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Coronary heart disease differences in Eastern versus Western Europe: A demanding situation

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There are more than 4 million cardiovascular disease (CVD) related deaths each year in Europe, thus representing the main cause of deaths (47% of total: 52% of deaths in women and 42% in men). Notably, the main forms of CVD are coronary heart disease (CHD: about half of all CVD) and stroke (about 1/4 in men and 1/3 in women). If one considers geographic distribution of CVD deaths, CVD is the main cause of death for women in all countries of Europe for which we have mortality data and it is the main cause of death for men in all but 6 of these countries (exceptions are France, Israel, the Netherlands, San Marino, Slovenia and Spain). Indeed, CVD causes more than 50% of deaths in women in 29 countries, mostly in Central and Eastern Europe. In 9 countries (Azerbaijan, Belarus, Bulgaria, Georgia, Montenegro, Romania, FYR Macedonia, Ukraine and Uzbekistan) CVD causes more than 50% of deaths in men [1].

Death rates from CHD are generally higher in Central and Eastern Europe than in Northern, Southern and Western Europe. For example the death rate for men aged under 65 living in the Russian Federation is more than 13 times higher than in France, and for women it is almost 16 times higher. Western European countries generally have higher rates than Southern European countries. For example the death rate for both men and women aged under 65 living in Ireland is 1.7 times higher than in Italy [1]. These contemporary results were repeatedly stressed in the past [2–4] to the extent that the SCORE Project was forced to produce risk charts according to geographic distributions of the populations at risk [5,6].

Over the past 30 years, death rates from CHD have been consistently falling in most Northern and Western European countries, however trends in Central and Eastern European countries have been more mixed, including relative stability in some places for example Bulgaria and rapid increases in countries including Ukraine and Belarus. By the time of the MONICA Project (1980–1995), of the 28 areas investigated several Eastern European countries still presented increasing CHD incidence and mortality [7], a situation that is not so evident at present [1]. Around 2000–2005 rates are falling in the majority of Central and Eastern European countries although among men aged under 65 living in Iceland and the Netherlands there was a fall by 57% and 55% respectively, while in countries such as Ukraine, the Russian Federation and Lithuania, there was no more than around or less than 10% decreases in death rate, hiding steep increases until the mid-2000s, followed by equally steep falls in more recent years [1].

Table 1 presents a comparison of 7 selected, but representative Western versus 7 Eastern European countries and shows in men and women 25-year crude percent changes, starting from 1980, in age-standardized CHD mortality both for all ages and for people <45 years old, derived from a very important recent report [8]. Average results were provided to give a summary impression. Among Eastern European countries it was not possible to include Croatia and Serbia (the former Yugoslavia) whose data were published [1] just relative, respectively, to 1985–2009 and 1998–2009. With these limitations in mind, there is first of all a roughly double age-standardized average CHD mortality (per 100,000 inhabitants) in the chosen Eastern versus Western European countries in 1980–1984, which is true for both genders and both age groups. Secondly, there is a large contrast in the overall 25-year crude CHD mortality decrease in men and women from Western Europe (around −50%) as compared to people from Eastern Europe (between −14 and −19%), only in part ameliorated among relatively younger (<45 years old) individuals. Finally, in Romania at least (but data exist also for other Eastern European countries) there were notable overall increasing rather than decreasing CHD mortality trends and very little decreases in younger people. It is probable that these very recent changes mask in some way a condition that was seen previously when trends were increasing in most Eastern European countries whereas concomitantly they were decreasing in Western Europe [4].

There are several causes to potentially explain the abovementioned differences in CHD mortality and CHD mortality trends [4,9]. One of these relates to changes in diet [4,10,11] and probably, more in general, in life-style habits of which diet is a fundamental component in addition to smoking habits and physical activity [12,13]. These habits are

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Table 1
Age-standardized CHD mortality per 100,000 inhabitants average rates among men and women, both all ages combined (A) and people <45 years old (B), in 2 quinquennial periods and the respective 25-year crude % changes in 7 selected Western and 7 selected Eastern European Countries, condensed from [8].

	Men						Women					
	1980–1984		2005–2009		25-year crude % change		1980–1984		2005–2009		25-year crude % change	
	A	B	A	B	A	B	A	B	A	B	A	B
Belgium	187	7.9	93	2.7	−50	−66	90	1.9	41	0.7	−48	−64
Finland	421	14.6	192	3.1	−54	−79	169	1.4	89	0.4	−47	−69
France	111	4.6	57	2.3	−40	−50	48	0.6	22	0.5	−54	−19
Germany	249	7.4	127	3.1	−49	−58	109	1.2	67	0.8	−39	−30
Italy	171	7.0	85	2.3	−50	−67	84	1.1	43	0.4	−49	−60
Spain	114	6.8	74	3.1	−36	−55	51	1.0	31	0.6	−39	−44
United Kingdom	371	12.4	132	4.5	−64	−64	164	2.1	61	1.0	−63	−52
Western Europe	232	8.6			−50	−63	89	1.3			−48	−48
Bulgaria	244	12.7	188	9.8	−23	−23	155	1.9	97	1.7	−37	−9
Estonia	646	25.7	348	6.4	−46	−75	366	2.4	172	0.9	−53	−61
Hungary	334	26.5	309	9.7	−7	−64	168	5.1	178	2.7	+6	−47
Latvia	604	34.5	426	14.6	−30	−58	344	5.0	207	1.9	−40	−62
Lithuania	511	23.2	462	14.2	−10	−39	343	2.8	251	2.5	−27	−11
Romania	199	12.8	257	11.3	+29	−12	140	2.9	160	2.6	+15	−8
Slovakia	381	15.1	337	6.3	−12[a]	−58[a]	206	1.8	214	1.3	+4[a]	−27[a]
Eastern Europe	417	21.5			−14	−47	246	3.1			−19	−32

[a] Not precise as in 1980–1984 data were common to Czech Republic. Average results are here just to provide a summary impression from 1980 to 2009. In [1] data were also published for Croatia (1985–2009) and Serbia (only 1998–2009).

concordantly bad in the presence of socio-economic situations accompanied by the transition from the pre-industrial to the industrial society whereby cultural approach changes toward health [9]. Healthier dietary habits are abandoned and the amount of working physical activity decreases dramatically which may be causative of changes and among these of serum cholesterol increases [10,11]. Long-term effects of these changes may relate to increased incidence of CHD and CHD mortality, a typical presentation seen in transitional countries [4] whose mechanisms should be actively looked for if one is to decrease CHD burden there and the various clinical presentations from acute coronary syndromes (especially in relatively younger individuals) to congestive heart failure and sudden death [14–17].

Total serum cholesterol was recently presented as the differentiating covariate of CHD incidence and death versus other deaths in a 50-year long follow-up leading to the quasi extinction of a residential and middle-aged male cohort in Italy [18]. This was an important result obtained by applying competing risk analysis based on the Fine-Gray model, using the cumulative incidence function that prevents overestimation of risks due to Kaplan–Meier based methods such as Cox analysis. It enabled the discovery of an opposite mathematical sign when CHD incidence and deaths were the primary event (positive relation with total cholesterol levels) as opposed to when the other deaths were the primary event (negative relation with total cholesterol levels) [18]. This means that the risk of CHD incidence and death is increased as a function of total cholesterol levels whereas cholesterol has an opposite relation with the other types of death. These results in an epidemiological investigation [18] may have a profound significance if one explores the natural history of patients who presented with an acute coronary syndrome and underwent percutaneous coronary intervention [14] among whom major adverse cardiovascular events occurring during follow-up were equally attributable to recurrence at the site of culprit lesions and to nonculprit lesions. Although nonculprit lesions that were responsible for unanticipated events were frequently angiographically mild, most were thin-cap fibroatheromas or were characterized by a large plaque burden, a small luminal area, or some combination of these characteristics, as determined by gray-scale and radiofrequency intravascular ultrasonography. It is possible that these coronary changes may have had a substrate consisting, among other factors, in the long-duration impact of increased serum cholesterol levels [16–18].

A localized, peculiar, but well documented example of CHD trends in Eastern Europe was provided by the experience of the Serbian cohorts of the Seven Countries of Cardiovascular Diseases: 3 Serbian cohorts of middle-aged men were enrolled between 1962 and 1964 and then followed up for 45 years, with data on 40 years of follow-up already partially published. They were the rural cohorts in the village of Velika Krsna, the workers in an agro-industry cooperative in Zrenjanin, in the province of Vojvodina and a cohort in Belgrade made by the Professors of the local University [19,20]. Entry levels on main CHD risk factors were relatively low in these cohorts, except mean serum cholesterol in Belgrade (around 210 mg/dl), that contrasted with the low levels in Velika Krsna (160 mg/dl) and Zrenjanin (170 mg/dl) [20].

During the first 10 years of follow-up all-cause and CHD death rates were also relatively low in Serbia compared with the high levels observed in USA, Finland, and the Netherlands, and similar to the low levels found in Italy, Greece and Japan [21]. Thereafter, 2 almost simultaneous phenomena were seen, i.e. large increase in risk factors mainly serum cholesterol, larger than in any other Seven Countries cohorts and not explained by aging, and an enormous increase in death rates from CHD. After 10 years serum cholesterol increased between 30 and 35 mg/dl in Velika Krsna and Belgrade and 50 mg/dl in Zrenjanin. Altogether, after 25 years, serum cholesterol had increased by 15% in Belgrade, 35% in Velika Krsna and 45% in Zrenjanin [21–24].

The increase in CHD mortality could be monitored inspecting the cumulated hazard rates derived from the Weibull distribution that represents the acceleration in mortality during the follow-up. These levels in Serbia overtook one by one (Fig. 1) those of all the other countries [25]. As a consequence of this acceleration, the CHD cumulative death rate in Serbia after 40 years reached the levels of the US and the Netherlands, lower only to the Finnish rate that was the highest in the Seven Countries.

A peculiarity within the Seven Countries cohorts was that incidence and mortality from CHD in Belgrade during the first 25 years of follow-up and even before were perfectly in line with the expectations, based on entry levels of serum cholesterol and saturated fatty acid consumption, while all-cause mortality was definitely the lowest within the Seven Countries Study countries and similar to that of Crete [19,20,26]. This suggests that the possible “healthy worker effect” and/or the higher socio-economic status of the Belgrade Professors was protective only for morbid and fatal conditions other than CHD. To complete the picture it should be recalled that in a large Serbian study started in the 1960s in collaboration with the Framingham Study group, incidence and mortality from CHD in the subsequent 7 years were relatively low, as in the Seven Countries Study data, with a level that was definitely lower than that recorded in the Framingham study [27,28].