Original Articles

Is Immigration Associated with an Increase in Risk Factors and Mortality among Coronary Artery Disease Patients? A Cohort Study of 13,742 Patients

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Abstract

Background: Clinical studies showing an association between immigration and increased prevalence of coronary risk factors or mortality rate in patients with coronary artery disease are scarce.

Objectives: To compare the risk profile and mortality of coronary patients born in Israel with those who immigrated to Israel, and to determine whether recent immigration is associated with greater risk among immigrants from the Soviet Union.

Methods: Demographic, clinical, and laboratory data were collected on chronic coronary artery disease patients from 18 Israeli medical centers during the screening period of the Bezafibrate Infarction Prevention Study in the early 1990s. Data on mortality after a mean 7.7 year follow-up were obtained from the Israel Population Registry.

Results: While significant differences in mortality (14.7% vs. 18.5%, $P < 0.001$) were observed between Israeli-born patients and immigrants respectively, the mortality in these groups was similar when compared within specific age groups. Immigrants suffered more from hypertension and angina pectoris, and their New York Heart Association functional limitation class was higher, as compared to their Israeli-born counterparts. A multivariate analysis of mortality comparing patients from the Soviet Union who immigrated after 1970 with those who immigrated before 1970 showed an increased risk for newer immigrants, with a hazard ratio of 1.69 (95% confidence interval 1.19-2.40) for those immigrating between 1970 and 1984, and 1.68 (95% CI 1.01-2.28) for those immigrating between 1985 and 1991.

Conclusion: The worse profile and prognosis observed among patients who recently emigrated from the Soviet Union cannot be explained by traditional risk factors for CAD such as smoking, diabetes, hypertension, and lipid disorders. Further investigation, including variables such as psychological stress to which immigrants are more exposed than others, is needed.

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It is well known that psychosocial factors such as emotional and occupational stress are strongly associated with the development and course of coronary disease [1–6]. Immigration is a complex process of adaptation to many environmental factors and can be adapted to a "live model" of sociopsychological stress. The ethnically diverse Israeli population comprises many immigrants, some of whom arrived in large waves of migration from several countries or geographic areas during specific periods throughout Israel's history. One of the more recent waves of immigration consisted of one million immigrants from the Soviet Union who arrived in Israel in the early 1990s.

The compiling of a registry of chronic coronary artery disease patients in Israel during the early nineties provided an opportunity to investigate differences in the prevalence of coronary risk factors and mortality between patients born in Israel and immigrants. In addition, the availability of data on the year of immigration to Israel enabled a comparison of risk according to length of time in Israel.

The purpose of the present analysis was to compare the CAD risk profile, functional limitations, and mortality between CAD patients who were born in Israel and those who immigrated to Israel. Furthermore, in the case of immigrants from the Soviet Union, an attempt was made to determine whether recent immigration is associated with greater risk than earlier immigration.

Patients and Methods

Between 1 February 1990 and 30 October 1992, clinical data on more than 20,000 male and female patients aged 45 to 74 years and presumed to have CAD were recorded in the log books of 18 cardiology departments in Israel. A total of 15,524 patients with an established diagnosis of CAD were screened for inclusion in the Bezafibrate Infarction Prevention Study, and they constitute the population of the BIP registry [7]. The BIP study, a placebo-controlled secondary prevention study, was conducted in 3,122 patients with the aim of assessing the efficacy of the long-term administration of bezafibrate on the reduction of fatal and non-fatal coronary events in CAD patients [7].

All the patients screened in the BIP study underwent a medical examination and a blood test after fasting for 14 hours. Medical, historical and demographic data, as well as date of immigration and drug intake data were recorded. The diagnosis of CAD was made in

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CI = confidence interval
CAD = coronary heart disease

BIP = Bezafibrate Infarction Prevention Study

patients with documented myocardial infarction or typical angina pectoris, a positive exercise test, evidence of myocardial ischemia revealed by radionuclear studies, or at least 60% stenosis of one of the major coronary arteries. Patients who had undergone percutaneous transluminal coronary angioplasty or coronary artery bypass graft were considered for inclusion if the procedure had been performed at least 6 months prior to the study.

Mortality data on the screened patients, after a mean follow-up period of 7.7 years (range 6–9 years), were obtained by matching the patients' identification numbers with the life status as recorded in the Israel Population Registry. Death certificates and diagnosis of hospital discharge were coded using the system described in the 9th edition of the International Classification of Disease (ICD-9). Data on mortality were unavailable for 827 patients who were therefore excluded from the present analysis. In addition, due to the vast cultural differences between Jewish and Arab patients as well as their exposure to different environmental factors, it was decided to exclude from analysis 922 Arab patients who had been screened for the BIP study. An additional 33 patients were excluded because of missing data regarding country of birth. The 13,742 remaining patients constitute the study population for this analysis.

In order to assess the association between immigration and coronary risk factors and mortality, several different comparisons were conducted. The first compared patients born in Israel (n = 1,850) with those who immigrated (n = 11,892). This comparison is also presented by age group due to significant differences in mean age between Israeli-born and immigrant patients. The age groups used were ⩽ 55 years, 56–65, and ⩾ 66.

An additional analysis focused specifically on CAD patients who emigrated from the Soviet Union, most of whom are Ashkenazi Jews, thus representing a large relatively homogeneous group without large ethnic variations. Those included in this study emigrated from the Soviet Union between January 1921 and January 1991 (n = 1,275), and were divided into three groups according to the length of time they had lived in Israel. The first group of patients immigrated to Israel between 1921 and 1970, and had lived in the country for more than 21 years (n = 359) at the time of screening for the BIP study. The second group immigrated between 1971 and 1984 (n = 688), and had lived in Israel for 7–20 years prior to screening. The third group comprises newer immigrants who had lived in Israel for less than 6 years, having immigrated between 1985 and 1991 (n = 228). The prevalence of CAD risk factors, functional limitation and mortality were compared among these groups.

Statistical methods

Results of continuous variables are reported as mean values ± SD. The chi-square and Student *t*-test or ANOVA were used to determine the significance of differences between proportions and means respectively. The adjusted relative risk of mortality associated with recent immigration was estimated using the Cox proportional hazard model, adjusting for age, female gender, past myocardial infarction, diabetes, hypertension, angina pectoris,

NYHA = New York Heart Association

Table 1. Baseline characteristics of immigrant vs. Israeli-born CAD patients

	All immigrants (n=11,892)	Israeli-born (n=1,850)	*P*
Morbidity (%)			
CVA	1.8	1.0	<0.01
Diabetes	18.8	17.9	0.3
PVD	4.2	3.6	0.2
MI per history	71.3	75.3	0.02
Hypertension	34.3	31.5	0.02
COPD	3.0	1.5	<0.001
TIA	0.9	1.1	0.6
Lipid profile (mean ± SD, mg/dl)			
Total cholesterol	224.1±39.3	225.3±39.1	0.12
HDL-cholesterol	38.1±10.3	37.0±9.7	<0.001
LDL-cholesterol	155.4±34.1	156.9±34.3	0.04
Triglycerides	154.8±86.1	160.0±90.2	0.02
CAD risk factors			
Smoking (%)	10.1	9.9	0.8
Systolic BP (mean, mmHg)	135.±19.6	131.8±18.1	<0.001
Diastolic BP (mean, mmHg)	81.5±9.8	81.1±10.1	0.07
Glucose (mean, mg/dl)	113.6±44.6	112.9±46.6	0.48
Body weight (kg)	74.5±11.4	78.5±12.1	<0.001

BP = blood pressure, COPD = chronic obstructive pulmonary disease, CVA = cerebrovascular accident, MI = myocardial infarction, PVD = peripheral vascular disease, TIA = transient ischemic attack

NYHA functional class ⩾ 2, history of stroke, peripheral vascular disease, chronic obstructive pulmonary disease, smoking, and inclusion in the BIP study.

Results

The comparison between immigrants and Israeli-born patients showed that immigrants were older, with a mean age of 60.6 vs. 56.6 years (*P* < 0.001), respectively, and they included a greater proportion of women (20.1% vs. 13.9%, *P* < 0.001). Table 1 summarizes the co-morbidity, lipid profile, and CAD risk factors of these two groups of patients. Immigrants were shown to have increased rates of morbidity from stroke and hypertension, as well as increased levels of systolic arterial pressure and diastolic arterial pressure. There were no differences in the prevalence of risk factors such as smoking, diabetes mellitus, total blood cholesterol and blood glucose. However, Israeli-born patients showed lower high density lipoprotein levels, higher low density lipoprotein and triglyceride levels and higher total body weight (78.5 vs.74.5 kg, *P* < 0.001). Immigrants suffered more often from angina pectoris (60.7 vs. 47.7%) and were more likely to use nitrates (51.0 vs. 40.9%, *P* < 0.0000) and calcium-channel blockers (51.5 vs. 40.9%, *P* < 0.001). A significant difference in mortality was observed between immigrants (18.5%) and patients born in Israel (14.7%) (*P* < 0.001).

Because of significant differences in the mean age of the immigrant and Israeli-born patients (60.6 vs. 56.6), and the substantial role that age plays in predicting mortality and risk factors, we divided the patients by age groups and compared mortality rates and risk factors in the same age groups [Table 2]. The groups of younger and middle-aged immigrants (aged ⩽ 65) included a greater proportion of women in comparison to Israeli-

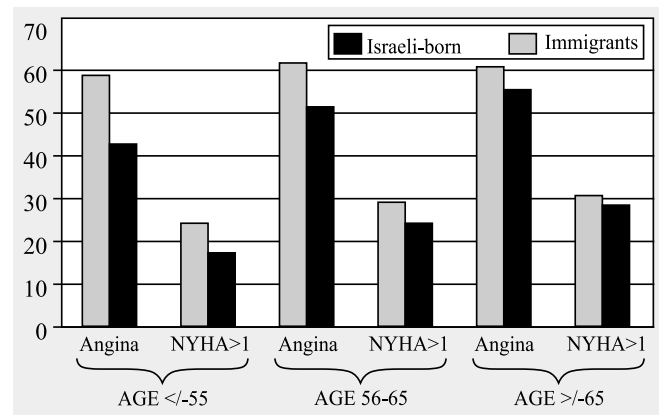Immigration and Prognosis of CAD Patients

Table 2. Baseline characteristics of immigrant vs. Israeli-born CAD patients by age group

Characteristics and co-morbidity (%)	Age ⩽ 55			Age 56–65			Age ⩾ 66		
	Immigrants (n=2,684)	Israeli-born (n=836)	P	Immigrants (n=2,684)	Israeli-born (n=836)	P	Immigrants (n=2,684)	Israeli-born (n=836)	P
Mean age (yr ± SD)	50.6±3.5	50.3±3.5	NS	60.9±2.8	60.3±2.9	<0.001	68.0±1.8	67.7±1.5	0.04
Women	12.0	9.4	0.04	20.9	16.8	<0.01	25.3	20.5	NS
CVA	1.4	0.8	0.2	1.9	1.0	0.08	2.2	1.9	0.8
MI per history	73.7	76.9	0.07	71.0	74.8	0.02	70.2	70.7	0.9
Hypertension	26.3	27.4	0.5	35.7	35.7	0.99	37.4	31.6	0.09
COPD	1.8	1.4	0.5	3.6	0.9	<0.001	3.2	4.2	0.4
Angina	57.6	42.2	<0.001	61.7	50.8	<0.001	60.1	54.9	0.13
NYHA class ⩾2	23.6	16.6	<0.001	28.2	23.8	<0.01	30.2	27.9	0.5
Lipid profile (mean ± SD, mg/dl)									
Total cholesterol	224.1 ±38.2	226.8 ±40.0	0.07	225.1 ±39.0	225.4 ±37.9	0.8	221.8 ±40.0	219.0 ±39.3	0.3
HDL-cholesterol	35.9 ±9.1	35.8 ±9.3	0.8	38.3 ±10.2	37.6 ±9.8	0.08	39.4 ±10.9	38.8 ±10.5	0.4
LDL-cholesterol	154.8 ±33.4	157.7 ±35.4	0.03	156.3 ±33.8	157.5 ±32.8	0.4	154.0 ±34.5	151.7 ±34.9	0.3
CHD risk factors									
Smoking (%)	15.4	11.5	<0.01	10.1	8.9	0.3	6.1	7.4	0.4
Systolic BP (mean, mmHg)	128.9 ±17.8	128.5 ±16.9	0.6	136.1 ±19.4	133.7 ±18.4	<0.001	139.2 ±19.8	137.7 ±19.0	0.3
Diastolic BP (mean, mmHg)	80.7 ±9.8	80.9 ±10.1	0.7	81.7 ±9.9	81.6 ±10.1	0.9	81.6 ±9.6	80.3 ±10.0	0.07
Glucose (mean, mg/dl)	112.6 ±47.7	109.2 ±43.6	0.07	114.2 ±43.6	116.1 ±49.5	0.3	113.0 ±43.1	115.7 ±46.4	0.4
Body weight (kg)	77.2 ±12.0	80.0 ±12.1	<0.001	74.6 ±11.3	78.0 ±12.1	<0.001	72.4 ±10.9	74.9 ±10.8	0.001
Medication (%)									
Nitrates	44.5	27.2	<0.001	51.0	42.3	<0.001	55.7	45.1	0.003
Ca-blockers	44.8	36.0	<0.001	52.9	46.2	<0.001	54.9	43.3	<0.001
ACE inhibitors	7.9	6.8	0.3	11.3	11.3	0.99	12.0	12.1	0.98
Aspirin	61.5	70.9	<0.001	57.9	66.7	<0.001	56.8	59.5	0.43
Diuretics	9.2	6.5	0.01	15.9	14.5	0.3	21.1	17.2	0.2

born patients. There were no differences between immigrants and Israeli-born patients with regard to the proportion of patients with a history of stroke, diabetes, peripheral vascular disease, or hypertension. A history of myocardial infarction was more common among middle-aged men who were Israeli-born than among immigrants, and a history of chronic obstructive pulmonary disease was more frequent among middle-aged immigrants than among Israeli-born patients in the same age group. Younger and middle-aged immigrants were more likely to suffer from angina (P < 0.001 for both age groups), and their NYHA functional class indicated greater limitation (P < 0.001 and P < 0.01 for young and middle-aged patients, respectively), in comparison to Israeli-born patients of the same age [Figure 1]. Younger immigrants were more likely to be smokers, but had lower LDL-cholesterol levels than Israeli-born patients (154.8 ± 33.4 vs. 157.7 ± 35.4 mg/dl, P = 0.03). Among patients aged 55–65, immigrants were older and had higher mean systolic blood pressure than Israeli-born patients. In all age groups, the body weight of immigrants was significantly lower than that of Israeli-born patients, and immigrant patients suffered more from angina pectoris and consequently took nitrates and Ca-channel blockers more frequently (P < 0.001) than their Israeli counterparts. The use of aspirin was less frequent among immigrants at younger ages (P < 0.001).

When analyzed by age group, mortality rates were similar among immigrants and Israeli-born patients (age ⩽ 55: 9.6 vs. 9.9%, age 56–65: 17.9 vs. 16.6%, age ⩾ 66: 26.8 vs. 26.0%).

A comparison among patients who immigrated to Israel from the Soviet Union by the time period in which they immigrated is presented in Table 3. A significant difference in mortality rates was found between immigrants who had lived in Israel for less than 20 years (18.8% and 17.0% for groups 2 and 3 respectively), and immigrants who had lived in Israel for more than 21 years (12.0%). Noteworthy is the absence of statistically significant differences

Figure 1. Angina and NYHA Functional Class of immigrant vs. Israeli-born CAS patients by age group

LDL = low density lipoprotein

Table 3. Characteristics of immigrants from the Soviet Union by time of immigration

	Group 1: Veterans >21 yr	Group 2: Veterans >7 yr	Group 3: New immigrants	P
Morbidity (%)				
MI	69.9	70.5	66.7	0.75
Diabetes mellitus	16.4	19.0	15.0	0.53
Hypertension	35.1	41.1	36.1	0.13
CVA	1.7	2.0	2.0	0.96
PVD	3.6	4.8	4.8	0.6
COPD	2.2	3.2	2.7	0.3
Lipid profile (mean ± SD, mg/dl)				
Total cholesterol	227.8±37.1	225.1±38.3	221.0±44.1	0.22
HDl-cholesterol	39.6±10.9	38.1±10.3	37.5±8.5	0.05
LDL-cholesterol	159.0±33.4	156.7±33.2	153.8±36.1	0.3
Triglycerides	150.7±83.2	153.0±81.8	140.3±67.4	0.1
CAD risk factors				
Smoking (%)	9.5	8.0	8.8	0.83
Systolic BP (mean, mmHg)	134.8±48.6	136.4±21.1	134.5±20.0	0.26
Diastolic BP (mean, mmHg)	81.1±9.1	82.0±10.8	80.7±10.5	0.18
Glucose (mean, mg/dl)	107.1±32.3	113.9±47.2	108.8±39.6	0.06
Body weight (kg)	74.3±11.8	76.2±10.9	75.1±11.0	0.06
Angina, NYHA functional class & mortality				
Angina pectoris (%)	61.3	70.8	76.9	<0.001
NYHA class ≥2 (%)	28.1	31.1	43.5	0.03
Mortality (%)	12.0	18.8	17.0	0.04

between the groups in the prevalence of most CAD risk factors, except for HDL level. However, newer immigrants suffered much more from angina pectoris and heart failure as defined by the NYHA functional limitation classification. The mean age of the patients in each of the three groups was similar: 60.9 years for those who immigrated between 1921 and 1970, 60.0 years for those who arrived in Israel between 1971 and 1984, and 61.2 years among newer immigrants (1985–1991).

A multivariate analysis of mortality, comparing patients who immigrated from the Soviet Union during the period 1971–1984 and 1985–1991 with those who immigrated before 1970, showed an increased risk for newer immigrants, indicated by a hazard ratio of 1.69 (95% CI: 1.19-2.40) for those immigrating between 1971 and 1984, and 1.68 (95% CI: 1.01-2.28) for those immigrating between 1985 and 1991.

Discussion

To the best of our knowledge, the literature does not contain studies on the effect of immigration, as an adaptation process, on risk factors and mortality of coronary artery disease patients. Problems of organism adaptation to environmental factors have been especially relevant to Israel for the past 25 years, during which more than 1 million people emigrated from the northern hemisphere. In the coming 5–10 years this flow is not expected to cease.

HDL = high density lipoprotein

New immigrants have to adapt themselves to numerous aspects of environment (weather-climatic, language, professional, social and psychological) which, occurring simultaneously, can be overwhelming for the majority of them, and under certain conditions may cause a rebuilding of metabolism with development of a state of stress. Reaction to environmental stress factors may be aggravated by personality disorders, social isolation, hopelessness, frustration, depressed affect, professional overloads of an emotional nature (lack of time, hyperstimulation), lack of emotional vents, and lack of job satisfaction [4,8,9]. Unfavorable stress influences the cardiovascular system and may be connected mainly with an increase in sympathetic nervous system tonus, which is followed by stimulation of heart metabolism, increase in blood pressure, blood coagulation rise, hypercholesterolemia, increase in myocardial unexcitability, and is often accompanied by heart system disorders, development of coronarospasm and anginal attack [8–12].

In a large Israeli population of CAD patients, we observed a lower total mortality in Israeli-born patients compared with immigrants. This can probably be explained by significant differences in mean ages of the groups (the Israeli-born are younger). Within specific age groups, total mortality rates of Israeli-born patients and immigrants were similar. However, immigrants suffered much more than Israeli-born patients from hypertension and angina pectoris, and used nitrates and Ca-channel blockers more frequently. Also, NYHA functional limitation class was higher in immigrants, especially younger ones. A similar pattern of mortality with respect to ethnic origin was observed in the SPRINT registry population, which comprised Israeli patients hospitalized for acute myocardial infarction between the years 1981 and 1983 [13].

The significantly higher rates of total mortality, angina pectoris, and heart failure observed in the group of patients who recently emigrated from the Soviet Union cannot be explained only by statistically significant differences in HDL blood levels, body weight, and blood glucose levels in comparison to immigrants who have been living in Israel for longer. The CAD patients who recently emigrated from the former USSR are a relatively homogeneous group, without significant age and ethnic variation.

The prevalence of other risk factors such as smoking, elevated total cholesterol, hypertension and high LDL levels in this group was similar to that of immigrants from the Soviet Union who had immigrated earlier. It is possible that there are other unknown factors that were not assessed in our study but affect newer immigrants. For example, one could speculate that psychological

and social stress, as well as misadaptation, which may have accompanied the process of acclimation to a new culture and environment, could have contributed to their increased mortality rate. An earlier study performed in Haifa showed that new immigrants had the largest number of cases of significant triple vessel disease in all age groups, including those under 50 [14].

It is also possible that the poorer cardiovascular profile of newer immigrants from the Soviet Union may be a reflection of the high rate of mortality that has been observed in Eastern European compared to Western European countries over the past few decades [15]. It has been suggested that the high death rates from coronary heart disease in Eastern Europe may be partially explained by the failure of the political and economic system to satisfy population needs, both from a material and psychosocial perspective [16]. Psychological stress experienced over an extended period in the Soviet Union, compounded by the psychological stresses of immigration, may explain the increased risk of these immigrants. In addition, these immigrants did not receive advanced western-standard medical treatment in their home country because of deficits and crises in medicine in the Soviet Union. They probably came to Israel with advanced coronary artery disease. Also, advanced techniques such as coronary angiography and cardiac scans, which enable early diagnosis of CAD, were not easily accessible to the immigrants before they left the Soviet Union. This may explain the insufficient early diagnosis of CAD in this country. CAD risk factors were not independently predictive of total mortality among the newer immigrant population.

On the basis of the above mentioned findings, further investigation of immigration is needed in order to assess the role of other possible risk factors, such as psychological stress. It is necessary to develop several approaches to increase our under-standing of the adaptive processes of large human contingents, which could aid in conducting prophylactic programs specific for immigrant populations.

References

1. Ketterer MW. Secondary prevention of ischemic heart disease. The case for aggressive behavioral monitoring and intervention. *Psychosomatics* 1993;34(6):478–84.
2. Suadicani P, Hein HO, Gyntelberg F. Are social inequalities as associated with the risk of ischemic heart disease a result of psychosocial working conditions? *Atherosclerosis* 1993;101(2):165–75.
3. Wahrborg P. Mental stress and ischaemic heart disease: an under-estimated connection. *Eur Heart J* 1998;19(Suppl):20–3.
4. Gonzalez MA, Rodriguez Artalejo F, Calero JR. Relationship between socioeconomic status and ischaemic heart disease in cohort and case-control studies. *Int J Epidemiol* 1998;27(3):350–8.
5. Emdad R, Belkic K, Theorell T, Cizinsky S, Savie C, Olsson K. Psychophysiologic sensitization to headlight glare among professional drivers with and without cardiovascular disease. *J Occup Health Psychol* 1998;3(2):147–60.
6. Stewart MJ, Hirth AM, Klassen G, Makrides L, Wolf H. Stress, coping, and social support as psychological factors in readmissions for ischaemic heart disease. *Int J Nurs Stud* 1997;34(2):151–63.
7. The BIP Study Group. Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: The Bezafibrate Infarction Prevention (BIP) Study. *Circulation* 2000;102:21–7.
8. Anda R, Williamson D, Jones D, et al. Depressed affect, hopelessness, and the risk of ischemic heart disease in a cohort of U.S. adults. *Schriftenr Ver Wasser Boden Lufthyg* 1993;88:135–66.
9. Netterstom B, Suadicani P. Self-evaluated job satisfaction and ischemic heart disease. A 10-year follow-up study of bus drivers in a big city. *Ugeskr Loeger* 1994;156(36):5110–14.
10. Valkonen T. Psychosocial stress and sociodemographic differentials in mortality from ischaemic heart disease in Finland. *Acta Med Scand Suppl* 1982;660:152–64.
11. Elliott SJ, Dean A. An ecologic analysis of psychosocial stress and heart disease in British Columbia. *Can J Public Health* 1998;89(2):137–41.
12. Belkic K, Emdad R, Theorell T. Occupational profile and cardiac risk: possible mechanisms and implications for professional drivers. *Int J Occup Med Environ Health* 1998;11(1):37–57.
13. The Secondary Prevention Reinfarction Israeli Nifedipine Trial (SPRINT) Study Group. Ethnic differences in mortality of male and female patients surviving acute myocardial infarction: long-term follow-up of 5,700 patients. *Eur J Epidemiol* 1997;13:745–54.
14. Abinader EG, Sharif DS, Kharash L, Mamedov K. The impact of new immigrants from the former Soviet Union on the severity of coronary angiographic findings in a public hospital in Israel. *IMAJ* 2000;2:274–7.
15. Marmot MG. Socio-economic factors in cardiovascular disease. *J Hypertension* 1996;14(Suppl 5):S201–5.
16. Bobak M. East-West mortality divide and its potential explanations: proposed research agenda. *Br Med J* 1996;312:421–5.

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