

# Regional Pattern of Cardiovascular Risk Burden in Croatia

Josipa Kern<sup>1</sup>, Ozren Polašek<sup>1</sup>, Sanja Musić Milanović<sup>2</sup>, Aleksandar Džakula<sup>1</sup>, Kristina Fišter<sup>1</sup>, Marija Strnad<sup>2</sup>, Davor Ivanković<sup>1</sup> and Silvijs Vuletić<sup>1</sup>

<sup>1</sup> »Andrija Štampar« School of Public Health, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>2</sup> Croatian National Institute of Public Health, Zagreb, Croatia

## ABSTRACT

*The objective of this study was to investigate regional gradient of a synthetic cardiovascular burden (CVRB) in Croatia. Analysis was based on a multistage stratified sample representative of general adult population in six regions of Croatia (Croatian Adult Health Survey). Synthetic CVRB was defined by incidents (heart attack, stroke), blood pressure, overweight/obesity (BMI, waist circumference), and risky behaviours (smoking, physical inactivity, high alcohol consumption, inadequate nutrition). Total CVRB in Croatia was 44.7% for men and 50.3% for women. Combining both high and moderate CVRB, men were found to be under more risk than women (72.8% vs. 61.7%, respectively). The result showed an east-north-west gradient in continental Croatia, with high CVRB in Eastern (40.2%) and Central region (44.3%), City of Zagreb (45.7%) and Northern region (53.1%). Mountainous region had the lowest prevalence of respondents with high CVRB (39.2%). Coastal region with the prevalence of 46.3% of high CVRB was nearly the same as the City of Zagreb. The results suggest the presence of substantial regional differences in the cardiovascular risk burden.*

**Key words:** cardiovascular risk burden, regional pattern, health behaviour, Croatian Adult Health Survey, Croatia

## Introduction

Within-country geographical variation in the prevalence of cardiovascular diseases (CVD) and mortality (CVM) have important implications for planning public health policy and intervention for primary and secondary prevention of cardiovascular diseases. Considerable variation in cardiovascular and all-cause mortality both on a national and on a regional level is seen in Europe. There is a clear north-east to south-west gradient in age-standardized mortality from ischemic heart disease and cerebrovascular disease combined<sup>1</sup>. Central and Eastern Europe has higher mortality rates compared with other European countries<sup>1</sup>.

Croatia ranks high among the European countries in terms of the prevalence of risk factors for developing cardiovascular disease. Compared with the neighbouring countries in year 2000, the age standardised CVD mortality rate among people aged 45–74 was 209 per 100000 in Croatia, 99 in Slovenia, 57 in Austria and 180 in Hungary<sup>2</sup>. Between neighbourhoods Croatia lie in a highest position.

Geographically, social-economically and culturally Croatia is heterogeneous country. There are general opinion and even stereotype that these differences reflect the way of living in three regions of Croatia, continental, mountainous and coastal regions, the last often described as Mediterranean. The Mediterranean is considered as the healthiest one, mainly due to so called Mediterranean nutrition characterized by unsaturated fat and high vegetable consumption. Consequently it is presumed that the Mediterranean area is characterized by not so high prevalence of cardiovascular diseases. Regional differences in the prevalence of cardiovascular diseases could be explained by the classic coronary risk factors such as smoking, hypertension, hyperlipidaemia, diabetes or overweight as well as socio-economic factors, life-style variables such as diet, alcohol use, physical activity, medical care, genetic factors and environmental conditions<sup>3</sup>.

Recent research in public health and epidemiology has tackled this problem of Mediterranean healthy way

of living. Two Croatian health surveys, one 1995–97 and the other 2001 presented the results by region<sup>4,5</sup>. Samples in both these surveys were not regionally stratified in advance. The results were later in the analysis suitable fit for some regions of Croatia. INTER-HEART 2 study<sup>6</sup>, LIBS 5<sup>7</sup>, and Croatian health surveys<sup>8–10</sup> study presented also their results by regions. The series of abstracts dealing with regionalism of CVD mortality, hypertension, overweight, smoking, physical inactivity, alcohol use, nutrition were presented in the AMZH Scientific Symposium, Regionalism of cardiovascular risk factors in the population of Croatia<sup>11–18</sup>. Most of these papers suggest there may be a north-south or continental-coastal gradient of cardiovascular risk factors in Croatia.

The objective of this paper is to examine whether the grades of a synthetic cardiovascular risk burden (CVRB) show any gradient of cardiovascular burden in Croatia.

### Sampling and Methods

Data for this study was taken from the 2003 Croatia Adult Health Survey (CAHS), a multistage stratified sample representative of general adult population in six regions of Croatia<sup>19</sup>.

Synthetic CVRB was defined taking into account various cardiovascular related incidents (heart attack, stroke), blood pressure, overweight/obesity (BMI, waist circumference), and risky behaviours (smoking, physical inactivity, high alcohol consumption, inadequate nutrition<sup>8</sup>). Current daily smokers and those who quit less than 10 years ago were classified as smokers. Those who fulfilled at least three of the following criteria were counted as physically inactive: driving to work, working in white collar occupations, taking less than two 30-minute sessions of exercise weekly in their leisure time, and having someone constantly advising them on the need for more physical activity. High alcohol consumption was defined as having a binge of heavy drinking at least once a week, drinking alcohol daily, or having someone constantly advising them on the need to cut down on alcohol consumption. Finally, those who fulfilled at least three of the following criteria were classified as having an inadequate diet: regularly eating food prepared with animal fat, regular consumption of full-fat (at least 3.2%) milk and milk products, low consumption of fruits, eating smoked meat at least twice a week, and adding salt to food before tasting.

Categories of synthetic CVRB were as follows: »High burden« was defined as at least one cardiovascular incident or blood pressure of 160/100 mm Hg or higher, BMI of 25 or higher, and high value of waist circumference (102 cm or higher for males and 88 cm or higher for females). »Moderate burden« was defined as not being high, but with blood pressure of 140/90 mm Hg and higher, and less than 160/100, and BMI of 25 or higher but less than 30 or high value of waist circumference. »Low burden« was defined as not being high or moderate, but with at least one of risky behaviours. »No bur-

den« means that neither of high, moderate nor low burdens exists.

### Definition of the regions in Croatia

Croatia is geographically defined by three natural-geographical areas, Panonic-Peripanonic, Dinaric mountains and Mediterranean areas. Six regions were defined according to geographical and ethno-cultural characteristics: Eastern, North, Central, City of Zagreb, Mountainous and Coastal regions. Eastern Croatia, consisting of Slavonia, south Baranja and west Srijem, is Croatian low-land. North-west Croatia is a hilly high populated area. Central region is part of Peripanonic area, most populated region and gravity centre of economic life in Croatia. Zagreb is a typical middle European city. Mountainous region is scarcely populated area of north-west Dinaric Mountains. Coastal region is an Adriatic sea area.

Applied statistical methods included prevalence and 95%CI. The bootstrap re-sampling method was used to compute standard deviations<sup>20</sup>. Data processing was done by SAS statistical package (SAS Institute Inc., Cary, NC, USA).

### Results

The distribution of CVRB according to age groups (to 34, 35–64, 65 and over) and gender is shown in Figures 1 and 2. The pattern of CVRB was similar in both genders, but age groups showed quite different patterns. High CVRB is characteristic for the oldest age group. CVRB was lower in the middle age group and the lowest in younger ones. Moderate CVRB was nearly equally distributed in all the age groups. Low CVRB and No CVRB were characteristics of the youngest age group.

The CVRB by regions for both sexes is presented in Tables 1 and 2. High CVRB is shown in Figures 3 and 4. The prevalence of CVRB in all regions exceeds 40%. Total CVRB in Croatia was 44.7% for men and 50.3% for women.

Eastern and Northern regions showed extreme prevalence of high CVRB in men. The Northern region showed the highest prevalence (53.1%), the Eastern the lowest

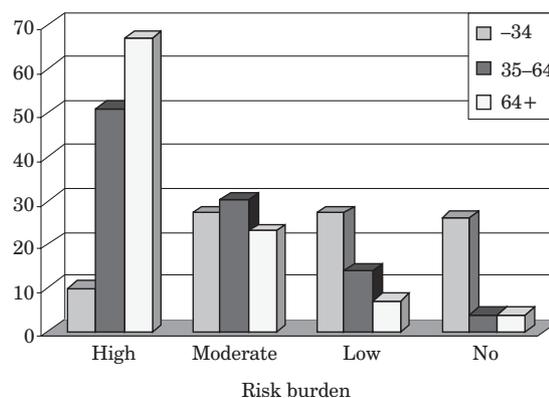


Fig. 1. Cardiovascular risk burden by age groups – men.

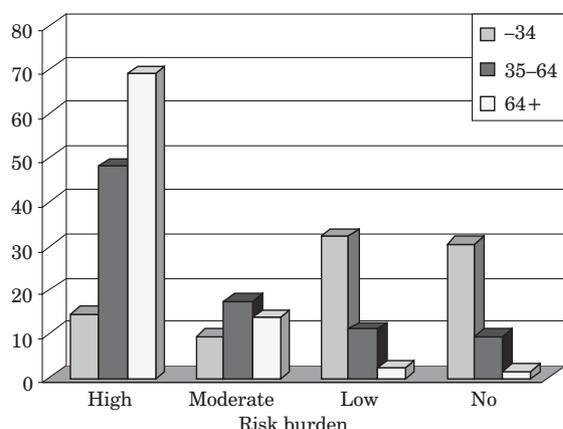


Fig. 2. Cardiovascular risk burden by age groups – women.

(40.2%). Confidence intervals did not overlap, pointing to the statistically significant difference at the level of  $p < 0.05$ . All other regions were in-between, with no statistical significance. Women showed a different pattern – continental regions (Eastern, North, Central) were higher than the city of Zagreb and Coastal region. The last two regions showed the high CVRB prevalence of less than 50%. Only the Coastal region and continental regions (Eastern, North, Central) showed statistically significant difference in the prevalence of high CVRB. No CVRB showed the highest prevalence in Coastal region in both, men (12.2%) and women (18.8%) (Table 3).

Figures of socio-demographic distribution by region point to the characteristics as follows: regions are comparable according to age distributions for men, but women of the oldest age group were somewhat underrepresented

**TABLE 1**  
CARDIOVASCULAR RISK BURDEN BY REGIONS – MEN

| Regions        | High burden %<br>(%,95% CI) | Moderate burden<br>(%,95% CI) | Low burden<br>(%,95% CI) | No burden<br>(%,95% CI) | Estimated population |
|----------------|-----------------------------|-------------------------------|--------------------------|-------------------------|----------------------|
| Eastern        | 40.2<br>(36.9–43.5)         | 26.7<br>(20.7–32.7)           | 23.7<br>(16.9–30.5)      | 9.5<br>(6.6–12.3)       | 331548               |
| Northern       | 53.1<br>(46.7–59.6)         | 27.0<br>(22.5–31.5)           | 12.1<br>(7.9–16.4)       | 7.8*<br>(7.9–16.4)      | 197580               |
| Central        | 44.3<br>(39.4–49.3)         | 27.1<br>(22.6–31.5)           | 18.36<br>(13.9–22.8)     | 10.2*<br>(5.6–14.8)     | 407898               |
| City of Zagreb | 45.7<br>(39.6–51.9)         | 29.7<br>(23.8–35.7)           | 13.1<br>(8.4–17.8)       | 11.4<br>(7.0–15.9)      | 279533               |
| Mountainous    | 39.2*<br>(17.2–61.3)        | 35.6<br>(29.4–45.7)           | 13.4*<br>(8.1–18.7)      | –**                     | 191479               |
| Coastal        | 46.3<br>(40.9–51.8)         | 27.1<br>(23.0–31.2)           | 14.4<br>(10.3–18.5)      | 12.2<br>(9.1–15.3)      | 533001               |
| Total          | 44.7                        | 28.1                          | 16.6                     | 10.6                    | 1640425              |

\* coefficient of variability between 16.6 and 33.3%

\*\* coefficient of variability greater than 33.3%

**TABLE 2**  
CARDIOVASCULAR RISK BURDEN BY REGIONS – WOMEN

| Regions        | High burden %<br>(%,95% CI) | Moderate burden<br>(%,95% CI) | Low burden<br>(%,95% CI) | No burden<br>(%,95% CI) | Estimated population |
|----------------|-----------------------------|-------------------------------|--------------------------|-------------------------|----------------------|
| Eastern        | 55.0<br>(51.5–58.5)         | 15.7<br>(13.6–17.8)           | 16.0<br>(12.9–19.1)      | 13.3<br>(10.2–16.4)     | 367100               |
| North          | 54.2<br>(49.5–58.9)         | 13.6<br>(10.8–16.4)           | 16.3<br>(11.9–20.7)      | 15.9<br>(12.1–19.7)     | 231547               |
| Central        | 56.5<br>(53.1–60.0)         | 15.5<br>(12.9–18.1)           | 14.4<br>(11.1–17.6)      | 13.7<br>(11.5–15.8)     | 414425               |
| City of Zagreb | 46.8<br>(43.7–49.8)         | 16.4<br>(14.0–18.8)           | 22.3<br>(19.6–25.2)      | 14.5<br>(11.9–17.1)     | 331939               |
| Mountainous    | 51.5<br>(42.0–61.0)         | 21.5<br>(14.7–28.2)           | –*                       | 13.6<br>(10.3–16.8)     | 168006               |
| Coastal        | 43.9<br>(41.4–46.4)         | 19.5<br>(17.0–21.9)           | 17.8<br>(15.1–20.4)      | 18.8<br>(17.0–20.6)     | 593929               |
| Total          | 50.3                        | 17.0                          | 17.3                     | 15.5                    | 1839163              |

\* coefficient of variability greater than 33.3%

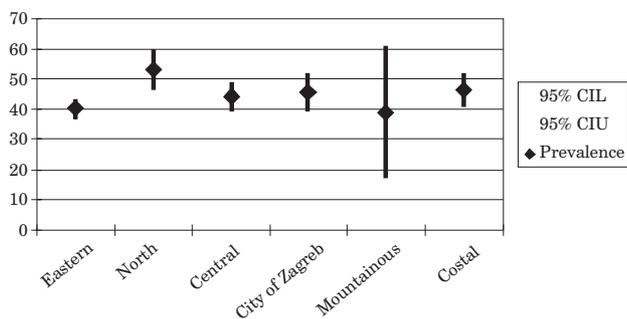


Fig. 3. High CVRB by region (prevalence and 95%CI) – men.

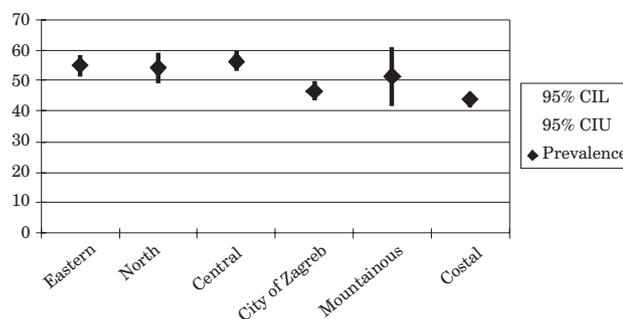


Fig. 4. High CVRB by region (prevalence and 95%CI) – women.



Fig. 3a. High CVRB prevalence by region – men.

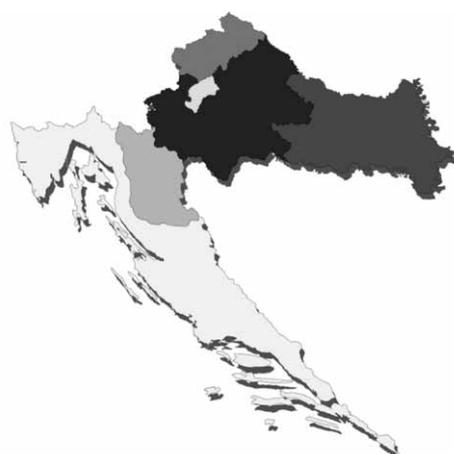


Fig. 4a. High CVRB prevalence by region – women.

**TABLE 3**  
NO-CVR BURDEN RANKS BY REGION AND SEX

| Region         | Men          |      | Women        |      |
|----------------|--------------|------|--------------|------|
|                | Prevalence % | Rank | Prevalence % | Rank |
| Eastern        | 9.5          | 4    | 13.3         | 6    |
| Northern       | 7.8          | 5    | 15.9         | 2    |
| Central        | 10.2         | 2    | 13.7         | 4    |
| City of Zagreb | 11.4         | 3    | 14.5         | 3    |
| Mountainous    | *            | *    | 13.6         | 5    |
| Coastal        | 12.2         | 1    | 18.8         | 1    |

\* coefficient of variability greater than 33.3%

in the North region. Education level was the lowest in Eastern region and the highest in the city of Zagreb, in both men and women. Income was the highest in the city of Zagreb in both men and women. The Coastal region was ranked as the next. All other regions were comparable according to income.

### Discussion

We hypothesized that an emerging property of combinations of gene influences, people’s lifestyles, socio-economic and cultural factors in the described Croatian re-

gions could result in the high prevalence of CVRB. Emergence is described as the phenomenon where global behaviour arises from the interaction between local parts of the system<sup>21</sup>. We may convey this definition as global regional pattern of cardiovascular risk burden is arising from complex interactions of gene influences and risky-life behaviour in the socio-cultural environment in transitional Croatia.

Croatia is a country characterized with highest cardiovascular mortality and high CVRB as well. The high CVRB is more prevalent in women (50.3%) than in men (44.7%). There is no value of high CVRB under 40 in all

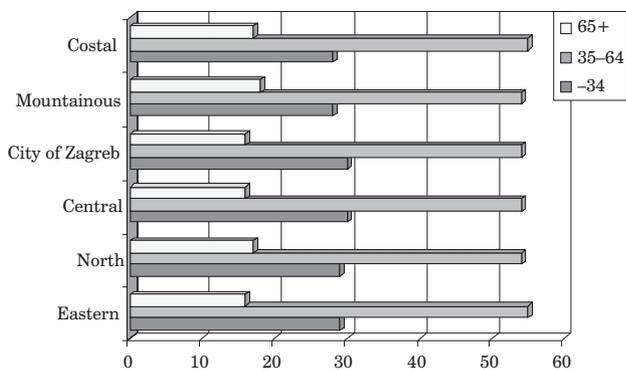


Fig. 5. Age distribution by region – men.

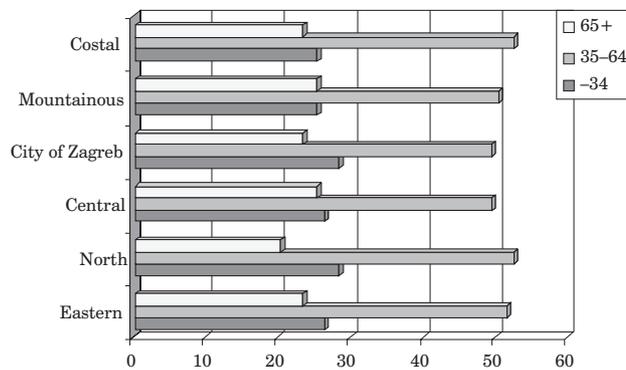


Fig. 6. Age distribution by region – women.

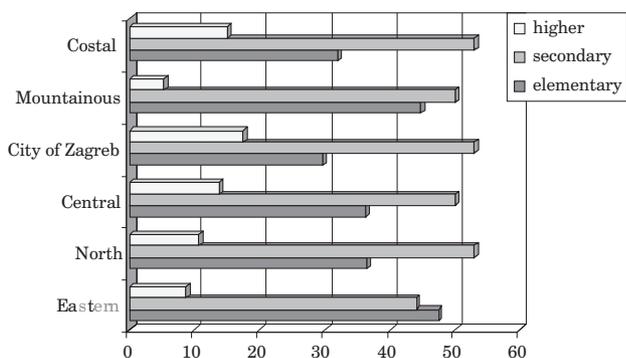


Fig. 7. Education level by region – men.

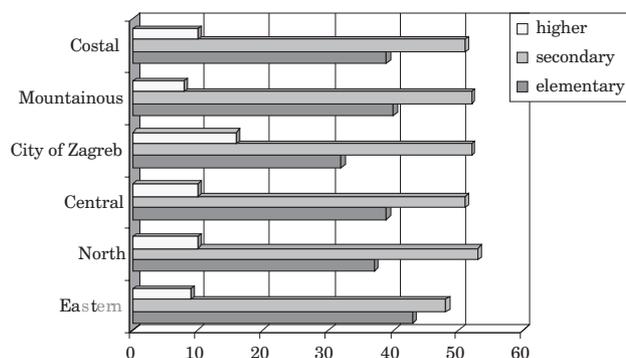


Fig. 8. Education level by region – women.

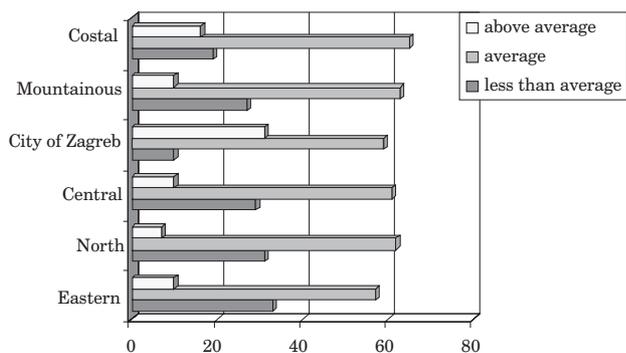


Fig. 9. Income by region – men.

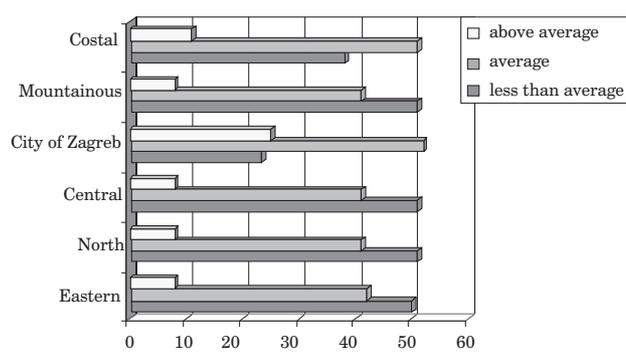


Fig. 10. Income by region – women.

regions. Half of the CVRB belongs to high grade of CVRB. Considering the moderate CVRB, it is much higher in men (28.1%) than in women (17.0%). Combining both high and moderate CVRB, men (72.8%) are more under risk than women (61.7%).

Men and women do not show the similar pattern of CVRB. We may state an east-north-west gradient in continental Croatia, with high CVRB in East region (40.2%), Central region (44.3%), City of Zagreb (45.7%) and North region (53.1%). Mountains region as a part of continental Croatia shows the lowest high CVRB (39.2%). Coastal region with the prevalence of 46.3% of high CVRB is nearly the same as the City of Zagreb. North and Central re-

gions in Croatia also have the highest cardiovascular mortality<sup>11</sup>.

On the contrary, CVRB in women shows some continental-coastal gradient of the high CVRB. Ranking high CVRB, the Central region ranks first (56.5%), followed by Eastern region (55.0%), Northern region (54.2%), Mountainous region (51.5%), City of Zagreb (46.8%), and Coastal region (43.9%). Considering the No CVR burden category there is no gradient at all. Just the Coastal area shows the highest value of people without CVR burden in both men and women. CVRB for Croatian health care system has very serious implications, causing a severe damage to the people's health.

The maximum value of high CVRB reaches as high as 60% of the population. There is no high burden under 40%. The health of these people is damaged and urgent target for secondary and tertiary prevention. Moderate CVRB is intervention target of primary health care, particularly family physicians. Low CVRB (risky lifestyle) is particularly an intervention target in the public health nursing system. No-CVRB is a target for health promotion activities in both health and social community. The achievement is aimed primarily at inter-sector coordination between health care professions working at the level of primary health care, secondary and tertiary health care, and social community.

How to explain the CVRB in all regions in Croatia? All regions are comparable by age groups, so in this analysis age is not considered a key variable. We must suppose that the genetic background of cardiovascular diseases like burden or manifest disease, open population could not account for differences of high CVRB between regions. The genomic medicine has started, but at least, on the population level it is not yet measurable. The next candidate to explain high CVRB is risky life behaviour.

## REFERENCES

- MUELLER-NORDHORN J, BINTING S, ROLL S, WILLICH SN, Eur Heart J, 29 (2008) 1316. — 2. Croatian Health Service Yearbook 2005 (Croatian National Institute of Public Health, Zagreb, 2006). — 3. DE BACKER G, AMBROSONI E, BORCH-JOHNSEN K, BROTONS C, CIFKOVA R, DALLONGEVILLE J, EBRAHIM S, FAERGEMAN O, GRAHAM I, MANCIA G, MANGER CATS V, ORTH-GOMÉR K, PERK J, PYÖRÄLÄ K, RODICIO JL, SANS S, SANSOY V, SECHTEM U, SILBER S, THOMSEN T, WOOD D, Eur Heart J, 24 (2003) 1601. — 4. TUREK S, RUDAN I, SMOLEJ-NARANCIĆ N, SZIROVICZA L, CUBRILLO-TUREK M, ZERJAVIĆ-HRABAK V, RAK-KAIĆ A, VRHOVSKI-HEBRANG D, PREBEG Z, LJUBIČIĆ M, JANIČIJEVIĆ B, RUDAN P, Coll Antropol, 25 (2001) 77. — 5. JUREŠA V, IVANKOVIĆ D, VULETIĆ G, BABIĆ-BANASZAK A, SRCEK I, MASTILICA M, BUDAK A, Coll Antropol 24 (2000) 69. — 6. RUMBOLDT Z, INTER-HEART: svjetsko istraživanje čimbenika koronarnog rizika [in Croatian], U: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 7. BERGOVEC M, MILIČIĆ D, REINER Ž, MIHATOV Š, Liječ Vjesn, 127 (supl.3) (2005) 40. — 8. KERN J, STRNAD M, ČORIĆ T, VULETIĆ S, BMJ, 331 (2005) 208. — 9. KERN J, IVANKOVIĆ D, SOGORIĆ S, VULETIĆ S, Med Arh, 58 (2004) 351. — 10. BÉCUE-BERTAUT M, KERN J, HERNÁNDEZ-MALDONADO ML, JUREŠA V, VULETIĆ S, Public Health, 122 (2008) 140. — 11. STRNAD M, ČORIĆ T, KERN J, POLAŠEK O, Mortalitet od kardiovaskularnih bolesti [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 12. ERCEG M, HRABAK-ŽERJAVIĆ V, IVIČEVIĆ-UHERNIK A, Hrvatska zdravstvena anketa: povišeni krvni tlak [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 13. HEIM I, KRUCHEK LEONTIĆ D, Pretilost i prekomjerna tjelesna težina u Hrvatskoj [in Croatian], In: Knjiga sažetaka (Prostorna

Smoking, unhealthy diet, physical inactivity, heavy alcohol drinkers, overweight and elevated blood pressure are neither individually nor by health care system controlled. In our health care system focus on 'population approach' (reducing risk in whole population) and 'high risk approach' (reducing risk in individuals at high risk of CVD) is not appropriately developed. Primary intervention for CVRB at the population level is practically non-existent. Risky people's life-behaviour and lack of inter-sector activity on the primary health care level should be the main intervention target in the prevention of cardiovascular diseases. The coordination and balance of downstream health improvement work focused on lifestyles with more upstream work, particularly through the community planning process<sup>22</sup>.

## Acknowledgements

The study is supported by the Ministry of Science, Education and Sport of the Republic of Croatia (Regionalism of cardiovascular behavioral risk factors – model of intervention; No: 108-1080135-0264).

- distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 14. MIŠIGOJ-DURAKOVIĆ M, HEIMER S, GREDELJ M, HEIMER Ž, Nedovoljna tjelesna aktivnost [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 15. KOVAČIĆ L, GAZDEK D, SAMARDŽIĆ S. Hrvatska zdravstvena anketa: Pušenje [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 16. MUSTAJ-BEGOVIĆ J, DOKO JELINIĆ J, PUCARIN-CVETKOVIĆ J, MILOŠEVIĆ M, ŽUŠKIN Ž, Hrvatska zdravstvena anketa: Potrošnja alkohola [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 17. KAIĆ-RAK A, KULIER I, PUCARIN-CVETKOVIĆ J, Prehrambene navike [in Croatian], In: Knjiga sažetaka (Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj, AMZH, Zagreb, 2005). — 18. VULETIĆ S, KERN J, IVANKOVIĆ D, POLASEK O, BRBOROVIĆ O, Acta Med Croatica, 61 (2007) 239. — 19. VULETIĆ S, POLAŠEK O, KERN J, STRNAD M, BAKLAJČIĆ Ž, Coll Antrop, 33 Suppl 1 (2009) 3. — 20. BELLAND Y, BAILIE L, PAGE J, Statistics Canada, Croatian Ministry of Health, Central Bureau of Statistics: a joint effort of implementing the 2003 Croatian adult health survey, In: Proceedings (Proceeding of the American Statistical Association on Meeting on survey research methods, Toronto, American Statistical Association, 2004.). — 21. DE WOLF T, HOLVOET T, Emergence and Self-Organisation: a statement of similarities and differences, accessed on May 16th, 2008, available at: URL: [http://www.omegafield.net/library/morphogenesis/emergence\\_and\\_self\\_organisation.pdf](http://www.omegafield.net/library/morphogenesis/emergence_and_self_organisation.pdf). — 22. LOWTHER M, MORDUE A, Primary Prevention of cardiovascular Disease in Scotland, 2006, accessed on May 16th, 2008, available at URL: <http://www.vhscotland.org.uk/library/misc/NHS-CVD%20Full%20Doc.pdf>.

J. Kern

University of Zagreb, School of Medicine, »Andrija Štampar« School of Public Health, Rockefellerova 4, 10000 Zagreb, Croatia  
e-mail: [jkern@snz.hr](mailto:jkern@snz.hr)

## **PROSTORNA DISTRIBUCIJA KARDIOVASKULARNOG BREMENA U HRVATSKOJ**

### **S A Ž E T A K**

Cilj ovog rada bio je ispitati postoji li gradijent u prostornoj distribuciji sintetičkog kardiovaskularnog bremena (CVRB) u Hrvatskoj. Analiza se temelji na višestupanjskom stratificiranom uzorku odrasle populacije u šest hrvatskih regija. Sintetički CVRB se definira incidentima (srčani infarkt, moždani udar), krvnim tlakom, prekomjernom tjelesnom težinom, abdominalnom debljinom i rizičnim ponašanjem (pušenje, fizička neaktivnost, pretjerano pijenje alkohola, neadekvatna prehrana). Ukupni CVRB u Hrvatskoj je procijenjen na 44,7% za muškarce i 50,3% za žene. Kombinirajući visoki i srednji rizik, prevalencija u muškaraca se procjenjuje na 72,8% a u žena na 61,7%. Rezultati pokazuju gradijent istok-sjever-zapad u kontinentalnom dijelu Hrvatske s visokim CVRB: u istočnoj regiji 40,2%, centralnoj 44,3%, gradu Zagrebu 45,7%, i sjevernoj regiji 53,1%. Gorska Hrvatska pokazuje najmanju prevalenciju visokog CVRB (39,2%). Jadranska regija s prevalencijom visokog CVRB od 46,3% je gotovo jednaka gradu Zagrebu.