Chapter

Sex Differences in Long-Term Trends of Psychosocial Factors and Gender Effect on Risk of Cardiovascular Diseases: Arterial Hypertension, Myocardial Infarction and Stroke

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Abstract

Introduction: The study aimed to determine gender differences in the prevalence and dynamics of affective states over a long period, i.e., 23 years, and to establish their effect on the risk of cardiovascular diseases (CVD), i.e., arterial hypertension (AH), myocardial infarction (MI), and stroke among the population aged 25–64 in Russia / Siberia. Methods: Between 1994 and 2017, we conducted 4 screening surveys of representative samples (totalling 4,815 people) under the international programs MONICA and HAPIEE in Russia / Siberia. To determine the sex differences in cardiovascular risk from 1994 to 2010, we observed cohorts formed from the screened individuals without CVD and diabetes mellitus (DM). Results: High levels of affective states in the period from 1994 to 2003, especially in women, were replaced by a downward trend in 2013. At the same time, there was a reduction in the gender gap in terms of frequency of depression lower 1%, and men in the younger age groups reported higher levels of personal anxiety (49.3% vs 46.1% in adults aged 35-44y) and vital exhaustion (16.9% vs 15.6%) than women in 2017. We found that men with unfavourable levels of affective states have a 3–5 fold higher risk of hypertension and stroke, while women have a higher risk of myocardial infarction (p for all < 0.05). Hostility in men is associated with a negative risk of myocardial infarction and stroke (HR=0.3 and HR=0.29, respectively; p for all < 0.05). However, this was levelled out by unfavourable social characteristics. Conclusions: The downward trends in prevalence of psychosocial factors were unstable and associated with reduced gender gap for affective states. It had a significant impact on the gender magnitude of cardiovascular risk.

Keywords: anxiety, depression, vital exhaustion, hostility, social support, population, risk, sex differences, arterial hypertension, myocardial infarction, stroke, marital status, education, occupational status

1. Introduction

The widespread and widely discussed opinion in the mass media that the number of people with anxiety, depression and other affective states is increasing year to year implies a relative increase in these disorders over the past decades. Nevertheless, the study of literary sources has provided multifaceted estimates of the prevalence of psychosocial factors (PSF). Due to the different recording methods in epidemiological studies, the heterogeneity of the data is too high to make a proper comparison. According to the available epidemiological findings, one-third of the population of the United States and European countries is susceptible to anxiety disorders [1]. At the same time, the prevalence of psychosocial factors depending on sex is also different. Negative psychological characteristics (e.g., anxiety and depression) are twice as common in women and often have a more severe form and an earlier onset [2].

The impact of PSF on health is unequal in terms of gender. For example, depressive disorders are on the list of the leading widespread diseases in the world among women, but not men, according to Global Burden Diseases (2002) [3]. And this may be an echo of other common negative psychosocial factors, such as high anxiety, vital exhaustion, and stress in the family and workplace. A number of these states are inextricably linked to the XX or XY genotype or are due to sex differences in functioning (i.e., susceptibility to diseases). For other psychological factors, there is a clear link to work and social environment, which differs for both sexes [4, 5].

Cardiovascular effects of stress and other psychological factors may also differ in women and men [6]. Large-scale studies show that particular psychosocial characteristics, such as stress or depression, are associated with cardiovascular health to the same degree in men and women, while others, i.e., vital exhaustion, anxiety signs and low life satisfaction, are associated with heart disease rates in women but not in men.

Analysis of recent studies and meta-analyses [7] indicates that social gradient, as a mediator, as well as the sex differences, boost the effect of psychosocial characteristics on cardiovascular health,.

Different levels of PSF are not always adverse, but can also serve as protective factors concerning physical and mental health. Thus, a favourable profile of social contacts with relatives or friends is associated with favourable indicators of mental health and serves as a barrier to depression and perceived stress. In addition, the social support received from friends is positively correlated with the lifestyle, in particular, with intensive physical activities [8]. The accumulation of data on the influence of psychosocial factors on the risk of cardiovascular events is a prerequisite for the creation of authoritative working groups and the development of international regulations and recommendations [9]. Yet the question of the impact of gender differences remains unresolved.

In Russia, such studies are rare, but the differences in the studied population and the tools used do not allow us to give comparative estimates in the dynamics of the prevalence of PSF. Moreover, there are no available cohort studies at all.

Our study identified gender differences in the prevalence and dynamics of affective states over a long period, i.e., 23 years, and determined their impact on the risk of developing CVD (such as arterial hypertension, myocardial infarction, stroke) among the population aged 25–64.

2. Methods

This study is based on the survey of the male and female population living in one of the districts of Novosibirsk (Russia). The research was carried out within the framework of screenings conducted in 1994–1995, 2003–2005, 2013–2016, and 2016–2017.

In 1994–1995, the third screening under the WHO program Multinational Monitoring of Trends and Determinants of Cardiovascular Disease – Optional Psychosocial Sybstudy (MONICA-MOPSY) examined individuals aged 25–64 (n = 1527, 43% men, mean age – 44.85 ± 0.4 years, response rate – 77.3%) [10].

Another international project HAPIEE (Health, Alcohol and Psychosocial Factors in Eastern Europe) in 2003–2005 examined 45–64-year-old individuals (n = 1650, 34.9% of men, mean age – 54.25 ± 0.2 year, response rate – 66.5%) [11].

In 2013–2016, a survey of a random representative sample aged 25–44 was conducted as part of screening studies under the budgeting scheme of The Institute of Internal and Preventive Medicine, state reg. no. 01201282292 (n = 975, 43.8% men, mean age 34.5 ± 0.4 years, response rate – 71.5%).

In 2016–2017, the International PCDR project (The International Project on Cardiovascular Disease in Russia) examined 35–64-year-old individuals (n = 663, 41.3% men, mean age – 51.95 ± 0.32 years, response rate – 73.6%). The study surveyed the residents of the same district of Novosibirsk as in the previous years.

All samples were formed based on electoral rolls using a random number table. We used a random mechanical selection method. The general examination was conducted according to the standard methods accepted in epidemiology and included in the program. The methods were strictly standardised and conformed to the requirements of the MONICA project protocol. The material was validated and processed under the WHO program MONICA-psychosocial in the Information Collection Center of the MEDIS Institute in Munich, Germany (Institut für Medizinische Informatik und Systemforschung). Quality control was carried out in MONICA quality control centres: Dundee (Scotland), Prague (Czech Republic), Budapest (Hungary). The results presented were considered satisfactory.

2.1 Psychosocial testing

Anxiety traits levels were assessed using the Spielberger test (Anxiety subscale, as a personality trait). Interpretation of the data was based on the following criteria: the assessment of a trait of anxiety less than 30 corresponded to low anxiety (LAL); the score from 31 to 44 was a sign of moderate anxiety (MAL); and a score of more than 45 indicated high anxiety level (HAL).

A depression scale blank, i.e., the MOPSY test (Depression Scale, MMPI Adopted by MONICA protocol), consisting of 15 questions, was used to assess depression. For each question, there are two answers: "I agree" and "I disagree". The severity of depression was evaluated as no depression (ND), moderate (MD), or major (major D).

The vital exhaustion level was studied using the MOPSY questionnaire (Maastricht Vital Exhaustion Questionnaire). The test consisted of 14 statements. To respond to each statement, there are 3 answers: "yes", "no", "I don't know". The level of vital exhaustion was estimated as no vital exhaustion (NVE), moderate vital exhaustion (MVE), or high vital exhaustion (HVE).

Hostility (Hostility Scale, Cook-Medley test). The test consisted of 20 statements. 2 answers, "agree" and "disagree", were provided to respond to each statement. Hostility expression was assessed as low, moderate, or high.

Social support (Berkman-Syme test) [12]. A 17-point index of close contacts (ICC) was determined. It was evaluated as low, moderate, or high. Social Network Index (SNI), consisting of 9 points, was assessed as low, moderate-1, moderate-2, or high.

The subjects were asked to answer the scale questions on their own according to the given instructions. Individuals who did not fill out the questionnaire were not included in the sample.

2.2 Endpoints

The study identified the following “endpoints”: the first cases of arterial hypertension (AH), myocardial infarction (MI), and stroke. All MI cases were recorded under the WHO epidemiological program Register of acute myocardial infarction, conducted in Novosibirsk from 1978 to the present day [13]; newly occuring cases of hypertension and stroke were recorded during the observation of the cohort. Sources used to identify cases of AH and stroke included population-based cohort study (annually), medical history, hospital discharge, medical records in polyclinics or general practices documents, death certificates, interviews with relatives, pathological and forensic reports. AH was defined as a condition in which SBP was 140 mmHg and above and/or DBP – 90 mmHg and/or antihypertensive medication was taken.

2.3 Participants

The object for the study of CVD risk was the cohort formed from the number of 25–64-year-old individuals examined at the III MONICA-psychosocial screening. The prospective follow-up period for the participants was 16 years (1994–2010). A total of 384 women and 190 men, with a baseline age of 25–64 years without CVD or DM at the time of screening, were included in the analysis. Over 16 years, the cohort had 15 cases of first-onset MI in women and 30 in men, and 35 cases of the first-onset stroke in women and 22 in men. During the same period, 229 cases of first-time AH were detected in women and 46 cases in men.

3. Results and discussion

3.1 Sex differences in the dynamics of psychosocial factors from 1994 to 2017

The results of the study showed that high levels of anxiety traits were present in two-third of the female population aged 25–64 in 1994 (**Table 1**). Whereas among men, high anxiety was found in less than half of those surveyed. Among the male population in 1994, the frequency of high anxiety increased linearly from younger to older age groups. In contrast, among women, high levels of AT were more common in the younger age groups of 25–34 and 35–44. Between 2003 and 2005, the maximum HAL values among both sexes, except for men in the 45–54 year group, were observed. In 2013–2016, there was a significant decrease in the prevalence of HAL in young groups in both sexes (**Table 1**). By 2016–2017, only the female population of 35–64-year- olds had consolidated such a favourable trend, but in men, the prevalence of high anxiety was back to 1994 levels. Thus, for the first time, the frequency of HAL among men 35–44 years was higher than in women of the same age group, although the differences did not reach statistical significance. The increase in anxiety levels among men is likely due to peak values of social tensions amid the economic crisis that began to gain momentum after 2014. Subsequently, we should expect similar changes among the female population.

The study of sex differences in epidemiological studies in the United States showed that the prevalence of anxiety changed slightly from 1990 to 2003 and averaged about 30% among women and 20% among men [14, 15]. This is lower

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Low	1994	12	6.8	0	0	4	2.2	1	0.6	0	0	1	0.5	0	0	2	1.2	16	4.5	1	0.3
Moderate		96	54.9	56	35.4	86	48.6	48	30.2	57	42	85	46.2	67	39.6	76	45	182	51.7	104	32.8
High		67	38.3	102	64.6	87	49.2	110	69.2	79	58	98	53.3	102	60.4	91	53.8	154	43.8	212	66.9
Total		175	100	158	100	177	100	159	100	136	100	184	100	169	100	169	100	352	100	317	100
		χ^2 = 28.982 df = 2 p < 0.001				χ^2 = 14.338 df = 2 p = 0.001				χ^2 = 1.39 df = 2 p = 0.499				χ^2 = 3.193 df = 2 p = 0.203				χ^2 = 15.937 df = 2 p < 0.001			
Low	2005									7	2.3	2	0.4	8	2.9	0	0	15	2.6	2	0.2
Moderate										135	44.4	113	20.4	79	29	70	13.5	214	37.2	183	17
High										162	53.3	439	79.2	185	68	450	86.5	347	60.2	889	82.8
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										χ^2 = 65 df = 2 p = 0.0001				χ^2 = 45.98 df = 2 p < 0.001				χ^2 = 14.51 df = 2 p < 0.001			
Low	2013	31	18.8	15	7	29	11.1	15	4.5									60	14.1	30	5.5
Moderate		97	58.8	113	53.1	145	55.3	141	42.1									242	56.7	254	46.4
High		37	22.4	85	39.9	88	33.6	179	53.4									125	29.3	264	48.2
Total		165	100	213	100	262	100	335	100									427	100	548	100
		χ^2 = 19.89 df = 2 p = 0.0001				χ^2 = 27 df = 2 p = 0.0001												χ^2 = 45.6 df = 2 p = 0.0001			
Low	2017					2	2.9	10	11.2	3	4	15	10.3	7	3	8	5.4	12	4.5	33	8.6
Moderate						33	47.8	38	42.7	45	56	53	36.3	57	48.7	72	48.3	135	50.8	163	42.4
High						34	49.3	41	46.1	32	40	78	53.4	53	45.3	69	46.3	119	44.7	188	49
Total						69	100	89	100	80	100	146	100	117	100	149	100	266	100	384	100
						χ^2 = 3.869 df = 2 p > 0.05				χ^2 = 9.418 df = 2 p < 0.01				χ^2 = 0.060 df = 2 p > 0.05				χ^2 = 6.740 df = 2 p = 0.035			

Abbreviations: M- males; F – females; N – numbers (absolute).

Table 1.
Gender differences in the dynamic of anxiety traits levels in age groups of a population aged 25–64 years in 1994–2017.

than presented in our study. Similarly, a comparison of data from the European Union showed no significant change in the rates of anxiety disorders between 2005 and 2011. Anxiety was more often recorded among the female population, but its prevalence, on the contrary, was higher among middle-aged Europeans [1, 16]. Significant differences in prevalence are related to the use of different instruments to assess anxiety in our study [17].

Depression (D) occurred in more than half of the female population aged 25–64 in 1994 (**Table 2**). The prevalence of D among men was less than 30%. At the same time, the frequency of major depression among women is 4 times higher on average than among men ($p < 0.001$). The prevalence of major D in 1994 in men increased with age and was unexpectedly higher among 45–54-year-olds. Among women of 45–54 years old, major D in 2003 increased by 2% over 1994, but the 4-fold drop in major D in the 55–64-year-olds group was reflected in a decline in the overall average major depression rates of that period. In 2013, in the young-age population, there was an increase in the high prevalence of major D among men, and we observed a tendency of the narrowing gap in the prevalence of depression with the female population. In 2017, high levels of major D persisted among men and women in the younger age group of 35–44 years old, and even an explosive increase in major D was found in the category of 55–64-year-old women. At the same time, the proportion of individuals with no D in the population aged 45–64 years of both sexes was higher than in 1994.

Sex distribution was studied in 2006–2009 and 2013–2015 as part of the first and second waves of the European health interview survey (EHIS). The proportion of people suffering from depressive disorders among women was higher than among men in each of the EU member states [18]. Portugal recorded the largest gender gap: the proportion of Portuguese women with chronic depression was 11.3% higher than men. The third wave of the European health interview survey (EHIS) was scheduled to start in 2019, but the COVID-19 pandemic is delaying new findings to help understand the current trend in the prevalence of depression depending on sex and age in the Eurozone.

The prevalence of high VE in 1994 was 2 times higher among women than men in the open population aged 25–64 (14.6% and 31%, for men and women of 25–64 years old, respectively; $p < 0.001$). In 1994, both men and women showed a non-linear increase in the frequency of high VE from younger to older age groups (**Table 3**). Between 2003 and 2005, the increase in average levels of VE compared to 1994 reduced the proportion of those who did not experience vital exhaustion. The gender gap in high VE levels was heterogeneous across age groups. The 2013–2016 trend for a significant decrease in high and average VE levels in men and women in 2017 remained only in the 35–44-year-olds group. However, in older age categories, the decrease in VE occurred only among the female population of 45–64 years old, whereas in men of this age, the levels of vital exhaustion did not decrease, but, on the contrary, slightly increased compared to 2003. Then, for the first time in the entire 23-year follow-up period, men were more likely to report VE than women (16.9% and 15.6% for men and women of 35–64 years old, respectively, n.s.).

According to The Copenhagen City Heart Study, the prevalence of medium and high VE levels measured between 1991 and 1994 was 25% in the population, of which 58.5% were women. It should be noted that in this study, the examined population was quite old: the average age was 60 [19]. In a large-scale epidemiological study in the United States, high levels of VE were observed in 24% of the participants, and average levels of VE were found in 44% of the surveyed. Women were more likely than men to report high VE levels [20].

More than half of the male and female population have high or average levels of hostility (**Table 4**). At the same time, the prevalence of hostility in 1994 was

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Major	1994	1	0.6	10	9.7	3	1.8	18	13.6	9	6.9	1	2.9	6	4	8	18.6	19	3.1	37	11.8
Moderate		39	23.4	44	42.7	39	23.9	53	40.2	35	26.9	17	48.6	44	29.5	20	46.5	157	25.8	134	42.8
No D		127	76	49	47.6	121	74.2	61	46.2	86	66.2	17	48.6	99	66.4	15	34.9	433	71.1	142	45.4
Total		167	100	103	100	163	100	132	100	130	100	35	100	149	100	43	100	609	100	313	100
		χ^2 = 28.674 df = 2 p < 0.001				χ^2 = 29.695 df = 2 p < 0.001				χ^2 = 6.219 df = 2 p = 0.045				χ^2 = 18.210 df = 2 P < 0.001				χ^2 = 66.724 df = 2 p < 0.001			
Major	2005									4	1.3	28	5.1	11	4	22	4.2	15	2.6	50	4.7
Moderate										75	24.7	179	32.3	62	22.8	161	31	137	23.8	340	31.7
No D										225	74	347	62.6	199	73.2	337	64.8	424	73.6	684	63.7
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										χ^2 = 15.036 df = 2 p = 0.001				χ^2 = 6.088 df = 2 P = 0.048				χ^2 = 17.541 df = 2 p < 0.001			
Major	2013	11	6.7	36	16.9	29	11.1	54	16.1									>40	9.4	90	16.4
Moderate		36	21.8	50	23.5	54	20.6	97	29									90	21.1	147	26.8
No D		118	71.5	127	59.6	179	68.3	184	54.9									297	69.5	311	56.8
Total		165	100	213	100	262	100	335	100									427	100	548	100
		χ^2 = 9.97 df = 2 p = 0.007				χ^2 = 11.08 df = 2 p = 0.004												χ^2 = 18.531 df = 2 p < 0.001			
Major	2017					8	11.6	11	12.4	3	4	14	9.5	4	3.4	30	20.1	15	5.6	55	14.3
Moderate						11	15.9	22	24.7	17	21	36	24.7	29	24.8	31	20.8	57	21.4	89	23.2
No D						50	72.5	56	62.9	60	75	96	65.8	84	71.8	88	59.1	194	73	240	62.5
Total						69	100	89	100	80	100	146	100	117	100	149	100	266	100	384	100
						χ^2 = 1.980 df = 2 p = 0.372				χ^2 = 3.239 df = 2 p = 0.199				χ^2 = 16.430 df = 2 p < 0.001				χ^2 = 13.779 df = 2 p < 0.002			

Abbreviations: M- males; F – females; N – numbers (absolute); D – depression.

Table 2.
Gender differences in the dynamic of depression levels in age groups of a population aged 25–64 years in 1994–2017.

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
High	1994	8	4.8	23	22.3	23	13.9	45	33.3	29	22.5	10	25	29	19.3	26	44.8	89	14.6	104	31
Moderate		80	48.5	49	47.6	78	47.3	63	46.7	65	50.4	17	42.5	95	63.3	19	32.8	318	52.2	148	44
No VE		77	46.7	31	30.1	64	38.8	27	20	35	27.1	13	32.5	26	17.3	13	22.4	202	33	84	25
Total		165	100	103	100	165	100	135	100	129	100	40	100	150	100	58	100	609	100	336	100
		χ^2 = 21.085 df = 2 p = 0.001				χ^2 = 20.967 df = 2 p = 0.001				χ^2 = 0.785 df = 2 p = 0.675				χ^2 = 17.991 df = 2 p < 0.001				χ^2 = 36 df = 2 p < 0.001			
High	2005									50	16.4	172	31	59	21.7	148	28.5	109	18.9	320	29.8
Moderate										174	57.2	303	54.7	157	57.7	314	60.4	331	57.5	617	57.4
No VE										80	26.3	79	14.3	56	20.6	58	11.2	136	23.6	137	12.8
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										χ^2 = 31.794 df = 2 p < 0.001				χ^2 = 14.38 df = 2 p = 0.001				χ^2 = 4.086 df = 2 p = 0.13			
High	2013	7	4.2	24	11.3	19	7.3	65	19.4									26	6.1	89	16.2
Moderate		52	31.5	82	38.5	91	34.7	135	40.3									143	33.5	217	39.6
No VE		106	64.2	107	50.2	152	58	135	40.3									258	60.4	242	44.2
Total		165	100	213	100	262	100	335	100									427	100	548	100
		χ^2 = 10.112 df = 2 p = 0.006				χ^2 = 26.23 df = 2 p = 0.001												χ^2 = 35.77 df = 2 p = 0.001			
High	2017					4	5.8	10	11.2	14	17.5	17	11.6	27	23.1	33	22.1	45	16.9	60	15.6
Moderate						22	31.9	38	42.7	19	23.7	68	46.6	56	47.9	67	45	97	36.5	173	45.1
No VE						43	62.3	41	46.1	47	58.8	61	41.8	34	29	49	32.9	124	46.6	151	39.3
Total						69	100	89	100	80	100	146	100	117	100	149	100	266	100	384	100
						χ^2 = 4.425 df = 2 p > 0.05				χ^2 = 11.401 df = 2 p < 0.01				χ^2 = 0.451 df = 2 p > 0.05				χ^2 = 4.927 df = 2 p = 0.086			

Abbreviations: M- males; F – females; N – numbers (absolute); VE – vital exhaustion.

Table 3.
Gender differences in the dynamic of vital exhaustion levels in age groups of a population aged 25–64 years in 1994–2017.

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
High	1994	52	31.7	48	46.6	53	33.8	54	40	37	30.3	15	37.5	50	33.6	24	41.4	192	32.4	141	42
Moderate		25	15.2	26	25.2	37	23.6	38	28.1	24	19.7	7	17.5	27	18.1	15	25.9	113	19.1	86	25.6
Low		87	53.4	29	28.2	67	42.6	43	31.9	61	50	18	45	72	48.4	19	32.8	287	48.4	109	32.4
Total		164	100	103	100	157	100	135	100	122	100	40	100	149	100	58	100	592	100	336	100
		χ^2 = 16.08 df = 2 p < 0.001				χ^2 = 3.622 df = 2 p = 0.001				n.s.				n.s.				χ^2 = 22.58 df = 2 p < 0.001			
High	2005									138	45.4	189	34.1	111	40.8	183	35.2	249	43.2	372	34.6
Moderate										58	19.1	132	23.8	51	18.8	120	23.1	109	18.9	252	23.5
Low										108	35.5	233	42.1	110	40.4	217	41.7	218	37.8	450	41.9
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										χ^2 = 10.657 df = 2 p = 0.005				n.s.				n.s.			
High	2013	61	37	62	29.1	90	34.4	100	29.9									151	35.4	162	29.6
Moderate		46	27.9	45	21.1	70	26.7	85	25.4									116	27.2	130	23.7
Low		58	35.2	106	49.8	102	38.9	150	44.8									160	37.5	256	46.7
Total		165	100	213	100	262	100	335	100									427	100	548	100
		χ^2 = 8.103 df = 2 p = 0.017				n.s.												χ^2 = 8.451 df = 2 p = 0.015			
High	2017					22	31.9	27	30.3	20	25	50	34.2	46	39.3	42	28.2	88	33.1	119	31
Moderate						32	46.4	26	29.2	22	27.5	26	17.8	24	20.5	38	25.5	78	29.3	90	23.4
Low						15	21.7	36	40.4	38	47.5	70	47.9	47	40.2	69	46.3	100	37.6	175	45.6
Total						69	100	89	100	80	100	146	100	117	100	149	100	266	100	384	100
						χ^2 = 7.365 df = 2 p < 0.05				n.s.				n.s.				χ^2 = 4.687 df = 2 p = 0.096			

Abbreviations: M- males; F – females; N – numbers (absolute).

Table 4.
Gender differences in the dynamic of hostility levels in age groups of a population aged 25–64 years in 1994–2017.

unexpectedly higher among the female population in all age groups. However, in further follow-up periods, from 2003 to 2017, men showed higher levels of hostility compared to women. This reinforces our theory that trajectories in the prevalence of psychosocial characteristics change during periods of changing socio-economic patterns in society. Between 2013 and 2016, the trend in the prevalence of men over women with high hostility was consolidated by reducing its prevalence among the female population to historically low values of less than 30% in the 25–34- and 35–44-year-olds groups. In 2017, this trend was also recorded in the older age groups, where the lowest levels of high hostility were observed among men of 45–54 years old and women of 55–64 years old for the entire observation period between 1994 and 2017.

What makes our results unique is that reports on the prevalence of affective states are limited and more commonly cited in clinical groups. Concerning the frequency of hostility in other populations, the most informative is the CARDIA study, which included more than 5,000 men and women aged 18–30. At the time of the initial survey (1985–1986), the high level of hostility was 23.4% in the study population, the average was 52.3%, and was more common among men, compared to women [21].

Sex differences in the dynamics of social support levels are presented in **Tables 5** and **6**. The higher prevalence of low close contact (ICC) among men, compared to women, was reported in both the youngest 25–34-year-olds group (63.8% vs. 57.7%) and older age groups of 45–54 and 55–64 (64% vs. 54%, respectively) in 1994. In 2003 and 2013, there was a downward trend in the frequency of the low close contact index to 46–50%, although ICC levels did not differ depending on sex. In 2017, on the contrary, women were 14.4% more likely to show a lack of social support, in comparison with men, and completely levelled the emerging favourable trend of 2013.

The prevalence of a low social network index (combined indicator: low and moderate-1) in the open population among men and women aged 25–64 was equally high in 1994 and between 2003 and 2005. Between 2013 and 2016, there was an unstable trend toward an increase in the level of social ties among young age groups of both sexes. Later, over a short period, this trend reversed, marking an unfavourable increase, predominantly among the female population of 35–64 years old, reaching, on average, 75% of the values in the frequency of the low index of social ties. Such differences are explained by the fact that women have better social connections and receive support from multiple sources, but satisfaction with close contacts is reflected in the perception of social support and the effect on health [22, 23].

3.2 Gender effect in the risk of AH in individuals with unfavourable levels of PSF

In our study of the risk of AH development depending on PSF levels, we obtained the following results. Among men and women with HAL, the risk of AH was higher in the "stronger sex", with an increased risk demonstrated in the first five years of follow-up (**Figure 1**). The magnitude of risk in men was maximum after 10 years of follow-up (HR = 5.75), and in women in the first five years – HR = 2.38 (95% CI: 1.13–4.99). And this is despite the fact that the prevalence of HAL is higher in women. Indeed, BigData analysis showed that age and male sex are associated risk factors for AH in individuals with anxiety disorders [24]. In a multivariate model adjusted for social characteristics and age, the risk of AH was also higher among men (HR = 4.57; 95% CI:2.07–10.08). While age was a determinant of AH risk in women (HR = 7.93; $p < 0.01$ for the oldest age category), marital

DOI: http://dx.doi.org/10.5772/intechopen.99767

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Low	1994	102	63.8	82	57.7	85	55.9	86	60.6	79	64.2	72	54.1	102	64.6	71	54.2	368	62	311	56.8
Moderate		39	24.4	50	35.2	44	28.9	45	31.7	33	26.8	52	39.1	37	23.4	55	42	153	25.9	202	36.9
High		19	11.9	10	7	23	15.1	11	7.7	11	8.9	9	6.8	19	12	5	3.8	72	12.1	35	6.4
Total		160	100	142	100	152	100	142	100	123	100	133	100	158	100	131	100	593	100	548	100
		χ^2 = 5.27 df = 2 p = 0.072				n.s.				n.s.				χ^2 = 14.85 df = 2 p < 0.001				χ^2 = 22.603 df = 2 p < 0.001			
Low	2005									140	46.1	298	53.8	129	47.4	251	48.3	269	46.7	549	51.1
Moderate										141	46.4	231	41.7	118	43.4	240	46.2	259	45	471	43.9
High										23	7.6	25	4.5	25	9.2	29	5.6	48	8.3	54	5
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										χ^2 = 6.567 df = 2 p = 0.038				n.s.				n.s.			
Low	2013	79	47.9	95	44.6	130	49.6	167	49.9									209	48.9	262	47.8
Moderate		66	40	96	45.1	105	40.1	141	42.1									171	40	237	43.2
High		20	12.1	22	10.3	27	10.3	27	8.1									47	11	49	8.9
Total		165	100	213	100	262	100	335	100									427	100	548	100
		n.s.				n.s.												n.s.			
Low	2017					34	49.3	49	55.1	38	47.5	98	67.1	49	41.9	83	55.7	121	45.5	230	59.9
Moderate						30	43.5	32	36	35	43.75	46	31.5	53	45.3	55	36.9	118	44.4	133	34.6
High						5	7.2	8	8.9	7	8.75	2	1.4	15	12.8	11	7.4	27	10.1	21	5.5
Total						69	100	89	100	80	100	146	100	117	100	149	100	266	100	384	100
						n.s.				χ^2 = 12.537 df = 2 p < 0.01				n.s.				χ^2 = 14.554 df = 2 p < 0.001			

Abbreviations: M- males; F – females; N – numbers (absolute).

Table 5.
Gender differences in the dynamic of close contact index in age groups of a population aged 25–64 years in 1994–2017.

Levels		25–34 years				35–44 years				45–54 years				55–64 years				25–64 years			
		M		F		M		F		M		F		M		F		M		F	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Low	1994	122	76.3	111	78.2	113	74.4	110	77.4	94	72.9	104	78.2	128	81.6	98	74.8	457	76.4	423	77.2
Moderate		28	17.5	28	19.7	33	21.7	29	20.4	26	20.2	23	17.3	21	13.4	31	23.7	108	18.1	111	20.3
High		10	6.3	3	2.1	6	3.9	3	2.1	9	7	6	4.5	8	5.1	2	1.5	33	5.5	14	2.5
Total		160	100	142	100	152	100	142	100	129	100	133	100	157	100	131	100	598	100	548	100
		χ^2 = 15.894 df = 3 p = 0.001				n.s.				n.s.				χ^2 = 7.217 df = 2 p = 0.028				χ^2 = 6.867 df = 2 p = 0.033			
Low	2005									233	76.7	444	80.2	202	74.3	416	80	435	75.5	860	80.1
Moderate										59	19.4	97	17.5	61	22.4	90	17.3	120	20.8	187	17.4
High										12	3.9	13	2.3	9	3.3	14	2.7	21	3.7	27	2.5
Total										304	100	554	100	272	100	520	100	576	100	1074	100
										n.s.				n.s.				χ^2 = 5.001 df = 2 p = 0.083			
Low	2013	98	59.4	123	57.8	158	60.3	212	63.3									256	60	335	61.1
Moderate		53	32.1	71	33.3	88	33.6	99	29.6									141	33	170	31
High		14	8.5	19	8.9	16	6.1	24	7.2									30	7	43	7.9
Total		165	100	213	100	262	100	335	100									427	100	548	100
		n.s.				n.s.												n.s.			
Low	2017					53	73.6	66	68	46	56.8	119	85	67	65.1	97	70.3	166	64.8	282	75.2
Moderate						16	22.2	23	23.7	29	35.8	19	13.6	31	30.1	34	24.6	76	29.7	76	20.3
High						3	4.2	8	8.2	6	7.4	2	1.4	5	4.9	7	5.1	14	5.5	17	4.5
Total						72	100	97	100	81	100	140	100	103	100	138	100	256	100	375	100
						n.s.				χ^2 = 22.212 df = 2 p < 0.001				n.s.				χ^2 = 8.175 df = 2 p = 0.017			

Abbreviations: M- males; F – females; N – numbers (absolute).

Table 6.
Gender differences in the dynamic of social networks index in age groups of a population aged 25–64 years in 1994–2017.

status was also important in men: divorced and widowed appeared to be more vulnerable (HR = 4.30 and HR = 4.84, respectively; p for all <0.001).

The risk of AH in men with D was high already in the first 5 years of follow-up observations, 6.7 times higher, gradually decreasing 10 and 16 years after screening, but it remained significant. In women, a significant cohort outcome was determined only 10 years after screening and was 1.7 times higher for those with depression. Multivariate analysis also identified a higher risk of AH among men rather than women: HR = 5.3 and HR = 1.4 (95%CI:1.04–1.98), respectively. As with high anxiety, women's risk was higher in the older age groups of 45–54 and of 55–64, significantly outpacing men in these categories, reaching HR = 6.9. At the same time, the mean level of education was a protective factor for women (HR = 0.56; p < 0.05). In men, everything is different. Divorced (HR = 3.0), those with primary education (HR = 5.6), and manual labour workers (HR = 2.8) with D had higher risks of AH compared with married men with higher education and higher occupational status (the white-collars, e.g., engineers and technicians, managers) (p for all <0.05).

Similarly revealing, in terms of gender differences, is a recent report by Kao W. T. et al. (2019). In this 10-year study, men with depression had a higher risk of AH than those without D [25]. In women, the results were contradictory: some risk models showed a decrease in the development of AH among women with depression; but using a model adjusted for other covariates, they showed an increased risk of AH in women, compared with individuals without D. The authors considered social factors to be among the many reasons for the higher risk of AH among men rather than women.

The maximum risk of hypertension in men with VE was recorded in the first five years from the start of the study HR = 3.2 (95% CI:1–7.3). Further, this risk decreased but remained significant by the end of the follow-up period. Women with VE had a 2-fold higher risk of AH after 5 years of observation, but after 10 years it was no longer statistically significant. In the multivariate model, the risk of AH was also higher in the male cohort HR = 2.9 (95%CI:1–7.9). In women, the social parameters (i.e. marital status, education, occupational status) and age included in the model reduced the risk to a greater extent than in men, although it remained significant, HR = 1.34 (95% CI:0.99–1.82). Age over 34 years (HR = 2.3) and primary education (HR = 1.8) were additional predictors of AH risk among women with VE. In the ARIC Study, the highest quartile of VE was also associated with lower educational attainment and higher systolic BP [20]. In men, the age limit was significantly higher (over 54 years old), but the increase in risk at this age was more than 5 times higher for people with VE as well. In addition, divorce played a significant role in the occurrence of AH in men with VE (HR = 3.3). This is probably the case when VE is a potential response to intractable problems in life and the inability to adapt to prolonged exposure to psychological stressors [26].

The risk of developing AH, during the first 5 years of follow-up, was already 2 times higher in both men and women with a low index of close contacts (ICC) as compared to those with higher indices. Among those with low social network indices (SNI), the risk of developing AH was 5.9 times higher among men and 1.8 times higher among women in the first 5 years of follow-up. The multivariate model retained a statistically significant risk of developing AH only in men with low ICC (HR = 1.2). At the same time, the marital status "unmarried" (i.e. single/divorced/widowed) significantly increased the risk level to the limit of 7.1 times (for widowers). It should be noted that in widowed women, the risk of AH was also significant (HR = 2.7 95% CI: 1.03–7.35), although not as high as in men.

In women, there was also a tendency of an increased 2-fold risk of AH among those who had primary education (p = 0.06).

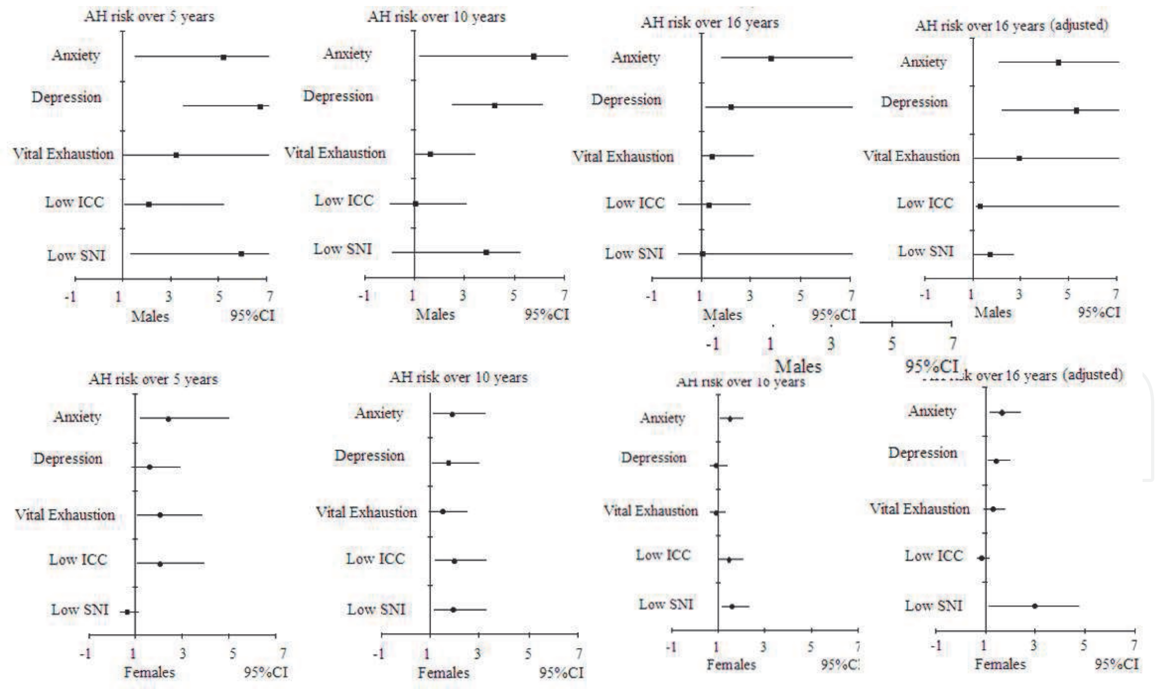

Figure 1.
Gender differences in risk of an arterial hypertension incidence in a cohort aged 25–64 with anxiety traits, depression, vital exhaustion and low social support. Abbreviations: AH- arterial hypertension; CI- confidence interval; ICC – Index of close contacts; SNI – Social network index.

The effect of low social ties on the risk of AH in the multivariate model was 1.7 times higher in men and 2.9 times higher in women. The effect of marital status "single" was statistically significant only in men, as well as heavy physical labour, which increased the risk by almost 3 times. However, the initial level of educational attainment was statistically significant for both sexes: the risk of AH was 1.4 times higher in men and 2 times higher in women with low SNI. In both sexes, age was a more significant risk factor because it had a linear effect on the risk of AH, being the maximum in the age group of 55–64, reaching HR = 8 in women.

In our study, marital status "unmarried" (divorced, single, or widowed) determined the extreme degree of social isolation in men with low ICC / SNI, which was reflected in a higher risk of AH in them, compared to the "tender gender", where marital status was not always a significant risk factor [27]. In the ELSA study (n = 8310), loneliness remained a significant predictor of cardiovascular events regardless of sociodemographic factors and social isolation; even after the inclusion of traditional RFS to the model, the association between loneliness and CVD was maintained [28].

3.3 Gender effect in the risk of MI in individuals with unfavourable levels of PSF

The risk of myocardial infarction for 16 years of follow-up was slightly higher among women with high anxiety compared to men (HR = 4.19 and HR = 3.7, respectively), but the inclusion of social characteristics and age in the model increased the risk value among women to HR = 5.16 (p for all <0.05). In men, the risk in the multivariate model decreased but remained significant HR = 1.79 (**Figure 2**). A great risk share in this model was explained by age over 54; however, these associations were not statistically significant in women.

The risk of a heart attack in men with depression was 2 and in women 2.5 times higher. In the multivariate model, the risk of MI in men was reduced but remained significant, and in women with D, statistics were no longer valid. In the age group

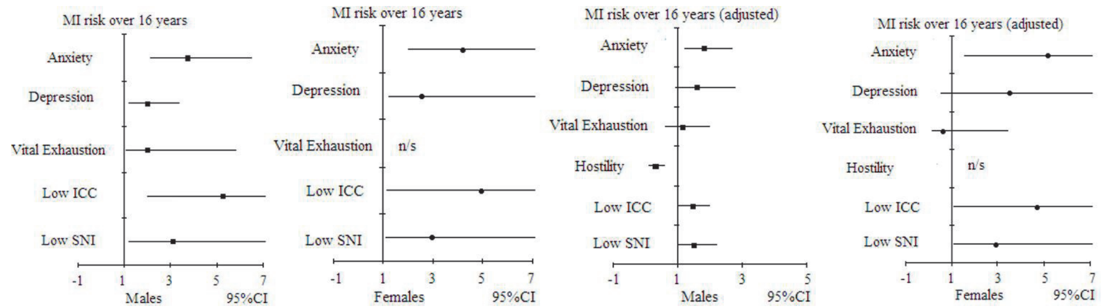

Figure 2.
Gender differences in risk of myocardial infarction incidence in a cohort aged 25–64 years with anxiety traits, depression, vital exhaustion, hostility and low social support. Abbreviations: CI- confidence interval; ICC – Index of close contacts; MI- myocardial infarction; SNI – Social network index.

of 55–64, the risk of MI was highest in men (HR = 6.8) and women (HR = 6.3). Marital status "single" (HR = 6), primary education (HR = 3.2), and manual labour (HR = 6.7) were predictors of high risk of MI in men with D (p for all <0.05). No such associations were found in women.

A recent publication of the ESC 2018 working group cites several studies concerning sex differences in the risk of coronary heart disease (CHD) and CVD mortality [9]. Studies of young population samples (under 40) found that the effect of depression on the risk of CHD was higher among women than in men. In the NHANES III study, a history of major depression was associated with an almost 15-fold increased risk of CHD in women and 3.5-fold in men [29]. This confirms our earlier findings [30], but in our present study, the sex differences were not as significant in risk.

In the simple risk model, VE did not affect the development of MI in women, whereas in men it was 2 times higher compared to those in whom vital exhaustion was not found. The multivariate model reduced the magnitude of risk after adjusting for socio-demographic characteristics, but the statistical significance for men remained the same. Living out of wedlock, age over 44, and blue-collar occupations were associated with a 3–7-fold increase in risk for men. Divorced status in women also increased the risk of myocardial infarction (5 times higher).

In our study, the moderate to high levels of hostility reduced the risk of MI by 70%. However, some social characteristics changed this ratio unfavourably. Living out of wedlock has been associated with the risk of MI in men who demonstrate hostility. The increase in risk was particularly significant among the widowed (12 times higher). Primary education and age over 44 also increased the risk of MI. Executive positions combined with hostility is associated with a 9-fold increased risk of MI compared to engineering professions. No significant associations and effects on the risk of MI in women with hostility during the 16-year follow-up period were found.

A recent meta-analysis assessing the impact of hostility showed that anxiety, depression, and psychological stress, but not anger or hostility, were associated with CHD risk in women. In men, on the contrary, anger is one of the leading psychosocial risk factors for cardiovascular events [31]. Our study complements these conclusions by showing that the risk of IM is manifested only in a certain social environment.

The risk of MI in individuals with low indices of close contacts and social ties was significantly higher but did not differ significantly depending on sex, slightly predominating in men. At the same time, the lack of close contacts increased the risk more significantly (5 times), rather than a poor social network (3 times). Interestingly, the multivariate model practically did not weaken the risk of MI in women, which increased significantly among women with low ICC and primary education (HR = 15.4). In men, primary education had a comparatively smaller effect on risk, giving preference to age, living out of wedlock (single, divorced, widowed status), and having an engineering or technician occupation, or physical labour. Similar associations were found for the social network index (SNI) in the multivariate model, where the risk of MI was higher in women compared to men. In contrast to close contacts, the lack of social connections combined with age, primary education and physical labour increased the risk of MI − 3-3.7 times in women. For men, such factors as marital status "single", age, primary education, and physical labour remained significant. Importantly, low SNI combined with a mid-level executive position also increased the risk of MI (2.5 times). A similar effect was not observed in women.

3.4 Gender effect in the risk of stroke in individuals with unfavourable levels of PSF

The risk of stroke was higher among men with HAL, HR = 4.43 (95% CI:2.8–6.9), rather than among women, HR = 3.5. In the multivariate model, the risk of stroke was lower for men than for women. Adverse changes in marital status (divorce or death of a spouse), as well as age over 54 years, were associated with an increase in the risk of stroke (3.8–5.8 times higher) in men, but not women.

Stroke is the fourth leading cause of death in the female population [32]. Recent studies indicate an independent influence of anxiety in stroke risk [33, 34]. This confirms the results obtained earlier [35]. The overall risk of stroke according to the meta-analysis, which included 950 thousand participants, was 1.24. It is reported that individuals with more severe anxiety may have a higher risk [36]. In multivariate models, a higher risk of stroke was observed among men, people with low education attainment, and those living out of wedlock [32], as well as in our study. Our study confirms the need to consider the social gradient in terms of the effect of PSF on the risk of CVD in the general population.

Depression increased the risk of stroke more strongly in men (by 5.8 times) than in women (HR = 4.6). However, including social and demographic variables in the model increased the risk of stroke in women 8.5 times. At the same time, the combination of age over 54 years with depression increased the risk of stroke (6.9 times in women, and 3.1 times in men). Depression in widowed men with primary education increased the risk more than 8 times. A tendency toward increased risk was observed in men with D in low-skilled jobs.

A meta-analysis of more than 17 cohort studies found a 1.34-fold increase in the risk of stroke among people with depression [37], which again confirms our results [30]. In this analysis, the differences in risk among men and women were not so significant (HR = 1.49 and 1.35), which may be explained by a shift in the evaluation due to differences between studies, since some studies were performed among the male population [38]. Yet individual studies show a significantly higher risk of stroke in women than in men [39]. In addition, the influence of age is also significant, increasing the effect of depression in the group of people under 65 years (**Figure 3**) [39].

Vital exhaustion increased the risk of stroke equally in men and women in both the simple and multivariate models, although the inclusion of social and demographic characteristics reduced the risk value; it remained high: 2.6 times higher in men and 2.53 times higher in women in the multivariate model. The age of 55–64 years was significant in the development of stroke, increasing the risk in men 2.4 times, in women 2.9 times. Marital status and educational attainment were associated with stroke risk only in men, but not in women. Being divorced and having an

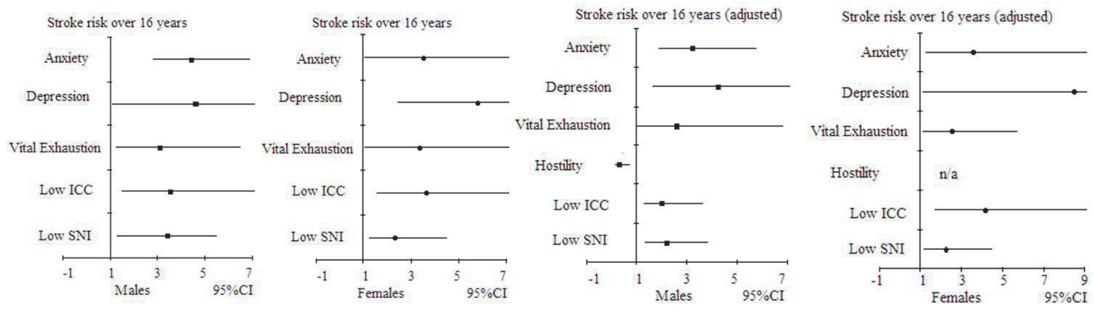

Figure 3.
Gender differences in risk of stroke incidence in a cohort aged 25–64 years with anxiety traits, depression, vital exhaustion, hostility and low social support. Abbreviations: CI- confidence interval; ICC – Index of close contacts; SNI – Social network index.

elementary level of education increased the risk of stroke in the cohort of men by 3.8–4.8 times. The tendency toward risk is also observed among widows.

Gender differences in stroke risk were also studied in the Copenhagen City Heart Study. The researchers found that women with high levels of VE had a 2.27-fold risk of stroke, which was slightly reduced in a multivariate analysis. Yet no association was found with stroke in men with VE. A longer cohort study might have levelled the gender difference in this longitudinal study: it estimated 6–9 years in this study [40].

Hostility in men has a negative association with stroke risk (HR = 0.29, 95% CI:0.1–0.7). Divorce, primary education, and the age of 55–64 are associated with a 3.2–4.6-fold increase in the risk of stroke. The maximum risk values were observed among pensioners (HR = 14.5) in comparison with executives. There was no association with stroke in women with hostility during the 16-year follow-up period.

The low level of close contacts increased the risk of stroke to the same degree in men and women – 3.5 times. But a poor social network (low SNI) was more important for men, increasing the risk of stroke 3.4 times, and for women 2.3 times. Adding social parameters and age to the analysis reduced the risk value in men with low ICC to HR = 2 (95% CI:1.27–3.61), while the risk of stroke increased 4.13-fold in women. Only women with higher education and a favourable level of close contact were resistant to the risk of stroke. In men, only primary education was associated with a twofold risk of stroke. Moreover, being a divorced or widowed blue-collar was associated with an increased risk of stroke in men but not women. However, age over 54 was critically important in the risk of stroke in both sexes, but with a greater magnitude among women (HR = 5.19; $p < 0.05$).

In contrast to the simple model, in the multivariate Cox model, SNI increased the risk of stroke in the same way in men and women (2.2 times). As in the case of low ICC, any level of education attainment, apart from higher education, increased the risk of stroke in women; while in men, only primary education was significant, in case of poor social ties. Women aged 55–64 were 2 times more likely than men of the same age group to have a stroke. Yet occupational status, as well as marital status, were statistically significant only in men. Being a blue-collar worker and having the status of a divorced or a widower, combined with a low SNI, increased the risk of stroke 4.8–6.9 times. Literary sources show that the socially isolated, i.e., deprived of social contacts and not participating in social activities, lonely or not satisfied with the quality of their social contacts, have a 30% higher risk of CHD, stroke and early mortality [41]. Such studies only add to the significance of the influence of the social gradient described in our previous works [42].

4. Conclusions

In the period from 1994 to 2003/05, our study registered high levels of negative psychological characteristics, which prevailed among women. The favourable trend of 2013 in the reduction of affective states reversed shortly. By 2017, younger men for the first time began reporting higher levels of anxiety and vital exhaustion than women. For 23 years, against the background of an increase in the proportion of people of both sexes without negative psychological conditions, the gender gap in the frequency of major depression decreased. Such multifaceted trends are due to a decrease in the average levels of PSF in our study.

It is worth mentioning that an increased level of hostility in the Russian/Siberian population is associated with a negative risk of stroke. It can be assumed that a low level of hostility is probably not the most advantageous, from an evolutionary point of view, tool of adaptability in the conditions of the permanent crisis in Russia in the post-Soviet period. At the same time, high anxiety, as a personality trait, develops in character over many years, activates biological mechanisms and leads to the development of cardiovascular events. This also applies to other psychosocial factors. It should be pointed out that the increase in the risk of CVD is observed already in the first 5 years after the initial study and remains significant for a long period – 16 years in both sexes. The magnitude of the risk depends on gender. Its higher values were determined in men with unfavourable levels of PSF in the development of AH and stroke. Yet the inclusion of social characteristics to the model often changed this ratio, weakening the risk magnitude in men, but maintaining the same or increasing in women. This is explained by the high sensitivity of men to living outside wedlock, increasing the risk of CVD among divorced and, especially, widowed (6–8 times). In women, such associations were not typical. Obviously, more men benefit from being married rather than women who have to bear the domestic burden. These explanations can be found in our earlier works. The influence of occupational status was also decisive for men. Working professions are associated with a higher risk of CVD in men compared to engineers, technicians and managers. In women, the prognostically unfavourable factor was the initial level of education attained and age over 44 years in combination with affective states. Among men, the impact of these factors was less significant.

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