Acta Med. Nagasaki 57: 13－18

Impact of Hypertension, Diabetes and Dyslipidemia on Ischemic Heart Disease among Japanese: A Case-Control Study Based on National Health Insurance Medical Claims

Hairong HUANG,[1] Zhaojia YE,[1] Iyoko NAGAHAMA,[2] Hideaki TAZOE,[2] Yasuyo ABE,[1] Kiyoshi AOYAGI[1]

[1]Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
[2]Nagasaki National Health Insurance Organizations

Aim Although the important role of conventional risk factors (cigarette smoking, hypertension, diabetes and dyslipidemia) in the pathogenesis of ischemic heart disease (IHD) has been established, how frequently IHD is preceded by exposure to conventional risk factors remains controversial. The present study aimed to identify the prevalence of hypertension, diabetes and dyslipidemia among patients with IHD and examine associations between each of them with IHD in a Japanese population.
Methods Data were collected from health insurance claims in May 2010 for National Health Insurance beneficiaries aged 40-79 years in Nagasaki Prefecture, Japan. One sex- and age-matched control was randomly selected for each of 42,236 patients with IHD (International Classification of Diseases, 10th Revision code: I20-25). The prevalence of hypertension, diabetes and dyslipidemia and the number of these risk factors were compared between the patients and controls. Associations between risk factors and IHD were examined using a conditional logistic regression model.
Results Over 90% of patients with IHD had at least one of hypertension, diabetes or dyslipidemia. The odds of IHD were 4.5-fold (95% confidence interval [CI]: 4.3, 4.7), 4.2-fold (95% CI: 3.9, 4.6) and 5.3-fold (95% CI: 4.9, 5.7) higher for patients with hypertension, diabetes and dyslipidemia, respectively, compared with patients without any of these risk factors. Patients with several risk factors were at increased risk for IHD.
Conclusion Comprehensive risk reduction strategies that encourage a healthy lifestyle and diet and promote the recognition, evaluation and management of conventional risk factors are important to prevent IHD.

ACTA MEDICA NAGASAKIENSIA 57: 13－18, 2012

Keywords: Hypertension, diabetes, dyslipidemia, ischemic heart disease, medical claim

Introduction

Ischemic heart disease (IHD) is the most common cause of disability and death worldwide.[1] With the increasing use of new medical technologies such as percutaneous intracoronary intervention (PCI), off-pump coronary artery bypass surgery and laparoscopic surgery, the impact of IHD on healthcare expenditures has substantially and simultaneously increased.[2,3] Thus, the prevention of IHD is a public health priority. Cigarette smoking, hypertension, diabetes, dyslipidemia, obesity and psychosocial factors are established independent risk factors for IHD.[4-11] Treatment for hypertension,[12,13] diabetes[14] and dyslipidemia[15] has convincingly helped to decrease the risk of IHD. Because of the strength of evidence supporting their role in the pathogenesis of IHD, the four major risk factors of cigarette smoking, hypertension, diabetes and dyslipidemia have been labeled as conventional risk factors. Although the importance of

Address correspondence: Zhaojia Ye, PhD
Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, 1-12-4 Sakamoto, Nagasaki 852-8523 Japan
Tel: +81-95-819-7067, Fax: +81-95-819-7069, E-mail: zj-ye@nagasaki-u.ac.jp

Received Nobember 25, 2011; Accepted January 19, 2012

these risk factors in the development of IHD is established, some studies indicate that over 50% of patients with IHD do not have them.[16-18] Furthermore, the identification of non-conventional risk factors such as novel molecular and genetic biomarkers that might play a role in the development of IHD has recently received considerable attention.[19, 20] On the other hand, recent epidemiological studies have challenged this assertion by demonstrating that most patients with IHD in Western populations have at least one conventional risk factor.[21, 22]

However, the prevalence of conventional risk factors among patients with IHD in the Japanese population is poorly described. A good understanding of the risk factors for IHD is important to guide clinical medicine, public health policies and research efforts. We therefore conducted a case-control study to identify the prevalence of hypertension, diabetes and dyslipidemia among patients with IHD and examined associations between these risk factors and IHD in a representative Japanese population.

Methods

The Japanese health system provides universal coverage for the general population through a health insurance system for employees and their families (60% of the population) and through a National Health Insurance (NHI) system for the self-employed, retired and unemployed (40% of the population). Hospitals and clinics submit monthly claims to the insurers that include the diagnoses and costs for direct reimbursement after patients have been treated.

Data were collected from health insurance claims in May 2010 for NHI beneficiaries aged 40-79 years in Nagasaki Prefecture, Japan. Among 391,485 beneficiaries (women: 211,495, 54.0%), 258,293 (66.0%; women: 146,309, 56.6%) were identified from health insurance claims as having received medical care during May 2010.

Diseases were coded following the International Classification of Diseases, 10th Revision (ICD-10). Overall, 42,236 patients were defined as having IHD (ICD 10 code: I20-25). Among the remaining 216,057 patients, those with a diagnosis of cardiovascular disease (ICD-10 code: I60-69), arteries, arterioles and capillaries diseases(ICD-10 code:I70-79), liver disease (ICD-10 code: K70-77) or kidney failure (ICD-10 code: N17-19) were excluded, leaving 155,726 patients (women: 92,731, 59.5%). One sex- and age-matched (within 5-year age groups) control patient was randomly selected for each patient with IHD. The prevalence of hypertension, diabetes and dyslipidemia was compared between patients with IHD and controls. Hypertension was defined as a record of ICD-10 code I10-13. Diabetes was defined as a record of ICD-10 code E11-14, and dyslipidemia was defined as a record of ICD-10 code E78.

Data were analyzed using SAS software version 9.1.3 (SAS Institute, Cary, NC, USA). The prevalence of hypertension, diabetes and dyslipidemia and the number of risk factors were compared between patients with IHD and controls. Differences in categorical variables between patients with IHD and controls were examined using the chi-square test. The strength of the association between hypertension, diabetes and dyslipidemia and IHD was estimated using a conditional logistic regression model (SAS PHREG procedure) and is expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Associations between combinations or numbers of conventional risk factors and IHD were also estimated.

Results

Figure 1 shows the number of medical care claims submitted due to IHD per 100 beneficiaries by sex and age. The average numbers of IHD per 100 beneficiaries were 10.6 and 11.1 for women and men, respectively. More men than women had IHD in every age group. The number of patients with IHD per 100 beneficiaries increased from 0.7 to 22.1 for men and from 0.9 to 20.7 for women for age groups 40-44 years to 75-79 years, respectively.

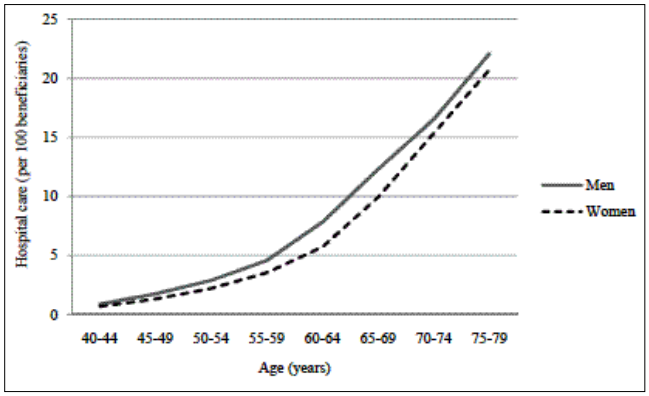

Figure 1. Number of medical cares for ischemic heart disease per 100 beneficiaries according to sex and age, Nagasaki Prefecture, Japan, 2010 (n = 391,485).

Figure 2 shows that the proportions of patients with IHD accompanied by one, two and all three conventional risk factors were 31.1%, 38.3% and 22.3%, respectively; only 8.3% of patients had no apparent risk factors. The prevalence

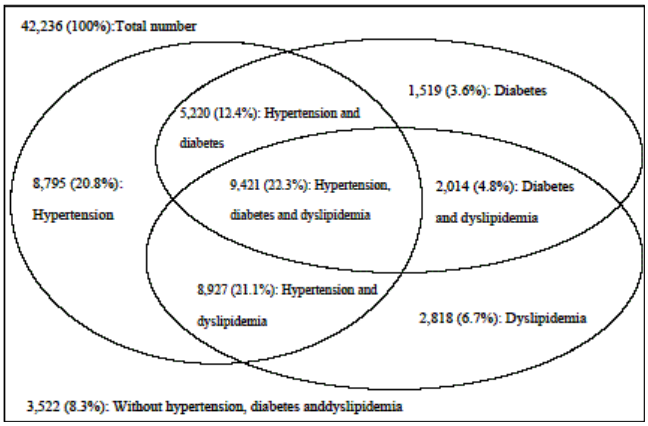

Figure 2. Prevalence of hypertension, diabetes and dyslipidemia among patients with ischemic heart disease, Nagasaki Prefecture, Japan, 2010 (n = 42,236).

of hypertension, diabetes and dyslipidemia among patients with IHD was 76.6% (78.2% in men and 75.2% in women), 43.0% (50.0% in men and 36.8% in women) and 54.9% (49.5% in men and 59.7% in women), respectively.

Table 1 shows the baseline characteristics of the patients with IHD and controls. Over 90% of the patients with IHD were over 60 years of age and more of them were women (52.9% vs. 47.1%, P < 0.001). Patients with IHD had a significantly higher overall prevalence of hypertension (76.6% vs. 47.5%, P < 0.001), diabetes (43.0% vs. 19.9%, P < 0.001) and dyslipidemia (54.9% vs. 27.5%, P < 0.001) than controls. The proportion of individuals without any of these conventional risk factors was significantly higher among controls than patients with IHD (39.5% vs. 8.3%, P < 0.001).

Table 2 shows the prevalence of conventional risk factors among patients with IHD and controls according to sex and age. The prevalence of all three conventional risk factors in each sex and age group was significantly higher among patients with IHD than controls (P < 0.01). The proportion of individuals without any of the three conventional risk factors decreased significantly with increasing age (P < 0.01 for trend).

Table 3 shows the results of conditional logistic regression analysis. The ORs were 4.5 (95% CI: 4.3, 4.7), 4.2 (95% CI: 3.9, 4.6) and 5.3 (95% CI: 4.9, 5.7) for patients with hypertension, diabetes and dyslipidemia, respectively, compared with those without any of these risk factors. The OR was higher for dyslipidemia than those for hypertension and diabetes. Any combination of these conventional risk factors was associated with a higher risk of IHD. Notably, the OR was 16.4 (95% CI: 15.4, 17.5) among patients with all three risk factors. The association between risk factors and IHD analyzed based on numbers of risk factors was close and graded (Figure 3).

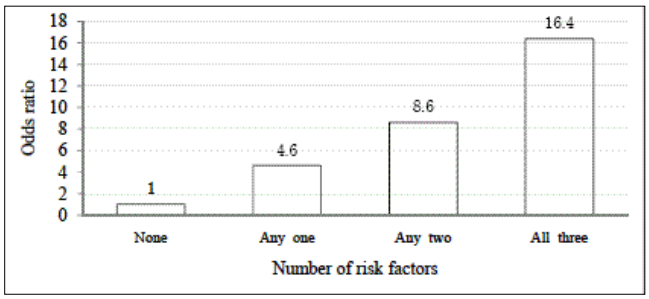

Figure 3. Risk of ischemic heart disease according to numbers of conventional risk factors of hypertension, diabetes or dyslipidemia.

Table 1. Baseline characteristics of the patients.

Characteristic	Patients (N = 42,236)	Controls (N = 42,236)	P value
	N (%)		
Age (years)			
40-49	501 (1.2)	501 (1.2)	
50-59	2,430 (5.8)	2,430 (5.8)	
60-69	11,735 (27.8)	11,735 (27.8)	
70-79	27,570 (65.3)	27,570 (65.3)	
Women	22,343 (52.9)	22,343 (52.9)	
Hypertension	32,363 (76.6)	20,080 (47.5)	<0.001
Diabetes	18,174 (43.0)	8,387 (19.9)	<0.001
Dyslipidemia	23,180 (54.9)	11,636 (27.5)	<0.001
Number of risk factors			
0	3,522 (8.3)	16,693 (39.5)	
1	13,132 (31.1)	13,737 (32.5)	
2	16,161 (38.3)	9,052 (21.4)	
3	9,421 (22.3)	2,754 (6.5)	<0.001

Table 2. Prevalence of conventional risk factors among patients with IHD and controls according to sex and age.

	Age (years)							
	40-49		50-59		60-69		70-79	
	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
Men								
Number	298	298	1,371	1,371	5,980	5,980	12,244	12,244
Hypertension	58.7	16.1	72.2	33.7	78.3	45.5	79.3	48.8
Diabetes	45.0	12.1	47.5	18.6	50.9	23.6	50.0	23.6
Dyslipidemia	49.3	13.1	54.1	17.2	53.0	20.5	47.2	19.7
Number of risk factors								
0*	17.4	71.1	10.7	53.6	7.3	42.0	7.4	39.8
1	30.9	18.8	29.5	27.6	29.0	32.8	31.5	34.1
2	32.9	7.7	35.1	14.4	38.0	18.9	38.1	20.0
3	18.8	2.3	24.7	4.4	25.7	6.3	22.9	6.0
Women								
Number	203	203	1,059	1,059	5,755	5,755	15,326	15,326
Hypertension	48.3	10.3	63.9	28.6	71.4	42.0	77.8	53.1
Diabetes	41.4	4.4	34.5	12.6	35.8	16.2	37.3	17.7
Dyslipidemia	37.9	7.4	51.1	20.8	61.6	33.7	59.9	36.2
Number of riskfactors								
0*	26.6	82.8	17.4	58.2	9.5	42.6	7.8	33.4
1	34.5	13.3	32.0	25.8	32.3	29.4	31.1	33.7
2	23.6	3.0	34.4	12.0	38.1	21.5	39.4	25.3
3	15.3	1.0	16.2	4.1	20.1	6.5	21.7	7.5

Data are expressed as ratios (%). Prevalence differences between patients with IHD and controls are statistically significant at $P < 0.01$ unless otherwise noted.
*$P < 0.01$ for trend with increasing age in patients with IHD and controls.

Table 3. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for ischemic heart disease.

Risk factor	OR (95% CI)
None	1.0
Hypertension	4.5 (4.3-4.7)
Diabetes	4.2 (3.9-4.6)
Dyslipidemia	5.3 (4.9-5.7)
Hypertension+Diabetes	9.0 (8.4-9.6)
Hypertension+Dyslipidemia	8.5 (8.0-9.0)
Diabetes+Dyslipidemia	8.6 (7.8-9.4)
Hypertension+Diabetes+Dyslipidemia	16.4 (15.4-17.5)

Discussion

Our study used claims-based diagnoses to investigate relationships between IHD and hypertension, diabetes and dyslipidemia among a Japanese population. We found that over 90% and over 50% of patients with IHD had at least one and at least two conventional risk factors, respectively. All three of the conventional risk factors were significantly associated with IHD and individuals with multiple risk factors were at increased risk for IHD.

The prevalence of conventional risk factors for IHD in Western populations has been reported. Khot et al.[21] analyzed data from 14 randomized clinical trials (n = 122,458) and found that 80-90% of patients who developed clinically significant IHD had at least one conventional risk factor. Greenland et al.[22] studied three large long-term prospective US cohorts (n = 386,915), and found that 87-100% of patients who experienced a fatal IHD event had at least one conventional risk factor. Our findings indicated that over 90% of Japanese patients with IHD have at least one of hypertension, diabetes or dyslipidemia, which is similar to the findings from non-Japanese populations.

The prevalence of conventional risk factors was higher in the present, than in other published studies. Nieto et al.[23] demonstrated that 84% and 42% of hypertensive and

hypercholesterolemic individuals, respectively, aged 45 to 64 years in the United States were aware of their conditions. Franse et al.[24] demonstrated a respective 15.6% and 8.0% prevalence of diagnosed and undiagnosed diabetes in an older population in the United States. Most previous studies analyzed data from community dwelling populations, whereas the present study included only data from individuals who had used medical services and used claim-based diagnoses to identify conventional risk factors, which provides proven accurate and dependable information about diseases.[25-27] These differences might explain the higher prevalence of conventional risk factors identified in the present study.

Consensus regarding the role of conventional risk factors in the development of IHD worldwide is growing. Yusuf and colleagues[4] showed that dyslipidemia, smoking, hypertension, diabetes and psychosocial factors were the most important risk factors for acute myocardial infarction in a case-control study of 52 countries that represented every inhabited continent. Stamler et al.[28] indicated that individuals without any conventional risk factors had an 80-90% lower risk of coronary heart disease mortality compared with the rest of the population in five US cohorts. Furthermore, nonsmokers with low blood pressure and a low cholesterol level in Göteborg had an age-adjusted relative risk of 0.09 compared with the average population of that city.[29] Wald and Law[30] suggested that a combination of statins, antihypertensive drugs, folic acid and aspirin could potentially reduce IHD events by over 80%. In addition, lifestyle modification to prevent the development of conventional risk factors, including increased consumption of fruits and vegetables, moderate activity and avoidance of smoking, also appears to reduce the risk of IHD.[31-33] Our findings that hypertension, diabetes and dyslipidemia were significantly associated with IHD and that having multiple risk factors increased the risk for IHD reinforce the important role of conventional risk factors in the development of IHD.

Studies of novel molecular and genetic biomarkers, such as C-reactive protein, fibrinogen, lipoprotein and homocysteine, might provide insight into the pathogenesis of IHD and into the monitoring and treatment of patients.[19] They may also play a role in risk assessment in specific clinical situations.[20] However, their optimal application to routine screening and risk stratification remains to be determined, and they are unlikely to have major public health importance.[19, 20] Based on the high prevalence of conventional risk factors among patients with IHD and their role in the development of IHD, we suggest that clinical medicine, public health policies and research efforts should place more emphasis on conventional risk factors. An aggressive prevention strategy including lifestyle modification to prevent the development of conventional risk factors and early medical intervention to treat hypertension, diabetes and dyslipidemia would contribute to reducing IHD.

The strengths of our study include a large sample population of over 40,000 patients with IHD and controls from the same region and claims-based diagnoses of risk factors. These factors improved the accuracy of risk factor estimation and the applicability of our findings to the general population. Policy makers and physicians can better understand the impact of preventing or modifying these risk factors on the risk of future IHD based on the present findings.

However, some limitations must be considered in the interpretation of our findings. Firstly, we assessed conventional risk factors at the time of IHD diagnosis, not years in advance. Secondly, information about some important risk factors such as cigarette smoking, obesity and psychosocial factors was unavailable. Thirdly, since conditions were diagnosed only from health insurance claims during a period of one month, information about patients who did not visit medical facilities has been missed. These patients might tend to have clinically mild to moderate IHD. Diagnostic criteria for diseases might vary among different doctors. These factors might have caused sampling bias in this study. In addition, information about the severity and treatment of IHD and its associated conventional risk factors was also unavailable from health insurance claims. Further studies to assess the effect of medical treatment of conventional risk factors on risk of IHD would be helpful to improve the effectiveness of IHD reduction strategies.

In conclusion, our findings show that over 90% of a Japanese population with IHD had at least one of hypertension, diabetes or dyslipidemia and that all of these risk factors were significantly associated with IHD. Comprehensive risk reduction strategies that encourage a healthy lifestyle and dieting, and promote the recognition, evaluation and management of conventional risk factors are important to prevent IHD.

Acknowledgements

This study was funded by Nagasaki National Health Insurance Organizations and Nagasaki Prefectural Government.

References

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 349: 1498-1504, 1997.
2. Clark MA, Bakhai A, Lacey MJ, Pelletier EM, Cohen DJ. Clinical and economic outcomes of percutaneous coronary interventions in the elderly: an analysis of medicare claims data. *Circulation* 110: 259-264, 2004.
3. Menzin J, Wygant G, Hauch O, Jackel J, Friedman M. One-year costs of ischemic heart disease among patients with acute coronary syndromes: findings from a multi-employer claims database. *Curr Med Res Opin* 24: 461-468, 2008.
4. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 364: 937-952, 2004.
5. Suh I, Oh KW, Lee KH, Psaty BM, Nam CM, Kim SI, et al. Moderate dietary fat consumption as a risk factor for ischemic heart disease in a population with a low fat intake: a case-control study in Korean men. *Am J Clin Nutr* 73: 722-727, 2001.
6. Sorrentino MJ. Implications of the metabolic syndrome: the new epidemic. *Am J Cardiol* 96: 3E-7E, 2005.
7. Xu W, Zhao Y, Guo L, Guo Y, Gao W. Job stress and coronary heart disease: a case-control study using a Chinese population. *J Occup Health* 51: 107-113, 2009.
8. Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 364: 953-962, 2004.
9. Almdal T, Scharling H, Jensen JS, Vestergaard H. The independent effect of type 2 diabetes mellitus on ischemic heart disease, stroke, and death: a population-based study of 13,000 men and women with 20 years of follow-up. *Arch Intern Med* 164: 1422-1426, 2004.
10. Katanoda K, Marugame T, Saika K, Satoh H, Tajima K, Suzuki T, et al. Population attributable fraction of mortality associated with tobacco smoking in Japan: a pooled analysis of three large-scale cohort studies. *J Epidemiol* 18: 251-264, 2008.
11. Saito I, Kokubo Y, Yamagishi K, Iso H, Inoue M, Tsugane S. Diabetes and the risk of coronary heart disease in the general Japanese population: the Japan Public Health Center-based prospective (JPHC) study. *Atherosclerosis* 216: 187-191, 2011.
12. Collins R, Peto R, MacMahon S, Hebert P, Fiebach NH, Eberlein KA, et al. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 335: 827-838, 1990.
13. Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet* 362: 1527-1535, 2003.
14. Weitzman S, Maislos M, Bodner-Fishman B, Rosen S. Association of diabetic retinopathy, ischemic heart disease, and albuminuria with diabetic treatment in type 2 diabetic patients. A population-based study. *Acta Diabetol* 34: 275-279, 1997.
15. Collins R, Armitage J, Parish S, Sleigh P, Peto R. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 361: 2005-2016, 2003.
16. Futterman LG, Lemberg L. Fifty percent of patients with coronary artery disease do not have any of the conventional risk factors. *Am J Crit Care* 7: 240-244, 1998.
17. Braunwald E. Shattuck lecture--cardiovascular medicine at the turn of the millennium: triumphs, concerns, and opportunities. *N Engl J Med* 337: 1360-1369, 1997.
18. Hennekens CH. Increasing burden of cardiovascular disease: current knowledge and future directions for research on risk factors. *Circulation* 97: 1095-1102, 1998.
19. Hackam DG, Anand SS. Emerging risk factors for atherosclerotic vas cular disease: a critical review of the evidence. *JAMA* 290: 932-940, 2003.
20. Dent TH. Predicting the risk of coronary heart disease. II: the role of novel molecular biomarkers and genetics in estimating risk, and the future of risk prediction. *Atherosclerosis* 213: 352-362, 2010.
21. Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, et al. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 290: 898-904, 2003.
22. Greenland P, Knoll MD, Stamler J, Neaton JD, Dyer AR, Garside DB, et al. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. *JAMA* 290: 891-897, 2003.
23. Nieto FJ, Alonso J, Chambless LE, Zhong M, Ceraso M, Romm FJ, et al. Population awareness and control of hypertension and hypercholesterolemia. The Atherosclerosis Risk in Communities study. *Arch Intern Med* 155: 677-684, 1995.
24. Franse LV, Di Bari M, Shorr RI, Resnick HE, van Eijk JT, Bauer DC, et al. Type 2 diabetes in older well-functioning people: who is undiagnosed? Data from the Health, Aging, and Body Composition study. *Diabetes Care* 24: 2065-2070, 2001.
25. Bullano MF, Kamat S, Willey VJ, Barlas S, Watson DJ, Brenneman SK. Agreement between administrative claims and the medical record in identifying patients with a diagnosis of hypertension. *Med Care* 44: 486-490, 2006.
26. Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. *Am Heart J* 148: 99-104, 2004.
27. Kawasumi Y, Abrahamowicz M, Ernst P, Tamblyn R. Development and validation of a predictive algorithm to identify adult asthmatics from medical services and pharmacy claims databases. *Health Serv Res* 46: 939-963, 2011.
28. Stamler J, Stamler R, Neaton JD, Wentworth D, Daviglus ML, Garside D, et al. Low risk-factor profile and long-term cardiovascular and noncardiovascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women. *JAMA* 282: 2012-2018, 1999.
29. Rosengren A, Dotevall A, Eriksson H, Wilhelmsen L. Optimal risk factors in the population: prognosis, prevalence, and secular trends; data from Goteborg population studies. *Eur Heart J* 22: 136-144, 2001.
30. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ* 326: 1419, 2003.
31. Joshipura KJ, Hu FB, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, et al. The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann Intern Med* 134: 1106-1114, 2001.
32. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 343: 16-22, 2000.
33. Pais PS. Early intervention and prevention of myocardial infarction. *J Hypertens Suppl* 24: S25-30, 2006.