

# Changes in the exposure to cardiovascular disease risk factors in an 18 year follow-up study of a cohort of middle age urban residents. The Polish arm of the HAPIEE study

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## Abstract

**Background:** *Cross-sectional studies revealed that risk factor exposure increases with age but after reaching its peak decreases. This decline may be attributed to higher mortality among exposed individuals, lifestyle, or natural physiological changes related to age. Only prospective observations at the individual level provide credible insights of exposure during the transition from middle to old age. This study addresses changes in cardiovascular risk factors among older urban residents in Poland over an 18-year period.*

**Methods:** *The study analyzed data from the Polish arm of the Health, Alcohol and Psychosocial factors In Eastern Europe (HAPIEE) project, a prospective cohort study investigating cardiovascular disease determinants. The sample included 312 participants (46–69 years). Data on demographic characteristics, blood lipids, blood pressure, body mass index (BMI), fasting glucose, and smoking status were collected at baseline and during re-examination.*

**Results:** *The analysis yielded a decrease in diastolic blood pressure, total cholesterol, LDL-cholesterol, and non-HDL cholesterol concentrations. However, BMI and fasting glucose levels increased. The decrease in blood pressure was mainly attributed to treatment effects, while the reduction in lipid concentrations was observed regardless of treatment. In addition, smoking prevalence decreased over the course of 18 years.*

**Conclusions:** *The results of the prospective nearly 20 year observation at the individual level confirm findings from repeated cross-sectional studies on decrease in lipid concentrations, blood pressure and prevalence of smoking in older individuals. (Cardiol J 2024; 31, 5: 690–698)*

**Keywords:** cardiovascular disease, cross-sectional studies, heart disease risk factors, body mass index, lipids

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## Introduction

A substantial reduction in cardiovascular disease (CVD) mortality is possible mainly by reducing exposure to major risk factors in a population which contributes to a decrease of the incidence. In Poland, there was a dynamic decline in mortality due to the diseases of circulatory system after 1991 which slowed down after 1999 and a large increase was observed from 2020 which reflected the 2<sup>nd</sup> and consecutive waves of the COVID-19 pandemic [1, 2]. The results of IMPACT modeling for Poland indicated that the 54% reduction in coronary heart disease mortality observed in Poland between 1991 and 2005 could be attributed to favorable changes in exposure to major risk factors [3].

Later, repeated cross-sectional studies of Polish population samples showed not only a lack of beneficial changes in exposure to risk factors in the last decades, but even some unfavorable changes have been noted. A significant increase in the prevalence of hypertension (from 36% to 43%) was confirmed in WOBASZ studies. The frequency of obesity increased from 22% to 26% and at the same time a proportion of low physically active people increased from 52% to 55%. The WOBASZ studies confirmed the overtime increase in the frequency of diabetes and showed that the prevalence of fasting glucose  $\geq 7\text{mmol/L}$  increased from 9% to 18%. There was no significant growth in the prevalence of dyslipidemia, which affects nearly 70% of the adult population and there was some reduction in the frequency of smoking (31% to 25%) [4–10].

Data from a United States (US) population of adults also showed no significant improvement in the prevalence of major risk factors. In the serial cross-sectional survey study, conducted between 1999 and 2018, the increase in mean body mass index (BMI) was reported from  $28.0\text{ kg/m}^2$  to  $29.8\text{ kg/m}^2$ , mean glycated hemoglobin A increased from 5.4% to 5.7%, and no overtime change in mean systolic blood pressure was observed. On the other hand, mean serum total cholesterol was reduced from 203.3 mg/dL to 188.5 mg/dL and smoking prevalence decreased from 24.8% to 18.1% [11]. In the prospective study from China, changes in the prevalence of individual CVD risk factors over 7 years were insignificant, but overtime increase in 10-year risk of atherosclerotic CVD was observed in 30% of participants while the decrease was found only in 6% of individuals [12].

Polish cross-sectional studies which involved a national sample yielded that the exposure to risk factors increased with age and after reaching a peak

in upper middle age or early old age decreases. Smoking rates peak at age 45–54 years both in men and in women and in the older age groups fall to about 16% in men and 3% in women in the age group 75–84 years [8]. Hypercholesterolemia peaks at age 45–54 years and then levels in men and peaks at age 55–64 years and decreases then after in women [13]. Obesity and overweight peak at age 55–79 years in men and at age 65–75 years in women [5]; hypertension peaks at age 70–79 years in both sexes [4] and diabetes at age 65–74 years [14]. One explanation of the decline of the prevalence of risk factors is an effect of greater mortality of the exposed individuals in comparison to not-exposed but, even the differences in the age of reaching the peak of exposure between risk factors (smoking and hypercholesterolemia peak approximately a decade before obesity, hypertension and diabetes) suggest that there are other reasons of the decline which might include changes in the lifestyle, chronic diseases, treatment received or natural physiological changes which reflect ageing. An investigation of changes in the exposure to risk factors which are not related to mortality require prospective observations at the individual level which cover the period of the passing from middle to old age [15].

The aim of the present study was to assess the changes in blood lipids, blood pressure, body mass index, fasting glucose and smoking in 18-year follow-up of older urban residents.

## Methods

### Studied sample

The studied group consisted of participants of the Polish arm of the HAPIEE (*Health, Alcohol and Psychosocial factors In Eastern Europe*) project, which was a prospective cohort study aimed to investigate determinants of cardiovascular disease (CVD) and other chronic conditions in Central and Eastern Europe. Detailed descriptions of the study design and methods have been published elsewhere [16]. Brief information, relevant for this paper is given below. A random sample of 10,728 men and women aged 45–69 years old, stratified by gender and 5-year age groups, was selected from Krakow population register. The baseline examination was carried out between 2002 and 2005; response rate was 61% [16]. The HAPIEE study was approved by ethics committees at University College London and at the Jagiellonian University Medical College. All participants gave written informed consent. For the purpose of this paper, data was collected in

two time points: at baseline and at re-examination carried out between December 2019 and March 2020. The re-examination was planned to include the entire Polish HAPIEE cohort but was interrupted by the COVID-19 pandemic outbreak, when 464 participants were interviewed (participation rate 49%).

Current analysis included 312 participants for whom data from the interview and measurements of blood lipids, blood pressure and body weight and height from both examinations (at baseline and in re-examination) were available.

## Data

The same data collection methods were used both at baseline and in re-examination. Participants were first visited at home by trained nurses to complete a standardised questionnaire which included questions about health, health behaviours and socioeconomic characteristics. Then, all participants were invited to a clinic for anthropometric and blood pressure measurements and blood collection for biochemical tests.

A standardised questionnaire was used to obtain data on age, sex, education (primary/secondary/university), smoking status (current/former/never), perceived health (very good/good/average/poor/very poor). Participants were asked about medical history of diagnosis of hypertension, diabetes and hypercholesterolemia, and in those with positive answers, the information about the use of pharmacological treatment was collected.

The information on treatment for hypertension, hypercholesterolemia or diabetes was obtained based on the answers to the questions whether participant was taking drugs for lowering blood pressure, lowering blood cholesterol or blood glucose (yes/no) in people who had previously been diagnosed by the doctor as having hypertension, hypercholesterolemia, or diabetes.

Blood pressure was measured in a sitting position on the right arm, after at least a 5-minute rest, three times at 2-minute intervals using an Omron M5-I digital blood pressure monitor. In the analysis, the average of the last two measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were used. Body weight and height were measured in a standing position with no shoes and without outer garments. Based on anthropometric measurements body mass index (BMI,  $\text{kg}/\text{m}^2$ ) was calculated. Venous blood was collected using vacuum tubes from participants after overnight fasting. Blood was stored at  $+4^\circ\text{C}$  and centrifuged within 4 hours of the venepuncture. The analyses

were carried out on the same day. Blood lipids were determined by the automated enzymatic colorimetric method. Low-density lipoprotein cholesterol was calculated by the Friedewald formula. Non-HDL was calculated as the difference between total cholesterol and HDL cholesterol. Glucose concentration in plasma was assessed using the enzymatic method.

## Statistical analysis

Continuous variables were presented as means with standard deviations (SD). The Shapiro-Wilk test was used to test the normal distribution of variables. Categorical variables were reported as numbers and percentages. Changes in numerical and categorical variables were assessed using paired t-test and McNemar-Bowker test, respectively. The ANCOVA for repeating measurements was used to take into account the influence of covariates (age, sex, BMI, educational level, smoking status and perceived health) The analysis was performed with stratification by medication use (hypertension, hypercholesterolemia and diabetes as appropriate). Statistical analyses were performed using IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp. P-values  $< 0.05$  were accepted as statistically significant.

## Results

The sample included 312 participants between 46 and 69 years of age at baseline. The distributions of age, gender, education, perceived health, and smoking are shown in Table 1. There were 154 (49.4%) men, and 128 (41.0%) participants with university education. Almost half of the sample (46.5%) had good or very good perceived health, and approximately 28% (86) were current smokers.

Participants included in the analysis were younger (55 years, SD = 6.3 vs. 58 years, SD = 7.0), better educated (41% vs. 28% with university education) and healthier (46.5% vs. 35.2%, with good or very good perceived health) compared to non-responders. However, there was no statistically significant difference in prevalent myocardial infarction, stroke and gender distribution (49% men vs. 49% men) (Suppl. Table S1).

The distribution of smoking status at baseline and at the re-examination is presented in Table 2. Over 70% of the participants declared the same smoking status at both phases of the study, however, there was a significant change in smoking status observed. There were 38 (12%) people who

**Table 1.** Distribution of age, sex, perceived health and smoking status at baseline

Age, mean (SD)	55 (6.3)
Sex — male, n (%)	154 (49.4%)
<b>Education, n (%)</b>	
Primary	61 (19.6%)
Secondary	123 (39.4%)
University	128 (41.0%)
<b>Perceived health, n (%)</b>	
Very good	14 (4.5%)
Good	131 (42.0%)
Average	140 (44.9%)
Poor	25 (8.0%)
Very poor	2 (0.6%)
<b>Smoking status, n (%)</b>	
Current	86 (27.7%)
Former	116 (37.2%)
Never	109 (35.1%)

stopped smoking, and they constituted the largest group of those who changed smoking status. There was no significant change in perceived health between baseline and re-examination (**Suppl. Table S2**).

Changes in blood pressure, BMI, blood lipids, and glucose concentration in the entire sample are presented in Table 3. There was a lower mean DBP observed at the re-examination, compared to the baseline (mean difference: 2.6 mmHg); however, the significant change was found only in SBP. There were significant decreases in blood lipids concentrations: by 0.98 mmol/L in total cholesterol, 0.97 mmol/L in LDL-cholesterol, and by 0.99 mmol/L in non-HDL cholesterol. No significant changes in HDL-cholesterol or triglyceride (TG) levels were observed. An increase in mean BMI by 1.2 kg/m<sup>2</sup> was found. Also, there were higher mean glucose concentrations in re-examination compared to baseline (5.8 mmol/L vs. 5.1 mmol/L). After adjusting for age, sex, education level, smoking

status, and perceived health, the direction and magnitude of significant differences remained almost unchanged.

In the Table 4, there are presented mean values of blood pressure, blood lipids, and glucose concentrations in participants who were treated for hypertension, hypercholesterolemia and diabetes, respectively, presented separately for baseline and the re-examination. In the re-examination, the number of participants treated for hypertension more than doubled, those treated for hypercholesterolemia increased by 2.5 times, and number of people treated for diabetes increased by 5 times. Participants treated for these conditions in re-examination had lower mean values of SBP, DBP, total cholesterol, LDL-cholesterol and non-HDL cholesterol than participants treated in baseline. Concentration of fasting glucose was higher in participants treated for diabetes in re-examination.

The right section of the Table 4 shows a comparison of mean values of blood pressure, blood lipids, and glucose concentrations in participants treated for hypertension, hypercholesterolemia and diabetes, respectively in both phases of the study. After adjusting for covariates, among participants continuing treatment for hypertension in both phases of the study a significant decrease in SBP and DBP, by approximately 9 mmHg was observed and in participants treated for hypercholesterolemia in both phases of the study a significant decrease in total cholesterol, LDL-cholesterol and non-HDL cholesterol were found by 1.69 mmol/L, 1.6 mmol/L and 1.67 mmol/L, respectively. Adjusted difference for fasting glucose was impossible to estimate due to the small number of participants.

By analogy with Table 4, the results for participants not treated for the conditions mentioned above are presented in Table 5. The number of untreated participants declined substantially over time. In participants declaring no treatment for hypertension in baseline and re-examination mean SBP and DBP were within normal blood pressure limits. In participants not using medication for hypercholesterolemia, mean TC, LDL-cholesterol and non-HDL-cholesterol were lower in

**Table 2.** Smoking status at baseline and re-examination

Smoking status at baseline	Smoking status at re-examination			
	Current	Former	Never	
Current	40 (12.9%)	38 (12.2%)	8 (2.6%)	< 0.001
Former	12 (3.9%)	77 (24.8%)	27 (8.7%)	
Never	1 (0.3%)	3 (1.0%)	105 (33.8%)	



**Table 3.** Difference in mean blood pressure, BMI, blood lipids and fasting glucose concentrations between re-examination and baseline

	Baseline		Re-examination		Difference (re-examination — baseline)			Adjusted difference* (re-examination — baseline)		
	N	mean (SD)	mean (SD)	Δ	95% CI	p	Δ	95% CI	p	
Systolic blood pressure [mmHg]	312	132.1 (17.75)	131.8 (16.74)	-0.388	(-2.754; 1.979)	0.75	-0.39	(-2.763; 1.983)	0.76	
Diastolic blood pressure [mmHg]	312	83.7 (11.2)	81.1 (9.4)	-2.601	(-4.121; 1.081)	0.008	-2.597	(-4.104; -1.090)	< 0.001	
Body Mass Index [kg/m <sup>2</sup> ]	311	27.3 (4.07)	28.5 (5.61)	1.188	(0.73; 1.646)	< 0.001	1.196	(0.746; 1.646)	< 0.001	
Total cholesterol [mmol/L]	312	5.8 (1.02)	4.8 (1.09)	-0.976	(-1.127; -0.825)	< 0.001	-0.971	(-1.110; -0.832)	< 0.001	
LDL cholesterol [mmol/L]	312	3.6 (0.94)	2.7 (0.97)	-0.973	(-1.11; -0.837)	< 0.001	-0.970	(-1.097; -0.843)	< 0.001	
NonHDL cholesterol [mmol/L]	312	4.3 (1.06)	3.3 (1.04)	-0.990	(-1.143; -0.838)	< 0.001	-0.986	(-1.125; 0.846)	< 0.001	
HDL cholesterol [mmol/L]	312	1.5 (0.37)	1.5 (0.39)	0.015	(-0.018; 0.047)	0.37	0.015	(-0.018; 0.05)	0.368	
Triglycerides [mmol/L]	312	1.5 (0.68)	1.4 (0.63)	-0.032	(-0.111; 0.048)	0.43	-0.0281	(-0.104; 0.048)	0.466	
Fasting glucose [mmol/L]	311	5.1 (0.71)	5.8 (1.25)	0.791	(0.664; 0.918)	< 0.001	0.791	(0.665; 0.920)	< 0.001	

\*After adjustment for age, sex, education level, smoking status and perceived health

**Table 4.** Difference in mean blood pressure, blood lipids and fasting glucose concentrations between re-examination and baseline in participants treated for hypertension, hypercholesterolemia and diabetes

Treatment for:	Treated at baseline		Treated at re-examination		Continued treatment at baseline and re-examination						
	N	mean (SD)	N	mean (SD)	N	mean (SD)	P				
Hypertension	83	142.9 (16.98)	171	133.1 (18.14)	76	143.2 (17.46)	134.4 (17.38)	0.001	-8.809	(-13.994; -3.632)	0.001
	83	90.0 (11.59)	171	80.3 (9.16)	76	90.4 (11.53)	81.2 (9.95)	< 0.001	-9.14	(-12.328; -5.954)	< 0.001
Hypercholesterolemia	48	6.16 (1.04)	119	4.34 (0.94)	29	6.09 (0.88)	4.4 (0.98)	< 0.001	-1.69	(-2.116; -1.264)	< 0.001
	48	3.93 (0.96)	119	2.22 (0.84)	29	3.88 (0.87)	2.28 (0.84)	< 0.001	-1.6	(-1.966; -1.235)	< 0.001
Diabetes	48	4.71 (1.11)	119	2.912 (0.94)	29	4.62 (1.00)	2.95 (0.96)	< 0.001	-1.673	(-2.093; -1.253)	< 0.001
	48	1.44 (0.35)	119	1.432 (0.36)	29	1.46 (0.35)	1.45 (0.37)	0.71	-0.017	(-0.1123; 0.077)	0.709
	48	1.71 (0.92)	119	1.517 (0.64)	29	1.625 (0.80)	1.471 (0.65)	0.2	-0.153	(-0.393; -0.086)	0.197
	9	6.58 (0.78)	55	7.233 (1.99)	8	6.7 (0.73)	8.36 (3.15)	0.16			

\*After adjustment for age, sex, education level, smoking status and perceived health

**Table 5.** Difference in mean blood pressure, blood lipids and fasting glucose concentrations between re-examination and baseline in participants without treatment for hypertension, hypercholesterolemia and diabetes

No treatment for:	Not treated at baseline			Not treated at re-examination			No treatment at baseline and re-examination					
	N	mean (SD)	N	mean (SD)	N	mean (SD)	Adjusted difference* (re-examination — baseline)			P	95% CI	P
							mean (SD)	mean (SD)	mean (SD)			
Hypertension	228	128.2 (16.43)	141	130.09 (14.77)	133	122.0 (12.42)	130.2 (14.82)	< 0.001	8.137	(5.417; 10.857)	< 0.001	
	228	81.5 (10.23)	141	82.1 (9.63)	133	78.7 (9.29)	82.4 (9.69)	< 0.001	3.701	(1.778; 5.643)	< 0.001	
Hypercholesterolemia	263	5.70 (0.99)	193	5.09 (1.07)	174	5.49 (0.856)	5.12 (1.027)	< 0.001	-0.366	(-0.521; -0.210)	< 0.001	
	263	3.58 (0.92)	193	2.94 (0.95)	174	3.39 (0.765)	2.97 (0.917)	< 0.001	-0.413	(-0.554; -0.273)	< 0.001	
	263	4.23 (1.02)	193	3.58 (1.02)	174	3.98 (0.863)	3.60 (0.981)	< 0.001	-0.376	(-0.529; -0.223)	< 0.001	
	263	1.47 (0.37)	193	1.51 (0.41)	174	1.51 (0.382)	1.52 (0.406)	0.65	0.01	(-0.035; 0.056)	0.65	
	263	1.42 (0.60)	193	1.39 (0.63)	174	1.29 (0.542)	1.39 (0.619)	0.052	0.087	(-0.002; 0.177)	0.056	
Diabetes	302	5.01 (0.661)	256	5.56 (0.74)	255	4.90 (0.531)	5.55 (0.744)	< 0.001	0.646	(0.558; 0.734)	< 0.001	

\*After adjustment for age, sex, education level, smoking status and perceived health

re-examination. A higher concentration of fasting glucose by 0.54 mmol/L was found in re-examination among participants not treated for diabetes. After adjusting for age, gender, education, smoking and perceived health, participants who had not been treated for hypertension throughout the study period had a significant increase in mean SBP and DBP by 8 mmHg and 3.7 mmHg, respectively. Beneficial changes in the lipid profile were observed; significant decreases in concentrations of total cholesterol, LDL-cholesterol and non-HDL by 0.37 mmol/L, 0.41 mmol/L and 0.38 mmol/L were found. Participants not treated for diabetes experienced significant increases in fasting glucose concentration.

### Discussion

The current study suggests that over 18 years, blood pressure and cholesterol concentration decreased in the studied group while BMI and glucose concentration increased, independently of age, sex, education, smoking and perceived health. The reduction in mean blood pressure was driven mainly by the effect of treatment. Decrease in blood lipid concentration was observed regardless of the treatment, but the reduction in treated patients was more pronounced.

The present findings are consistent with other studies assessing trajectories of long-term patterns of cardiovascular disease risk in population-based cohort study. It found that in all trajectory groups, unfavorable increasing in fasting glucose, but favorable raising in HDL and decreasing smoking and total cholesterol happened over time. It has been observed that the medium-medium and high-high risk groups had a significantly higher CVD incidence than the low-low risk [17]. A systematic review on the association between trajectories of risk factors and risk of cardiovascular disease confirmed the increased CVD risk with an increasing trajectory of blood pressure and worse diabetes control [18].

Observed beneficial changes in exposure to cigarette smoking reflects trends observed across the Europe [8, 19], where reduction in smoking among older adults was found. The increase of BMI in the present study is in line with age-related changes observed in body composition of older ages which include

a progressive increase in fat mass and a decline in lean mass [20]. However, overweight and obesity in seniors were not significantly associated with deterioration of physical and cognitive function or with increased mortality [21]. Thus, the observed increase in BMI in the current study does not necessarily have to be considered undoubtedly negative as more and more often it is raised that the optimum range of BMI levels for older adults is higher than the range recommended by WHO for adults [22, 23].

The observation of increased fasting glucose concentrations which were found both in the whole sample and in the strata by diabetes treatment are consistent with the latest global data. The prevalence of 24% among older adults in 2021 is predicted to increase substantially by 2045. In Poland, the percentage of people with diabetes is also increasing, and in older age groups the observed increase was the largest (18% to 27%) [14, 24].

In the present study, the decrease in mean systolic blood pressure in treated individuals is large and varies between 8.8 mmHg and 9.75 mmHg. This may indicate some increase in the effectiveness of blood pressure control in the elderly population. According to the data of the PolSenior2 study great progress has been made in the control of hypertension in people aged 60 and over. In the age group from 60 to over 90 years of age, systolic and diastolic blood pressures were significantly reduced. However, the proportion of successfully treated seniors is still below expectations [25]. As could be expected, based on the literature, the knowledge about the increase in blood pressure with age, people who did not declare that they were treated for hypertension, an increase in mean blood pressure was observed. However, the mean blood pressure in this group was at the level of high normal blood pressure which is in line with the observations on improvement of the detection of hypertension in elderly populations [4, 20].

In the present analysis, beneficial changes in blood lipid concentration were observed. The changes were substantial, significant and stable, regardless of the covariates included or the stratification applied. Given the significant changes in the availability and use of lipid-lowering drugs (ezetimibe, PCSK9 inhibitors) and the increasingly restrictive targets of lipid-lowering treatment in recent years, beneficial changes in the lipid profile of the population, including its oldest populations could be expected. However, the fact that improvement was observed not only in treated

participants may indicate that some beneficial changes in lifestyle or other spontaneous changes in the population could explain the finding. Data from the Framingham Heart Study on the longitudinal trajectories of cholesterol concentration from midlife to later life also showed a decrease in total cholesterol concentration with age, observed regardless of the treatment. The authors pointed to genetic factors, which might additionally affect changes in diet, body composition and physical activity observed over the course of life [26].

There are several limitations in the interpretation of the results presented that should be considered. The participation rate in baseline examination achieved 60% and it is known that the examination included a healthier part of the general population [27]. In the later stages of the study, all participants diagnosed with health-threatening conditions, including exposure to risk factors, were instructed to contact a physician. Finally, the present analysis included only the participants who survived and participated in the study for almost two decades after the baseline observation. In consequence, the studied group, although selected from the general population, is not fully representative for the general population. However, to understand the difference between participants who took part in the study and those who did not, a finding that the participants examined were a little younger, healthier and better educated might be important. Fact that the analysis was performed on the healthier part of the sample might have led to an underestimation of the exposure. However, we do not present data on prevalence, awareness or control of risk factors which are more sensitive to the effect of earlier participation in the study, than the values of objective measurements. Due to the restrictions related to the pandemic, a relatively small group of people was examined. However, it was a random subsample of the participants of the study, and despite being relatively small, its size assured enough statistical power to show significant relationships.

There are however some strengths of the study that should be emphasized. Changes in risk factors in the general population of older adults, not patients, were assessed. According to available research, this is the first Polish study that assessed changes in risk factors over such a long period of observation in the same study participants and was related to the period of passing from the middle to old age. The longitudinal study design allowed us to estimate real within-individual age-related change in CVD risk factors. The same tightly

controlled research procedures were used in both studies to minimize systematic error. The influence of confounders was taken into account in the analysis.

## Conclusions

In conclusion, the results of this prospective study, after nearly 20 years of observation at the individual level, confirm findings from repeated cross-sectional studies on decrease in lipid concentrations, blood pressure and prevalence of smoking in older individuals.

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