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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Global cardiovascular mortality risk in the adult Polish population: prospective assessment of the cohorts studied in multicentre national WOBASZ and WOBASZ Senior studies

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Abstract

Background and aim: To develop a global cardiovascular disease (CVD) mortality risk model for the Polish population and to verify these data in the context of the SCORE risk algorithm.

Methods: We analysed data obtained in two multicentre national population studies, the WOBASZ study which was conducted in 2003–2005 and included 14,769 subjects aged 20–74 years, and the WOBASZ Senior study which was conducted in 2007 and included 1096 subjects above 74 years of age. All these subjects were followed for survival status until 2012 and the cause of death was determined. The mean duration of follow-up was 8.2 years for WOBASZ study participants and about 5 years for WOBASZ Senior study participants. Overall, 1436 subjects died, including 568 due to CVD. For the purpose of our analysis of overall and CVD mortality, 15 established risk factors were selected. Survival was analysed separately in WOBASZ and WOBASZ Senior study participants. Statistical methods included descriptive statistics, Kaplan-Meier curves, Cox proportional hazard models, and the SCORE risk algorithm. Measure of incompatibility of the SCORE risk model to the Polish population was determined as the difference between mortality rates by the SCORE risk quartiles and the Cox approach.

Results: During the 8-year follow-up of the WOBASZ study population, mortality due to CVD was 38% among men and 31% among women. The most common causes of CVD mortality were ischaemic heart disease (IHD, 33%) followed by cerebrovascular disease (17%) in men, and cerebrovascular disease (31%) followed by IHD (23%) in women. We found significant differences between men and women in regard to survival curves for both overall mortality and CVD mortality ($p < 0.0001$). For overall mortality among men and women, nearly all selected risk factors were shown to be significant in univariate analyses, except for high density lipoprotein cholesterol (HDL-C) level and the total cholesterol/HDL-C ratio in men, and smoking status in women. In multivariate analysis, independent predictors in men included age, glucose level, systolic blood pressure, and smoking status. In women, independent predictors were age, smoking status, and diabetes. During the 5-year follow-up of the WOBASZ Senior study population, mortality due to CVD was 48% among men and 58% among women. The most common cause of CVD mortality in both men and women was IHD (29% and 24%, respectively), followed by cerebrovascular disease (16% and 21%, respectively). We found significant differences between men and women in regard to survival curves for overall mortality ($p < 0.0001$) but not for CVD mortality ($p = 0.0755$). Due to the fact that survival curves for CVD mortality did not differ between men and women, we estimated the cut-off age for no survival difference in the WOBASZ study. By selecting the oldest patients and adding them to the WOBASZ Senior cohort, we obtained the cut-off age of 70 years above which the survival curves were not significantly different between men and women. In univariate analyses, independent predictors in men were age and creatinine level. These factors remained significant in multivariate analysis. In women above 74 years of age, independent predictors in univariate analyses included age, HDL-C level, creatinine level, total cholesterol/HDL-C ratio, and smoking status. Age, HDL-C level, creatinine level, and smoking status remained independent predictors of overall mortality in multivariate analysis. For CVD mortality, significant predictors were the same as for overall mortality. In women, significant predictors in uni- and multivariate analyses were age and smoking status. Overall disagreement between CVD mortality rates by the SCORE risk model and the Cox model was 5.7% in men and 2% in women.

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Conclusions: 1. Long-term follow-up of WOBASZ and WOBASZ Senior study participants allowed assessment of the independent association of the evaluated cardiovascular risk factors with CVD mortality in the Polish population. 2. Validation of the SCORE risk algorithm to estimate individual global CVD risk in the Polish population showed a high predictive value of this algorithm.

Key words: WOBASZ, WOBASZ Senior, cardiovascular disease, global risk, SCORE

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INTRODUCTION

Cardiovascular disease (CVD) is a major cause of morbidity, disability, and premature mortality. A reduction in CVD mortality has been observed in Poland since early 1990s, amounting to 30% in 1997–2001. However, mortality rates remain worse compared to other European Community countries, e.g. they continued to be nearly 2-fold higher in 2011. Notably, these adverse mortality rates are mostly seen among young and middle-age subjects, with mortality in this age group being 2.5-fold higher compared to other European Community countries. Large regional differences are also observed in Poland, estimated at about 25–30% among those aged 20–74 years. Reasons for this variation are complex. They may depend on socioeconomic conditions, lifestyle, and the regional healthcare level [1, 2].

The idea of a risk factor for a given event has originated from the Framingham and Seven Countries studies [3]. According to the definition by Simborg [4], risk factor is a feature or symptom occurring in the population which is statistically associated with an increased disease incidence or mortality. Risk factors define subjects at a risk of future pathology despite its absence at the time of evaluation. The value of a specific risk factor is an individual feature that affects the likelihood of occurrence of the event being studied. A world literature review by Hopkins and Williams [5] identified at least 246 factors that showed a significant correlation with ischaemic heart disease (IHD) incidence in at least one study.

Long-term epidemiological studies showed that concomitant presence of several risk factors resulted in a synergistically and not additively increased risk. Then, the global risk may be much more increased with even modest elevation of several risk factors compared to that associated with highly elevated but single risk factors.

Conclusion from these studies prompted a research interest in multivariate statistical analyses. Based on such analyses performed in the United States in the early 1960s, American Heart Association first published tables [6] that allowed estimation of the likelihood of IHD incidence in relation to such factors as gender, age, cigarette smoking, blood pressure (BP), serum cholesterol level, glucose, tolerance, and electrocardiographic evidence of left ventricular hypertrophy, followed by development, with a support from Merck Sharp & Dohme, of a risk calculator known as Coronary Risk Assessor.

This risk calculator also allowed comparing an individual risk with a hypothetical individual of the same gender and age but free from the risk factors, thus increasing patients' motivation for lifestyle changes.

In Europe, the European Systematic COronary Risk Evaluation (SCORE) algorithm is used since 2003 to estimate the 10-year CVD mortality risk in relation to risk factors including gender, age, total cholesterol level, systolic BP, and cigarette smoking [7]. The global SCORE risk has been used to develop guidelines and recommendations to increase public awareness of the need for lifestyle changes, e.g. smoking cessation and dietary modification. Based on the SCORE risk algorithm, the European Society of Cardiology guidelines for the prevention of CVD have been developed and endorsed by the Polish Cardiac Society and the Polish Society of Hypertension [8–11].

Since that time, the concept of global risk has been frequently used to develop preventive recommendations for multiple types of CVD.

It is known, however, that the use of an algorithm developed to estimate the risk in a given population may lead to risk overestimation or underestimation in other populations [12]. Thus, the SCORE risk algorithm that is currently used in guidelines targeted at the Polish population needs to be validated.

Based on the results of multicentre national study to evaluate the health status of the Polish population (*Wieloośrodkowe Ogólnopolskie Badanie Stanu Zdrowia Ludności* [WOBASZ]), the SCORE risk algorithm has been validated for the Polish population aged 35–64 years.

The aim of the present study was to develop a global CVD mortality risk model for the Polish population and to verify these data in the context of the SCORE risk algorithm.

METHODS

Patients

We analysed data obtained in two research projects, the WOBASZ study which was conducted in 2003–2005 and included 14,769 subjects aged 20–74 years, and the WOBASZ Senior study which was conducted in 2007 and included 1096 subjects above 74 years of age. Study goals, patient samples, and methods used in these two projects were reported previously [13]. In both studies, methods were similar and included evaluation of the prevalence and levels of selected CVD risk factors.

Table 1. Mean (± standard deviation [SD]) duration of the follow-up

Gender	WOBASZ		WOBASZ Senior	
	N	Mean ± SD	N	Mean ± SD
Men	6977	8.12 ± 1.54	555	4.69 ± 1.76
Women	7792	8.36 ± 1.05	541	5.06 ± 1.5

For the purpose of the present analysis, we selected 15 variables which are established CVD mortality risk factors.

To accomplish study goals, we conducted a prospective follow-up of participants of both studies. The follow-up of the WOBASZ study participants included two stages in 2007–2009 (the Polish Ministry of Health projects under the POLKARD programme) and 2012–2014 (a grant from the National Science Centre). In 2003–2008 (5-year follow-up), a total of 507 deaths were identified (including 352 among men and 155 among women), and when the follow-up was extended to 2012 (8-year follow-up), overall 1085 deaths were identified, including 385 deaths due to CVD (274 among men and 111 among women).

Previously, the WOBASZ Senior study participants have not been subjected to a prospective follow-up and the survival status in this cohort was established for the first time. In 2007–2012, 351 subjects died, including 101 men and 82 women due to CVD.

Determination of survival status and the cause of death

To determine survival status of the WOBASZ and WOBASZ Senior study participants, we used the Polish national personal identification number database (Universal Electronic System for Registration of the Population, *Powszechny Elektroniczny System Ewidencji Ludności* [PESEL]) run by the Ministry of the Interior. After obtaining information on patients' deaths with their dates, we used yearly mortality databases run by the Central Statistical Office (*Główny Urząd Statystyczny* [GUS]). Based on 4 identifying features including the address, gender, date of birth, and date of death, the cause of death was retrieved from the GUS database. If the cause of death could not be precisely ascertained (due to several records with the same 4 identifying features), death was classified as due to non-cardiac reasons.

Table 1 shows the mean duration of follow-up in the WOBASZ and WOBASZ Senior studies.

Statistical analysis

Statistical analysis included descriptive statistics for the basic sample estimators, levels of selected mortality risk factors, and determination of predictors of all-cause and CVD mortality. Hypotheses were verified using parametric (Student *t* test) and non-parametric (Wilcoxon test and χ^2 test) tests, depending on the distribution of the analysed variables.

In statistical analyses of CVD mortality, deaths due to non-CVD causes were treated as censored observations.

Survival was evaluated using Kaplan-Meier curves. Survival curves were compared using the log-rank test. Predictive value of selected risk factors was determine using uni- and multivariate Cox proportional hazard regression models [14]. Variables showing significance in a multivariate model were selected using the stepwise approach. Personal index (PI) values obtained for each patient in multivariate Cox model were correlated with SCORE risk values determined using the algorithm reported previously [7].

Evaluation of the concordance of global SCORE risk estimates in the Polish population

Based on published 10-year CVD mortality risk estimates using the SCORE risk algorithm [7, 12], an individual 10-year risk value was determined for each WOBASZ study participant aged 35–64 years. The SCORE risk algorithm was validated in the Polish population by comparing mortality rates in SCORE risk quartiles and mortality risk quartiles by the Cox approach. The sum of absolute differences between these mortality rates in all quartiles is the measure of disagreement [15].

All statistical analyses were performed separately for men and women.

Statistical conclusions were based on two-tailed test with the significance level set at alpha = 0.05. Statistical calculations were performed using the SAS package, version 9.2.

RESULTS

Baseline characteristics of the WOBASZ and WOBASZ Senior study participants were reported previously [16].

Tables 2 and 3 show basic parameters of the analysed risk factors for all-cause and CVD mortality.

Statistically significant differences in most established CVD risk factors were found between the genders in the Polish population aged 20–74 years. The mean levels of these risk factors were mostly higher in men, with the exception of abdominal obesity which was more common among women. Also the mean high density lipoprotein cholesterol (HDL-C) level was adversely lower in men compared to women.

Among the WOBASZ Senior study participants (above 74 years of age), major differences in the mean levels and rates of the analysed risk factors were also observed between the two genders but adversely higher mean values were noted in women.

Table 2. Description of the study material (mean ± standard deviation [SD], median, and interquartile range) — WOBASZ study

Risk factor	Men		Women		P
	Mean ± SD	Median (25%; 75%)	Mean ± SD	Median (25%; 75%)	
Age [years]	45.6 ± 15.2	46 (33;57)	45.2 ± 15.1	46 (32; 56)	0.0852[a]
Body mass index [kg/m^2]	26.6 ± 4.5	26.2 (23.5; 29.2)	26.1 ± 5.6	25.1 (21.9; 29.4)	< 0.0001[a]
Glucose [mmol/L]	5.12 ± 1.47	4.8 (4.4; 5.4)	4.88 ± 1.34	4.7 (4.3; 5.1)	< 0.0001[a]
Cholesterol [mmol/L]	5.38 ± 1.15	5.31 (4.57; 6.07)	5.37 ± 1.19	5.27 (4.54; 6.08)	0.2422[a]
HDL-C [mmol/L]	1.36 ± 0.41	1.30 (1.08; 1.55)	1.54 ± 0.38	1.51 (1.28; 1.77)	< 0.0001[a]
LDL-C [mmol/L]	3.35 ± 1.05	3.25 (2.62; 4.02)	3.31 ± 1.06	3.23 (2.54; 3.92)	0.1208[a]
Triglycerides [mmol/L]	1.68 ± 1.50	1.31 (0.93; 1.93)	1.32 ± 0.95	1.10 (0.81; 1.57)	< 0.0001[a]
Total cholesterol/HDL-C ratio	3.36 ± 1.54	3.1 (2.2; 4.2)	2.72 ± 1.35	2.4 (1.8; 3.4)	< 0.0001[a]
Diastolic BP [mm Hg]	83.7 ± 11.8	82.5 (75.5; 90)	81.4 ± 11.8	80 (73; 88)	< 0.0001[a]
Systolic BP [mm Hg]	137.3 ± 18.9	134.5 (125; 146)	129.9 ± 21.8	125 (115; 139)	< 0.0001[a]
Smokers [%]	42.2		27.2		< 0.0001[c]
Abdominal obesity [%][1]	24.9		38.4		< 0.0001[c]
Diabetes [%][2]	7.2		6.1		0.0049[c]
Hypertension [%][3]	40.1		32.1		< 0.0001[c]

[a]Wilcoxon test; [c]Chi-square test; [1]Waist circumference: men ≥ 102 cm, women ≥ 88 cm; [2]Glucose level ≥ 7.0 mmol/L and/or use of glucose-lowering drugs; [3]Systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg and/or use of antihypertensive drugs; BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

Table 3. Description of the study material (mean ± standard deviation [SD], median, and interquartile range) — WOBASZ Senior study

Risk factor	Men		Women		P
	Mean ± SD	Median (25%; 75%)	Mean ± SD	Median (25%; 75%)	
Age [years]	79.0 ± 3.9	78 (76; 81)	79.2 ± 3.4	79 (77; 81)	0.0269[a]
Body mass index [kg/m^2]	27.1 ± 4.2	26.6 (24.3; 29.10)	28.8 ± 5.9	28.0 (24.6; 32.4)	< 0.0001[a]
Glucose [mmol/L]	5.56 ± 2.08	5.0 (4.6; 5.7)	5.71 ± 2.11	5.10 (4.7; 5.8)	0.2695[a]
Cholesterol [mmol/L]	4.95 ± 1.02	4.89 (4.31; 5.60)	5.40 ± 1.13	5.44 (4.64; 6.20)	< 0.0001[b]
HDL-C [mmol/L]	1.31 ± 0.37	1.27 (1.06; 1.51)	1.39 ± 0.38	1.34 (1.10; 1.63)	0.0006[a]
Creatinine [μmol/L]	88.4 ± 27.9	82 (72; 96)	75.4 ± 40.6	68 (59; 83)	< 0.0001[a]
LDL-C [mmol/L]	3.23 ± 0.96	3.23 (2.60; 3.76)	3.50 ± 1.06	3.47 (2.79; 4.22)	< 0.0001[b]
Triglycerides [mmol/L]	1.17 ± 0.59	1.04 (0.78; 1.37)	1.48 ± 0.74	1.31 (1.00; 1.72)	< 0.0001[a]
Total cholesterol/HDL-C ratio	3.02 ± 1.33	2.78 (2.16; 3.63)	3.12 ± 1.31	2.87 (2.28; 3.66)	0.2317[a]
Diastolic BP [mm Hg]	83.7 ± 11.4	83.0 (75.5; 90.5)	86.7 ± 12.9	87.0 (79; 94.5)	< 0.0001[b]
Systolic BP [mm Hg]	151.2 ± 23.2	147.5 (133.5; 166.5)	155.0 ± 24.5	153 (137; 170)	0.0086[a]
Smokers [%]	14.2		3.3		< 0.0001[c]
Abdominal obesity [%][1]	38.1		72.3		< 0.0001[c]
Diabetes [%][2]	16.9		18.8		0.4077[c]
Hypertension [%][3]	74.9		86.6		< 0.0001[c]

[a]Wilcoxon test; [b]Student *t* test; [c]Chi-square test; [1]Waist circumference: men ≥ 102 cm, women ≥ 88 cm; [2]Glucose level ≥ 7.0 mmol/L and/or use of glucose-lowering drugs; [3]Systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg and/or use of antihypertensive drugs; BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

Tables 4 and 5 show the number of deaths overall and due to CVD during the 8-year follow-up of the WOBASZ study participants and 5-year follow-up of the WOBASZ Senior study participants.

During the 8-year follow-up of the younger population, mortality due to CVD was 38% among men and 31% among women. The most common causes of CVD mortality were IHD (33%) followed by cerebrovascular disease (17%) in

Table 4. Number of deaths among WOBASZ study participants

Years of follow-up	Men		Women	
	Deaths overall	Deaths due to CVD	Deaths overall	Deaths due to CVD
Within one year	68	33	20	7
I year	80	28	37	15
II year	82	36	36	12
III year	77	26	33	9
IV year	87	21	48	13
V year	86	28	47	11
VI year	84	36	61	20
VII year	96	42	50	13
VIII year	67	24	26	11
Overall	727	274	358	111

CVD — cardiovascular disease

Table 5. Number of deaths among WOBASZ Senior study participants

Years of follow-up	Men		Women	
	Deaths overall	Deaths due to CVD	Deaths overall	Deaths due to CVD
Within one year	42	23	22	11
I year	33	18	24	13
II year	41	17	23	12
III year	29	11	33	18
IV year	33	18	21	15
V year	31	14	19	13
Overall	209	101	142	82

CVD — cardiovascular disease

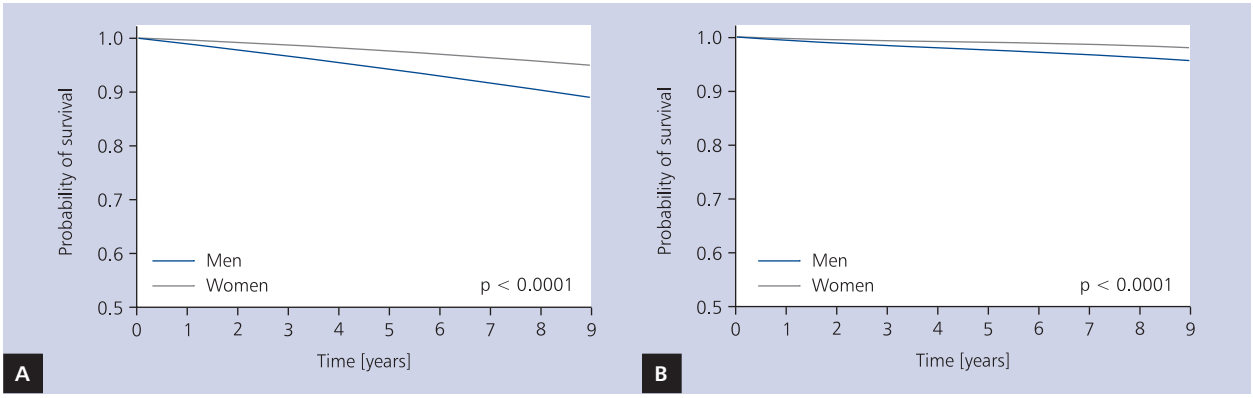

Figure 1. Kaplan-Meier 8-year survival curves for the Polish population aged 20–74 years estimated for WOBASZ study participants; **A**. Total mortality; **B**. Cardiovascular disease mortality

men, and cerebrovascular disease (31%) followed by IHD (23%) in women.

During the 5-year follow-up of the older population, mortality due to CVD was 48% among men and 58% among women. The most common cause of CVD mortality in both men and women was IHD (29% and 24%, respectively), followed by cerebrovascular disease (16% and 21%, respectively).

Figure 1 shows survival curves for overall mortality during 8 years of follow-up, and survival curves for CVD mortality.

Table 6. Uni- and multivariate Cox analysis findings in the WOBASZ study — relative risk (95% confidence interval) for overall mortality

Risk factor	Men		Women	
	Univariate model	Multivariate model	Univariate model	Multivariate model
Age	1.086 (1.079–1.093)	1.092 (1.084–1.100)	1.097 (1.087–1.108)	1.103 (1.091–1.115)
Body mass index	1.032 (1.017–1.048)	–	1.068 (1.051–1.085)	–
Glucose	1.167 (1.136–1.200)	1.079 (1.038–1.121)	1.212 (1.174–1.252)	–
Total cholesterol	1.190 (1.121–1.263)	–	1.239 (1.150–1.336)	–
HDL-C	1.137 (0.956–1.352)	–	0.699 (0.523–0.934)	–
LDL-C	1.005 (1.003–1.007)	–	1.006 (1.004–1.008)	–
Triglycerides	1.000 (1.000–1.001)	–	1.001 (1.001–1.002)	–
Total cholesterol/HDL-C ratio	1.076 (0.982–1.179)	–	1.180 (1.080–1.289)	–
Diastolic BP	1.024 (1.018–1.030)	–	1.034 (1.027–1.042)	–
Systolic BP	1.021 (1.018–1.024)	1.008 (1.001–1.014)	1.025 (1.021–1.029)	–
Smoking status	1.114 (1.062–1.290)	1.791 (1.531–2.096)	0.958 (0.757–1.213)	2.278 (1.742–2.980)
Abdominal obesity	1.980 (1.705–2.300)	–	2.415 (1.952–2.986)	–
Diabetes	2.608 (2.138–3.181)	–	4.782 (3.729–6.132)	2.018 (1.547–2.632)
Hypertension	2.362 (2.036–2.740)	–	4.045 (3.253–5.029)	–

BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

We found significant differences between men and women in regard to survival curves for both overall mortality and CVD mortality ($p < 0.0001$).

Predictive value of the analysed risk factors for overall mortality in uni- and multivariate models is shown in Table 6.

For overall mortality among men and women, nearly all selected risk factors were shown to be significant in univariate analyses, except for HDL-C level and the total cholesterol/HDL-C ratio in men, and smoking status in women.

In multivariate analysis, independent predictors in men included age, glucose level, systolic BP, and smoking status. In women, independent predictors were age, smoking status, and diabetes.

Predictive value of the analysed risk factors for CVD mortality is shown in Table 7.

For CVD mortality among men and women, nearly all selected risk factors were shown to be significant in univariate analyses, except for HDL-C, triglycerides, and the total cholesterol/HDL-C ratio in men, and triglycerides and smoking status in women.

In multivariate analysis, independent predictors in men included age, glucose level, smoking status, and hypertension. In women, independent predictors were age, systolic BP, and diabetes.

Survival curves in the WOBASZ Senior study are shown in Figure 2.

We found significant differences between men and women in regard to survival curves for overall mortality ($p < 0.0001$) but not for CVD mortality ($p = 0.0755$).

Due to the fact that survival curves for CVD mortality did not differ between men and women, we estimated the cut-off age for no survival difference in the WOBASZ study. By selecting the oldest patients and adding them to the WOBASZ Senior cohort, we obtained the cut-off age of 70 years above which the survival curves were not significantly different between men and women (Fig. 3).

Predictive value of the analysed risk factors for overall mortality in uni- and multivariate models for the WOBASZ Senior study participants is shown in Table 8.

In univariate analyses, independent predictors in men were age and creatinine level. These factors remained significant in multivariate analysis. In women above 74 years of age, independent predictors in univariate analyses included age, HDL-C level, creatinine level, total cholesterol/HDL-C ratio, and smoking status. Age, HDL-C level, and smoking status remained independent predictors of overall mortality in multivariate analysis.

Predictive value of the analysed risk factors for CVD mortality is shown in Table 9.

For CVD mortality, significant predictors were the same as for overall mortality. In women, significant predictors in uni- and multivariate analyses were age and smoking status.

In the next step, we estimated the goodness of fit of the SCORE risk model to the Polish population aged 35–64 years. Table 10 shows the findings of the multivariate Cox analysis of the factors included in the SCORE risk model. In the Polish population, we found no statistical significance of total cholesterol level in the Cox model that included the

Table 7. Uni- and multivariate Cox analysis findings in the WOBASZ study — relative risk (95% confidence interval) for cardiovascular mortality

Risk factor	Men		Women	
	Univariate model	Multivariate model	Univariate model	Multivariate model
Age	1.094 (1.083–1.106)	1.090 (1.077–1.104)	1.129 (1.106–1.152)	1.107 (1.082–1.133)
Body mass index	1.043 (1.018–1.069)	–	1.075 (1.045–1.105)	–
Glucose	1.172 (1.121–1.225)	1.081 (1.014–1.151)	1.248 (1.187–1.312)	–
Total cholesterol	1.270 (1.156–1.396)	–	1.256 (1.100–1.435)	–
HDL-C	1.124 (0.845–1.494)		0.442 (0.256–0.765)	–
LDL-C	1.007 (1.004–1.010)	–	1.007 (1.003–1.011)	–
Triglycerides	1.000 (0.999–1.001)	–	1.002 (0.998–1.002)	–
Total cholesterol/HDL-C ratio	0.975 (0.834–1.140)	–	1.234 (1.096–1.390)	–
Diastolic BP	1.029 (1.019–1.038)	–	1.044 (1.031–1.058)	–
Systolic BP	1.024 (1.019–1.029)	–	1.033 (1.027–1.039)	1.011 (1.003–1.020)
Smoking status	1.477 (1.244–1.768)	1.647 (1.270–2.137)	0.516 (0.312–1.855)	–
Abdominal obesity	2.217 (1.741–2.824)	–	3.244 (2.184–4.818)	–
Diabetes	2.916 (2.136–3.982)	–	7.017 (4.671–10.543)	2.538 (1.636–3.938)
Hypertension	3.200 (2.487–4.119)	1.598 (1.215–2.100)	5.533 (3.649–8.389)	–

BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

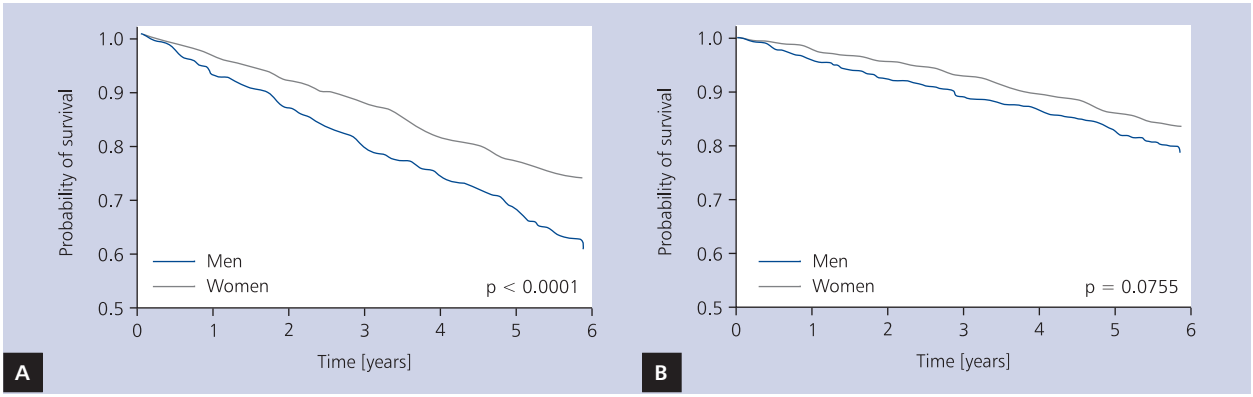

Figure 2. Kaplan-Meier 5-year survival curves for the Polish population aged 75 years and above estimated based on data from the WOBASZ Senior study; **A**. Total mortality; **B**. Cardiovascular disease mortality

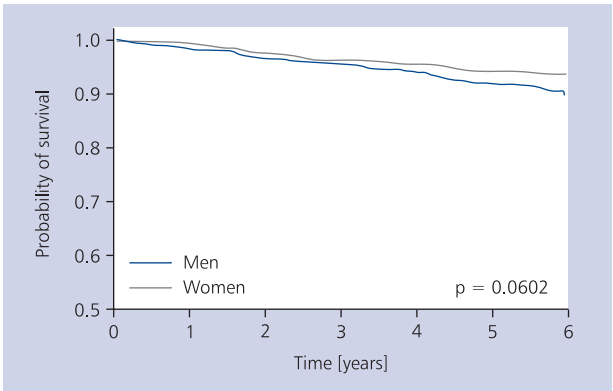

Figure 3. Kaplan-Meier survival curves for men and women aged 70 years and above

four variables included in the SCORE risk model. In women, smoking status was also not significant.

Tables 11 and 12 show CVD mortality rates in the SCORE risk model and the Cox model quartiles along with discrepancies between these rates.

DISCUSSION

Confirmation of the fact that modifiable risk factors (elevated cholesterol, body mass index, and BP, cigarette smoking, and others) affect CVD morbidity and mortality justifies preventive efforts. The degree of an event risk is measured by individual patient status that encompasses a range of personal characteristics. These characteristics, analysed using statistical methods and used to model the studied phenomenon, allow

Table 8. Uni- and multivariate Cox analysis findings in the WOBASZ Senior study — relative risk (95% confidence interval) for overall mortality

Risk factor	Men		Women	
	Univariate model	Multivariate model	Univariate model	Multivariate model
Age	1.099 (1.069–1.131)	1.096 (1.063–1.130)	1.131 (1.086–1.177)	1.128 (1.072–1.187)
Body mass index	1.002 (0.968–1.036)	–	0.997 (0.968–1.027)	–
Glucose	1.016 (0.950–1.087)	–	1.034 (0.958–1.116)	–
Total cholesterol	1.080 (0.934–1.239)	–	0.885 (0.752–1.041)	–
HDL-C	1.015 (0.672–1.534)	–	0.435 (0.258–0.731)	0.579 (0.337–0.993)
Creatinine	1.012 (1.007–1.016)	1.011 (1.006–1.016)	1.007 (1.004–1.010)	1.007 (1.004–1.010)
LDL-C	1.048 (0.897–1.225)	–	0.872 (0.732–1.038)	–
Triglycerides	1.001 (0.998–1.003)	–	0.999 (0.997–1.005)	–
Total cholesterol/HDL-C ratio	1.081 (0.965–1.210)	–	1.155 (1.013–1.317)	–
Diastolic BP	0.991 (0.979–1.003)	–	0.994 (0.981–1.008)	–
Systolic BP	1.001 (0.995–1.007)	–	1.000 (0.993–1.007)	–
Smoking status	1.167 (0.805–1.693)	–	2.094 (1.026–4.275)	3.582 (1.640–7.826)
Abdominal obesity	1.200 (0.911–1.581)	–	1.014 (0.695–1.479)	–
Diabetes	1.301 (0.930–1.819)	–	1.022 (0.672–1.555)	–
Hypertension	1.044 (0.760–1.435)	–	1.074 (0.655–1.761)	–

BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

Table 9. Uni- and multivariate Cox analysis findings in the WOBASZ Senior study — relative risk (95% confidence interval) for cardiovascular mortality

Risk factor	Men		Women	
	Univariate model	Multivariate model	Univariate model	Multivariate model
Age	1.146 (1.106–1.187)	1.143 (1.101–1.187)	1.116 (1.056–1.179)	1.120 (1.046–1.199)
Body mass index	1.018 (0.970–1.068)	–	1.000 (0.962–1.040)	–
Glucose	1.052 (0.976–1.133)	–	1.038 (0.940–1.147)	–
Total cholesterol	1.089 (0.889–1.334)	–	0.945 (0.765–1.169)	–
HDL-C	0.795 (0.436–1.449)	–	0.555 (0.287–1.072)	–
Creatinine	1.013 (1.007–1.019)	1.010 (1.004–1.017)	1.004 (0.997–1.010)	–
LDL-C	1.073 (0.863–1.333)	–	0.915 (0.728–1.148)	–
Triglycerides	1.002 (0.999–1.006)	–	0.999 (0.996–1.006)	–
Total cholesterol/HDL-C ratio	1.148 (0.989–1.333)	–	1.115 (0.935–1.329)	–
Diastolic BP	0.981 (0.963–1.000)	–	0.998 (0.980–1.016)	–
Systolic BP	1.001 (0.993–1.010)	–	1.001 (0.992–1.010)	–
Smoking status	0.760 (0.406–1.421)	–	1.809 (1.662–4.943)	3.291 (1.182–9.159)
Abdominal obesity	1.363 (0.919–2.021)	–	1.094 (0.658–1.819)	–
Diabetes	1.565 (0.990–2.475)	–	1.053 (0.610–1.818)	–
Hypertension	1.179 (0.735–1.892)	–	1.114 (0.575–2.160)	–

BP — blood pressure; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol

determination of the overall risk which is a measure of the likelihood of disease occurrence, presence, or severity, or the occurrence of death. Determination of the overall patient risk, also known as global risk, should be a responsibility of a physician. In the Framingham study, the algorithm to estimate the likelihood of CVD symptom occurrence within a specified period of time (from 4 to 12 years) was based on systolic BP, total cholesterol and HDL-C level, electrocardiographic evidence of left ventricular hypertrophy, age, and the presence of diabetes [17].

Table 10. Relative risk and 95% confidence interval values for global SCORE risk components in the Polish population aged 35–64 years

Risk factor	Men	Women
Age	1.082 (1.056–1.109)	1.062 (1.010–1.118)
Cholesterol	1.146 (0.988–1.328)	0.991 (0.750–1.310)
Systolic blood pressure	1.012 (1.004–1.020)	1.024 (1.010–1.037)
Smoking status	1.675 (1.192–2.353)	1.087 (0.515–2.294)

Table 11. Cardiovascular mortality rates in risk quartiles by SCORE and Cox model in men aged 35–64 years in the WOBASZ study; ∑ difference = 5.7%

Algorithm	1st quartile	2nd quartile	3rd quartile	4th quartile
SCORE	1.4%	1.3%	4.0%	13.9%
Cox	0%	1.6%	2.8%	11.1%
Difference	1.4%	0.3%	1.2%	2.8%

Table 12. Cardiovascular mortality rates in risk quartiles by SCORE and Cox model in women aged 35–64 years in the WOBASZ study; ∑ difference = 2.0%

Algorithm	1st quartile	2nd quartile	3rd quartile	4th quartile
SCORE	0.3%	0.5%	1.0%	5.4%
Cox	0%	0.4%	0.6%	4.2%
Difference	0.3%	0.1%	0.4%	1.2%

In the PROCAM study, the algorithm to determine 8-year probability of myocardial infarction or sudden death due to CVD was based on such risk factors as age, systolic BP, HDL-C and low density lipoprotein cholesterol level, triglycerides, smoking, the presence of diabetes and angina pectoris, and a positive family history of myocardial infarction [17].

The 10-year CVD mortality risk estimated using the SCORE risk algorithm is based on four risk factors including age, total cholesterol, systolic BP, and smoking status, with separate estimations for men and women. Patients with diabetes or glucose level ≥ 7 mmol/L, and those with a history of myocardial infarction or coronary artery disease are considered high risk.

In contrast to the above algorithms, the global CVD mortality risk model for the Polish population aged 20–74 years did not include lipid levels including HDL-C, total cholesterol, and triglycerides. The WOBASZ study population was characterised by high HDL-C levels (mean levels 1.36 mmol/L and 1.54 mmol/L, respectively, in men and women) with distribution close to a uniform one (low standard deviation values). For this reason, HDL-C level did not reach significance in the multivariate model. A similar scenario was noted for total cholesterol level, with the coefficient of variation up to 21%. A strong correlation between triglyceride levels and age is observed in the Polish population. When age was introduced into the model as the strongest non-modifiable risk factors, triglyceride level was excluded.

Our observations confirm a significant association between systolic BP and CVD mortality, similarly to the mentioned global risk models.

Prospective studies confirmed clinical observations of an increased CVD incidence associated with the presence of diabetes. In the Framingham study, diabetes was associated with a 2-fold increase in CVD mortality [17].

The SCORE risk algorithm to estimate a 10-year risk of a cardiac event in men and women aged 35–64 years has been based on multinational, multicentre prospective studies. To develop a model of a 10-year CVD mortality risk, data from 12 European cohort studies were used, performed in Finland, Russia, Norway, United Kingdom (two cohorts), Denmark, Sweden, Belgium, Germany, Italy, France, and Spain. The analysis included 88,080 women and 117,098 men aged 45–64 years. During the follow-up, 7934 CVD deaths occurred, including 5652 deaths due to IHD. The cohorts were divided into two groups corresponding to low- and high-risk countries, with a SCORE risk algorithm developed separately for each of these groups [7]. Data from the Polish population were not included, and thus SCORE risk model parameters do not take into account the characteristics of the Polish population. The algorithm used in the WOBASZ study was based on the SCORE risk algorithm for high-risk countries.

Use of a multivariate Cox proportional hazard model based on risk factors included in the SCORE risk algorithm showed that in the Polish population, only three of them in men (age, smoking, and elevated systolic BP) and two in women (age and elevated systolic BP) were predictors of fatal CVD events. In contrast, elevated total cholesterol level was not a significant risk factor in this population. The latter observation is apparently at variance with the widely accepted notion of a significant association between total cholesterol level and CVD mortality. In the recent study by Bandosz et al. [18], a reduction in cholesterol level was shown to be responsible for 39% of the IHD mortality reduction observed in Poland in 1991–2005. To explain these discrepant conclusions, it should be noted that in analyses from the WOBASZ study, cholesterol level was a significant predictor of CVD mortality but only in an univariate analysis. A positive association between age and cholesterol level is known. In multivariate analyses that include both these variables, only one of them, i.e. age, remained significant due to the strength of this correlation. Data used for the analyses reported in the IMPACT study [18] characterised the general Polish population aged 20–74 years in terms of the mean values of continuous variables, such as cholesterol level, and event rates, such as smoking, hypertension, and others (not individual patient-level data). At each time point in 1991–2005, the age range in the study population was the same and thus the effect of total cholesterol level was independent from the patient's age, consistent with a univariate effect.

After a Cox proportional hazard model based on the same set of variables was applied to the collected data, specific risk values were determined for the Polish population. Goodness of fit of both models, i.e. SCORE and Cox, to the observed CVD deaths was evaluated based on mortality rates in risk quartiles.

Due to the fact that mortality risk was estimated using the maximum likelihood ratio method, the best (model) fit of the observed mortality rates was obtained in the Cox model risk quartiles. The difference between mortality rates in risk quartiles by the SCORE risk algorithm and the Cox model describes risk over- or underestimation in a specific SCORE risk quartile compared to the Cox model risk quartile. In both Tables presented, mortality rates in SCORE risk quartiles were overestimated compared to Cox model risk quartiles. The sum of absolute differences between these CVD mortality rates in all quartiles is the measure of disagreement of the SCORE risk algorithm in the Polish population versus the risk estimated using a Cox model. Overall disagreement was 5.7% in men and 2% in women. We believe these values are not high, if compared to previous Warsaw Pol-MONICA studies [15].

CONCLUSIONS

1. Long-term follow-up of WOBASZ and WOBASZ Senior study participants allowed assessment of the independent association of the evaluated cardiovascular risk factors with CVD mortality in the Polish population.
2. Validation of the SCORE risk algorithm to estimate individual global CVD risk in the Polish population showed a high predictive value of this algorithm.

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Ryzyko globalne zgonu z powodu chorób sercowo-naczyniowych dorosłej populacji polskiej: ocena prospektywna kohort zbadanych w wieloośrodkowych ogólnopolskich badaniach stanu zdrowia ludności — WOBASZ i WOBASZ Senior

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Streszczenie

Wstęp i cel: Celem pracy było znalezienie dla populacji polskiej modelu ryzyka globalnego zgonu sercowo-naczyniowego i zweryfikowanie uzyskanych danych w kontekście ryzyka ocenianego wg algorytmu SCORE.

Metody: Materiał empiryczny stanowiły dane uzyskane z **W**ieloośrodkowych **O**gólnopolskich **Ba**dań **S**tanu **Z**drowia — WOBASZ i WOBASZ Senior. W latach 2003–2005 zbadano 14769 osób w wieku 20–74 lat w ramach badania WOBASZ, a w 2007 r. zbadano 1096 osób w wieku powyżej 74 lat w ramach badania WOBASZ Senior. Do 2012 r. zbierano informacje na temat wszystkich tych osób dotyczące wystąpienia zgonu oraz określono przyczynę zgonu. Średni okres obserwacji dla pacjentów z badania WOBASZ wynosił 8,2 roku, a dla pacjentów z badania WOBASZ Senior — około 5 lat. Ogółem zmarło 1436 osób, zgonów kardiologicznych było 568. Do analiz statystycznych umieralności ogółem i spowodowanej chorobami układu sercowo-naczyniowego (CVD) wybrano 15 uznawanych czynników ryzyka. Analizę przeżywalności wykonano oddzielnie dla respondentów badań WOBASZ i WOBASZ Senior. Zastosowano metody statystyki opisowej, krzywe Kaplana-Meiera, model hazardów proporcjonalnych Coxa i algorytmu ryzyka incydentu sercowo-naczyniowego SCORE. Miarę niezgodności modelu SCORE do polskiej populacji określono jako różnicę między częstościami zgonów w kwartylach ryzyka wg skal SCORE i Coxa.

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Wyniki: W okresie 8 lat umieralność z powodu CVD stanowiła w „młodszej" (WOBASZ) populacji 38% wśród mężczyzn i 31% wśród kobiet ogółu zmarłych. Najczęstszymi przyczynami zgonu kardiologicznego u mężczyzn były: choroba niedokrwienna serca (33%) i choroby naczyń mózgu (17%), a u kobiet — choroby naczyń mózgu (31%) i choroba niedokrwienna serca (23%). Stwierdzono istotne statystycznie zróżnicowanie krzywych przeżycia między mężczyznami i kobietami zarówno dotyczących umieralności ogólnej ($p < 0,0001$), jak i umieralności z powodu CVD ($p < 0,0001$). Dla umieralności ogółem wśród mężczyzn i kobiet prawie wszystkie wybrane czynniki okazały się istotne statystycznie w analizach jednoczynnikowych, z wyjątkiem stężenia cholesterolu o wysokiej gęstości (HDL) i wskaźnika aterogenności u mężczyzn oraz statusu palenia tytoniu u kobiet. Jako niezależne w analizie wieloczynnikowej dla mężczyzn okazały się: wiek, stężenie glukozy, wartość ciśnienia tętniczego skurczowego i status palenia tytoniu, natomiast u kobiet niezależnymi predykatorami były: wiek, status palenia tytoniu i cukrzyca. W okresie 5 lat umieralność z powodu CVD stanowiła w „starszej" (WOBASZ Senior) populacji 48% wśród mężczyzn i 58% wśród kobiet ogółu zmarłych. Najczęstszymi przyczynami zgonu kardiologicznego zarówno u mężczyzn, jak i u kobiet była choroba niedokrwienna serca, odpowiednio 29% i 24%, a następnie choroby naczyń mózgu, odpowiednio 16% i 21%. Wśród starszych pacjentów stwierdzono istotne statystycznie zróżnicowanie krzywych przeżycia dla umieralności ogółem między mężczyznami i kobietami ($p < 0,0001$), natomiast nie zanotowano statystycznego zróżnicowania umieralności spowodowanej CVD ($p = 0,0755$). W związku z faktem braku zróżnicowania krzywych przeżycia dla mężczyzn i kobiet dla umieralności z powodu CVD, wykonano estymację punktu odcięcia dla wieku w badaniu WOBASZ, przy którym rozpoczyna się brak zróżnicowania przeżywalności; wynosi on 70 lat. Począwszy od tego wieku przeżywalność z powodu CVD mężczyzn i kobiet nie różnią się istotnie. Dla umieralności ogółem wśród mężczyzn istotnymi statystycznie w analizach jednoczynnikowych okazały się: wiek i stężenie kreatyniny. Czynniki te pozostały istotne także w analizie wieloczynnikowej. Wśród kobiet w wieku powyżej 74 lat istotnymi czynnikami okazały się, pojedynczo, wiek, stężenie cholesterolu HDL, kreatyniny, wskaźnik aterogenności i palenie tytoniu. W modelu wieloczynnikowym natomiast niezależnymi predykatorami umieralności ogólnej pozostały: wiek, stężenie cholesterolu HDL, kreatyniny i palenie tytoniu. Dla umieralności spowodowanej CVD istotnymi czynnikami ryzyka okazały się te same zmienne co w przypadku umieralności ogółem. Wśród kobiet w analizach jednoczynnikowych i w analizie wieloczynnikowej istotnymi predykatorami były wiek i palenie tytoniu. Uzyskano 5,7% niezgodności częstości zgonów między ryzykiem SCORE i ryzykiem Coxa u mężczyzn i 2% u kobiet.

Wnioski: 1. Wdrożenie programu obserwacji odległej osób zbadanych w programach WOBASZ i WOBASZ Senior, które były badaniami o zasięgu ogólnopolskim, stworzyło możliwość prześledzenia niezależnego związku analizowanych czynników ryzyka sercowo-naczyniowego z wystąpieniem zgonu z powodu CVD w populacji polskiej. 2. Weryfikacja algorytmu SCORE do oceny indywidualnego globalnego ryzyka CVD w populacji polskiej pokazała dużą wartość predykcyjną tego narzędzia.

Słowa kluczowe: WOBASZ, WOBASZ Senior, choroby układu sercowo-naczyniowego, ryzyko globalne, SCORE

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