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Associations between Area of Residence and Cardiovascular Risk

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Abstract

Cardiovascular disease (CVD) is the primary cause of death in many developing countries. The most preventable form of CVD is coronary heart disease (CHD). The present study aimed to identify cardiovascular risk factors and correlation with atherosclerotic cardiovascular disease in 364 patients from a rural community in Romania. There were assessed the traditional risk factors for cardiovascular disease. We used descriptive statistic method to calculate the average and standard deviation of assessed parameters. The data were processed by using the Kolmogorov-Smirnov (K-S) test. Risk scores were calculated by using the University of Edinburgh Risk Calculator. The mean value of systolic blood pressure was 130.9 mmHg, total cholesterol of 3.38 mmol/l, and HDLc 1.33 mmol/l. The risk of coronary heart disease (CHD) was significantly higher in urban than in rural (8.03% vs 6.6%). The risk of myocardial infarction (MI) was higher in urban than in rural, too (4.5% vs 2.8%). The risk for cardiovascular disease was significantly higher in urban than in rural (19.4% vs 12.9%). There was no significant risk of stroke, coronary heart disease or death due to cardiovascular disease in urban or rural. Further studies will establish the main mechanism of linkage between and tightly correlation with cardiovascular risk factors.

Keywords: cardiovascular disease, cardiovascular risk, coronary heart disease, myocardial infarction, area of residence.

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Introduction

The assessment of the developing risk for a cardiovascular disease, in general population, is based on assessing the complete profile of cardiovascular risk factors. Despite recent declines in age-adjusted mortality, cardiovascular disease (CVD) is the primary cause of death in many developing countries. The most preventable form of CVD is coronary heart disease (CHD). In the United States, CHD annually results in 502,000 deaths, of which 185,000 are due to myocardial infarction (MI); economic burden is $133 billion (Tamam, 2014). American Health Association policy statement concluded that costs will rise to more than $1 trillion annually in the United States by the year 2030 and preventive measures are required (Weintraub *et al.*, 2011). By the year 2020, CHD is estimated to become the leading cause of death and disability worldwide. Evidence show that atherosclerotic disease and its consequences may be slowed down by preventive measures. Primordial prevention usually refers to healthy lifestyle choices to prevent the development of coronary risk factors (Strasser, 1978). A review which examined 55 trials that intended to reduce multiple risk factors suggested that intervention results in small reductions in risk factors (blood pressure, cholesterol, and smoking), but has little or no impact on the risk of CHD mortality or morbidity (Ebrahim *et al.*, 2011). That suggests that especially in developing countries a different approach to behavior change is needed. Global cardiovascular risk assessment represents an important goal to be achieved not only in individuals with overt clinical manifestations of atherosclerotic disease; it has the same importance in healthy individuals. Early detection of risk factors is important to establish both primary and secondary preventive measures which may lead to decreased morbidity and mortality and reduced hospitalization costs. In a much broader sense, risk factors include characteristics of lifestyle, certain biochemical and physiological characteristics and some individual modifiable factors (Mahmood *et al.*, 2014).

The term “risk factor” appeared around 1960's when many epidemiological data suggested a high correlation between some population characteristics and the prevalence of ischaemic heart disease. The Framingham Heart Study is the origin of the term risk factor. Thomas Dawber was the director of the study between 1949 and 1966, his name being close related by the future epidemiological research of risk factors (Dawber *et al.*, 1951).The objective of the Framingham Heart Study was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke. The researchers recruited 5,209 men and women aged between 30 and 62 years from the town of Framingham, Massachusetts, and began the first round of extensive physical examinations and lifestyle interviews that they would later analyze for common patterns related to CVD development.

In the 1950s, it was believed that atherosclerosis was a normal phenomenon of aging and occurred universally as people became older. High blood pressure and elevated serum cholesterol were also seen as normal consequences of aging in the 1950s. These and further risk factors, e.g., homocysteine, were gradually discovered over the years (Kannel *et al.*, 1976, Lloyd-Jones *et al.*, 2001, Sundstrom *et al.*, 2005, O'Donnell *et al.*, 2008). A microorganism involved in respiratory infections, *Chlamydophila pneumonia*, was first associated with atherosclerosis and coronary heart diseases in 1986, and this bacteria is highly likely to be a modifiable risk factor that may be a target of future therapies (Blasi *et al.*, 2009).

The Framingham Heart Study, along with other important large studies, e.g., the Seven Countries Study, Nurses' Health Study, Women's Health Initiative, also showed the importance of healthy diet, not being overweight or obese, and regular exercise in maintaining good health, and that there are differences in cardiovascular risk between men and women (Millen *et al.*, 2001). It also confirmed that cigarette smoking is a highly significant factor in the development of heart disease, leading to angina pectoris, myocardial infarction (MI), and coronary death (Freund *et al.*, 1993, Doll *et al.*, 2004).

Major findings from the Framingham Heart Study, according to the researchers themselves were: (1) In 1960 was established that cigarette smoking, increased cholesterol and elevated blood pressure increase risk of heart disease and they were considered major risk factors for ischaemic heart disease. Exercise decreases risk of heart disease, and obesity increases it; (2) In 1970 – was established that elevated blood pressure increases risk of stroke. In women who are postmenopausal, risk of heart disease is increased, compared with women who are premenopausal. Psychosocial factors were involved as risk factors for heart disease. In 1980 was established that high levels of HDL cholesterol reduce risk of heart disease; (3) In 1990 left ventricular hypertrophy was incriminated to increase risk of stroke. Elevated blood pressure can progress to heart failure. Framingham Risk Score is published, and correctly predicts 10-year risk of future coronary heart disease (CHD) events. At 40 years of age, the lifetime risk for CHD is 50% for men and 33% for women (Murabito, 1995); (4) In 2000 – a new term – the so called "high normal blood pressure" was incriminated to increase risk of cardiovascular disease (high normal blood pressure is defined as a systolic pressure of 120–139 mm Hg and/or a diastolic pressure of 80–89 mm Hg). Lifetime risk of developing elevated blood pressure is 90%. Obesity is considered also a risk factor for heart failure. Serum aldosterone levels predict risk of elevated blood pressure. Lifetime risk for obesity is approximately 50%. The "SHARe" project is announced, a genome wide association study within the Framingham Heart Study. Social contacts of individuals are relevant to whether a person is obese, and whether cigarette smokers decide to quit smoking. Four risk factors for a precursor of heart failure are discovered. 30-year risk for serious cardiac events can be calculated. American Heart Association considers certain genomic findings of the

Framingham Heart Study one of the top research achievements in cardiology. Some genes increase risk of atrial fibrillation.

Busselton Health Study has been carried out since 1966 in a high proportion of the residents of Busselton, a town in Western Australia, over a period of many years. A database has been com-piled and is managed by the School of Population Health at the University of Western Australia. Although the results of the Busselton Health Study and the Framingham Heart Study are similar in many aspects, the Busselton Health Study investigated also the influence of some factors that had not been investigated in the Framingham Heart Study, e.g., sleep apnea (Knuiman *et al.*, 1997, Marshall *et al.*, 2009). The Caerphilly Heart Disease Study, also known as the Caerphilly Prospective Study (CaPS), is an epidemiological prospective cohort, set up in 1979 in a representative population sample drawn from a typical small town in South Wales, UK. The study has collected wide ranging data and has led to over 400 publications in the medical press, notably on vascular disease, cognitive function and healthy living (The Caerphilly and Speedwell Collaborative Group, 1984, Elwood *et al.*, 2013). China-Cornell-Oxford Project, also known as "China-Oxford-Cornell Study on dietary, lifestyle and disease mortality characteristics in 65 rural Chinese counties". This study was later referred to as "China Study I". The successor study is named "China Study II" (Segelken, 2001). There should be underlined that risk factors have a high predictibility for atherosclerosis and ischemic heart disease; the relationship is not strictly causal. They especially indicate a "predisposition" for disease (Elwood *et al.*, 2010). Multidisciplinary research has identified three major risk factors: hypertension, dyslipidemia and smoking. Cardiovascular risk factors may be modifiable (ie those factors that can be modified by diet or pharmacological measures, such as smoking, dyslipidemia, hypertension, obesity, diabetes) or non-modifiable (age, sex, genetic factors).

A population-based study conducted more recently in 2004 in 52 countries, 5 continents (the INTERHEART study) led to the identification of nine risk factors involved in the onset of acute myocardial infarction: smoking, dyslipidemia, hypertension, diabetes, obesity diet, physical inactivity, alcohol consumption, psychosocial factors. A number of risk factors are involved in the occurrence of other cardiovascular disease, coronary heart disease outside: chronic alcoholism is associated with increased incidence of dilated cardiomyopathy and arrhythmias (Annand *et al.*, 2008). Starting from these theoretical premises, the present study aimed to identify cardiovascular risk factors and correlation with atherosclerotic cardiovascular disease in a rural community in Romania.

Material and method

The study was conducted by general practitioners in Suceava County. The study group consisted in 364 patients, from rural and urban area, followed by general practitioners. The exclusion criteria in this study were: previous personal history of cerebrovascular diseases (stroke, acute coronary syndrome), patients younger than 18 years, patient refusal, presence of psychiatric, cognitive or other diseases that might alter the understanding of the study objectives or the ability to provide accurate information. Those who did not complete the interview were recorded as having refused to participate and were taken into account when calculating the refusal rate, but excluded from the final analysis. Thus, 12,1% of the initial sample's participants were excluded. Descriptive statistics was used to calculate the average and standard deviation of assessed parameters. The data didn't have Gaussian distribution so the nonparametric statistical tests were used. For all analyses a p value < 0.05 was considered significant; all were undertaken using the Statistical Package for Social Science (SPSS) program for Windows Version 13.0 (SPSS 13.0, Chicago, IL, USA). The traditional risk factors for cardiovascular disease were assessed. A standardized questionnaire provided information on age, area of residence, smoking status and the number of cigarettes smoked on a daily basis. Weight, height and blood pressure were measured in duplicated and recorded according to the standard protocol. In order to determine cardiovascular risk scores plasma cholesterol levels, HDLc, LDLc, and glycaemia were determined. The presence of diabetes was considered for those patients with history of diabetes or in the presence of 2 values of glycaemia higher than 126 mg/dl. Risk scores were calculated by using the University of Edinburgh Risk Calculator. Risk scores are for estimating the probability of cardiovascular disease for individuals who have not already developed any major atherosclerotic disease. This calculator is intended for use by health professionals. It was originally developed to provide online charts based on the design of the well known Joint British Societies (JBS) Cardiovascular Disease Risk Prediction Charts, developed by The University of Manchester, and published in the British National Formulary (BNF). The calculator can produce risk scores based on the following scores: Framingham, Joint British Societies (JBS) / British National Formulary (BNF), ASSIGN. Time period to calculate risk over can be varied between 4 and 12 years for any of the Framingham calculations, but it is fixed at 10 years for the BNF or ASSIGN scores. The main parameters we used were: age, gender, smoking, number of cigarettes/day, family history of diabetes, Scottish Index of Multiple Deprivation (SIMD) which was considered as value of 20, systolic arterial blood pressure, total cholesterol and HDL (mmol/l). We used the Edinburgh Risk Calculator to determine the probability to develop a myocardial infarction, cerebral stroke and death in next 10 years.

Results and discussions

In the analyzed group predominated women (n = 195; 61.1%) and people in rural areas (n = 228; 71.5%). It assessed the presence of traditional risk factors. Thus 63 persons (19.7%) were smokers, 70 (21.9%) had one first degree relative with cerebrovascular disease and 55 (17.2%) were known to have diabetes. Smokers admitted to smoking an average of 11.05 ± 4.97 cigarettes/day. The mean value of systolic blood pressure was 130/90 mmHg, total cholesterol of 3.38mmol/l, and HDLc 1.33 mmol/l. These parameters were assessed to estimate the risk of coronary heart disease, myocardial infarction, stroke and death due to cardiovascular disease over 10 years (Table 1). Using the University of Edinburgh Risk Calculator we noticed that in the study group, the probability to develop a myocardial infarction, in next 10 years, was 3.37%, and for cerebral stroke was 4.08%. The probability of death due to cardiovascular disease was 3.99% (Table 2). The risk of coronary heart disease (CHD) estimated by Framingham equation was significantly higher in urban than in rural (8.03% vs 6.6%; Std. Deviation 6.31; p = 0.034). The risk of myocardial infarction (MI) was higher in urban than in rural, too (4.5% vs 2.8%; Std. Deviation of 5.02; p = 0.002). There was no significant risk of stroke, cardiovascular disease, death due to coronary heart disease or death due to cardiovascular disease in urban or rural. The risk for cardiovascular disease estimated by ASSIGN equation was significantly higher in urban than in rural (19.4% vs. 12.9%; Std. Deviation 15.9; p = 0.002) (Table 3).

In some studies, the authors showed that case-fatality rates were highest in the middle- and low-income countries. In total, in high-income countries, 6.5% of individuals died following an MI, stroke, or heart-failure hospitalization in high-income countries vs. 15.86% in middle-income countries and 17.28% in low-income countries (O'Riordan, 2014). A population-based study of Ontario patients with chronic CAD found differences in use of laboratory testing and apparent access to physicians in rural vs. urban dwellers, but these did not affected the rates of hospitalization or 1-year survival or any differences in risk adjusted mortality or in cardiac hospitalizations (47.2% vs. 46.3%) (Busko, 2014).

In Tehran lipid and glucose study, performed in 15005 subjects, the prevalence and distribution of high blood pressure, cigarette smoking, dyslipoproteinemia, diabetes mellitus, and obesity was determined. In adults, 78% of men and 80% of women presented at least one CVD risk factor. The percentage of adult women with two or more risk factors was significantly greater than for men. The Prevalence of DM was 9.8%, of hypertension 20.4%, of total cholesterol 19.3% and smoking was 22.3% (Azizi, 2002). Another study, including a cohort of 4535 Indian adults, investigated the prevalence of cardiovascular risk factors by socio-economic position. This study showed that lower fruit intake and higher tobacco and alcohol use were found in those with lower socio-economic conditions. They had less blood pressure, glucose or cholesterol screening and less knowledge of

nine cardiovascular risk factors. Overweight, physical inactivity, diabetes, hypertension, family history of cardiovascular disease and previous CVD (men only) were greater in persons with higher socio-economic positions (Zaman *et al.*, 2012). Unwin *et al.* (2010) showed in 206 subjects, in which were investigated the changes and their determinants in cardiovascular risk factors on rural to urban migration after 1 and 3 months of migration, that physical activity declined (79.4% to 26.5% in men, 37.8% to 15.6% in women, $p < 0.001$), and weight increased.

In a review of 71 papers comprising 207 populations and over 100,000 spousal pairs, the greatest majority of data indicated the existence of positive correlations between spouses for both traditional and emerging risk factors of ischemic cardiovascular disease. There were positive correlations between blood pressure, smoking habits, cholesterol (total and LDL), triglycerides, and factors linked to body weight. A clear concordance for hypertension, smoking, diabetes, and obesity was observed. Cardiovascular mortality may be affected by marital status. Increased mortality risk was higher for subjects who were unmarried, probable based on physiologic pathways (Di Castelnuovo *et al.*, 2009).

Table 1. *Cardiovascular Risk Factors - descriptive characterization*

	N	Minimum	Maximum	Mean	Std. Deviation
SBP	319	85	220	130.09	21.738
T-chol	318	2.1250	6.4300	3.394654	.7439428
HDLc	317	.5775	3.6500	1.333730	.4204228

SBP = Systolic Blood Pressure; T-chol = total cholesterol;HDLc = High Density Lipoprotein cholesterol

Table 2. *The Risk of Cardiovascular Disease - descriptive data*

	N	Minimum	Maximum	Mean	Std. Deviation
MI	317	.0099	24.7894	3.372604	4.2736717
STROKE	317	.2168	43.5244	4.080486	4.6289745
CVD	319	11.2022	40.8416	40.748682	1.6594873
CHD death	317	.0018	16.3834	1.757731	2.6533844
CVD death	317	.0236	37.2948	3.990897	5.5570532
BNF	317	.9221	61.8891	11.113396	9.6911638
ASSIGN	317	2.4295	90.6166	17.570963	14.5106022

MI = myocardial infarction; CVD = cardiovascular disease; CHD = coronary heart disease; BNF = British National Formulary; ASSIGN = ASSIGN definition

- any cardiovascular death, CHD (ICD-9 410–414, ICD-10 I20-I25) including angioplasty and bypass grafting, cerebrovascular disease.

Table 3. *Assessment of Cardiovascular Risk Factors According to Aria of Residence*

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		p*
					Lower Bound	Upper Bound	
CHD	urban	91	8.033024	6.3188378	6.717062	9.348986	**.034**
	rural	226	6.630209	5.8517163	5.863167	7.397252	
MI	urban	91	4.590432	5.0230511	3.544331	5.636533	**.002**
	rural	226	2.882239	3.8363231	2.379374	3.385104	
STROKE	urban	91	3.592701	3.4451816	2.875208	4.310195	.331
	rural	226	4.276895	5.0210467	3.618737	4.935054	
CVD	urban	91	40.515888	3.1070524	39.868813	41.162963	.113
	rural	228	40.841596	.0000000	40.841596	40.841596	
CHD_DEATH	urban	91	1.721808	2.3134704	1.240004	2.203611	.705
	rural	226	1.772196	2.7832227	1.407371	2.137020	
CVD_DEATH	urban	91	2.800629	3.3392035	2.105206	3.496052	.057
	rural	226	4.470165	6.1730545	3.661001	5.279328	
BNF	urban	91	11.625725	9.1741489	9.715116	13.536334	.305
	rural	226	10.907104	9.9039703	9.608893	12.205316	
ASSIGN	urban	91	19.430564	15.9863413	17.335075	21.526052	.002
	rural	226	12.952614	8.3745706	11.208525	14.696703	

MI = myocardial infarction; CVD = cardiovascular disease; CHD = coronary heart disease; BNF = British National Formulary; ASSIGN = ASSIGN definition - any cardiovascular death, CHD (ICD-9 410–414, ICD-10 I20-I25) including angioplasty and bypass grafting, cerebrovascular disease.

In AFINOS study, Martinez-Gomez et al (2010) investigated the association between sedentary behavior and cardiovascular risk factors in 210 adolescents, demonstrating that adolescents with a high level of sedentary behavior had less favorable systolic blood pressure, triglycerides levels and cardiac risk factors

scores than adolescents with a high level of overall adiposity. In an observational study performed in 71018 women in 5 years Chomistek et al (2013), starting free of cardiovascular disease, with sedentary behavior and normal weigh at baseline, demonstrated that prolonged sitting time was associated with increased cardiovascular disease risk, independent of leisure-time physical activity; combination of low physical activity and prolonged sitting augments cardiovascular disease risk. Changes in population diet are likely to reduce cardiovascular disease and cancer, but the effect of dietary advice is uncertain. In an update of a previous review in Cochrane Database, Rees et al (2013) assessed the effects of providing dietary advice to achieve sustained dietary changes or improved cardiovascular risk profile among healthy adults. The authors concluded that dietary advice appears to be effective in bringing modest beneficial changes in cardiovascular risk factors over approximately 12 months. A systematically review of 58 epidemiological studies about the role of Mediterranean diet in the prevention of cardiovascular diseases showed favorable effects but a certain degree of controversy remains. Important methodological differences and limitations in the studies make difficult to compare results, thus further studies, particularly randomized clinical trials, are needed to finally substantiate the benefits of Mediterranean diet (Grossoa *et al.*, 2014, Aragaki *et al.*, 2013).

Conclusions

Cardiovascular disease is the primary cause of death in many developing countries. Early detection of risk factors is important to establish both primary and secondary preventive measures which may lead to decreased morbidity and mortality and reduced hospitalization costs. In our study we noted a predominance of women (n = 195; 61.1%) and persons with environment of origin from rural (n = 228; 71.5%). The risk of coronary heart disease (CHD) estimated by Framingham equation was significantly higher in urban than in rural (8.03% vs. 6.6%. The risk of myocardial infarction (MI) was higher in urban than in rural, too (4.5% vs. 2.8%). There was no significant risk of stroke, coronary heart disease or death due to cardiovascular disease in urban or rural. The risk for cardiovascular disease estimated by ASSIGN equation was significantly higher in urban than in rural (19.4% vs. 12.9%). Further studies will establish the main mechanism of linkage between environment of origin and tightly correlation.

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References

Anand, S., Islam, S., Rosengren, A., Franzosi, M.G., Steyn, K., Yusufali, A., Keltai, M., Diaz, R., Rangarajan, S., Yusuf, S. (2008). Risk factors for myocardial infarction in women and men: insights from the INTERHEART study, DOI, 932-940 http://dx.doi.org/10.1093/eurheartj/ehn018

Aragaki, A.K., Manson, J.E., Stefanick, M.L., Lu, B., Sands-Lincoln, M., Going, S.B., Garcia, L., Allison, M.A., Sims, S.T., LaMonte, M.J., Johnson, K.C., Eaton, C.B. (2013). Relationship of sedentary behavior and physical activity to incident cardiovascular disease: results from the Women's Health Initiative. *Journal of the American College of Cardiology*, *61*(23), 2346-54.

Azizi, F., Rahmani, M., Emami, H., Mirmiran, P., Hajipour, R., Madjid, M., Ghanbili, J., Ghanbarian, A., Mehrabi, Y., Saadat, N., Salehi, P., Mortazavi, N., Heydarian, P., Sarbazi, N., Allahverdian, S., Saadati, N., Ainy, E., Moeini, S. (2002). Cardiovascular risk factors in an Iranian urban population: Tehran lipid and glucose study (phase 1). *Soz Praventivmed, 47*(6), 408-26.

Blasi, F., Tarsia, P., & Alberti, S. (2009). Chlamydophila pneumonia. *Clinical Microbiology and Infection*, *15*, 29-35.

Busko, M. (2014). Differences in Rural, Urban CAD Care Processes Don't Affect Outcomes: Canada Data, *Heartwire,* http://www.medscape.com/viewarticle/834002

Dawber, T.R., Meadors, G.F. & Moore, F.E. (1951). Epidemiological Approaches to Heart Disease. The Framingham Study. American Journal of Public Health and the Nation's Health, *41*(3), 279-281.

Di Castelnuovo, A., Quacquaruccio, G., Donati, M.B., De Gaetano, B., Iacoviello, L. (2009). Spousal Concordance for Major Coronary Risk Factors: A Systematic Review and Meta-analysis. *American Journal of Epidemiology, 169*(1), 1-8.

Doll, R., Peto, R., Boreham, J., Sutherland, I. (2004). Mortality in relation to smoking: 50 years' observations on male British doctors. *British Medical Journal*, *328* (7455), 1519.

Ebrahim, S., Taylor, F., Ward, K., Beswick, A., Burke, M., Davey Smith, G. (2011). Multiple risk factors interventions for primary prevention of coronary heart disease. *Cochrane Database of Systematic Reviews*, *1*, 1-171.

Elwood, P., Galante, J., Pickering, J., *et al.* (2013). Healthy Lifestyles Reduce the Incidence of Chronic Diseases and Dementia: Evidence from the Caerphilly Cohort Study. *PLOS ONE*, *8*(12), e81877.

Elwood, P.C., & Longley, M. (2010). My Health–Whose Responsibility - a jury decides. *Journal of Epidemiology and Community Health, 64*, 761-764.

Freund, K.M., Belanger, A.J., D'Agostino, R.B., & Kannel, W.B. (1993). The health risks of smoking. The Framingham Study: 34 years of follow-up. *Annals of Epidemiology*, *3*(4), 417-24.

Govindaraju, D.R., Cupples, L.A., Kannel, W.B., O'Donnell, C.J., Atwood, L.D., D'Agostino, R.B.Sr., Fox, C.S., Larson, M., Levy, D., Murabito, J., Vasan, R.S., Splansky, G.L., Wolf, P.A., & Benjamin, E.J. (2008). Genetics of the Framingham Heart Study population. *Advances in Genetics, 62*, 33-65.

Grossoa, G., Mistrettaa, A., Frigiolab, A., Gruttadauriac, S., Biondid, A., Basiled, F., Vitaglionee, P., D'Oraziof, N., Galvanog, F. (2014). Mediterranean Diet and

Cardiovascular Risk Factors: A Systematic Review. *Food Science and Nutrition*, *5*, 593-610.

Kannel, W.B. (1976). Some lessons in cardiovascular epidemiology from Framingham. *American Journal of Cardiol*ogy, *37*(2), 269-282.

Knuiman. M.W., Vu, H.T. (1997). Prediction of coronary heart disease mortality in Busselton, Western Australia: an evaluation of the Framingham, national health epidemiologic follow up study, and WHO ERICA risk scores. *Journal of Epidemiology and Community Health, 51*(5), 515-9.

Lloyd-Jones, D.M.,O'Donnell, C.J., D'Agostino, R.B., Massaro, J., Silbershatz, H., Wilson, P.W. (2001). Applicability of cholesterol-lowering primary prevention trials to a general population: the Framingham Heart Study. *Archives of Internal* Medicine, *161*(7), 949-954.

Mahmood, S.S., Levy, D., Vasan, R.S., & Wang, T.J. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet*, 383(9921), 999-1008.

Marshall, N.S., Wong, K.K., Phillips, C.L., Liu PY, Knuiman MW, Grunstein RR (2009). Is sleep apnea an independent risk factor for prevalent and incident diabetes in the Busselton Health Study? *Journal of Clinical Sleep Medicine*, *5*(1), 15-20.

Martinez-Gomez, D.I., Eisenmann, J.C., Gomez-Martinez, S., Veses A, Marcos A, Veiga OL (2010). Sedentary behavior, adiposity and cardiovascular risk factors in adolescents. The AFI-NOS study. *Revista Espanola de Cardiologia*, *63*(3), 277-285.

Mendis, S., Puska, P., Norrving, B. (2011). Global Atlas on Cardiovascular Disease Prevention and Control. Editors *World Health Organization* (in collaboration with the World Heart Federation and World Stroke Organization).

Millen, B.E., & Quatromoni, P.A. (2001). Nutritional research within the Framingham Heart Study. The *Journal of Nutrition Health and Aging*, *5*(3), 139-143.

Murabito, J.M. (1995). Women and cardiovascular disease: contributions from the Framingham Heart Study. *Journal of the American Medical Women's Association*, *50*(2), 35-9.

O'Donnell, & C.J., Elosua, R. (2008). Cardiovascular risk factors. Insights from Framingham Heart Study. *Revista Espanola de Cardiologia, 61*(3), 299-310.

O'Riordan, M. (2014). Higher Risk, Better CVD Outcomes in Rich Countries; Opposite Holds for Poorer Countries, Heartwire, http://www.medscape.com/viewarticle/830498.

Rees, K,, Dyakova, M., Ward, K., Thorogood, M., Brunner, E. (2013). Dietary advice for reducing cardiovascular risk. *Cochrane Database of Systematic Reviews*, 28, 3:CD002128. doi: 10.1002/14651858.CD002128.pub4.

Segelken, R. (2001). Asians' switch to Western diet might bring Western-type diseases, new China-Taiwan study suggests. *Cornell Chronicle*.

Strasser, T. (1978). Reflections on cardiovascular diseases. *Interdisciplinary Science Review*, *3*, 225-30.

Sundstrom, J., Vasan, R.S. (2005). Homocysteine and heart failure: a review of investigations from the Framingham Heart Study. *Clinical Chemistyry and Laboratory Medicine*, *43*(10), 987-992.

Tamam, N.M. (2014). Primary and Secondary Prevention of Coronary Artery Disease, http://emedicine.medscape.com/article/164214-overview=a1.

The Caerphilly and Speedwell Collaborative Group (1984). Caerphilly and Speedwell collaborative heart disease studies. *Journal of Epidemiology and Public Health*, *38*(3), 259-262.

Unwin, N., James, P., McLarty, D., Machybia, H., Nkulila, P., Tamin, B., Nguluma, M., McNally, R. (2010). Rural to urban migration and changes in cardiovascular risk factors in Tanzania: a prospective cohort study. *Biomedcentral Public Health, 10, 272*.

Weintraub WS, Daniels SR, Burke LE, et al (2011). Value of Primordial and Primary Prevention for Cardiovascular Disease: A Policy Statement From the American Heart Association. *Circulation.*, *124*(8), 967-990.

Zaman, M.J., Patel, A., Jan, S., Hillis, G.S., Raju, P.K., Neal, B., Chow, C.K. (2012). Socio-economic distribution of cardiovascular risk factors and knowledge in rural India. *.International Journal of Epidemiology, 41(5),* 1302-1314.