population variation in the association 1) between BMI and SBP or 2) between antihypertensive medication use and SBP (i.e., different slopes in different populations). The slopes variance is also a coefficient in a function that describes how the between-population variation in SBP changes with individual levels of BMI and antihypertensive medication use (10).

In addition, the VPC can be calculated as a function of BMI and antihypertensive medication use and plotted against BMI. In this way, the VPC provides information on the importance of the population effects on specific groups of individuals:

VPC = 
$$\frac{V_{\text{MSP(BMI + antihypertensive medication})}}{V_{\text{MSP(BMI + antihypertensive medication})} + V_{I(BMI)}} \times 100$$

where  $V_{I(\mathrm{BMI})}$  = variance between individuals as a function of individual BMI and  $V_{\text{MSP (BMI + antihypertensive medication)}} = \text{variance}$ between MONICA study population as a function of individual BMI and antihypertensive medication use.

To estimate the proportion of the variation in SBP explained by a model with more terms, we calculated the percentage of variance explained as

$$\frac{(V_0 - V_1)}{V_0} \times 100,$$

where  $V_0$  = variance of the initial model and  $V_1$  = variance of the model with more terms.

MLwiN software, version 1.1 (16), was used to perform the analyses. Parameters were estimated by using iterative generalized least squares. Use of restricted iterative generalized least squares gave very similar results.

TABLE 1. Characteristics of the 39 MONICA\* study populations that participated in the final survey of the World Health Organization MONICA Project during the early 1990s

	Median	First quartile	Third quartile
No. of women	626	552	693
No. of men	589	520	654
Overall participation rate (%)	74	68	78
Age (mean years)			
Women	49	49	50
Men	50	49	50
Body mass index (mean; kg/m²)			
Women	26.6	25.9	27.4
Men	26.7	26.4	27.2
Systolic blood pressure (mean; mmHg)†			
Women	130	127	135
Men	134	131	137
Systolic blood pressure (standard deviation)†	20	18	21
Use of blood pressure-lowering drugs (%)			
Women	13	12	17
Men	11	9	14
Smokers (%)			
Women	21	15	28
Men	34	29	42

<sup>\*</sup> MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease

# RESULTS

The characteristics of the 39 MONICA study populations that participated in the final population risk factor survey are presented in table 1. Detailed information about the MONICA study populations is available at http://www.ktl.fi/

Figure 1 shows the distribution of SBP in MONICA study populations grouped by median SBP. It is evident that whatever cutoff was used to define hypertension, the proportion of hypertensives in the population increased with higher median SBP levels. Figure 1 also illustrates that individual variability was greater at higher median SBP values.

Tables 2 and 3 indicate that there was considerable between-population variance in SBP. These tables also show that after accounting for the individual characteristics studied, population differences in SBP explained about 7 percent (for men) and 8 percent (for women) of the total individual differences (model ii). Thus, some evidence existed for a population effect in shaping a common individual SBP level.

Tables 2 and 3 also illustrate that compared with the rest of the population, men and women who used antihypertensive

<sup>†</sup> In the MONICA study population.

TABLE 2. Multilevel regression analysis\* of systolic blood pressure in the 23,796 men aged 35–64 years from 39 MONICA study populations that participated in the final survey of the World Health Organization MONICA Project during the early 1990s

			Mo	del ii	Model iii	
Regression coefficients Mode		Model i Beta (mmHg)		95% CI†	Beta (mmHg)	95% CI
	Individua	al-level	variables			
Antihypertensive medication use			13.09	11.59, 14.58	13.09	11.60, 14.57
BMI‡			0.94	0.85, 1.04	0.94	0.84, 1.04
Smoking (yes vs. no)			-0.04	-0.51, 0.43	-0.05	-0.52, 0.42
Educational achievement (tertiles)						
High	Refere		Reference	•	Reference	
Medium			1.17	0.61, 1.74	1.18	0.62, 1.74
Low			2.11	1.56, 2.67	2.11	1.55, 2.66
Missing information			1.61	-3.61, 6.82	2.12	-2.32, 6.56
	Popul	ation va	riables			
Increasing SBP-SD†					1.05	0.41, 1.69
SBP measurement methods (random zero sphygmomanometer)					-2.82	-5.57, -0.07
<del>-</del>	Variance	SE†	Variance§	SE	Variance	SE
Variance						
Between populations	22.71	5.28	19.38	4.54	18.31	4.28
Between individuals	359.34	3.30	272.37	3.00	272.42	2.99
Antihypertensive medication use – SBP slope variance			16.95	5.08	16.67	5.02
BMI – SBP slope variance			0.06	0.02	0.06	0.02
BMI-related individual variance			0.54	0.13	0.54	0.13
Variance explained by the new model (%)						
Between populations	Reference		15		19	
Between individuals	Reference		24		24	
Variance partition coefficient¶ (%)	6		7		6.3	

<sup>\*</sup> Model i did not include any explanatory variables; model ii included individual variables; and, in model iii, model ii was extended and was adjusted for population characteristics. In models ii and iii, the coefficients for body mass index (BMI) and antihypertensive medication use were taken to be random at the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study population level, allowing for possible between-population differences in the association between these variables and systolic blood pressure (SBP) in each population (i.e., random slopes analysis).

- † CI, confidence interval; SBP-SD, standard deviation of SBP measurements in each population; SE, standard error.
- ‡ One whole unit (kg/m²) rise in BMI.
- § Also refer to figure 2.
- ¶ The variance partition coeffficient (VPC) is the percentage of the variance in SBP attributed to the MONICA study population (MSP) level and is therefore a measure of population effect. In models ii and iii, because the variance at both the individual and the MSP level of analysis is a function of BMI, and a function of antihypertensive medication use at the MSP level, the distribution of components of variance also becomes a function of BMI and antihypertensive medication use rather than being one single value as in model i. These variance functions were used to calculate the VPC:

$$VPC = \frac{V_{MSP(BMI + antihypertensive \ medication)}}{V_{MSP(BMI + antihypertensive \ medication)} + V_{I(BMI)}} \times 100$$

where  $V_{I\,(BMI)}$  = variance between individuals as a function of individual BMI and  $V_{MSP\,(BMI\,+\,antihypertensive\,medication)}$  = variance between MONICA study population as a function of individual BMI and antihypertensive medication use.

medication (and who presumably suffered from hypertension) had an SBP that was, on average, 13 mmHg and 15 mmHg higher, respectively. A one-unit rise in BMI was associated with about a 1-mmHg higher SBP in both men and women. SBP was about 1.4 mmHg lower in women who

smoked, but there was no apparent effect of smoking on SBP for men. Further investigations indicated that the effect of smoking on lowering blood pressure was also present for men, but it was reduced after adjustment for BMI (not shown in tables). Education showed a dose-response association

TABLE 3. Multilevel regression analysis\* of systolic blood pressure in the 24,986 women aged 35-64 years from 39 MONICA study populations that participated in the final survey of the World Health Organization MONICA Project during the early 1990s

Decrees in a settinion to	Model i		Model ii		Model iii	
Regression coefficients			Beta (mmHg)	95% CI†	Beta (mmHg)	95% CI
	In	dividual-le	vel variables			
Antihypertensive medication			14.79	13.15, 16.43	14.80	13.16, 16.44
BMI‡			0.86	0.76, 0.97	0.86	0.76, 0.97
Smoking (yes vs. no)			-1.36	-1.89, -0.83	-1.36	-1.89, -0.83
Educational achievement (tertiles)			Reference		Reference	
High						
Medium			1.58	1.03, 2.13	1.58	1.02, 2.13
Low			2.71	2.16, 3.26	2.71	2.16, 3.26
Missing information			-0.85	-6.13, 4.44	2.09	-2.64, 6.81
		Population	n variables			
Increasing SBP-SD†					1.08	0.40, 1.76
SBP measurement methods (random zero sphygmomanometer)					-2.20	-5.14, 0.74
_	Variance	SE†	Variance§	SE	Variance	SE
Variance						
Between populations	35.29	8.12	22.24	5.34	15.46	3.64
Between individuals	433.36	3.88	280.81	3.02	280.82	3.02
Antihypertensive medication use – SBP slope variance			22.00	6.19	21.99	6.12
BMI - SBP slope variance			0.09	0.03	0.09	0.03
BMI-related individual variance			0.17	0.08	0.17	0.08
Variance explained by the new model (%)						
Between populations	Reference		34		56	
Between individuals	Reference		35		35	
Variance partition coefficient¶ (%)	8		8		5	

<sup>\*</sup> Model i did not include any explanatory variables; model ii included individual variables; and, in model iii, model ii was extended and was adjusted for population characteristics. In models ii and iii, the coefficients for body mass index (BMI) and antihypertensive medication use were taken to be random at the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study population level, allowing for possible between-population differences in the association between these variables and systolic blood pressure (SBP) in each population (i.e., random slopes analysis).

- † CI, confidence interval; SBP-SD, standard deviation of SBP measurements in each population; SE, standard error.
- ‡ One whole unit (kg/m²) rise in BMI.
- § Also refer to figure 3.

¶ The variance partition coeffficient (VPC) is the percentage of the variance in SBP attributed to the MONICA study population (MSP) level and is therefore a measure of population effect. In models ii and iii, because the variance at both the individual and the MSP level of analysis is a function of BMI, and a function of antihypertensive medication use at the MSP level, the distribution of components of variance also becomes a function of BMI and antihypertensive medication use rather than being one single value as in model i. These variance functions were used to calculate the VPC:

$$VPC = \frac{V_{MSP(BMI + antihypertensive medication)}}{V_{MSP(BMI + antihypertensive medication)} + V_{I(BMI)}} \times 100$$

where  $V_{I(BMI)}$  = variance between individuals as a function of individual BMI and  $V_{MSP\ (BMI\ +\ antihypertensive\ medication)}$  = variance between MONICA study population as a function of individual BMI and antihypertensive medication use.

with SBP, which was 2 mmHg higher in men and 3 mmHg higher in women with the lowest educational achievement.

For men, adjustment for age, antihypertensive medication use, smoking habits, BMI, and educational achievement explained 15 percent of the age-adjusted variation in SBP between the MONICA study populations and 24 percent of the variance between individuals (table 2, model ii). For women, this adjustment had a larger effect, explaining 34 percent of the population differences and 35 percent of the individual differences (table 3, model ii).

Higher BMI and antihypertensive medication use were associated with higher SBP in all populations, but this association (the slope in the regression analysis) varied between populations (figure 2, a and b; figure 3, a and b). At both the individual and population levels, differences (i.e., variance) in SBP increased with higher BMI values (figure 2, c; figure 3, c). The VPC (i.e., the percentage of the total variance explained by the population level) appeared to have a U-shaped relation with BMI for women (figure 3, d) and for men who did not use antihypertensive medication (figure 2, d). For men versus women, the population level had a smaller influence on SBP, but, as for women, the population effect was higher for antihypertensive medication users than for nonusers (figure 2, d; figure 3, d).

Results for model iii in tables 2 and 3 indicate that over and above the individual characteristics studied and the methods used for measuring blood pressure, SBP increased as SBP-SD increased. As expected, use of a random zero sphygmomanometer led to a slightly lower SBP.

The data from each MONICA study population were subjected to central quality assessment and received a summary score for the quality of the different variables. The quality score was low for BMI in one MONICA study population, for blood pressure measurement in two MONICA study populations, and for antihypertensive medication information in three MONICA study populations. Excluding these MONICA study populations (6,323 individuals) from the analysis did not alter our conclusions because parameter estimates changed only slightly.

### **DISCUSSION**

We found empirical evidence of a population phenomenon affecting individual SBP over and above individual factors. Our findings suggest that even an apparently individual characteristic, such as blood pressure level, is in part conditioned by the population in which one lives. This population effect remained after we accounted for differences between the individual composition of MONICA study populations regarding their age, use of antihypertensive medication, smoking habits, BMI, and educational achievement. On average, about 7–8 percent of the total individual differences in SBP in the MONICA Project were attributed to the population in which a person was living. However, the population effect was found to be much stronger for certain groups; for example, it was considerably larger for overweight women using antihypertensive medication (a VPC of about 20 percent).

The size of the population effect found in this study was not surprising since the MONICA Project covers a large number of populations with widely different economic, health care, social, genetic, and lifestyle characteristics, as well as varying environments. When populations in more limited geographic contexts are compared, or if underlying individual-population heterogeneity is not investigated, the VPC may be much lower, as has been observed in the city of Malmö, Sweden (17) and in Scotland (18).

The rationale for mass preventive strategies is supported by the data in figure 1. As explained by Rose (13), lowering the average level of blood pressure in the population would result in a decrease in the prevalence of hypertension. However, multilevel analysis further shows that a mass preventive strategy aimed at shifting the whole blood pressure distribution in the population in a favorable direction by reducing individual BMI would have different effects in different populations. The likely SBP reduction for a specific BMI reduction would be higher in some populations than in others, and variability would be especially large for people who are overweight and for those receiving antihypertensive medication treatment. In this study, we focused on the effects of BMI on SBP, but other unmeasured characteristics (e.g., reduced salt intake, genetic factors) may present a similar pattern of individual-environment interactions (19).

The relatively large population effect among antihypertensive medication users (i.e., a VPC of about 12 percent for men and 18 percent for women) compared with all nonusers (a VPC of about 6 percent for men and 10 percent for women) probably reflects differences in therapeutic practice between MONICA study populations, such as different blood pressure thresholds for initiating pharmacologic treatment, use of different drugs, and differences in the promotion of treatment adherence (20). Shared diagnostic and therapeutic procedures in a specific MONICA study population would influence all persons in the MONICA study population simultaneously, thus resulting in a common level of SBP in a population over and above individual characteristics. For clinicians, the challenge is to recognize that the usual levels of blood pressure they find in a population are not necessarily optimal. In part, this issue is related to adoption of evidence-based best practice that has the potential to improve diagnosis and treatment for the whole population. Also important is for clinicians to understand that the population approach to prevention—for example, lowering blood pressure through population-wide reductions in body weight—adds considerable value to the high-risk strategy of medical treatment of those people with hypertension.

The smaller VPC for nonusers of antihypertensive medication indicates that individual SBP levels in this group seem less influenced by environmental factors. It is likely that factors related to pharmacologic treatment of high blood pressure are more susceptible than those associated with untreated blood pressure level to current contextual influences. It is known that determinants of many biomedical variables are more properly understood from a life-course perspective (21). Therefore, the influence of population factors on untreated SBP would be better investigated by longitudinal, rather than cross-sectional, multilevel analysis.

When we compared populations, we observed that increased SBP variation within populations (i.e., SBP-SD) was associated with higher SBP. From a multinational perspective, high within-population variation in SBP levels may reflect an array of societal factors that affect determinants of SBP and increase blood pressure in the population. Therefore, preventive strategies that consider heterogeneity among individuals and are directed to the whole population have the potential to reduce individual differences at the same time they reduce population means.

At the individual level, the observed educational gradient in SBP level confirms previous investigations (22). It was present even when BMI, a factor in the pathway between

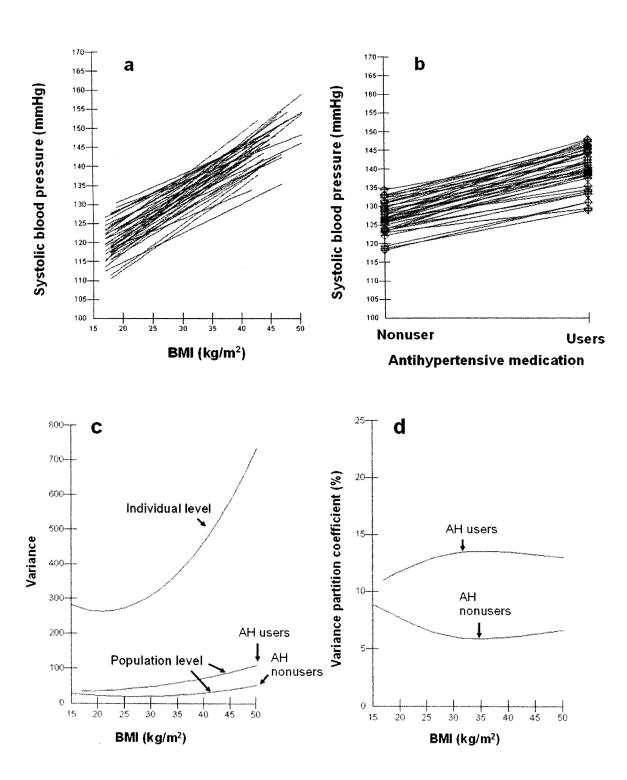


FIGURE 2. Information on the 23,796 men aged 35-64 years from 39 Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study populations that participated in the final risk factor survey of the World Health Organization MONICA Project, 1989–1997. The upper part shows the heterogeneity of the slopes for the association between (a) systolic blood pressure and body mass index (BMI) and (b) systolic blood pressure and blood pressure-lowering drugs (antihypertensive (AH) medication) in the 39 MONICA study populations. The lower part shows (c) the variance in individual systolic blood pressure as a function of individual BMI and the variance in mean systolic blood pressure at the MONICA study population level as a function of BMI and use of antihypertensive medication and (d) the variance partition coefficient—the percentage of the variance in individual systolic blood pressure attributed to the MONICA study population level—as a function of BMI and use of antihypertensive medication. Values were adjusted for age and blood pressure measurement techniques.

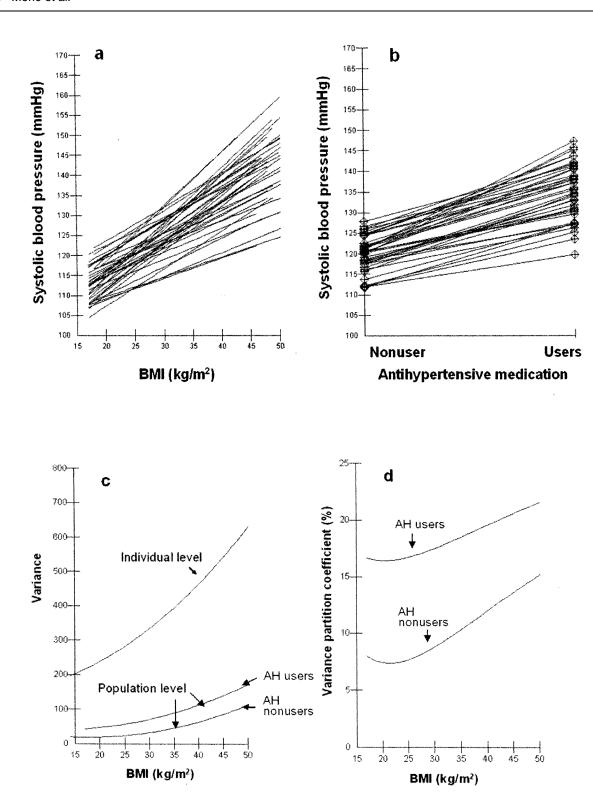


FIGURE 3. Information on the 24,986 women aged 35–64 years from 39 Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study populations that participated in the final risk factor survey of the World Health Organization MONICA Project, 1989–1997. The upper part shows the heterogeneity of the slopes for the association between (a) systolic blood pressure and blood pressure-lowering drugs (antihypertensive (AH) medication) in the 39 MONICA study populations. The lower part shows (c) the variance in individual systolic blood pressure as a function of individual BMI and the variance in mean systolic blood pressure at the MONICA study population level as a function of BMI and use of antihypertensive medication and (d) the variance partition coefficient—the percentage of the variance in individual systolic blood pressure attributed to the MONICA study population level—as a function of BMI and use of antihypertensive medication. Values were adjusted for age and blood pressure measurement techniques.

educational achievement and SBP level, was taken into account.

The role of BMI as a main risk factor for elevated blood pressure (23) was confirmed in our investigation. The dependence of the VPC on individual BMI supports the contention that SBP is strongly influenced by the environment in which people live (24). One plausible explanation is that diet, exercise, and other aspects of healthy lifestyle and/or slim body ideals are conditioned by common social processes (25, 26). Thus, population factors may influence SBP by operating as determinants of individual characteristics (27, 28).

Multilevel variance analysis provided an innovative way of understanding the distribution and determinants of individual and population SBP (29). By considering that individuals are nested within populations, the multilevel approach appears both statistically and conceptually more appropriate than single-level ecologic analysis that disregards the natural structure of the data.

In this study, we found empirical evidence of a population effect on individual SBP over and above individual factors. The effects of antihypertensive medication use and BMI on SBP were modified by the population in which a person lived, especially for women. The results suggest the existence of a considerable potential for preventive strategies focused on the population level and directed to both pharmacologic and lifestyle-related factors (e.g., medical practice habits, societal attitudes toward healthy lifestyles). The effectiveness of these environmental strategies would improve if they were specifically shaped in each population and were designed to reach susceptible groups of people such as overweight women.

# **ACKNOWLEDGMENTS**

Dr. Merlo's work is supported by the Faculty of Medicine in Lund, the Council for Pharmacoepidemiology at the County of Skåne, The NEPI Foundation, and the Swedish Council for Working Life and Social Research (document 2003-0580). Dr. Asplund receives support from grants from the Swedish Research Council, the Swedish Council for Working Life and Social Research, the Heart and Chest Fund, Västerbotten and Norrbotten County Councils, and the Strategic Research Fund. Dr. Lynch's work is supported by a Robert Wood Johnson Investigator in Health Policy Award.

MONICA Centres were funded predominantly by regional and national governments, research councils, and research charities. Coordination was the responsibility of the World Health Organization, assisted by local fund-raising for congresses and workshops. The World Health Organization also contributed to the MONICA Data Centre in Helsinki, which was supported by the National Public Health Institute of Finland. A contribution to the World Health Organization from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, provided some support for the MONICA Data Centre and the Quality Control Centre for Event Registration in Dundee, Scotland. Grants from ASTRA Hässle AB, Sweden; Hoechst AG, Germany;

Hoffman-La Roche AG, Switzerland; and the Institut de Recherches International Servier (IRIS), France supported data analysis and preparation of previous publications.

The authors express their gratitude to Dr. Susana Sans, Director of the Monitoring and Research Programme on Chronic Diseases at the Institute of Health Studios in Barcelona, Spain, for her comments on the final version of the manuscript.

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#### **APPENDIX**

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