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Original Research Article

Utilization of cardiovascular medicines and cardiovascular mortality in Lithuania, Sweden and Norway in 2003–2012

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ABSTRACT

Objective: The aim of this ecological study was to evaluate whether any changes in cardiovascular (CV) medicine utilization, population, socioeconomic and health system factors were associated with CV mortality in Lithuania, Sweden and Norway in 2003–2012.

Materials and methods: CV drug utilization was calculated using the Anatomical Therapeutic Chemical/Defined Daily Dose (DDD) methodology and expressed as a number of DDD per 1000 inhabitants per day (DDD/TID). The CV age-standardized death rate (CV-SDR) and risk factors data were obtained from the WHO, EUROSTAT, and FAOSTAT databases. The multiple linear regression model was used for modeling outcome measures - the relationship between the CV-SDR and CV medicine utilization including socioeconomic (GDP, unemployment and divorce rate), population (alcohol consumption, smoking and amount of kcal per day, consumption of fruit and vegetables, health status self-evaluation) and health system factors (number of hospital beds, practicing physicians and health care expenditure).

Results: The higher CV medicine utilization in Sweden (307–455 DDD/TID, $P < 0.001$) and Norway (306–394 DDD/TID, $P < 0.001$) was associated with a definite decline in CV-SDR (in Norway from 215 to 146 and in Sweden from 233 to 174). In Lithuania, the increasing but lower consumption of CV medicines (135–360 DDD/TID, $P < 0.001$) and twice higher CV-SDR (from 541 to 447) was registered. A significant inverse correlation was observed between CV-SDR and DDD/TID. We found a strong association between the DDD/TID and the CV-SDR ($R^2 = 0.67$, $P < 0.001$). There was a strong correlation between CV-SDR and nine factors ($P < 0.05$), except the number of practicing physicians, amount of kcal per day. There was a strong correlation between DDD/TID and nine factors ($P < 0.05$), except the unemployment rate and amount of kcal per day. Association between an increase in the use of medicines and a decrease in CV-SDR was stronger in the case of higher alcohol consumption, higher number of available beds in hospitals and the lower unemployment rate.

Conclusions: We confirmed the strong negative correlation between CV medicine utilization and CV mortality in all countries. The strong correlation was found between CV-SDR and nine factors, also between the use of CV medicines and nine factors. The impact of factors on

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the medicines induced decrease in CV-SDR showed the stronger influence in case of lower unemployment, higher alcohol consumption and higher number of beds for hospitalization.

1. Introduction

Although cardiovascular (CV) disease remains a leading cause of mortality globally, a decrease in CV mortality has been observed in Europe during the last 30 years [1]. This decrease is a result of reduction in major risk factors, improved treatment and strengthened prevention measures. However, great regional differences in death rates from CV disease are observed in Europe, generally being higher in Central and Eastern Europe than in Northern, Southern and Western Europe [2,3]. It is reported that mortality from CV disease is more than twice and mortality from coronary heart disease and cerebrovascular disease is more than 3–5 times higher in Lithuania than in Scandinavian countries [4,5]. Despite significant increase in the use of CV medicines, the mortality rate remains high in Lithuania.

The use of CV drugs has not been studied in Lithuania, and it is unknown what utilization pattern of CV medicines is, and what impact the use of these medicines makes on CV mortality.

The main objective of this ecological study was to examine an association between the use of CV medicines and CV mortality in Lithuania and in geographically neighboring countries of Northern Europe – Sweden and Norway.

We have also analyzed possible associations between the changes in utilization of CV medicines and risk factors related to life style, socioeconomic status, health system, and mortality from CV disease, and the influence of these risk factors on association between the use of CV medicines and CV mortality. In addition, we will discuss possible actions to optimize risk factors and treatment of CV disease based on the results of this study.

2. Materials and methods

2.1. Sources of data

In this ecological study, we analyzed drug utilization data from Lithuania, Sweden and Norway over the period from 2003 to 2012 (2004–2012 for Norway). The data on the use of CV medicines was retrieved from national databases. For Lithuania, the database of Lithuanian National Health Insurance Fund ''SVEIDRA'' was used. This database contains information on all dispensed prescriptions of reimbursed medicines, and covers up to 100% of insured population (about 98% of population is covered by health insurance) [6].

For Norway, the data was extracted from the Norwegian Prescription Database (NorPD) at the Norwegian Institute of Public Health. The NorPD monitors drugs dispensed by prescription in Norway and cover 100% of the population [7].

For Sweden, the data was obtained from the database of the National Board of Health and Welfare under the Ministry of Health and Social Affairs (Socialstyrelsen). This database contains information on prescription medicines dispensed by community pharmacies and covers 100% of the outpatient visits [8].

Age-standardized CV death rate per 100,000 population (CV-SDR) was obtained from the World Health Organization database: WHO Health for All: European Mortality Indicator Database (WHO HFA-MDB) [9].

Eleven risk factors that may influence CV mortality have been chosen in this study. Selection of factors was based on the European guidelines on CV disease prevention in clinical practice (version 2012), which includes tobacco use, an unhealthy diet, physical inactivity, and excessive stress, which all together result in obesity, arterial hypertension, dyslipidemia, and elevated blood glucose [10].

We use corresponding data from publicly available databases, such as the WHO, the EUROSTAT, the Food and Agriculture Organization of the United Nations (FAO) databases, which directly or indirectly reflects the above-mentioned risk factors [11–18].

These databases contain the aggregated comparable data at the population level over the period of 2003–2012. We divided the factors into three categories: population related factors, socioeconomic factors and health care system related factors. Population related factors include alcohol consumption, smoking, energetic value of consumed food per day, consumption of fruits and vegetables, and personal perception of health condition. Socioeconomic factors include gross domestic product [GDP], unemployment rate and crude divorce rate. Health care system related factors are number of beds in hospitals, number of practicing physicians and health care expenditure per capita. Detailed description of the factors and data sources is presented in Table 1. There is no publicly available data on obesity and adequate physical activity. We replaced these factors by indirect factor, such as self-reported health status of the population. Despite the subjective nature, this factor could be used as relevant and reliable estimators of the health status of populations as well as good predictors of health care needs [19].

2.2. Methods and statistical analysis

Drug utilization was calculated using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology and ATC/DDD Index, 2014. The results were expressed as a number of Defined Daily Doses per 1000 inhabitants per day (DDD/TID) [20].

The utilization of CV medicines was analyzed regardless of the indication. The following ATC groups were included to the analysis: C01, cardiac therapy; C02, antihypertensive drugs

Table 1 – List of factors included in analysis.

Factor	Code	Description	Source
Socioeconomic factors			
Gross domestic product (GDP)	F1	GDP, expressed as US$ per capita, is the sum of gross value added by all resident producers in the economy plus any product taxes and minus any subsidies not included in the value of the products [11]	WHO HFA-DB
Unemployment rate	F2	The unemployment rate is the number of people unemployed as a percentage of the labor force. Unemployed persons are all persons 15–74 years of age who were not employed during the reference week, had actively sought work during the past four weeks, and were ready to begin working immediately or within two weeks [12]	EUROSTAT
Crude divorce rate	F3	Crude divorce rate is the ratio of the number of divorces during the year to the average population in that year. The value is expressed per 1000 inhabitants [13]	EUROSTAT
Population related factors			
Alcohol consumption	F4	Recorded alcohol consumption is defined as the recorded amount of alcohol consumed per adult (15+ years) over a calendar year in a country, in liters of pure alcohol. The indicator only takes into account the consumption that is recorded from production, import, export, and sales data often via taxation [11]	WHO HFA-DB
Smoking	F5	This indicator is expressed as the percentage of regular daily smokers in the population aged 15 years and above. This indicator is measured using the standard questionnaire during a health interview of a representative sample of the population [11]	WHO HFA-DB
Energetic value of consumed food per day	F6	Total amount of food converted into kilocalories, which is available for consumption per person per day [14]	FAOSTAT
Fruits and vegetables consumption	F7	Fruits and vegetables consumption is expressed as kg per capita per year [14]	FAOSTAT
Personal perception of health condition	F8	The concept is operationalized by a question on how a person perceives his/her health in general using one of the answer categories very good/good/fair/bad/very bad. The data are expressed by percentage of population, which estimate self-health condition as very good and good [15]	EUROSTAT
Health care system related factors			
Number of beds in hospitals	F9	This indicator is expressed as number of available beds in hospitals per 100,000 inhabitants [16]. Total hospital beds are all hospital beds which are regularly maintained and staffed and immediately available for the care of admitted patients	EUROSTAT
Number of practicing physicians	F10	Number of practicing physicians who provide services directly to patients per 100,000 population were obtained from database [17]	EUROSTAT
Health care expenditure per capita	F11	Health care expenditure expressed as EURO per capita [18]	EUROSTAT

(centrally and peripherally acting antiadrenergic agents); C03, diuretics; C04, peripheral vasodilators, C07 – beta blocking agents (BBs); C08, calcium channel blockers (CCBs); C09, agents acting on the renin–angiotensin system (RAS); and C10, lipid modifying agents.

2.3. Statistical analysis

The strength of the associations between the use of CV medicines and CV-SDR in three countries was examined using Pearson's correlation coefficient. The Pearson's correlation coefficient also was used to evaluate the influence of the factors on the use of CV medicines and on CV-SDR.

The multiple linear regression model, adjusted for multicollinearity and interaction terms, was used for modeling the outcome – the relationship between CV-SDR and the use of CV medicines including a series of other changing variables (the risk factors presented in Table 1). Regression analysis was performed, using the following equation:

$$\text{CV-SDR} = \text{CV medicines} + F_n + (\text{CVM medicines} * F_n)$$

CV-SDR – CV mortality (dependent variable), CV medicines – utilization of CV medicines expressed in DDD/TID (independent variable), F_n – value of factor, included to analysis (independent variable).

This equation presents variation in CV-SDR induced by changes of the use of CV medicines while F_n is fixed. Independent variables were centered prior to analysis.

Partial correlation analysis was performed in order to get a correct picture of the relationship between the use of CV medicines and CV-SDR by controlling the variables, and to study the effect of each variable separately.

A P value of <0.05 was considered statistically significant. No extrapolation based on available risk factor trends was made if data were not available in databases.

JMP statistical software (version 8.0; SAS, Cary, NC) was used for all data analysis.

2.4. Ethics statement

All data were congregated at the population level and publicly accessible with the exception of data from the database of the National Health Insurance Fund. No individual patient-level information was used in this analysis. The Regional Biomedical Research Ethics Committee (Medical Faculty of Vilnius University, Vilnius, Lithuania) issued the approval for this study.

3. Results

3.1. Trends and pattern of utilization of CV medicines

The use of CV medicines increased over the time in all three countries. Although the use of CV medicines was higher in Sweden (307 DDD/TID in 2003 and 455 DDD/TID in 2013; annual growth 4.8%; $P < 0.001$) and Norway (306 DDD/TID in 2004 and 394 DDD/TID in 2012; annual growth 3.2%; $P < 0.001$), the increase in the use of CV medicines was considerably higher in Lithuania (135 DDD/TID in 2003 and 360 DDD/TID in 2012, annual growth 16.7%; $P < 0.001$) (Fig. 1).

The analysis of the pattern of utilization of CV medicines showed that the most used groups of drugs in all three countries were agents acting on RAS, BBs and CCBs.

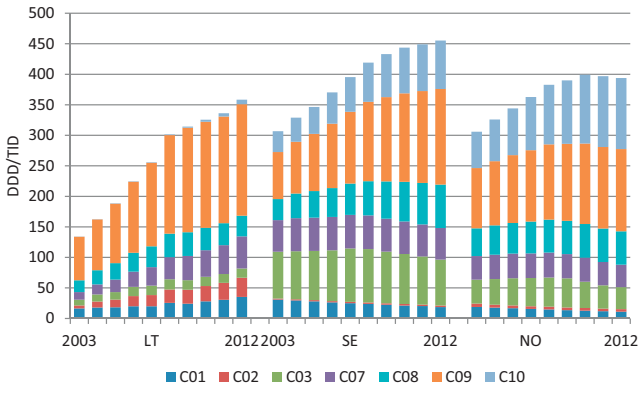

Fig. 1 – Utilization of different groups of CV medicines in Lithuania, Sweden and Norway in 2003–2012. DDD/TID, number of DDD per 1000 inhabitants per day; LT, Lithuania; SE, Sweden; NO, Norway. C04 utilization was <1 DDD/TID and it is not included in the figure.

The increase in utilization of agents acting on RAS was seen in all three countries: from 71.2 to 182.7 DDD/TID in Lithuania, from 77.1 to 156.6 DDD/TID in Sweden and from 98.7 to 134.6 DDD/TID in Norway.

The use of BBs in Lithuania has increased during the period from 12.5 in 2003 to 52.6 DDD/TID in 2012, and became similar to the utilization in Sweden (51.8 DDD/TID) and Norway (38.6 DDD/TID). The consumption of CCBs over period was about two times lower in Lithuania (19.4 DDD/TID in 2003 and 33.8 DDD/TID in 2012) than in Sweden (34.5 DDD/TID in 2003 and 71.2 DDD/TID in 2012) and Norway (45.5 DDD/TID in 2004 and 54.7 DDD/TID in 2012).

The marked differences were observed in the use of antiadrenergics, diuretics and lipid-modifying agents (Fig. 1). The use of centrally and peripherally acting antiadrenergic agents in 2012 in Lithuania was more that twelve times higher than in Sweden and more than seven times higher than in Norway (31.5 DDD/TID, 2.5 DDD/TID and 4.1 DDD/TID respectively).

In contrary, the use of plain diuretics was low in Lithuania (9.4 DDD/TID in 2003 and 15.2 DDD/TID in 2012) compared to Sweden (76.7 DDD/TID in 2003 and 75.3 DDD/TID in 2012) or Norway (47.9 DDD/TID in 2004 and 36 DDD/TID in 2012).

A striking difference in the use of statins was noticed between countries over period. In 2012 the use of statins was just 7.4 DDD/TID in Lithuania compared to 79.3 DDD/TID in Sweden and 116 DDD/TID in Norway.

3.2. Associations between the CV medicine utilization, risk factors and their combinations on cardiovascular mortality

The CV-SDR has decreased during the study period in all three countries (Fig. 2). However, in Lithuania, it was about 2.4 times higher at the beginning of the study period and 3 times higher in 2012.

A significant negative correlation (r value from -0.96 to -0.82) was observed between the CV-SDR and the use of CV medicines in all three countries (Fig. 2).

The Pearson correlation coefficients between the use of CV medicines, CV-SDR and risk factors are shown in Table 2. Strong negative correlation was found between CV-SDR and the following factors: GDP, consumption of fruit and vegetables, self-assessment of personal health ($P < 0.001$) and health care expenditure per capita ($P < 0.01$).

On the contrary, strong and moderate positive association was seen between unemployment rate, crude divorce rate, alcohol consumption, available beds in hospital and CV-SDR ($P < 0.001$).

The strong positive correlation was found between the use of CV medicines and GDP, personal health assessment and health care expenditure. The negative correlation was seen between the alcohol consumption, smoking, crude divorce rate and the rate of available beds in hospitals and the use of CV medicines ($P < 0.001$) (Table 2).

The analysis of the multiple regression models revealed a strong association between the use of CV medicines and CV-SDR ($R^2 = 0.67$; $P < 0.001$), that means that 67% change in CV-SDR could be explained by the increased use of CV medicines.

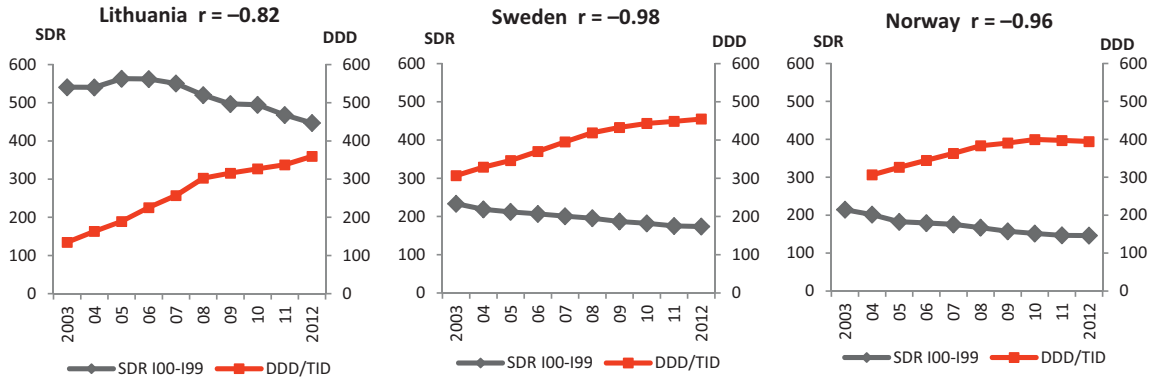

Fig. 2 – Age-standardized death rates from CV disease (SDR I00-I99) and utilization of CV medicines – trends and correlation in different countries. *r*, Pearson correlation coefficient.

Table 2 – Correlation coefficients between the use of CV medicines, CV age-standardized death rates and risk factors.

Factor	Correlation coefficient between CVD-SDR and F_n	*P*	Correlation coefficient between DDD/TID and F_n	*P*
F1	−0.88	<0.001	0.66	<0.001
F2	0.59	<0.001	−0.19	0.233
F3	0.94	<0.001	−0.68	<0.001
F4	0.95	<0.001	−0.64	<0.001
F5	0.55	<0.01	−0.85	<0.001
F6	0.41	<0.05	−0.04	0.711
F7	−0.73	<0.001	0.52	<0.05
F8	−0.97	<0.001	0.82	<0.001
F9	0.86	<0.001	−0.84	<0.001
F10	−0.19	0.462	0.57	<0.01
F11	−0.90	<0.001	0.64	<0.001

CVD-SDR – age-standardized death rates from CV disease.
DDD/TID-CVM utilization expressed by number of defined daily dose per 1000 inhabitants per day.

Eleven models were used to analyze the effect of the use of CV medicines on CV-SDR taking into account an additional factor.

The more significant impact of increased CV medicine utilization on CV-SDR was found in the country where the higher alcohol consumption, higher number of available beds in hospitals and the lower unemployment rate were registered (Table 3). Other factors do not change the impact of CV medicine utilization on CV-SDR in this model.

Partial correlation analysis showed that personal perception of health condition and number of beds in hospitals influenced the CV-SDR so strongly that they suppressed the direct impact of the utilization of CV medicines on CV-SDR (Table 4).

Table 3 – Summary of models, which estimate changes of CV age-standardized death rates caused by the use of CV medicines, risk factors and their interactions.

F*	DDD/TID Coef	SE	*T*	*P*	F* Coef	SE	*T*	*P*	DDD/TID* F* Coef	SE	*T*	*P*
F1	−0.61	0.24	−2.49	<0.05	0.00	0.00	−7.57	<0.001	0.00	0.00	0.84	0.41
F2	−1.54	0.12	−12.45	<0.001	20.62	2.52	8.17	<0.001	0.18	0.05	3.83	<0.001
F3	−0.56	0.18	−3.16	<0.01	237.49	21.80	10.89	<0.001	−0.21	0.35	−0.61	0.55
F4	−0.57	0.09	−6.38	<0.001	41.58	1.94	21.39	<0.001	−0.08	0.04	−2.15	<0.05
F5	−2.20	0.68	−3.22	<0.01	−11.58	10.43	−1.11	0.28	−0.01	0.08	−0.09	0.93
F6	−1.56	0.15	−10.74	<0.001	0.47	0.08	6.16	<0.001	−0.00	0.00	−1.50	0.15
F7	−1.24	0.23	−5.45	<0.001	−3.48	0.88	−3.95	<0.001	−0.01	0.01	−.80	0.43
F8	0.02	0.19	0.10	0.92	−10.20	0.88	−11.63	<0.001	0.01	0.01	1.64	0.18
F9	0.30	0.43	0.70	0.49	0.88	0.18	4.90	<0.001	−0.00	0.00	−2.87	<0.01
F10	−2.03	0.30	−6.69	<0.001	1.83	1.13	1.61	0.12	−0.04	0.02	−1.93	0.07
F11	−0.59	0.21	−2.85	<0.01	−0.05	0.01	−9.43	<0.001	0.00	0.00	1.68	0.11

Table 4 – Partial correlation analysis of impact of factors on correlation between CV age-standardized death rates and the use of CV medicines.

Confounding variable	Impact of factor on correlation between SDR and CVM	R^2 coefficient	P
F1	−0.69	0.48	<0.01
F2	−0.89	0.79	<0.01
F3	−0.72	0.51	<0.01
F4	−0.89	0.79	<0.01
F5	−0.73	0.54	<0.01
F6	−0.92	0.85	<0.01
F7	−0.78	0.60	<0.01
F8	−0.12	0.01	0.583
F9	−0.33	0.11	0.110
F10	−0.79	0.62	<0.01
F11	−0.73	0.54	0.701

4. Discussion

This is the first total population-based study analyzing the use of CV medicines and its association with CV mortality in Lithuania. Our analysis confirmed findings of other studies that the increase in the use of CV medicines is associated with the decrease in CV mortality [21].

However, a 3-fold increase in utilization of CV medicines in Lithuania during the study decade was not associated with substantial decrease in CV mortality. At the same time, the further decline of initially lower CV mortality was more pronounced in Sweden and Norway than in Lithuania [9]. This difference may be related to wide variation in prevalence of some CV risk factors, as well as genetic, socioeconomic, environmental and medical care factors in the countries [22,23]. It is well known that arterial hypertension and dyslipidemia are important risk factors for CV mortality [24,25]. It has been shown that timely and appropriate correction (including pharmacological) of high blood pressure and dyslipidemia is associated with decrease in CV morbidity and mortality [26,27]. Although the utilization of CV medicines increased in all three countries, the data from other studies showed that optimal control of blood pressure was achieved only in 12.6% of men and in 16.6% of women in Lithuania compared with 52–58% of patients in Sweden and 71% of patients in Norway [28–31]. Further studies are needed to evaluate treatment persistency and compliance with treatment in order to explain the findings.

According to our results, the pattern of the use of CV medicines differed between Scandinavian countries and Lithuania. The most used group of drugs was agents acting on RAS in all countries. Some differences were seen in utilization of BBs (similar utilization in Sweden and Lithuania, but lower in Norway) and CCBs (the highest utilization in Sweden and lowest in Lithuania). The main differences were seen in utilization of diuretics, centrally acting antiadrenergic drugs and statins. Although the outcome trials confirmed the efficacy of diuretics in preventing major forms of cardiovascular disease, the use of plain diuretics was very low in Lithuania compared to Sweden or Norway [32–34]. It should be noticed that the growing use of ACEI and ARB diuretic combinations might compensate the low use of plain diuretics.

Our analysis revealed extremely high utilization of centrally acting antiadrenergic drugs in Lithuania despite the limited evidence on the beneficial effect of this class on CV mortality [32,35]. The use of statins was extremely low in Lithuania despite appreciable evidence on efficacy of these medicines in prevention of CV mortality [36,37]. Such low utilization of statins may be partially explained by very strict reimbursement policy in Lithuania. Up to 2006, only cardiologists could prescribe statins for secondary prevention and for 6-months period. Although since 2009, the family doctors can prescribe generic statins, their utilization remains very low in Lithuania [38].

It is well known that CV morbidity and mortality is influenced by many CV risk factors: tobacco use, an unhealthy diet, physical inactivity, and excessive stress, which all together result in obesity, arterial hypertension, dyslipidemia, and elevated blood glucose. These risk factors are listed in European Guidelines on Cardiovascular Disease Prevention in Clinical Practice [10].

The negative effect of low socioeconomic status has been documented in many trials and meta-analysis as a possible predictor of health care utilization, non-adherence to prescribed treatment, morbidity and premature death [39,40].

We consider an unemployment rate as a factor representing the socioeconomic status and the divorce rate as a stress-conveying factor linked to poor health outcomes [39,40].

GDP and national health care expenditure could give a wider view of economical factors as it partially reflects patient's accessibility to medical care. Therefore, three socioeconomic factors, such as GDP, unemployment rate and crude divorce rate, were included to our analysis.

In order to assess influence of health care system on CV mortality we included three health care system related factors: health care expenditure per person, number of available hospital beds and number of practicing physicians [41].

The high prevalence of cardiovascular risk factors confirmed worse situation in Lithuania, which could significantly contribute to CV mortality.

We noticed the following differences in the values of risk factors in Lithuania compared to Scandinavian countries: 4–7 times lower GDP, 5.6–10 times lower health care expenditure per inhabitant; 1.7–4 times higher unemployment rate, 1.4–1.8 times higher divorce rate, 2 times higher alcohol consumption, 1.5 times higher (although decreasing) percentage of smokers in population, lower availability of fruit and vegetables (137.5 vs. 201.6 kg/year per person) [11–18].

Seven factors in our model (the increase in GDP, health care expenditure, consumption of fruits and vegetables and the decrease in the unemployment, divorce, alcohol and food consumption rates) were associated with lower CV-SDR mortality rate as expected.

The proportion of people who perceived their health as very good or good ranged from 71.7 to 80.9% in Sweden, from 73.7 to 78.7% in Norway and only from 41.5 to 44.3% in Lithuania [15]. It seems that health self-perception could influence risk behaviors that may have an effect on health. Individuals who

self-perceive their health as very good and good tend to have less risk behaviors and the necessity of medication could be decreased.

The number of hospital beds for 100,000 inhabitants was twice as high in Lithuania than in Sweden or in Norway [16]. The number of hospital beds could be considered as an indicator of the capacity of health care system [42].

There is limited evidence on how reduction in number of hospital beds affects the quality of care and the health status of the population. The most effective way to reduce the need for hospital beds is prevention of admission by enhancing the health of the population. It could be achieved by promoting healthy life style and implementing disease prevention and screening programs at the primary care level, improving diagnostic and treatment efficiency. Our analysis revealed the inverse correlation between the number of hospital beds and CV medicine utilization, which may be an indicator of diagnostic and treatment non-efficiency.

The finding of positive association between the number of hospital beds and CV-SDR is controversial and needs further studies.

There was no big difference in the number of practicing physicians per 100,000 population between three countries. Despite the comparison of the effectiveness of primary care and specialist care is controversial and varying between studies, there is some evidence that the greater number of primary care physicians in the area was associated with lower all-cause and CV mortality [43–46].

We tried to determine whether there is any relation between CV medicine utilization and CV-SDR in populations with different CV risks, and whether this relation changes over the time. Some researchers have attempted to find explanation about the trends in risk factors for CV mortality and changes in management of CV disease, using different techniques. There are some data showing that additional reduction in CV mortality is possible by either improving the distribution of risk factors in the population or raising the percentage of patients receiving evidence-based treatments, but the extent of their contribution have wide variations between the countries [47,48]. Our model, analyzing the impact of factors on the medicine-induced decrease in CV-SDR, showed the stronger influence in the case of lower unemployment rate, higher alcohol consumption and higher number of available hospital beds.

We acknowledge that this study has several limitations related to the weakness of ecological study design, data availability and quality. Almost all data were obtained from freely accessible databases, so we accepted all possible biases related to collection of these data. The selection of risk factors was limited to data availability. Our analysis of drug utilization was based on dispensed data, thus we do not have any information on real use of medicines. We did not analyze the use of medicines at the patient level: no information on indications, initiation of treatment and persistency of drug use and treatment compliance was collected. Information on effectiveness of treatment was also not available. In addition, we have not studied the utilization of antithrombotic agents, which can also have an impact on CV mortality.

5. Conclusions

Our study showed the strong negative correlation between CV medicines utilization and CV mortality in Lithuania, Sweden and Norway. Strong negative correlation was found between CV-SDR and the following risk factors: GDP, consumption of fruit and vegetables, self-assessment of personal health and health care expenditure per capita. A positive association was seen between unemployment rate, crude divorce rate, alcohol consumption, available beds in hospital and CV-SDR. A strong positive correlation was found between the use of CV medicines and GDP, personal health assessment and health care expenditure. A negative correlation was seen between the alcohol consumption, smoking, crude divorce rate and the rate of available beds in hospitals and the use of CV medicines. Our model analyzing the impact of factors on the medicines induced decrease in CV-SDR showed the stronger influence in the case of lower unemployment rate, higher alcohol consumption and higher amount of available beds for hospitalization.

Our findings confirmed the necessity of complex approach in order to decrease CV mortality. It is important to ensure appropriate preventive measures to control risk factors and rational evidence based therapy of cardiovascular disease. This can be achieved by education of prescribers, economical incentives, implementation of evidence-based guidelines and some enforcement measures.

Conflict of interest

The authors state no conflict of interest.

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