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# Five-Year Cumulative Incidence of Hypertension in Adult Croatian Population: the CroHort Study

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## ABSTRACT

*The aim of this study was to establish a five-year cumulative incidence of arterial hypertension (hereinafter 5-CIAH) and its dependence on initial prehypertension, body weight, age and gender. »Croatian Adult Health Cohort Study (CroHort)« data collected during 2003 and 2008 for the 1383 subjects aged 18 + with initially normal blood pressure (systolic <140 mmHg and diastolic <90 mmHg, and not taking medication) was analysed. Methods of descriptive statistics, Student's t-test,  $\chi^2$ -test and logistic regression were used. The recorded 5-CIAH in male cohort was 36.9% [32.1 to 41.6] and 33.0% [30.1 to 36.0] in women and was higher in subjects with initial prehypertension (men 43.3% [37.5 to 49.0] versus 9.6% [12.1 to 27.2]; women 42.3% [38.1 to 46.6] versus 22.3% [18.5 to 26.1]). The development of arterial hypertension was affected by age (OR=2.2168), initial prehypertension (OR=2.1987) and overweight (OR=1.9399).*

**Key words:** CroHort study, hypertension, cumulative incidence, prehypertension, body mass index

## Introduction

Hypertension (hereinafter AH) is an important public health challenge due to its high prevalence and strong association with cardiovascular disease and premature death<sup>1</sup>. High blood pressure is the leading cause of death among women, accounting for 19% of all female deaths, and the second leading cause of death among men (second to smoking)<sup>1</sup>.

The estimated AH prevalence rate of the global adult population (older than 20) was 26.4% (1 billion) in 2000, and there are projections of growth up to 29.2% (1.56 billion) by 2025<sup>1</sup>. The estimated prevalence of hypertension in developed countries was 37.4% in men and 37.2% in women<sup>2</sup>. Prevalence rates in USA (20.3%) and Canada (21.4 %) were lower than those recorded in Europe<sup>3,4</sup>. Several AH prevalence rates were also published in Croatia<sup>5-9</sup>. The Croatian AH rate in 2003 was 44.2%<sup>8</sup>, closely nearing that of Spain (45.1%), lower than the rate reported for Germany (55.3%), and higher than those for Great Britain (38.8%), Italy (37.7%), Sweden (38.4%) and Greece (28.4%)<sup>3</sup>. Limited information is available about the incidence of hypertension because it requires a follow-up of a population for a prolonged period of time<sup>10</sup>. The first AH incidence rate was estimated in the Fra-

mingham cohort follow-up study which gave insight into older age as a risk factor<sup>10</sup>. Several longitudinal cohort studies in USA have shown race differences in the incidence of AH indicating that African Americans' rates were an average of two times higher than Caucasians<sup>11-15</sup>. In the Atherosclerosis Risk in Communities Study, the 6-year incidence of hypertension was 13.9 percent and 12.6 percent in White men and women, while 24.9 percent and 30.3 percent in African American men and women aged 45-49, respectively<sup>12</sup>.

According to the results of an Italian cohort study, 31.3% subjects had the initial stage of AH (systolic blood pressure (hereinafter SBP) >140 mmHg and <160 mmHg; diastolic blood pressure (hereinafter DBP) 90-95 mmHg), while 14.6% had the second stage (SBP >160 mmHg; DBP >95)<sup>16</sup>. A Dutch study showed that 7% of those who had had DBT <75 mmHg at the beginning developed AH, as did 15% of those who had initial DBT <85 mmHg and 30% with DBP 85-94 mmHg<sup>17</sup>. A French study reported that the incidence of AH in the working population was 3.0% in males and 1.34% in females<sup>18</sup>. Cumulative incidence of AH in a four-year period in Turkey was documented at a share of 21.4%, while the high-

est rate was recorded in the 65+ group (43.3%)<sup>18</sup>. In the ATTICA study, the annual incidence of AH was 2.86 per 100 males and 2.68 per 100 females<sup>20</sup>. Crude AH incidence rate in a Portuguese study was 6.23 (5.26–7.20) per 100 person years<sup>21</sup>.

Lower rates were recorded in a Indian cohort (2.8/1000 in the 25–64 age group)<sup>22</sup>. In a Taiwanese cohort, the incidence rate was 27%<sup>23</sup>. Age-adjusted incidence rate in a Chinese cohort was 12.75% in men and 10.4% in women<sup>24</sup>.

Framingham study showed that the lifetime risk for developing hypertension was 90 % for 55 years old participants<sup>25</sup>.

The literature supporting the linear associations between higher body mass index (hereinafter BMI) and hypertension is well established, and overweight and obesity are major modifiable risk factors<sup>26,27</sup>. Initial higher values of blood pressure or prehypertension have been recognized as another important risk factor for AH<sup>28–30</sup>. High sodium intake, physical inactivity, heavy alcohol intake, low potassium intake, and a Western-style diet constitute additional risk factors for hypertension<sup>31,32</sup>.

At the moment, no data on AH incidence in Croatia are available. This paper will, for the first time in Croatia, present a 5-year cumulative incidence of AH (further 5-CIAH) in a cohort of initially normotensive subjects.

## Materials and Methods

The paper analyzes the data collected in the Croatian Adult Health Cohort Study (*CroHort*) project of the Ministry of Science, Education and Sport, No. 108-1080135-0264, started in 2003 and finished in 2008. The methodology of the *CroHort* Study, as a tool for monitoring risk factors for cardiovascular diseases, was described in a special paper in this issue<sup>33</sup>. Answers and measurements were collected for 1383 respondents (396 males and 987 females) who fulfilled initial inclusion criteria (SBP < 140 mmHg and DBP < 90 mmHg and not using antihypertension medication statement).

Data was collected by visiting nurses in form of a structured questionnaire, which, among other things, included anthropometric measurements (height, weight and blood pressure), questions on diseases and taking medication, everyday habits and blood pressure measurements. Arterial pressure was measured by a calibrated mercury sphygmomanometer, which uses a standard cuff. Measurements were done in respondents' homes, in a sitting position. Values were read twice in intervals of 20 minutes or longer, and used to compute the average for every respondent.

The criteria for including respondents in the JNC-7<sup>32</sup> normal blood pressure group were SBP lower than 120 mmHg and DBP < 90 mmHg. The criteria for including respondents in the JNC-7<sup>32</sup> prehypertension group were SBP > 120 mmHg and SBP < 140 mmHg and/or DBP > 80 mmHg and < 90 mmHg. The criteria for including respondents in the JNC-7<sup>32</sup> group of hypertensive subjects

were SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or usage of antihypertensive drugs statement. The criterion for including respondents in the overweight group was BMI in a range of 25–29.9 kg/m<sup>2</sup> and BMI ≥ 30 kg/m<sup>2</sup> in the obese group.

The paper shows analytic results expressed in percentages of the 5-year cumulative incidence of AH (further 5-CIAH), their 95% confidence intervals (hereinafter 95%CI or [ ]), and 5-CIAH annual average. Student t-test, chi-square and logistic regression statistical method were used with p=0.05 as a cut-off value. Data processing was performed using the SPSS statistical package.

## Results

The average age of men (50.3±15.5 year) was significantly higher (t=4.7741; p<0.05) than of women (46.0±14.9). In the group of 396 men, 17.4% belonged to the 18–34 age group, 61.4% to the 35–64 age group and 21.2% were 65+. Among 987 females, 25.0% were aged 18–34, 61.4% were 35–64 and 13.6% were 65+. Age distribution differences between men and women were significant; the former had a distribution that significantly slanted towards the older age group ( $\chi^2=17.5$ ; d.f.=2; p<0.05).

Cohort crude 5-CIAH was 34.1% [31.6–36.6] and the average annual AH incidence rate was 6.8%. There were no significant differences in 5-CIAH between male (36.9% [32.1–41.6]) and female (33.0% [30.1–36.0]) groups. Annual average AH incidence rate was 7.4% in males and 6.6% in females.

Age-specific 5-CIAH values grew with age and the highest rates belonged to older age groups in both men and women (Figure 1). In the male 18–34 age group, 5-CIAH was 21.7% [CI 12.0–31.5], and 33.7% [CI 27.8–39.7] in the 35–64 age group. Significantly higher 5-CIAH rate was associated with the 65+ age group (58.3% [CI 47.8–68.9]) (Figure 1). In the female 18–34 age group, 5-CIAH was 18.2% [CI 13.4–23.0], in the 35–64 group it numbered 34.2% [CI 30.4–37.9], and 55.2% [CI 46.8–63.6] in the 65+ age group (Figure 1).

In the group of subjects with initially normal blood pressure, 5-CIAH was 19.0% [CI 12.1–27.2] in males and 26.1% [CI 18.5–26.1] in females. Significantly higher values of 5-CIAH were recorded in the group of initially prehypertensive men (48.3% [CI 37.5–49.0]) and women (42.3% [CI 38.1–46.6]) (Figure 2). The impact of initial values of blood pressure on AH incidence was analyzed in the group of males and females with normal BMI at the end of the follow-up. Among 135 males with normal BMI in the initially normotensive group, 7.1% (3 in 42) developed hypertension, which was significantly lower than 40.9% (38 in 93) in the prehypertensive group ( $\chi^2=15.5$ ; p<0.05) (Figure 3). Among 409 women with normal BMI in the group with initially normal blood pressure, 11% (24 of 218) developed hypertension, which was significantly lower than was the rate of 28.8% (55 of 191) in the prehypertensive group ( $\chi^2=20.6$ ; p<0.05) (Figure 3).

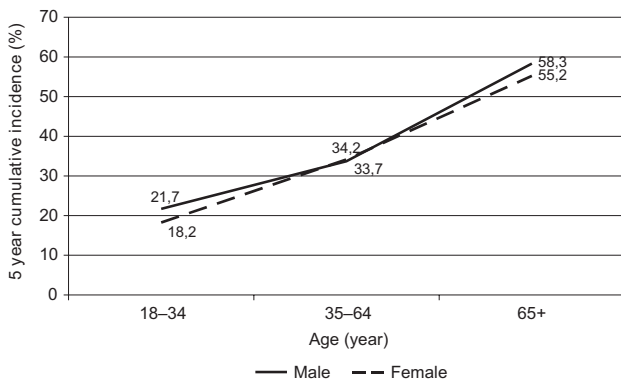


Fig. 1. Distribution of 5-year cumulative incidence of arterial hypertension in cohort of initially normotensive subjects by age and sex.

In the male group with normal BMI, 5-CIAH was 28.9% [CI 21.9–36.0] and 23.7% [CI 20.1–27.4] in the female group. Significantly higher values of 5-CIAH were recorded in the group of obese men than in the group with normal BMI (Figure 4). Values for 95%CI of 5-CIAH for the overweight population overlapped with those of the normal BMI and obesity groups; consequently no significant differences were noticed (Figure 4). In the female group, significant differences in 5-CIAH were recorded between the normal BMI and overweight/ obese populations (Figure 4).

Unconditional multivariate logistic regression was performed at the end of the follow-up as a criterion variable, while age, sex, body mass index (normal, overweight, obesity) and initial values of blood pressure (normal versus prehypertension) recorded at the beginning of the follow-up served as a predictor. Data for 1378 subjects was analyzed and the predictor of hypertension at the end of the follow-up were prehypertension, BMI and age (Table 1). Obesity (OR=2.22), prehypertension (OR=1.97), overweight (OR=1.59) and age (OR=1.03) of subjects contributed most to the hypertension development. No significant contribution of sex to hypertension development has been recorded.

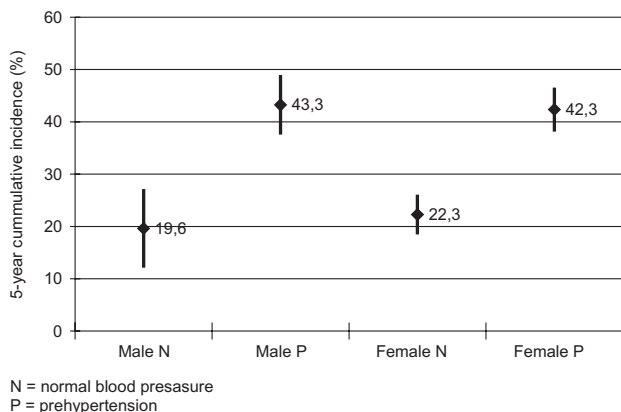


Fig. 2. Arterial hypertension 5-year cumulative incidence in cohort by initial blood pressure status and sex.

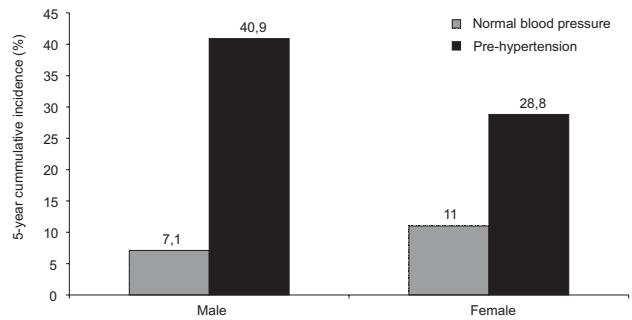


Fig. 3. Arterial hypertension 5-year cumulative incidence in cohort of subjects with normal body mass index by sex and initial blood pressure status (normal blood pressure=systolic <120 mmHg and diastolic <80mmHg or prehypertension=systolic pressure ≥120mmHg and <140mmHg and/or diastolic pressure ≥80mmHg and <90mmHg) sex.

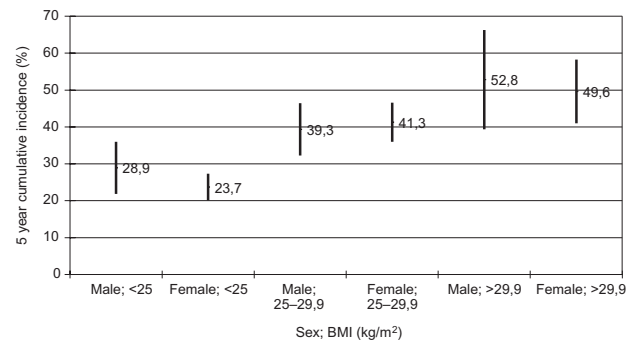


Fig. 4. Arterial hypertension 5-year cumulative incidence in cohort by initial body mass index and sex.

## Discussion and Conclusion

The measured 5-CIAH for the study cohort of subjects was 36.9% in the group of men and 33.0% in the group of women, with an average annual incidence of hypertension of 7.4% for men and 6.6% for women. The above mentioned values of 5-CIAH were for the first time reported in a study conducted in Croatia.

Due to inconsistent methods of research, rates between different countries cannot easily be compared based on the results published in the literature. Most research uses a method of direct standardization by age and sex, using its population as the standard, and for comparison of incidence trends over time<sup>10,11</sup>. However, due to differences in cohort size, age distribution and different time points in which the research was conducted, the value of the cumulative incidence of hypertension studied cohorts cannot be directly compared with the previously mentioned. The fact, however, remains that they are closer to the values recorded for the Black populations of the USA<sup>12</sup>, Portugal<sup>21</sup> and Turkey<sup>19</sup> than the White populations of the United States<sup>12,22</sup>, Greece<sup>20</sup> or China<sup>24</sup>.

**TABLE 1**  
RESULTS OF LOGISTIC REGRESSION ANALYSIS

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	p-Value
Sex	1.1372	0.8739	1.4797	0.1285	0.1343	0.9569	0.3386
Age	1.0316	1.0229	1.0403	0.0311	0.0043	7.2406	0
BMI (2/1)	1.5851	1.2202	2.0591	0.4606	0.1335	3.451	0.0006
BMI (3/1)	2.2239	1.5603	3.1697	0.7993	0.1808	4.4205	0
Prehypertension	1.9652	1.5142	2.5507	0.6756	0.133	5.0783	0

Legend: BMI 1 < 25 kg/m<sup>2</sup> < BMI 2 ≥ 25–29.9 kg/m<sup>2</sup> < BMI 3 > 29.9 kg/m<sup>2</sup>

Although the reported studied cohort 5-CIAH was slightly higher in men than women, this difference was not statistically significant. Earlier studies conducted in the United States found a significant difference in the incidence of hypertension between men and women<sup>11</sup>, whereas in recent studies significantly higher incidence of AH was established only for men and women of African American descent<sup>13</sup>.

In the monitored cohort, age-specific 5-CIAH increases with age in men and women and is the highest in the oldest age group. In other studies, the highest cumulative incidence rates were also recorded at the oldest age<sup>10,25</sup>. According to the results of the Framingham study, the incidence of hypertension in men grew from 3.3% at the age of 30–39 to 6.4% at 70–79, while in the group of women it grew from the initial 1.5% at the age of 30–39 to 6% at 70–79<sup>10</sup>.

Increase in the AH incidence with age is attributed to reduced elasticity of artery walls and increasing body mass<sup>10</sup>. A study conducted in a cohort of primitive tribes of Polynesia, which had a physically active lifestyle and lower dietary intake of fats and salt, could not correlate AH with age<sup>34</sup>.

In this research, no age differences in the specific 5-CIAH were found in relation to sex. According to the results of the Framingham study, men under 50 have higher rates of AH incidence than women, but women surpass men at an older age<sup>10</sup>.

It is not clear whether there are some unknown environmental factors and differences in behavior or if the reason lies in the fact that men over 50 are the ones who survived, not having died from heart and blood vessel diseases<sup>10</sup>.

A study conducted in a cohort population of China in men detected a higher incidence of AH (29.3%) than in women (23.4%)<sup>31</sup>. A study conducted in Greece could not identify differences in annual incidence by sex<sup>20</sup>.

According to available research, the incidence of AH increases in initially prehypertensive persons<sup>28–30</sup>. The

present study has demonstrated a higher incidence of AH in a cohort of men and women with initial prehypertension. This difference still remains after the analysis of only those subjects who had normal body weight. In the oldest age groups, no differences in the development of AH were noticed among normotensive or prehypertensive respondents. In a study conducted in Taiwan, in a cohort of middle-aged and elderly individuals, no differences in the development of the AH relative to the initial values of pressure were identified either<sup>28</sup>.

The results of this study have confirmed a link between obesity measured by BMI with the incidence of AH. The AH incidence increases with higher body mass index, as in those who are overweight or obese, which is consistent with the results of other studies<sup>26,27</sup>.

This research associates the development of AH with older age, higher body weight and initial values of blood pressure as independent predictors in a multivariate model, consistently with the results of studies carried out on other cohorts<sup>11,13,19,23,24</sup>.

Proper medication adherence and promotion of healthy nutrition and physical activity to achieve and maintain a normal body weight have the most significant impact on secondary and tertiary prevention and control of AH. Younger prehypertensive population should have at their disposal primary AH prevention programs that include promotion of physical activity and maintaining weight within the normal range.

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## PETOGODIŠNJA KUMULATIVNA INCIDENCIJA ARTERIJSKE HIPERTENZIJE – CroHort STUDIJA

### SAŽETAK

U radu su analizirani podaci za kohortu 1383 ispitanika u dobi 18+ iz Hrvatske kohortne studije kardiovaskularnog zdravlja prikupljeni tijekom intervjua provedenih tijekom 2003. i ponovljenih u 2008. godini. Cilj istraživanja bio je utvrditi kumulativnu petogodišnju incidenciju arterijske hipertenzije (dalje 5-CIAH) i njezinu zavisnost prema početnim vrijednostima arterijskog tlaka, tjelesnoj masi, dobi i spolu. Istraživanje je provedeno na kohorti ispitanika s početno normalnim arterijskim tlakom (sistolički <140 mmHg i dijastolički <90 mmHg i ne uzima lijekove). Podaci su prikupljeni metodom strukturiranog intervjua te antropometrijskim mjerenjima (visina, težina, krvni tlak). Krvni tlak izmjeren je dva puta tijekom istog posjeta i izračunat prosjek za svakog ispitanika. Rezultati su iskazani postotcima 5-CIAH te njihovim 95% intervalima pouzdanosti (dalje [ ]). Pored metoda deskriptivne statistike korišteni su Studentov t-test,  $\chi^2$ -test, te logistička regresija. Za statističku analizu korišten je statistički paket SPSS. U muškaraca kohorte za-bilježena 5-CIAH bila je 36,9% [32,1–41,6], a u žena 33,0% [30,1–36,0]. Ispitanici s početnom predhipertenzijom imali su više vrijednosti 5-CIAH u odnosu na one s početno normalnim tlakom (muškarci 43,3% [37,5–49,0] naprema 9,6% [12,1–27,2]; žene 42,3% [38,1–46,6] naprema 22,3% [18,5–26,1]). Razvoju arterijske hipertenzije najviše pridonosi starija dob ispi-tanika (OR=2,2168), početna predhipertenzija (OR=2,1987) te prekomjerna tjelesna masa (OR=1,9399), dok za spol to nije utvrđeno.