

A Population-Based Cross-Sectional Study of Cardiovascular Risk Factor in Latvia

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Key words: cardiovascular risk factors; population-based cross-sectional study.

Summary. *Background and Objective.* To date, the epidemiological studies of noncommunicable diseases in Latvia were more episodic and covered only selected areas. The first national cross-sectional population-based survey of cardiovascular risk factors after regaining independence was carried out to provide reliable information on the cardiovascular risk factor profile in adults.

Material and Methods. Computerized random sampling from the Registry of Latvian population was carried out. A total of 6000 enrolled subjects aged 25–74 years were divided into 10 age subgroups. The data of 3807 respondents (63.5% of all) were included into the final analysis.

Results. The mean number of cardiovascular risk factors was 2.99 ± 0.026 per subject: 3.45 ± 0.043 and 2.72 ± 0.030 for men and women, respectively. Of all the respondents, 75.2% had an increased total cholesterol level. Hypercholesterolemia was found in almost 56% of men and 41% of women in the age group of 25–34 years. Hyperglycemia was documented in 34.1% of the respondents (41.6% of men and 29.8% of women). More than two-thirds (67.8%) of the persons were overweight, while obesity was found in 25.6% of men and 32.6% of women. Arterial hypertension was identified in 44.8% of the respondents; its prevalence was higher in men than women (52.9% vs. 40.2%). There were more current smokers among men than women (30.5% vs. 11.4%).

Conclusions. The levels of cardiovascular risk factors in Latvia were found to be relatively high. The data can be utilized as baseline characteristics that can be compared down the road including the monitoring of health prevention activities.

Introduction

An increasing prevalence of noncommunicable diseases is a major public health concern in many countries as well as in Latvia. The health profile of the population reflects many of the trends of East Europe, including high morbidity and mortality due to cardiovascular diseases. During the last 20 years, according to Latvian mortality statistics, cardiovascular diseases accounted for 52%–54% of all deaths, and mortality rate remained to be high: 713.0 and 792.7 per 100 000 population in 2000 to 2010, respectively (1).

Limited information can be obtained from the morbidity data of the routine outpatient health statistics reports and public health databases for the assessment of disease prevalence. This is due to insufficient information about the causes of diseases and contributing risk factors as well as the association between these factors in the general population. With respect to this information, epidemiological studies present the opportunity to estimate

the prevalence of risk factors and thus assist in planning resources and improving prevention strategies. Thus, registries and epidemiological studies should be considered as two sides of the same coin: one deals with collecting data about morbidity, disability, and mortality; the other furnishes data about the prevalence of risk factors and their dynamics in relation to preventive measures. Only few cohort and population-based epidemiological studies have been carried out in Latvia during the last 20 years.

These population-based and cohort epidemiological studies mainly covered separate regions of Latvia (Rīga, Kuldīga, etc.), patients with a certain diagnosis (diabetes mellitus, hypertension), or scheduled outpatient visits to family doctors' practice (2–5). Moreover, to date, countrywide population studies have not been performed on regular basis in Latvia. The rationale for the evaluation of cardiovascular disease (CVD) risk in the Latvian population was based on the following: 1) the evidence that CVD is a major cause of morbidity and mortality, and it contributes to the increasing health care costs in Latvia; 2) CVDs are associated with modifiable lifestyle factors; and 3) the modification

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of the population risk factor profile has been shown as a substantial tool to improve the data on CVD morbidity and mortality (6).

The above-mentioned facts in Latvia encouraged the creation of a new epidemiological database comprising the entire Latvian population. The first national cross-sectional population survey on cardiovascular risk factors in Latvia was carried out in order to provide reliable information on the cardiovascular risk factor profile in an adult population. The survey was performed according to the internationally established standards and protocols (7, 8).

Material and Methods

This cross-sectional population-based survey was conducted from December 2008 to June 2009. The target population was all adults aged 25–74 years living in Latvia. The survey design and methodology was approved by the Ethics Committee of Research, Institute of Cardiology, University of Latvia.

The Registry of Latvian Population served as a basis for selecting the representatives for this cross-sectional study. Computerized simple random sampling was done, where each person had equal chances to be selected. A total number of selected persons in this study were 6000. They were divided into 10 subgroups by 5-year age intervals. There were 600 participants (300 men and 300 women) in each subgroup.

Recruitment of the subjects was performed by mobile study groups, which were temporarily located in local outpatient clinics of the selected urban areas for a number of days. The subjects from a definite area were informed about the study place and time in advance by mail and/or telephone, and they were invited to visit the study group.

Of the 6000 persons invited to the study, 4198 persons responded (communicated with us about

their agreement to take part in the study), and 4022 subjects came to the visit. A total of 176 persons were interviewed, but blood samples were not obtained; 39 persons refused to be interviewed. A complete study sample included 3807 respondents (63.5% of the overall study population).

The distribution of respondents by age and gender is seen in Table 1, and the distribution by sociodemographic characteristics is presented in Table 2.

The study procedures were carried out by health care professionals fully trained to perform the interview and examination. The training of the study staff was performed by specialists of the Research Institute of Cardiology, University of Latvia. Each study group had 2 training seminars. Overall, there were 3 mobile study groups consisting of 2 physicians/interviewers, a nurse, and an assistant/data manager (12 people totally). A standardized interview was carried out, together with the collection of anthropometric and biochemical data. The survey methodology was performed in accordance with the recommendations of the European Health Risk Monitoring Project (7).

The survey included an interview, based on a structured questionnaire, and physical examination.

The survey questionnaire was based on the WHO CINDI Health Monitor Survey including

Table 1. Distribution of Participants by Age and Gender

Age, years	Men		Women		Total	
	n	%	n	%	n	%
25–34	137	10.0	225	9.3	362	9.5
35–44	236	17.2	461	19.0	697	18.3
45–54	312	22.7	592	24.4	904	23.7
55–64	324	23.5	591	24.3	915	24.0
65–74	367	26.7	562	23.1	929	24.4
Total	1376	100	2431	100	3807	100

Table 2. Sociodemographic Characteristics of Study Population

	Men		Women		Gender Differences	
	%	95% CI	%	95% CI	χ^2	<i>P</i>
Education						
Primary	13.0	11.22–14.78	8.5*	7.39–9.61	21.15	0.0001
Secondary	25.1	22.81–27.39	24.7	22.99–26.41		
Secondary professional	33.3	30.81–35.79	34.8	32.91–36.69		
Higher	28.5	26.11–30.89	32.0*	30.15–33.85		
Marital status						
Married	77.9	75.71–80.09	60.8*	58.86–62.74	180.84	0.0001
Divorced	8.8	7.30–10.30	14.2*	12.81–15.59		
Widowers/widows	2.9	2.01–3.79	15.1*	13.68–16.52		
Never married	10.4	8.79–12.01	10.0	8.81–11.19		
Occupational status						
Laborers	44.1	43.68–44.52	32.2*	31.86–32.54	177.07	0.0001
White-collar workers	19.0	17.33–20.67	35.5*	34.98–36.02		
Employers	3.2	2.60–3.80	0.9*	0.21–1.59		
Jobless	5.5	4.57–6.43	3.8*	3.15–4.45		
Retired	23.7	22.61–24.79	22.1	21.86–22.34		
Others	4.6	3.59–5.61	5.5	4.98–6.02		

* $P < 0.05$ comparing men and women.

questions on socioeconomic status, symptoms, diseases, and health behavior (8). Additional questions on risk factors, diseases, and treatment were included from the EHRM protocol as well as from the WHO MONICA questionnaire. Smoking status was assessed using a standard set of questions following the European Health Risk Monitoring project protocol. The questionnaire was pretested during October–November 2008.

The questionnaire was completed, and height, weight, and blood pressure (BP) of the participants was recorded at the study place in the outpatient clinics. The examination was free of charge and lasted for an average of 35–40 minutes.

Weight was measured by a digital scale and height by a stadiometer, which was attached to a wall. Height and weight were used to calculate body mass index (BMI) in kg/m^2 .

BP was measured by an automated validated device (OMRON M6 Comfort) (9) with the subject in a sitting position, on the subject's right arm after having a rest for at least 5 minutes.

Three measurements were taken with an interval of 2–3 minutes. The last 2 measurements were averaged for the analysis. Venous blood samples were collected for fasting glucose (Glu), total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) measurements in the morning after an overnight fasting period. The analysis of these samples was done in the certified laboratories of one laboratory chain (10).

Another venous blood sample was taken and stored for future genetic analysis.

The following CVD risk factors were analyzed: 1) arterial hypertension, if systolic blood pressure was more than 140 mm Hg and/or diastolic blood pressure was more than 90 mm Hg or patients received antihypertensive treatment during the last 2 weeks; 2) the BMI cutoff points of 25 and 30 kg/m^2 were used to determine the overweight and obese subjects; 3) smoking status based on the responses; the participants were classified into 3 categories: daily smokers, ex-smokers, and never smokers. The cutoff points of dyslipidemias and hyperglycemia were as follows: TC, ≥ 5.0 mmol/L; TG, ≥ 1.70 mmol/L; low-density lipoprotein cholesterol (LDL-C), > 3.0 mmol/L; HDL-C, ≤ 1.0 mmol/L for men and ≤ 1.2 mmol/L women, and Glu, ≥ 5.6 mmol/L.

Data were analyzed using the SPSS for Windows, version 12.0.

The input of measurements in the database was performed by 2 specialists independently.

Differences in the mean values of CVD risk factors between men and women in total and each age groups were assessed using the Mann-Whitney test (Z). Differences in the prevalence of CVD risk factors between age groups and gender were estimated

by the chi-square test (χ^2) for categorical variables (AH, BMI, smoking, and biochemical parameters). The associations between AH and age, number of risk factors and age, and between gender groups were evaluated by the Spearman rank correlation (r_s). A P value of < 0.05 was accepted as statistically significant.

Two different coding systems were used. One coding system was used for phenotypic information; the other, for genotypic information. The phenotypic database was developed and stored in the Institute of Cardiology, University of Latvia. The genotypic database was created and stored in the Biomedical Study and Research Centre of Latvia.

The Steering Committee (3 persons) and the Scientific Board (7 persons) were set up to supervise the study.

Results

Cardiovascular Disease Risk Factors. The mean number of cardiovascular risk factors was 2.99 ± 0.026 per person for the overall study population. The male group had a significantly greater mean number of risk factors than the female group (3.45 ± 0.04 vs. 2.72 ± 0.03 , $Z = 13.557$, $P < 0.001$). Fig. shows that the number of risk factors increases with age both in men and women. A positive correlation between age (25–74 years) and number of risk factors was found ($r_s = 0.096$, $P < 0.001$, in men; and $r_s = 0.353$, $P < 0.001$ in women). In the age group of 65 years and more, the mean number of risk factors decreased in men and stabilized in women. When the oldest age group (65–74 years) was excluded from the analysis, a positive correlation between age and number of risk factors for men became stronger ($r_s = 0.207$, $P < 0.001$), but it did not change essentially for women ($r_s = 0.384$, $P < 0.001$).

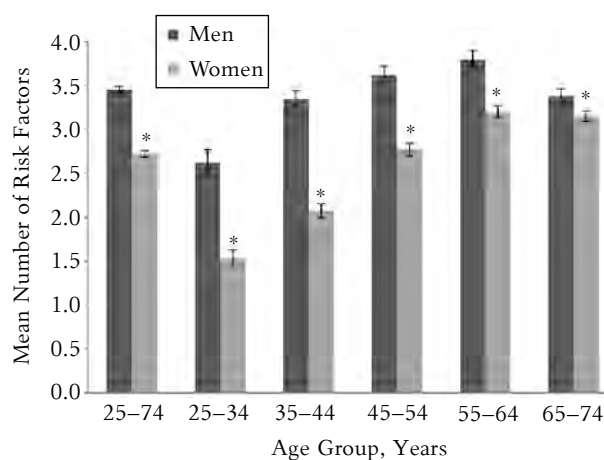


Fig. The mean number of risk factors per person by different age groups
Bars represent means \pm SE. * $P < 0.05$ comparing men and women.

Blood Pressure. The prevalence of hypertension in the general study population was 44.8%. The percentage of men with hypertension was significantly greater than that of women (52.9% vs. 40.2%, $P<0.001$) (Table 3).

The proportion of subjects with hypertension increased considerably with age in both genders (Table 4). This was confirmed by a positive correlation between both variables among men ($r_s=0.27$, $P<0.001$) and women ($r_s=0.40$, $P<0.001$).

Body Mass Index. The prevalence of overweight and obesity among the respondents was 37.7% and 30.1%, respectively. Significant gender differences were revealed ($P<0.001$): overweight was documented in 44.6% of men and 33.7% of women; obesity, in 25.6% of men and 32.6% of women (Table 3). Overweight as well as obesity increased with age among women and men ($P<0.001$) (Table 4).

Smoking. Less than one-third (30.5%) of men and 11.4% of women reported to be daily smokers (Table 3). The prevalence of daily smoking decreased with age in both the groups, but it was lower among women in all age groups (Table 4). There were more ex-smokers among older men aged 55–74 years as compared with younger men. The percentage of

men who were ex-smokers slightly increased with age ($P<0.008$), while the percentage of daily smokers significantly decreased ($P<0.001$).

The percentage of women who had never smoked was greater in older than younger age groups.

Lipids and Glucose. The data about the prevalence of dyslipidemia and hyperglyceridemia are presented in Tables 3 and 5. The prevalence of increased TC level was very high in both genders: 72.0% and 78.0% in men and women, respectively, with a significant intergroup difference ($P<0.003$). Moreover, the prevalence of increased LDL-C level was very high in both gender groups: 73.1% and 73.9% in men and women, respectively, but without a significant group difference. The prevalence of decreased HDL-C level was 16.3% in the overall study population with a statistically significant difference between gender groups ($P<0.01$). More than one-third (27%) of the overall study population had hypertriglyceridemia, and it was more prevalent among men than women (33.9% vs. 24.1%, $P<0.001$). Hyperglycemia was documented in 39.2% of the investigated persons with a statistically significant difference between gender groups ($P<0.001$) (Table 3). With an exception for HDL-C,

Table 3. Prevalence of Risk Factors in the Study Population

Risk Factor	All Population		Men		Women	
	%	95% CI	%	95% CI	%	95% CI
TC ≥ 5 mmol/L	75.2	73.83–76.57	72.0	69.63–74.37	78.0*	76.35–79.65
TG, ≥ 1.7 mmol/L	27.0	25.59–28.41	33.9	31.40–36.40	24.1*	22.40–25.80
LDL-C, ≥ 3 mmol/L	73.7	72.30–75.10	73.1	70.76–75.44	73.9	72.15–75.65
HDL-C, ≤ 1 mmol/L for men or ≤ 1.2 for women	16.3	15.13–17.47	17.0	15.02–18.98	15.9	14.45–17.35
Glucose, 5.6–6.99 mmol/L	28.7	27.89–29.51	35.3	32.77–37.83	24.9*	23.18–26.62
Glucose, ≥ 7 mmol/L	5.4	4.68–6.12	6.3	4.84–7.36	4.9	4.04–5.76
Arterial hypertension	44.8	43.22–46.38	52.9	50.26–55.54	40.2*	38.25–42.15
Body mass index						
Overweight	37.7	36.16–39.24	44.6	41.97–47.23	33.7*	31.82–35.58
Obesity	30.1	28.64–31.56	25.6	23.29–27.91	32.6*	30.74–34.46
Smoking						
Ex-smokers	15.1	13.96–16.24	25.8	23.49–28.11	9.1*	7.96–10.24
Daily smokers	18.2	16.98–19.42	30.5	28.36–33.24	11.4*	10.14–12.66

* $P<0.05$ comparing men and women.

TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Table 4. Prevalence of Arterial Hypertension, Overweight, Obesity and Smoking Habit in Men and Women in Different Age Groups

Category	25–34 years		35–44 years		45–54 years		55–64 years		65–74 years	
	%		%		%		%		%	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Arterial hypertension	23.7	8.2*	39.9	17.1*	50.2	33.0*	60.3	54.0	68.1	64.5
Body mass index										
Overweight	36.3	21.1*	43.3	29.5*	44.7	37.2*	47.8	36.9*	45.5	35.2*
Obesity	13.3	10.6	23.6	20.0	25.6	29.9	30.9	39.8*	26.8	46.9*
Smoking										
Ex-smokers	17.2	15.5	20.7	11.1*	26.2	9.8*	31.3	9.5*	27.2	3.9*
Daily smokers	46.3	22.3*	41.8	13.7*	38.8	15.4*	29.1	9.5*	11.5	2.9*

* $P<0.05$ comparing men and women.

Table 5. Prevalence of Dyslipidemia and Hyperglycemia in Men and Women in Different Age Groups

Category	25–34 yrs		35–44 yrs		45–54 yrs		55–64 yrs		65–74 yrs	
	%		%		%		%		%	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
TC \geq 5 mmol/L	55.9	40.6*	75.5	69.4	76.9	81.8	78.0	86.6*	67.5	81.9*
TG, \geq 1.7 mmol/L	29.4	11.2*	38.3	13.4*	37.0	22.4*	35.4	28.6*	29.5	29.9
LDL-C, \geq 3 mmol/L	55.9	37.5*	78.7	65.6*	77.3	80.1	81.5	82.8	68.2	77.8*
HDL-C, \leq 1 mmol/L for men or \leq 1.2 for women	22.8	12.5*	19.6	14.5	22.1	17.7	17.9	15.5	13.4	13.8
Glucose, 5.6–6.99 mmol/L	17.0	10.3*	28.1	15.9*	35.2	26.1*	41.0	32.5*	41.9	28.9*
Glucose, \geq 7 mmol/L	0.7	0.4	4.7	3.5	5.9	2.9*	9.6	6.2*	6.8	8.6

* $P < 0.05$ comparing men and women.

TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

the prevalence of all parameters showed a trend to increase with age in both gender groups (Table 5). However, it should be mentioned that in the age group of 65–74 years, the prevalence of dyslipidemia was lower in comparison with the age group of 55–64 years, especially in men.

Discussion

Some limitations should be acknowledged in this cross-sectional study. Particularly, the BP measurements were taken twice after a rest of at least 5 minutes but on the same occasion. It does not correspond to the hypertension diagnostic algorithm requiring 2 BP measurements on separate occasions (11). This fact may cause the overestimated prevalence of hypertension.

The level of nonresponse is a common problem, and this study was not an exception. A pretty high difference in the response rate was found between men and women as well as among some age subgroups. The level of responsiveness in both genders in the age group of 25–34 years did not reach the optimum; therefore, the results of this comparative analysis should be considered slightly limiting. The socioeconomic structure of the sample, compared to the background population from the 2009 census data, showed a little difference concerning the marital status and a slight underrepresentation of white-collar workers in the male group.

The strengths of this study include the large representative sample of general population from all regions of Latvia, the collection of data on various lifestyle and CVD risk factors, medical data and measurements by trained staff according to the internationally accepted protocols allowing comparisons among countries (12–14).

The obtained results confirmed the study hypothesis of high prevalence of cardiovascular risk factors in the Latvian population. Moreover, no significant improvements have been observed when compared with the previous epidemiological or health behavior studies (2–4, 15), especially for arterial blood pressure and body mass index.

A high number of risk factors in young male population are an unfavorable finding (>2.5 risk factors in men aged 25 to 34 years) showing the direction for preventive measures to be taken.

A decrease in the number of risk factors in men aged more than 64 years requires further analysis. A desirable explanation could be, for example, a decrease in the smoking prevalence. Nonetheless, the fact that the average life expectancy in Latvia in 2010 for men and women was 67.3 and 77.8 years, respectively, cannot be ignored (1). Therefore, a number of men at high cardiovascular risk do not survive over the age of 64 years. Obviously, the number and distribution of risk factors in men aged more than 64 years could undergo substantial changes. As a reason for the abovementioned could be the change of a positive correlation between age and number of risk factors if the older age/gender group (65–74 years) was excluded from the analysis. The correlation became stronger in the male group, while did not change essentially in women.

Overall, 44.8% of all the participants were recognized as hypertensive. The prevalence of hypertension seems to be close to the data from cross-sectional surveys conducted in several European countries (the United Kingdom, Spain, Italy, Hungary, Poland, and Germany) (12, 14). The results of the investigations revealed that in the same age group as in our study, the prevalence of hypertension was 60.1% in men and 38.5% in women in Germany (4000 people, 2001); in the UK national samples (1998 and 2003), 41.5% of men and 33.3% of women had AH, and in Poland, 44.0% and 35.0%, respectively. Both the primary prevention and the good management of hypertension will be future challenges in Latvia as the prevalence of some of the contributing factors, such as overweight and obesity, is likely to increase (2–4).

The high prevalence of obesity demonstrated in this study as well as the accumulation of other CVD risk factors in the middle-aged groups are likely to increase the burden of CVD and diabetes in the immediate future. The prevalence of hyperglycemia

(blood glucose level, ≥ 7.0 mmol/L) was approximately 5% and 6% in women and men, respectively. These data highlight the problem of diabetes mellitus in Latvia, although an increasing trend has already been expected (16).

The attention should be paid to the dyslipidemia profile found in this study: a very high prevalence of increased TC and LDL-C levels, increasing with age, a lower prevalence of abnormal TG level, which is stable in men with increasing age, and a low prevalence of decreased HDL-C. Of interest is the finding about the improvement of lipid profile in the age group of 65–74 years especially in men, if compared to younger age groups. We have no sufficient information about better medication strategy or better compliance in this age group that could explain this improvement of lipid profile. In addition, on the other hand, some other explanation could be the death of people with a very high level of risk factors in the middle-aged group, especially, among men. To note, the male life expectancy at birth in Latvia in 2009 was 68.3 years.

It is worth to note that the high prevalence of decreased HDL-C level and increased TG level has never been a problem in Latvia as it is shown in the previous epidemiological studies (3–4).

To note, the European Action on Secondary and Primary Prevention by Intervention to Reduce Events III (EUROASPIRE III) survey on the management of CVD prevention in Europe has reported the high prevalence of increased TC and LDL-C levels in Latvia: 64.0% of the coronary patients had a TC level of ≥ 4.5 mmol/L and 62.8% of patients had a LDL-C level of ≥ 2.5 mmol/L (17). These data reveal a problem at the level of secondary prevention. In Latvia, 73%–80% of the patients with coronary heart disease use lipid-lowering drugs in the framework of secondary prevention (17); thus, the lower prevalence of dyslipidemia was expected to be found in this patients' group in comparison with other European countries. Whatever the case could be, the reasons of the above-described dyslipidemia profile have to be investigated in future studies.

An ever-increasing number of epidemiological studies have identified smoking as one of the most important risk factors for noncommunicable diseases, including CVDs. The prevalence of smoking in Latvia is still rather high; however, the mean smoking prevalence has decreased in men in comparison with our previous cross-sectional population studies and the FINBALT health behavior study (2–4, 15). To note, it could be admitted that the lower prevalence of daily smoking among men in the current study might be caused by an insufficient representation of younger age groups. However, the comparison of smoking prevalence in our study with the data of the abovementioned studies (2–4, 15) clearly

demonstrated the decreased prevalence of smoking among men in all compared groups of equal age.

The finding that smoking is most prevalent in a younger age group, especially among women, might reflect the contemporary smoking habit in adolescence in general. This alarming fact was also confirmed by the study on smoking habits among teenagers performed within the framework of the WHO-supported International study "Health Behaviour in School-Aged Children" (18). It has been shown that in Latvia, 23.5% of 15-year-old adolescent boys and 15.4% of girls are daily smokers.

Comparing the risk factor profile in Latvia with the countries that have already dealt with the problem of CVD mortality, we can find some didactic correlations. The analysis of CVD risk factors within the 35-year period in Finland (6) has shown a tremendous improvement in the lipid profile: the prevalence of normal TC level (≤ 5.0 mmol/L) in 1972 was 6% for men and 7% for women, but in 2007, it increased to 36% and 46%, respectively. The dynamics of elevated BP and smoking is similar: the prevalence of elevated systolic BP declined from 64% in men and from 65% in women to 46% and 38%, respectively. The smoking prevalence decreased from 52% to 31% among men, but it increased from 10% to 18% among women. Therefore, we can say that the risk factor profile in Finland in 2007 was close to our findings in Latvia in 2009. The CVD mortality rate in Finland during the 35-year period declined to a range between 370 per 100 000 and 390 per 100 000 in men and women, respectively, which was explained by the decline of combined risk by 60% during these years (6). However, in Latvia, the CVD mortality rates during the last 5 years were found to be 2 times higher: 750–760 per 100 000 population in men and 780–790 per 100 000 population in women. From these comparisons of CVD risk factors and mortality rates, we can speculate that besides the impact of risk factors on mortality rates, there is a wider spectrum of other factors influencing CVD mortality in Latvia comparing to Finland including differences in a socioeconomic situation, access to medical services, etc.

Future longitudinal population-based studies should focus on more precise characterization of the data obtained in order to estimate the interaction of different risk factors and assess the contribution of each of them in the course of illness. This could help the option of adequate and effective intervention.

Conclusions

This first population-based cross-sectional epidemiological study of cardiovascular risk factors in Latvia covering the entire country has established a high prevalence of classical cardiovascular risk factors. The data can be utilized as baseline charac-

teristics against which other measurements can be compared down the road including the monitoring of health prevention activities.

Acknowledgments

This work was supported by the State Research Programme No. 8, the Ministry of Health, the Ministry of the Interior Affairs, the Ministry of Edu-

cation and Science, the Latvian Board of Science, Biomedical Research and Study Centre of Latvia, the Foundation of Innovative Medicine, the Latvian Society of Cardiology, and the Charity Foundation "Quinta" of Rietumu Banka.

Statement of Conflict of Interest

The authors state no conflict of interest.

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Received 2 September 2011, accepted 30 June 2012